ACC/AHA Clinical Practice Guideline

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Vascular Medicine

Endorsed by the Society of Hospital Medicine

WRITING COMMITTEE MEMBERS*

Lee A. Fleisher, MD, FACC, FAHA, Chair†; Kirsten E. Fleischmann, MD, MPH, FACC, Vice Chair†; Andrew D. Auerbach, MD, MPH†; Susan A. Barnason, PhD, RN, FAHA†; Joshua A. Beckman, MD, FACC, FAHA, FSVM*‡; Biykem Bozkurt, MD, PhD, FACC, FAHA*§; Victor G. Davila-Roman, MD, FACC, FASE*†; Marie D. Gerhard-Herman, MD†; Thomas A. Holly, MD, FACC, FASNC*‖; Garvan C. Kane, MD, PhD, FAHA, FASE¶; Joseph E. Marine, MD, FACC, FHRS#; M. Timothy Nelson, MD, FACS**; Crystal C. Spencer, JD††; Annemarie Thompson, MD‡‡; Henry H. Ting, MD, MBA, FACC, FAHA§§; Barry F. Uretsky, MD, FACC, FAHA, FSCAI‖‖; Duminda N. Wijeysundera, MD, PhD, Evidence Review Committee Chair

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply; see Appendix 1 for recusal information. †ACC/AHA Representative. ‡Society for Vascular Medicine Representative. §ACC/AHA Task Force on Practice Guidelines Liaison. ‖American Society of Nuclear Cardiology Representative. ¶American Society of Echocardiography Representative. #Heart Rhythm Society Representative. **American College of Surgeons Representative. ††Patient Representative/Lay Volunteer. ‡‡American Society of Anesthesiologists/Society of Cardiovascular Anesthesiologists Representative. §§ACC/AHA Task Force on Performance Measures Liasion. ‖‖Society for Cardiovascular Angiography and Interventions Representative. ¶¶ Former Task Force member; current member during the writing effort.

This document was approved by the American College of Cardiology Board of Trustees and the American Heart Association Science Advisory and Coordinating Committee in July 2014.

The online-only Comprehensive Relationships Data Supplement is available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIR.0000000000000106/-/DC1.

The online-only Data Supplement files are available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIR.0000000000000106/-/DC2.

The American Heart Association requests that this document be cited as follows: Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, Marine JE, Nelson MT, Spencer CC, Thompson A, Ting HH, Uretsky BF, Wijeysundera DN. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2014;130:e278–e333.

This article has been copublished in *Journal of the American College of Cardiology*.

Copies: This document is available on the World Wide Web sites of the American College of Cardiology (www.cardiosource.org) and the American Heart Association (my.americanheart.org). A copy of the document is available at http://my.americanheart.org/statements by selecting either the "By Topic" link or the "By Publication Date" link. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

Expert peer review of AHA Scientific Statements is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit http://my.americanheart.org/statements and select the "Policies and Development" link.

(*Circulation*. 2014;130:e278-e333.)

***Circulation* is available at http://circ.ahajournals.org** **DOI: 10.1161/CIR.0000000000000106**

ACC/AHA TASK FORCE MEMBERS

Jeffrey L. Anderson, MD, FACC, FAHA, Chair; Jonathan L. Halperin, MD, FACC, FAHA, Chair-Elect; Nancy M. Albert, PhD, RN, FAHA; Biykem Bozkurt, MD, PhD, FACC, FAHA; Ralph G. Brindis, MD, MPH, MACC; Lesley H. Curtis, PhD, FAHA; David DeMets, PhD¶¶; Lee A. Fleisher, MD, FACC, FAHA; Samuel Gidding, MD, FAHA; Judith S. Hochman, MD, FACC, FAHA¶¶; Richard J. Kovacs, MD, FACC, FAHA; E. Magnus Ohman, MD, FACC; Susan J. Pressler, PhD, RN, FAHA; Frank W. Sellke, MD, FACC, FAHA; Win-Kuang Shen, MD, FACC, FAHA; Duminda N. Wijeysundera, MD, PhD

Table of Contents

Preamble

The American College of Cardiology (ACC) and the American Heart Association (AHA) are committed to the prevention and management of cardiovascular diseases through professional education and research for clinicians, providers, and patients. Since 1980, the ACC and AHA have shared a responsibility to translate scientific evidence into clinical practice guidelines (CPGs) with recommendations to standardize and improve cardiovascular health. These CPGs, based on systematic methods to evaluate and classify evidence, provide a cornerstone of quality cardiovascular care.

In response to published reports from the Institute of Medicine[1,2] and the ACC/AHA's mandate to evaluate new knowledge and maintain relevance at the point of care, the ACC/AHA Task Force on Practice Guidelines (Task Force) began modifying its methodology. This modernization effort is published in the 2012 Methodology Summit Report[3] and 2014 perspective article.[4] The latter recounts the history of the collaboration, changes over time, current policies, and planned initiatives to meet the needs of an evolving healthcare environment. Recommendations on value in proportion to resource utilization will be incorporated as high-quality comparative-effectiveness data become available.[5] The relationships between CPGs and data standards, appropriate use criteria, and performance measures are addressed elsewhere.[4]

Intended Use—CPGs provide recommendations applicable to patients with or at risk of developing cardiovascular disease. The focus is on medical practice in the United States, but CPGs developed in collaboration with other organizations may have a broader target. Although CPGs may be used to inform regulatory or payer decisions, the intent is to improve quality of care and be aligned with the patient's best interest.

Evidence Review—Guideline writing committee (GWC) members are charged with reviewing the literature; weighing the strength and quality of evidence for or against particular tests, treatments, or procedures; and estimating expected health outcomes when data exist. In analyzing the data and developing CPGs, the GWC uses evidence-based methodologies developed by the Task Force.[6] A key component of the ACC/AHA CPG methodology is the development of recommendations on the basis of all available evidence. Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only selected references are cited in the CPG. To ensure that CPGs remain current, new data are reviewed biannually by the GWCs and the Task Force to determine if recommendations should be updated or modified. In general, a target cycle of 5 years is planned for full revision.[1]

The Task Force recognizes the need for objective, independent Evidence Review Committees (ERCs) to address key clinical questions posed in the PICOTS format (P=population; I=intervention; C=comparator; O=outcome; T=timing; S=setting). The ERCs include methodologists, epidemiologists, clinicians, and biostatisticians who systematically survey, abstract, and assess the quality of the evidence base.[3,4] Practical considerations, including time and resource constraints, limit the ERCs to addressing key clinical questions for which the evidence relevant to the guideline topic lends itself to systematic review and analysis when the systematic review could impact the sense or strength of related recommendations. The GWC develops recommendations on the basis of the systematic review and denotes them with superscripted "SR" (ie, [SR]) to emphasize support derived from formal systematic review.

Guideline-Directed Medical Therapy—Recognizing advances in medical therapy across the spectrum of cardiovascular diseases, the Task Force designated the term "guideline-directed medical therapy" (GDMT) to represent recommended medical therapy as defined mainly by Class I measures—generally a combination of lifestyle modification and drug- and device-based therapeutics. As medical science advances, GDMT evolves, and hence GDMT is preferred to "optimal medical therapy." For GDMT and all other recommended drug treatment regimens, the reader should confirm the dosage with product insert material and carefully evaluate for contraindications and possible drug interactions. Recommendations are limited to treatments, drugs, and devices approved for clinical use in the United States.

Class of Recommendation and Level of Evidence—Once recommendations are written, the Class of Recommendation (COR; ie, the strength the GWC assigns to the recommendation, which encompasses the anticipated magnitude and judged certainty of benefit in proportion to risk) is assigned by the GWC. Concurrently, the Level of Evidence (LOE) rates the scientific evidence supporting the effect of the intervention on the basis of the type, quality, quantity, and consistency of data from clinical trials and other reports (Table 1).[4]

Relationships With Industry and Other Entities—The ACC and AHA exclusively sponsor the work of GWCs,

Table 1. Applying Classification of Recommendations and Level of Evidence

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *No Benefit* or **CLASS III** *Harm* Procedure/Test — Treatment COR III: No benefit — Not Helpful — No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful — Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important key clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes mellitus, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative-effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

without commercial support, and members volunteer their time for this activity. The Task Force makes every effort to avoid actual, potential, or perceived conflicts of interest that might arise through relationships with industry or other entities (RWI). All GWC members and reviewers are required to fully disclose current industry relationships or personal interests, from 12 months before initiation of the writing effort. Management of RWI involves selecting a balanced GWC and requires that both the chair and a majority of GWC members have no relevant RWI (see Appendix 1 for the definition of relevance). GWC members are restricted with regard to writing or voting on sections to which their RWI apply. In addition, for transparency, GWC members' comprehensive disclosure information is available as an online supplement. Comprehensive disclosure information for the Task Force is also available at http://www.cardiosource.org/en/ACC/About-ACC/Who-We-Are/Leadership/Guidelines-and-Documents-Task-Forces.aspx. The Task Force strives to avoid bias by selecting experts from a broad array of backgrounds representing different geographic regions, genders, ethnicities, intellectual perspectives/biases, and scopes of clinical practice. Selected organizations and professional societies with related interests and expertise are invited to participate as partners or collaborators.

Individualizing Care in Patients With Associated Conditions and Comorbidities—The ACC and AHA recognize the complexity of managing patients with multiple conditions, compared with managing patients with a single disease, and the challenge is compounded when CPGs for evaluation or treatment of several coexisting illnesses are discordant or interacting.[7] CPGs attempt to define practices that meet the needs of patients in most, but not all, circumstances and do not replace clinical judgment.

Clinical Implementation—Management in accordance with CPG recommendations is effective only when followed; therefore, to enhance the patient's commitment to treatment and compliance with lifestyle adjustment, clinicians should engage the patient to participate in selecting interventions on the basis of the patient's individual values and preferences, taking associated conditions and comorbidities into consideration (eg, shared decision making). Consequently, there are circumstances in which deviations from these CPGs are appropriate.

The recommendations in this CPG are the official policy of the ACC and AHA until they are superseded by a published addendum, focused update, or revised full-text CPG.

Jeffrey L. Anderson, MD, FACC, FAHA
Chair, ACC/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Methodology and Evidence Review

The recommendations listed in this CPG are, whenever possible, evidence based. In April 2013, an extensive evidence review was conducted, which included a literature review through July 2013. Other selected references published through May 2014 were also incorporated by the GWC. Literature included was derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, Agency for Healthcare Research and Quality Reports, and other selected databases relevant to this CPG. The relevant data are included in evidence tables in the Data Supplement available online. Key search words included but were not limited to the following: *anesthesia protection; arrhythmia; atrial fibrillation; atrioventricular block; bundle branch block; cardiac ischemia; cardioprotection; cardiovascular implantable electronic device; conduction disturbance; dysrhythmia; electrocardiography; electrocautery; electromagnetic interference; heart disease; heart failure; implantable cardioverter-defibrillator; intraoperative; left ventricular ejection fraction; left ventricular function; myocardial infarction; myocardial protection; National Surgical Quality Improvement Program; pacemaker; perioperative; perioperative pain management; perioperative risk; postoperative; preoperative; preoperative evaluation; surgical procedures; ventricular premature beats; ventricular tachycardia;* and *volatile anesthetics.*

An independent ERC was commissioned to perform a systematic review of a key question, the results of which were considered by the GWC for incorporation into this CPG. See the systematic review report published in conjunction with this CPG[8] and its respective data supplements.

1.2. Organization of the GWC

The GWC was composed of clinicians with content and methodological expertise, including general cardiologists, subspecialty cardiologists, anesthesiologists, a surgeon, a hospitalist, and a patient representative/lay volunteer. The GWC included representatives from the ACC, AHA, American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society (HRS), Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society for Vascular Medicine.

1.3. Document Review and Approval

This document was reviewed by 2 official reviewers each from the ACC and the AHA; 1 reviewer each from the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, HRS, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, Society of Hospital Medicine, and Society for Vascular Medicine; and 24 individual content reviewers (including members of the ACC Adult Congenital and Pediatric Cardiology Section Leadership Council, ACC Electrophysiology Section Leadership Council, ACC Heart Failure and Transplant Section Leadership Council, ACC Interventional Section Leadership Council, and ACC Surgeons' Council). Reviewers' RWI information was distributed to the GWC and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACC and the AHA and endorsed by the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, Society of Hospital Medicine, and Society of Vascular Medicine.

1.4. Scope of the CPG

The focus of this CPG is the perioperative cardiovascular evaluation and management of the adult patient undergoing noncardiac surgery. This includes preoperative risk assessment and cardiovascular testing, as well as (when indicated) perioperative pharmacological (including anesthetic) management and perioperative monitoring that includes devices and biochemical markers. This CPG is intended to inform all the medical professionals involved in the care of these patients. The preoperative evaluation of the patient undergoing noncardiac surgery can be performed for multiple purposes, including 1) assessment of perioperative risk (which can be used to inform the decision to proceed or the choice of surgery and which includes the patient's perspective), 2) determination of the need for changes in management, and 3) identification of cardiovascular conditions or risk factors requiring longer-term management. Changes in management can include the decision to change medical therapies, the decision to perform further cardiovascular interventions, or recommendations about postoperative monitoring. This may lead to recommendations and discussions with the perioperative team about the optimal location and timing of surgery (eg, ambulatory surgery center versus outpatient hospital, or inpatient admission) or alternative strategies.

The key to optimal management is communication among all of the relevant parties (ie, surgeon, anesthesiologist, primary caregiver, and consultants) and the patient. The goal of preoperative evaluation is to promote patient engagement and facilitate shared decision making by providing patients and their providers with clear, understandable information about perioperative cardiovascular risk in the context of the overall risk of surgery.

The Task Force has chosen to make recommendations about care management on the basis of available evidence from studies of patients undergoing noncardiac surgery. Extrapolation from data from the nonsurgical arena or cardiac surgical arena was made only when no other data were available and the benefits of extrapolating the data outweighed the risks.

During the initiation of the writing effort, concern was expressed by Erasmus University about the scientific integrity of studies led by Poldermans.[9] The GWC reviewed 2 reports from Erasmus University published on the Internet,[9,10] as well as other relevant articles on this body of scientific investigation.[11–13] The 2012 report from Erasmus University concluded that the conduct in the DECREASE (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography) IV and V trials "was in several respects negligent and scientifically incorrect" and that "essential source documents are lacking" to make conclusions about other studies led by Poldermans.[9] Additionally, Erasmus University was contacted to ensure that the GWC had up-to-date information. On the basis of the published information, discussions between the Task Force and GWC leadership ensued to determine how best to treat any study in which Poldermans was the senior investigator (ie, either the first or last author). The Task Force developed the following framework for this document:

1. The ERC will include the DECREASE trials in the sensitivity analysis, but the systematic review report will be based on the published data on perioperative beta blockade, with data from all DECREASE trials excluded.
2. The DECREASE trials and other derivative studies by Poldermans should not be included in the CPG data supplements and evidence tables.
3. If nonretracted DECREASE publications and/or other derivative studies by Poldermans are relevant to the topic, they can only be cited in the text with a comment about the finding compared with the current recommendation but should not form the basis of that recommendation or be used as a reference for the recommendation.

The Task Force and the GWC believe that it is crucial, for the sake of transparency, to include the nonretracted publications in the text of the document. This is particularly important because further investigation is occurring simultaneously with deliberation of the CPG recommendations. Because of the availability of new evidence and the international impact of the controversy about the DECREASE trials, the ACC/AHA and European Society of Cardiology/European Society of Anesthesiology began revising their respective CPGs concurrently. The respective GWCs performed their literature reviews and analyses independently and then developed their recommendations. Once peer review of both CPGs was completed, the GWCs chose to discuss their respective recommendations for beta-blocker therapy and other relevant issues. Any differences in recommendations were discussed and clearly articulated in the text; however, the GWCs aligned a few recommendations to avoid confusion within the clinical community, except where international practice variation was prevalent.

In developing this CPG, the GWC reviewed prior published CPGs and related statements. Table 2 lists these publications and statements deemed pertinent to this effort and is intended for use as a resource. However, because of the availability of new evidence, the current CPG may include recommendations that supersede those previously published.

1.5. Definitions of Urgency and Risk

In describing the temporal necessity of operations in this CPG, the GWC developed the following definitions by consensus. An *emergency* procedure is one in which life or limb is threatened if not in the operating room where there is time for no or very limited or minimal clinical evaluation, typically within <6 hours. An *urgent* procedure is one in which there may be time for a limited clinical evaluation, usually when life or limb is threatened if not in the operating room, typically between 6 and 24 hours. A *time-sensitive* procedure is one in which a delay of >1 to 6 weeks to allow for an evaluation and significant changes in management will negatively affect outcome. Most oncologic procedures would fall into this category. An *elective* procedure is one in which the procedure could be delayed for up to 1 year. Individual institutions may use slightly different definitions, but this framework could be mapped to local categories. A *low-risk* procedure is one in which the combined surgical and patient characteristics predict a risk of a major adverse cardiac event (MACE) of death or myocardial infarction (MI) of <1%. Selected examples of low-risk procedures include cataract and plastic surgery.[34,35] Procedures with a risk of MACE of ≥1% are considered *elevated risk*. Many previous risk-stratification schema have included intermediate- and high-risk classifications. Because recommendations for intermediate- and high-risk procedures are similar, classification into 2 categories simplifies the recommendations without loss of fidelity. Additionally, a risk calculator has been developed that allows more precise calculation of surgical risk, which can be incorporated into perioperative decision making.[36] Approaches to establishing low and elevated risk are developed more fully in Section 3.

2. Clinical Risk Factors

2.1. Coronary Artery Disease

Perioperative mortality and morbidity due to coronary artery disease (CAD) are untoward complications of noncardiac surgery. The incidence of cardiac morbidity after surgery depends on the definition, which ranges from elevated cardiac biomarkers alone to the more classic definition with other signs of ischemia.[37–39] In a study of 15 133 patients who were >50 years of age and had noncardiac surgery requiring an overnight admission, an isolated peak troponin T value of ≥0.02 ng/mL occurred in 11.6% of patients. The 30-day mortality rate in this cohort with elevated troponin T values was 1.9% (95% confidence interval [CI]: 1.7% to 2.1%).[40]

Table 2. Associated CPGs and Statements

Title	Organization	Publication Year (Reference)
CPGs		
Management of patients with atrial fibrillation	AHA/ACC/HRS	2014[14]
Management of valvular heart disease	AHA/ACC	2014[15]
Management of heart failure	ACC/AHA	2013[16]
Performing a comprehensive transesophageal echocardiographic examination	ASE/SCA	2013[17]
Management of ST-elevation myocardial infarction	ACC/AHA	2013[18]
Focused update: Diagnosis and management of patients with stable ischemic heart disease	ACC/AHA/AATS/PCNA/SCAI/STS	2012[18a] 2014[19]
Focused update incorporated into the 2007 guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction*	ACC/AHA	2012[20]
Red blood cell transfusion	AABB	2012[21]
Management of patients with peripheral artery disease: focused update and guideline	ACC/AHA	2011[22] 2006[23]
Diagnosis and treatment of hypertrophic cardiomyopathy	ACC/AHA	2011[24]
Coronary artery bypass graft surgery	ACC/AHA	2011[25]
Percutaneous coronary intervention	ACC/AHA/SCAI	2011[26]
Perioperative transesophageal echocardiography	American Society of Anesthesiologists/SCA	2010[27]
Management of adults with congenital heart disease	ACC/AHA	2008[28]
Statements		
Perioperative beta blockade in noncardiac surgery: a systematic review	ACC/AHA	2014[8]
Basic perioperative transesophageal echocardiography examination	ASE/SCA	2013[29]
Practice advisory for preanesthesia evaluation	American Society of Anesthesiologists	2012[30]
Cardiac disease evaluation and management among kidney and liver transplantation candidates	AHA/ACC	2012[31]
Inclusion of stroke in cardiovascular risk prediction instruments	AHA/American Stroke Association	2012[32]
Perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management	HRS/American Society of Anesthesiologists	2011[33]

*The 2012 UA/NSTEMI CPG[20] is considered policy at the time of publication of this CPG; however, a fully revised CPG is in development, with publication expected in 2014.

AABB indicates American Association of Blood Banks; AATS, American Association for Thoracic Surgery; ACC, American College of Cardiology; AHA, American Heart Association; ASE, American Society of Echocardiography; CPG, clinical practice guideline; HRS, Heart Rhythm Society; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; SCA, Society of Cardiovascular Anesthesiologists; STEMI, ST-elevation myocardial infarction; STS, Society of Thoracic Surgeons; and UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction.

MACE after noncardiac surgery is often associated with prior CAD events. The stability and timing of a recent MI impact the incidence of perioperative morbidity and mortality. An older study demonstrated very high morbidity and mortality rates in patients with unstable angina.[41] A study using discharge summaries demonstrated that the postoperative MI rate decreased substantially as the length of time from MI to operation increased (0 to 30 days=32.8%; 31 to 60 days=18.7%; 61 to 90 days=8.4%; and 91 to 180 days=5.9%), as did the 30-day mortality rate (0 to 30 days=14.2%; 31 to 60 days=11.5%; 61 to 90 days=10.5%; and 91 to 180 days=9.9%).[42] This risk was modified by the presence and type of coronary revascularization (coronary artery bypass grafting [CABG] versus percutaneous coronary interventions [PCIs]) that occurred at the time of the MI.[43] Taken together, the data suggest that ≥60 days should elapse after a MI before noncardiac surgery in the absence of a coronary intervention. A recent MI, defined as having occurred within 6 months of noncardiac surgery, was also found to be an independent risk factor for perioperative stroke, which was associated with an 8-fold increase in the perioperative mortality rate.[44]

A patient's age is an important consideration, given that adults (those ≥55 years of age) have a growing prevalence of cardiovascular disease, cerebrovascular disease, and diabetes mellitus,[45] which increase overall risk for MACE when they undergo noncardiac surgery. Among older adult patients (those >65 years of age) undergoing noncardiac surgery, there was a higher reported incidence of acute ischemic stroke than for those ≤65 years of age.[46] Age >62 years is also an independent risk factor for perioperative stroke.[44] More postoperative complications, increased length of hospitalization, and inability to return home after hospitalization were also more pronounced among "frail" (eg, those with impaired cognition and with dependence on others in instrumental activities of daily living), older adults >70 years of age.[47]

A history of cerebrovascular disease has been shown to predict perioperative MACE.[32]

See Online Data Supplements 1 and 2 for additional information on CAD and the influence of age and sex. An extensive consideration of CAD in the context of noncardiac surgery, including assessment for ischemia and other aspects, follows later in this document.

2.2. Heart Failure

Patients with clinical heart failure (HF) (active HF symptoms or physical examination findings of peripheral edema, jugular venous distention, rales, third heart sound, or chest x-ray with pulmonary vascular redistribution or pulmonary edema) or a history of HF are at significant risk for perioperative complications, and widely used indices of cardiac risk include HF as an independent prognostic variable.[37,48,49]

The prevalence of HF is increasing steadily,[50] likely because of aging of the population and improved survival with newer cardiovascular therapies. Thus, the number of patients with HF requiring preoperative assessment is increasing. The risk of developing HF is higher in the elderly and in individuals with advanced cardiac disease, creating the likelihood of clustering of other risk factors and comorbidities when HF is manifest.

2.2.1. Role of HF in Perioperative Cardiac Risk Indices

In the Original Cardiac Risk Index, 2 of the 9 independent significant predictors of life-threatening and fatal cardiac complications—namely, the presence of preoperative third heart sound and jugular venous distention—were associated with HF and had the strongest association with perioperative MACE.[48] Subsequent approaches shifted the emphasis to history of HF[37] and defined HF by a combination of signs and symptoms, such as history of HF, pulmonary edema, or paroxysmal nocturnal dyspnea; physical examination showing bilateral rales or third heart sound gallop; and chest x-ray showing pulmonary vascular redistribution. This definition, however, did not include important symptoms such as orthopnea and dyspnea on exertion.[16] Despite the differences in definition of HF as a risk variable, changes in demographics, changes in the epidemiology of patients with cardiovascular comorbidities, changes in treatment strategies, and advances in the perioperative area, population-based studies have demonstrated that HF remains a significant risk for perioperative morbidity and mortality. In a study that used Medicare claims data, the risk-adjusted 30-day mortality and readmission rate in patients undergoing 1 of 13 predefined major noncardiac surgeries was 50% to 100% higher in patients with HF than in an elderly control group without a history of CAD or HF.[51,52] These results suggest that patients with HF who undergo major surgical procedures have substantially higher risks of operative death and hospital readmission than do other patients. In a population-based data analysis of 4 cohorts of 38 047 consecutive patients, the 30-day postoperative mortality rate was significantly higher in patients with nonischemic HF (9.3%), ischemic HF (9.2%), and atrial fibrillation (AF) (6.4%) than in those with CAD (2.9%).[53] These findings suggest that although perioperative risk-prediction models place greater emphasis on CAD than on HF, patients with active HF have a significantly higher risk of postoperative death than do patients with CAD. Furthermore, the stability of a patient with HF plays a significant role. In a retrospective single-center cohort study of patients with stable HF who underwent elective noncardiac surgery between 2003 and 2006, perioperative mortality rates for patients with stable HF were not higher than for the control group without HF, but these patients with stable HF were more likely than patients without HF to have longer hospital stays, require hospital readmission, and have higher long-term mortality rates.[54] However, all patients in this study were seen in a preoperative assessment, consultation, and treatment program; and the population did not include many high-risk patients. These results suggest improved perioperative outcomes for patients with stable HF who are treated according to GDMT.

2.2.2. Risk of HF Based on Left Ventricular Ejection Fraction: Preserved Versus Reduced

Although signs and/or symptoms of decompensated HF confer the highest risk, severely decreased (<30%) left ventricular ejection fraction (LVEF) itself is an independent contributor to perioperative outcome and a long-term risk factor for death in patients with HF undergoing elevated-risk noncardiac surgery.[55] Survival after surgery for those with a LVEF ≤29% is significantly worse than for those with a LVEF >29%.[56] Studies have reported mixed results for perioperative risk in patients with HF and preserved LVEF, however. In a meta-analysis using individual patient data, patients with HF and preserved LVEF had a lower all-cause mortality rate than did those with HF and reduced LVEF (the risk of death did not increase notably until LVEF fell below 40%).[57] However, the absolute mortality rate was still high in patients with HF and preserved LVEF as compared with patients without HF, highlighting the importance of presence of HF. There are limited data on perioperative risk stratification related to diastolic dysfunction. Diastolic dysfunction with and without systolic dysfunction has been associated with a significantly higher rate of MACE, prolonged length of stay, and higher rates of postoperative HF.[58,59]

2.2.3. Risk of Asymptomatic Left Ventricular Dysfunction

Although symptomatic HF is a well-established perioperative cardiovascular risk factor, the effect of asymptomatic left ventricular (LV) dysfunction on perioperative outcomes is unknown. In 1 prospective cohort study on the role of preoperative echocardiography in 1005 consecutive patients undergoing elective vascular surgery at a single center, LV dysfunction (LVEF <50%) was present in 50% of patients, of whom 80% were asymptomatic.[58] The 30-day cardiovascular event rate was highest in patients with symptomatic HF (49%), followed by those with asymptomatic systolic LV dysfunction (23%), asymptomatic diastolic LV dysfunction (18%), and normal LV function (10%). Further studies are required to determine if the information obtained from the assessment of ventricular function in patients without signs or symptoms adds incremental information that will result in changes in management and outcome such that the appropriateness criteria should be updated. It should be noted that the 2011 appropriate use criteria for echocardiography states it is "inappropriate" to assess ventricular function in patients without signs or symptoms of cardiovascular disease in the preoperative setting.[60] For preoperative assessment of LV function, see Section 5.2.

2.2.4. Role of Natriuretic Peptides in Perioperative Risk of HF

Preoperative natriuretic peptide levels independently predict cardiovascular events in the first 30 days after vascular surgery[61–66] and significantly improve the predictive performance of the Revised Cardiac Risk Index (RCRI).[61] Measurement of biomarkers, especially natriuretic peptides, may be helpful in assessing patients with HF and with diagnosing HF as a postoperative complication in patients at high risk for HF. Further prospective randomized studies are needed to assess the utility of such a strategy (Section 3.1).

2.3. Cardiomyopathy

There is little information on the preoperative evaluation of patients with specific nonischemic cardiomyopathies before noncardiac surgery. Preoperative recommendations must be based on a thorough understanding of the pathophysiology of the cardiomyopathy, assessment and management of the underlying process, and overall management of the HF.

Restrictive Cardiomyopathies: Restrictive cardiomyopathies, such as those associated with cardiac amyloidosis, hemochromatosis, and sarcoidosis, pose special hemodynamic and management problems. Cardiac output in these cardiomyopathies with restrictive physiology is both preload and heart rate dependent. Significant reduction of blood volume or filling pressures, bradycardia or tachycardia, and atrial arrhythmias such as AF/atrial flutter may not be well tolerated. These patients require a multidisciplinary approach, with optimization of the underlying pathology, volume status, and HF status including medication adjustment targeting primary disease management.

Hypertrophic Obstructive Cardiomyopathy: In hypertrophic obstructive cardiomyopathy, decreased systemic vascular resistance (arterial vasodilators), volume loss, or reduction in preload or LV filling may increase the degree of dynamic obstruction and further decrease diastolic filling and cardiac output, with potentially untoward results. Overdiuresis should be avoided, and inotropic agents are usually not used in these patients because of increased LV outflow gradient. Studies have reported mixed results for perioperative risk in patients with hypertrophic obstructive cardiomyopathy. Most studies were small, were conducted at a single center, and reflect variations in patient populations, types of surgery, and management.[67–69]

Arrhythmogenic Right Ventricular (RV) Cardiomyopathy and/or Dysplasia: In 1 autopsy study examining a series of 200 cases of sudden death associated with arrhythmogenic RV cardiomyopathy and/or dysplasia, death occurred in 9.5% of cases during the perioperative period.[70] This emphasizes the importance of close perioperative evaluation and monitoring of these patients for ventricular arrhythmia. Most of these patients require cardiac electrophysiologist involvement and consideration for an implantable cardioverter-defibrillator (ICD) for long-term management.

In a retrospective analysis of 1700 forensic autopsies of patients with sudden, unexpected perioperative death over 17 years, pathological examination showed cardiac lesions in 47 cases, arrhythmogenic RV cardiomyopathy in 18 cases, CAD in 10 cases, cardiomyopathy in 8 cases, structural abnormalities of the His bundle in 9 cases, mitral valve prolapse in 1 case, and acute myocarditis in 1 case, suggesting the importance of detailed clinical histories and physical examinations before surgery for detection of these structural cardiac abnormalities.[71]

Peripartum Cardiomyopathy: Peripartum cardiomyopathy is a rare cause of dilated cardiomyopathy that occurs in approximately 1 in 1000 deliveries and manifests during the last few months of pregnancy or the first 6 months of the postpartum period. It can result in severe ventricular dysfunction during late puerperium.[72] Prognosis depends on the recovery of the LV contractility and resolution of symptoms within the first 6 months after onset of the disease. The major peripartum concern is to optimize fluid administration and avoid myocardial depression while maintaining stable intraoperative hemodynamics.[73] Although the majority of patients remain stable and recover, emergency delivery may be life-saving for the mother as well as the infant. Acute and critically ill patients with refractory peripartum cardiomyopathy may require mechanical support with an intra-aortic balloon pump, extracorporeal membrane oxygenation, continuous-flow LV assist devices, and/or cardiac transplantation.[74]

See Online Data Supplement 3 for additional information on HF and cardiomyopathy.

2.4. Valvular Heart Disease: Recommendations

See the 2014 valvular heart disease CPG for the complete set of recommendations and specific definitions of disease severity[15] and Online Data Supplement 4 for additional information on valvular heart disease.

Class I

1. **It is recommended that patients with clinically suspected moderate or greater degrees of valvular stenosis or regurgitation undergo preoperative echocardiography if there has been either 1) no prior echocardiography within 1 year or 2) a significant change in clinical status or physical examination since last evaluation.[60]** ***(Level of Evidence: C)***
2. **For adults who meet standard indications for valvular intervention (replacement and repair) on the basis of symptoms and severity of stenosis or regurgitation, valvular intervention before elective noncardiac surgery is effective in reducing perioperative risk.[15]** ***(Level of Evidence: C)***

Significant valvular heart disease increases cardiac risk for patients undergoing noncardiac surgery.[37,48] Patients with suspected valvular heart disease should undergo echocardiography to quantify the severity of stenosis or regurgitation, calculate systolic function, and estimate right heart pressures. Evaluation for concurrent CAD is also warranted, with electrocardiography exercise testing, stress echocardiographic or nuclear imaging study, or coronary angiography, as appropriate.

Emergency noncardiac surgery may occur in the presence of uncorrected significant valvular heart disease. The risk of noncardiac surgery can be minimized by 1) having an accurate diagnosis of the type and severity of valvular heart disease, 2) choosing an anesthetic approach appropriate to the valvular heart disease, and 3) considering a higher level of perioperative monitoring (eg, arterial pressure, pulmonary artery pressure, transesophageal echocardiography), as well as managing the patient postoperatively in an intensive care unit setting.

2.4.1. Aortic Stenosis: Recommendation

Class IIa

1. **Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe aortic stenosis (AS).[48,75–84]** ***(Level of Evidence: B)***

In the Original Cardiac Risk Index, severe AS was associated with a perioperative mortality rate of 13%, compared with 1.6% in patients without AS.[48] The mechanism of MACE in patients with AS likely arises from the anesthetic agents and surgical stress that lead to an unfavorable hemodynamic state. The occurrence of hypotension and tachycardia can result in decreased coronary perfusion pressure, development of arrhythmias or ischemia, myocardial injury, cardiac failure, and death.

With the recent advances in anesthetic and surgical approaches, the cardiac risk in patients with significant AS undergoing noncardiac surgery has declined. In a single, tertiary-center study, patients with moderate AS (aortic valve area: 1.0 cm^2 to 1.5 cm^2) or severe AS (aortic valve area <1.0 cm^2) undergoing nonemergency noncardiac surgery had a 30-day mortality rate of 2.1%, compared with 1.0% in propensity score–matched patients without AS (P=0.036).[75] Postoperative MI was more frequent in patients with AS than in patients without AS (3.0% versus 1.1%; P=0.001). Patients with AS had worse primary outcomes (defined as composite of 30-day mortality and postoperative MI) than did patients without AS (4.4% versus 1.7%; P=0.002 for patients with moderate AS; 5.7% versus 2.7%; P=0.02 for patients with severe AS). Predictors of 30-day death and postoperative MI in patients with moderate or severe AS include high-risk surgery (odds ratio [OR]: 7.3; 95% CI: 2.6 to 20.6), symptomatic severe AS (OR: 2.7; 95% CI: 1.1 to 7.5), coexisting moderate or severe mitral regurgitation (MR) (OR: 9.8; 95% CI: 3.1 to 20.4), and pre-existing CAD (OR: 2.7; 95% CI: 1.1 to 6.2).

For patients who meet indications for aortic valve replacement (AVR) before noncardiac surgery but are considered high risk or ineligible for surgical AVR, options include proceeding with noncardiac surgery with invasive hemodynamic monitoring and optimization of loading conditions, percutaneous aortic balloon dilation as a bridging strategy, and transcatheter aortic valve replacement (TAVR). Percutaneous aortic balloon dilation can be performed with acceptable procedural safety, with the mortality rate being 2% to 3% and the stroke rate being 1% to 2%.[76–78,84] However, recurrence and mortality rates approach 50% by 6 months after the procedure. Single-center, small case series from more than 25 years ago reported the use of percutaneous aortic balloon dilation in patients with severe AS before noncardiac surgery.[79–81] Although the results were acceptable, there were no comparison groups or long-term follow-up. The PARTNER (Placement of Aortic Transcatheter Valves) RCT demonstrated that TAVR has superior outcomes for patients who are not eligible for surgical AVR (1-year mortality rate: 30.7% for TAVR versus 50.7% for standard therapy) and similar efficacy for patients who are at high risk for surgical AVR (1-year mortality rate: 24.2% for TAVR versus 26.8% for surgical AVR).[82,83] However, there are no data for the efficacy or safety of TAVR for patients with AS who are undergoing noncardiac surgery.

2.4.2. Mitral Stenosis: Recommendation

Class IIb

1. **Elevated-risk elective noncardiac surgery using appropriate intraoperative and postoperative hemodynamic monitoring may be reasonable in asymptomatic patients with severe mitral stenosis if valve morphology is not favorable for percutaneous mitral balloon commissurotomy.** ***(Level of Evidence: C)***

Patients with severe mitral stenosis are at increased risk for noncardiac surgery and should be managed similarly to patients with AS. The main goals during the perioperative period are to monitor intravascular volume and to avoid tachycardia and hypotension. It is crucial to maintain intravascular volume at a level that ensures adequate forward cardiac output without excessive rises in left atrial pressure and pulmonary capillary wedge pressure that could precipitate acute pulmonary edema.

Patients with mitral stenosis who meet standard indications for valvular intervention (open mitral commissurotomy or percutaneous mitral balloon commissurotomy) should undergo valvular intervention before elective noncardiac surgery.[85] If valve anatomy is not favorable for percutaneous mitral balloon commissurotomy, or if the noncardiac surgery is an emergency, then noncardiac surgery may be considered with invasive hemodynamic monitoring and optimization of loading conditions. There are no reports of the use of percutaneous mitral balloon commissurotomy before noncardiac surgery; however, this procedure has excellent outcomes when used during high-risk pregnancies.[86,87]

2.4.3. Aortic and Mitral Regurgitation: Recommendations

Class IIa

1. **Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable in adults with asymptomatic severe MR.** ***(Level of Evidence: C)***
2. **Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable in adults with asymptomatic severe aortic regurgitation (AR) and a normal LVEF.** ***(Level of Evidence: C)***

Left-sided regurgitant lesions convey increased cardiac risk during noncardiac surgery but are better tolerated than stenotic valvular disease.[88,89] AR and MR are associated with LV volume overload. To optimize forward cardiac output during anesthesia and surgery, 1) preload should be maintained because the LV has increased size and compliance, and 2) excessive systemic afterload should be avoided so as to augment cardiac output and reduce the regurgitation volume. For patients with severe AR or MR, the LV forward cardiac output is reduced because of the regurgitant volume.

Patients with moderate-to-severe AR and severe AR undergoing noncardiac surgery had a higher in-hospital mortality rate than did case-matched controls without AR (9.0% versus 1.8%; P=0.008) and a higher morbidity rate (16.2% versus 5.4%; P=0.003), including postoperative MI, stroke, pulmonary edema, intubation >24 hours, and major arrhythmia.[88] Predictors of in-hospital death included depressed LVEF (ejection fraction [EF] <55%), renal dysfunction (creatinine >2 mg/dL), high surgical risk, and lack of preoperative cardiac medications. In the absence of trials addressing perioperative management, patients with moderate-to-severe AR and severe AR could be monitored with invasive hemodynamics and echocardiography and could be admitted postoperatively to an intensive care unit setting when undergoing surgical procedures with elevated risk.

In a single, tertiary-center study, patients with moderate-to-severe MR and severe MR undergoing nonemergency noncardiac surgery had a 30-day mortality rate similar to that of propensity score–matched controls without MR (1.7% versus 1.1%; P=0.43).[89] Patients with MR had worse primary outcomes (defined as composite of 30-day death and postoperative MI, HF, and stroke) than did patients without MR (22.2% versus 16.4%; P<0.02). Important predictors of postoperative adverse outcomes after noncardiac surgery were EF <35%, ischemic cause of MR, history of diabetes mellitus, and history of carotid endarterectomy. Patients with moderate-to-severe MR and severe MR undergoing noncardiac surgery should be monitored with invasive hemodynamics and echocardiography and admitted postoperatively to an intensive care unit setting when undergoing surgical procedures with elevated risk.

2.5. Arrhythmias and Conduction Disorders

Cardiac arrhythmias and conduction disorders are common findings in the perioperative period, particularly with increasing age. Although supraventricular and ventricular arrhythmias were identified as independent risk factors for perioperative cardiac events in the Original Cardiac Risk Index,[48] subsequent studies indicated a lower level of risk.[37,90,91] The paucity of studies that address surgical risk conferred by arrhythmias limits the ability to provide specific recommendations. General recommendations for assessing and treating arrhythmias can be found in other CPGs.[14,92,93] In 1 study using continuous electrocardiographic monitoring, asymptomatic ventricular arrhythmias, including couplets and nonsustained ventricular tachycardia, were not associated with an increase in cardiac complications after noncardiac surgery.[94] Nevertheless, the presence of an arrhythmia in the preoperative setting should prompt investigation into underlying cardiopulmonary disease, ongoing myocardial ischemia or MI, drug toxicity, or metabolic derangements, depending on the nature and acuity of the arrhythmia and the patient's history.

AF is the most common sustained tachyarrhythmia; it is particularly common in older patients who are likely to be undergoing surgical procedures. Patients with a preoperative history of AF who are clinically stable generally do not require modification of medical management or special evaluation in the perioperative period, other than adjustment of anticoagulation (Section 6.2.7). The potential for perioperative formation of left atrial thrombus in patients with persistent AF may need to be considered if the operation involves physical manipulation of the heart, as in certain thoracic procedures. Ventricular arrhythmias, whether single premature ventricular contractions or nonsustained ventricular tachycardia, usually do not require therapy unless they result in hemodynamic compromise or are associated with significant structural heart disease or inherited electrical disorders. Although frequent ventricular premature beats and nonsustained ventricular tachycardia are risk factors for the development of intraoperative and postoperative arrhythmias, they are not associated with an increased risk of nonfatal MI or cardiac death in the perioperative period.[94,95] However, patients who develop sustained or nonsustained ventricular tachycardia during the perioperative period may require referral to a cardiologist for further evaluation, including assessment of their ventricular function and screening for CAD.

High-grade cardiac conduction abnormalities, such as complete atrioventricular block, if unanticipated, may increase operative risk and necessitate temporary or permanent transvenous pacing.[96] However, patients with intraventricular conduction delays, even in the presence of a left or right bundle-branch block, and no history of advanced heart block or symptoms, rarely progress to complete atrioventricular block perioperatively.[97] The presence of some pre-existing conduction disorders, such as sinus node dysfunction and atrioventricular block, requires caution if perioperative beta-blocker therapy is being considered. Isolated bundle-branch block and bifascicular block generally do not contraindicate use of beta blockers.

2.5.1. Cardiovascular Implantable Electronic Devices: Recommendation

See Section 6.4 for intraoperative/postoperative management of cardiovascular implantable electronic devices (CIEDs).

Class I

1. **Before elective surgery in a patient with a CIED, the surgical/procedure team and clinician following the CIED should communicate in advance to plan perioperative management of the CIED.** ***(Level of Evidence: C)***

The presence of a pacemaker or ICD has important implications for preoperative, intraoperative, and postoperative patient management. Collectively termed CIEDs, these devices include single-chamber, dual-chamber, and biventricular hardware configurations produced by several different manufacturers, each with different software designs and programming features. Patients with CIEDs invariably have underlying cardiac disease that can involve arrhythmias, such as sinus node dysfunction, atrioventricular block, AF, and ventricular tachycardia; structural heart disease, such as ischemic or nonischemic cardiomyopathy; and clinical conditions, such as chronic HF or inherited arrhythmia syndromes. Preoperative evaluation of such patients should therefore encompass an awareness not only of the patient's specific CIED hardware and programming, but also of the underlying cardiac condition for which the device was implanted. In particular, cardiac rhythm and history of ventricular arrhythmias should be reviewed in patients with CIEDs.

To assist clinicians with the perioperative evaluation and management of patients with CIEDs, the HRS and the American Society of Anesthesiologists jointly developed an expert consensus statement published in July 2011 and endorsed by the ACC and the AHA.[33] Clinicians caring for patients with CIEDs in the perioperative setting should be familiar with that document and the consensus recommendations contained within.

The HRS/American Society of Anesthesiologists expert consensus statement acknowledges that because of the complexity of modern devices and the variety of indications for which they are implanted, the perioperative management of patients with CIEDs must be individualized, and a single recommendation for all patients with CIEDs is not appropriate.[33] Effective communication between the surgical/procedure team and the clinician following the patient with a CIED in the outpatient setting is the foundation of successful perioperative management and should take place well in advance of elective procedures. The surgical/procedure team should communicate with the CIED clinician/team to inform them of the nature of the planned procedure and the type of electromagnetic interference (EMI) (ie, electrocautery) likely to be encountered. The outpatient team should formulate a prescription for the perioperative management of the CIED and communicate it to the surgical/procedure team.

The CIED prescription can usually be made from a review of patient records, provided that patients are evaluated at least annually (for pacemakers) or semiannually (for ICDs). In some circumstances, patients will require additional preoperative in-person evaluation or remote CIED interrogation. The prescription may involve perioperative CIED interrogation or reprogramming (including changing pacing to an asynchronous mode and/or inactivating ICD tachytherapies), application of a magnet over the CIED with or without postoperative CIED interrogation, or use of no perioperative CIED interrogation or intervention.[98,99] Details of individual prescriptions will depend on the nature and location of the operative procedure, likelihood of use of monopolar electrocautery, type of CIED (ie, pacemaker versus ICD), and dependence of the patient on cardiac pacing.

See Online Data Supplement 26 for additional information on CIEDs.

2.6. Pulmonary Vascular Disease: Recommendations

Class I

1. **Chronic pulmonary vascular targeted therapy (ie, phosphodiesterase type 5 inhibitors, soluble guanylate cyclase stimulators, endothelin receptor antagonists, and prostanoids) should be continued unless contraindicated or not tolerated in patients with pulmonary hypertension who are undergoing noncardiac surgery.** ***(Level of Evidence: C)***

Class IIa

1. **Unless the risks of delay outweigh the potential benefits, preoperative evaluation by a pulmonary hypertension specialist before noncardiac surgery can be beneficial for patients with pulmonary hypertension, particularly for those with features of increased perioperative risk.[100]*** ***(Level of Evidence: C)***

*Features of increased perioperative risk in patients with pulmonary hypertension include: 1) diagnosis of Group 1 pulmonary hypertension (ie, pulmonary arterial hypertension), 2) other forms of pulmonary hypertension associated with high pulmonary pressures (pulmonary artery systolic pressures >70 mm Hg) and/or moderate or greater RV dilatation and/or dysfunction and/or pulmonary vascular resistance >3 Wood units, and 3) World Health Organization/New York Heart Association class III or IV symptoms attributable to pulmonary hypertension.[101–107]

The evidence on the role of pulmonary hypertension in perioperative mortality and morbidity in patients undergoing noncardiac surgery is based on observational data and is predominantly related to Group 1 pulmonary hypertension (ie, pulmonary arterial hypertension).[101–107] However, complication rates are consistently high, with mortality rates of 4% to 26% and morbidity rates, most notably cardiac and/or respiratory failure, of 6% to 42%.[101–106] A variety of factors can occur during the perioperative period that may precipitate worsening hypoxia, pulmonary hypertension, or RV function. In addition to the urgency of the surgery and the surgical risk category, risk factors for perioperative adverse events in patients with pulmonary hypertension include the severity of pulmonary hypertension symptoms, the degree of RV dysfunction, and the performance of surgery in a center without expertise in pulmonary hypertension.[101–106] Patients with pulmonary arterial hypertension due to other causes, particularly with features of increased perioperative risk, should undergo a thorough preoperative risk assessment in a center with the necessary medical and anesthetic expertise in pulmonary hypertension, including an assessment of functional capacity, hemodynamics, and echocardiography that includes evaluation of RV function. Right heart catheterization can also be used preoperatively to confirm the severity of illness and distinguish primary pulmonary hypertension from secondary causes of elevated pulmonary artery pressures, such as left-sided HF. Patients should have optimization of pulmonary hypertension and RV status preoperatively and should receive the necessary perioperative management on a case-by-case basis.

See Online Data Supplement 6 for additional information on pulmonary vascular disease.

2.7. Adult Congenital Heart Disease

Several case series have indicated that performance of a surgical procedure in patients with adult congenital heart disease (ACHD) carries a greater risk than in the normal population.[108–113] The risk relates to the nature of the underlying ACHD, the surgical procedure, and the urgency of intervention.[108–113] For more information, readers are referred to the specific recommendations for perioperative assessment in the ACC/AHA 2008 ACHD CPG.[28] When possible, it is optimal to perform the preoperative evaluation of surgery for patients with ACHD in a regional center specializing in congenital cardiology, particularly for patient populations that appear to be at particularly high risk (eg, those with a prior Fontan procedure, cyanotic ACHD, pulmonary arterial hypertension, clinical HF, or significant dysrhythmia).

3. Calculation of Risk to Predict Perioperative Cardiac Morbidity

3.1. Multivariate Risk Indices: Recommendations

See Table 3 for a comparison of the RCRI, American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Myocardial Infarction and Cardiac Arrest (MICA), and American College of Surgeons NSQIP Surgical Risk Calculator. See Online Data Supplement 7 for additional information on multivariate risk indices.

Class IIa

1. **A validated risk-prediction tool can be useful in predicting the risk of perioperative MACE in patients**

Table 3. Comparison of the RCRI, the American College of Surgeons NSQIP MICA, and the American College of Surgeons NSQIP Surgical Risk Calculator

	RCRI[131]	American College of Surgeons NSQIP MICA[115]	American College of Surgeons NSQIP Surgical Risk Calculator[114]
Criteria	…	Increasing age	Age
	Creatinine ≥2 mg/dL	Creatinine >1.5 mg/dL	Acute renal failure
	HF	…	HF
	…	Partially or completely dependent functional status	Functional status
	Insulin-dependent diabetes mellitus	…	Diabetes mellitus
	Intrathoracic, intra-abdominal, or suprainguinal vascular surgery	Surgery type: • Anorectal • Aortic • Bariatric • Brain • Breast • Cardiac • ENT • Foregut/hepatopancreatobiliary • Gallbladder/adrenal/appendix/spleen • Intestinal • Neck • Obstetric/gynecological • Orthopedic • Other abdomen • Peripheral vascular • Skin • Spine • Thoracic • Vein • Urologic	Procedure (CPT Code)
	History of cerebrovascular accident or TIA	…	…
	…	…	American Society of Anesthesiologists Physical Status Class
	…	…	Wound class
	…	…	Ascites
	…	…	Systemic sepsis
	…	…	Ventilator dependent
	…	…	Disseminated cancer
	…	…	Steroid use
	…	…	Hypertension
	Ischemic heart disease	…	Previous cardiac event
	…	…	Sex
	…	…	Dyspnea
	…	…	Smoker
	…	…	COPD
	…	…	Dialysis
	…	…	Acute kidney injury
	…	…	BMI
	…	…	Emergency case
Use outside original cohort	Yes	No	No
Sites	Most often single-site studies, but findings consistent in multicenter studies	Multicenter	Multicenter

(*Continued*)

Table 3. Continued

	RCRI[131]	American College of Surgeons NSQIP MICA[115]	American College of Surgeons NSQIP Surgical Risk Calculator[114]
Outcome and risk factor ascertainment	Original: research staff, multiple subsequent studies using variety of data collection strategies	Trained nurses, no prospective cardiac outcome ascertainment	Trained nurses, no prospective cardiac outcome ascertainment
Calculation method	Single point per risk factor	Web-based or open-source spreadsheet for calculation (http://www.surgicalriskcalculator.com/miorcardiacarrest)	Web-based calculator (www.riskcalculator.facs.org)

BMI indicates body mass index; COPD, chronic obstructive pulmonary disease; CPT, current procedural terminology; ENT, ear, nose, and throat; HF, heart failure; NSQIP MICA, National Surgical Quality Improvement Program Myocardial Infarction Cardiac Arrest; NSQIP, National Surgical Quality Improvement Program; RCRI, Revised Cardiac Risk Index; TIA, transient ischemic attack; and ..., not applicable.

undergoing noncardiac surgery.[37,114,115] ***(Level of Evidence: B)***

Class III: No Benefit

1. **For patients with a low risk of perioperative MACE, further testing is not recommended before the planned operation.**[34,35] ***(Level of Evidence: B)***

Different noncardiac operations are associated with different risks of MACE. Operations for peripheral vascular disease are generally performed among those with the highest perioperative risk.[116] The lowest-risk operations are generally those without significant fluid shifts and stress. Plastic surgery and cataract surgery are associated with a very low risk of MACE.[34] Some operations can have their risk lowered by taking a less invasive approach. For example, open aortic aneurysm repair has a high risk of MACE that is lowered when the procedure is performed endovascularly.[117] The number of different surgical procedures makes assigning a specific risk of a MACE to each procedure difficult. In addition, performing an operation in an emergency situation is understood to increase risk.

The RCRI is a simple, validated, and accepted tool to assess perioperative risk of major cardiac complications (MI, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block).[37] It has 6 predictors of risk for major cardiac complications, only 1 of which is based on the procedure—namely, "Undergoing suprainguinal vascular, intraperitoneal, or intrathoracic surgery." A patient with 0 or 1 predictor(s) of risk would have a low risk of MACE. Patients with ≥2 predictors of risk would have elevated risk.

Two newer tools have been created by the American College of Surgeons, which prospectively collected data on operations performed in more than 525 participating hospitals in the United States. Data on more than 1 million operations have been used to create these risk calculators[114] (www.riskcalculator.facs.org).

The American College of Surgeons NSQIP MICA risk-prediction rule was created in 2011,[115] with a single study—albeit large and multicenter—describing its derivation and validation (http://www.surgicalriskcalculator.com/miorcardiacarrest). This tool includes adjusted ORs for different surgical sites, with inguinal hernia as the reference group. Target complications were defined as cardiac arrest (defined as "chaotic cardiac rhythm requiring initiation of basic or advanced life support") or MI (defined as ≥1 of the following: documented electrocardiographic findings of MI, ST elevation of ≥1 mm in >1 contiguous leads, new left bundle-branch block, new Q-wave in ≥2 contiguous leads, or troponin >3 times normal in setting of suspected ischemia). Using these definitions of outcome and chart-based data collection methods, the authors of the risk calculator derived a risk index that was robust in the derivation and validation stages and appeared to outperform the RCRI (which was tested in the same dataset) in discriminative power, particularly among patients undergoing vascular surgery.

The American College of Surgeons NSQIP Surgical Risk Calculator uses the specific current procedural terminology code of the procedure being performed to enable procedure-specific risk assessment for a diverse group of outcomes.[114] The procedure is defined as being an emergency case or not an emergency case. For the American College of Surgeons NSQIP, to be an emergency case, the "principal operative procedure must be performed during the hospital admission for the diagnosis AND the surgeon and/or anesthesiologist must report the case as emergent."[118] The calculator also includes 21 patient-specific variables (eg, age, sex, body mass index, dyspnea, previous MI, functional status). From this input, it calculates the percentage risk of a MACE, death, and 8 other outcomes. This risk calculator may offer the best estimation of surgery-specific risk of a MACE and death.

Some limitations to the NSQIP-based calculator should be noted: It has not been validated in an external population outside the NSQIP, and the definition of MI includes only ST-segment MIs or a large troponin bump (>3 times normal) that occurred in symptomatic patients. An additional disadvantage is the use of the American Society of Anesthesiology Physical Status Classification, a common qualitatively derived risk score used by anesthesiologists. This classification has poor inter-rater reliability even among anesthesiologists and may be unfamiliar to clinicians outside that specialty.[119,120] Clinicians would also need to familiarize themselves with the NSQIP definitions of functional status or "dependence," concepts that are thought to be important in perioperative risk assessment algorithms but that have not been included in multivariable risk indices to date (for more information on functional status, see Section 4).

3.2. Inclusion of Biomarkers in Multivariable Risk Models

Several studies have examined the potential utility of including biomarkers—most commonly preoperative natriuretic peptides (brain natriuretic peptide or N-terminal probrain natriuretic peptide) and C-reactive protein—in preoperative risk indices as an approach to identify patients at highest risk.[64,121–125] These studies and 2 subsequent meta-analyses suggest that biomarkers may provide incremental predictive value.[62,66] However, most studies had significant variation in the time frame in which these biomarkers were obtained, were observational, did not include a control arm, and did not require biomarkers routinely or prospectively. Furthermore, there are no data to suggest that targeting these biomarkers for treatment and intervention will reduce the postoperative risk. In addition, several of these studies were investigations conducted by Poldermans.[121,126–130]

4. Approach to Perioperative Cardiac Testing

4.1. Exercise Capacity and Functional Capacity

Functional status is a reliable predictor of perioperative and long-term cardiac events. Patients with reduced functional status preoperatively are at increased risk of complications. Conversely, those with good functional status preoperatively are at lower risk. Moreover, in highly functional asymptomatic patients, it is often appropriate to proceed with planned surgery without further cardiovascular testing.

If a patient has not had a recent exercise test before noncardiac surgery, functional status can usually be estimated from activities of daily living.[132] Functional capacity is often expressed in terms of metabolic equivalents (METs), where 1 MET is the resting or basal oxygen consumption of a 40–year-old, 70-kg man. In the perioperative literature, functional capacity is classified as excellent (>10 METs), good (7 METs to 10 METs), moderate (4 METs to 6 METs), poor (<4 METs), or unknown. Perioperative cardiac and long-term risks are increased in patients unable to perform 4 METs of work during daily activities. Examples of activities associated with <4 METs are slow ballroom dancing, golfing with a cart, playing a musical instrument, and walking at approximately 2 mph to 3 mph. Examples of activities associated with >4 METs are climbing a flight of stairs or walking up a hill, walking on level ground at 4 mph, and performing heavy work around the house.

Functional status can also be assessed more formally by activity scales, such as the DASI (Duke Activity Status Index) (Table 4)[133] and the Specific Activity Scale.[134] In 600 consecutive patients undergoing noncardiac surgery, perioperative myocardial ischemia and cardiovascular events were more common in those with poor functional status (defined as the inability to walk 4 blocks or climb 2 flights of stairs) even after adjustment for other risk factors.[132] The likelihood of a serious complication was inversely related to the number of blocks that could be walked (P=0.006) or flights of stairs that could be climbed (P=0.01). Analyses from the American College of Surgeons NSQIP dataset have shown that dependent functional status, based on the need for assistance with activities of daily living rather than on METs, is associated with significantly increased risk of perioperative morbidity and mortality.[135,136]

See Online Data Supplement 8 for additional information on exercise capacity and functional capacity.

4.2. Stepwise Approach to Perioperative Cardiac Assessment: Treatment Algorithm

See Figure 1 for a stepwise approach to perioperative cardiac assessment.

Table 4. Duke Activity Status Index

Activity	Weight
Can you…	
1. take care of yourself, that is, eating, dressing, bathing, or using the toilet?	2.75
2. walk indoors, such as around your house?	1.75
3. walk a block or 2 on level ground?	2.75
4. climb a flight of stairs or walk up a hill?	5.50
5. run a short distance?	8.00
6. do light work around the house like dusting or washing dishes?	2.70
7. do moderate work around the house like vacuuming, sweeping floors, or carrying in groceries?	3.50
8. do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?	8.00
9. do yardwork like raking leaves, weeding, or pushing a power mower?	4.50
10. have sexual relations?	5.25
11. participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?	6.00
12. participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?	7.50

Reproduced with permission from Hlatky et al.[133]

The GWC developed an algorithmic approach to perioperative cardiac assessment on the basis of the available evidence and expert opinion, the rationale of which is outlined throughout the CPG. The algorithm incorporates the perspectives of clinicians caring for the patient to provide informed consent and help guide perioperative management to minimize risk. It is also crucial to incorporate the patient's perspective with regard to the assessment of the risk of surgery or alternative therapy and the risk of any GDMT or coronary and valvular interventions before noncardiac surgery. Patients may elect to forgo a surgical intervention if the risk of perioperative morbidity and mortality is extremely high; soliciting this information from the patient before surgery is a key part of shared decision making.

5. Supplemental Preoperative Evaluation

See Table 5 for a summary of recommendations for supplemental preoperative evaluation.

5.1. The 12-Lead Electrocardiogram: Recommendations

Class IIa

1. **Preoperative resting 12-lead electrocardiogram (ECG) is reasonable for patients with known coronary heart disease, significant arrhythmia, peripheral arterial disease, cerebrovascular disease, or other significant structural heart disease, except for those undergoing low-risk surgery.[137–139]** ***(Level of Evidence: B)***

Class IIb

1. **Preoperative resting 12-lead ECG may be considered for asymptomatic patients without known coronary**

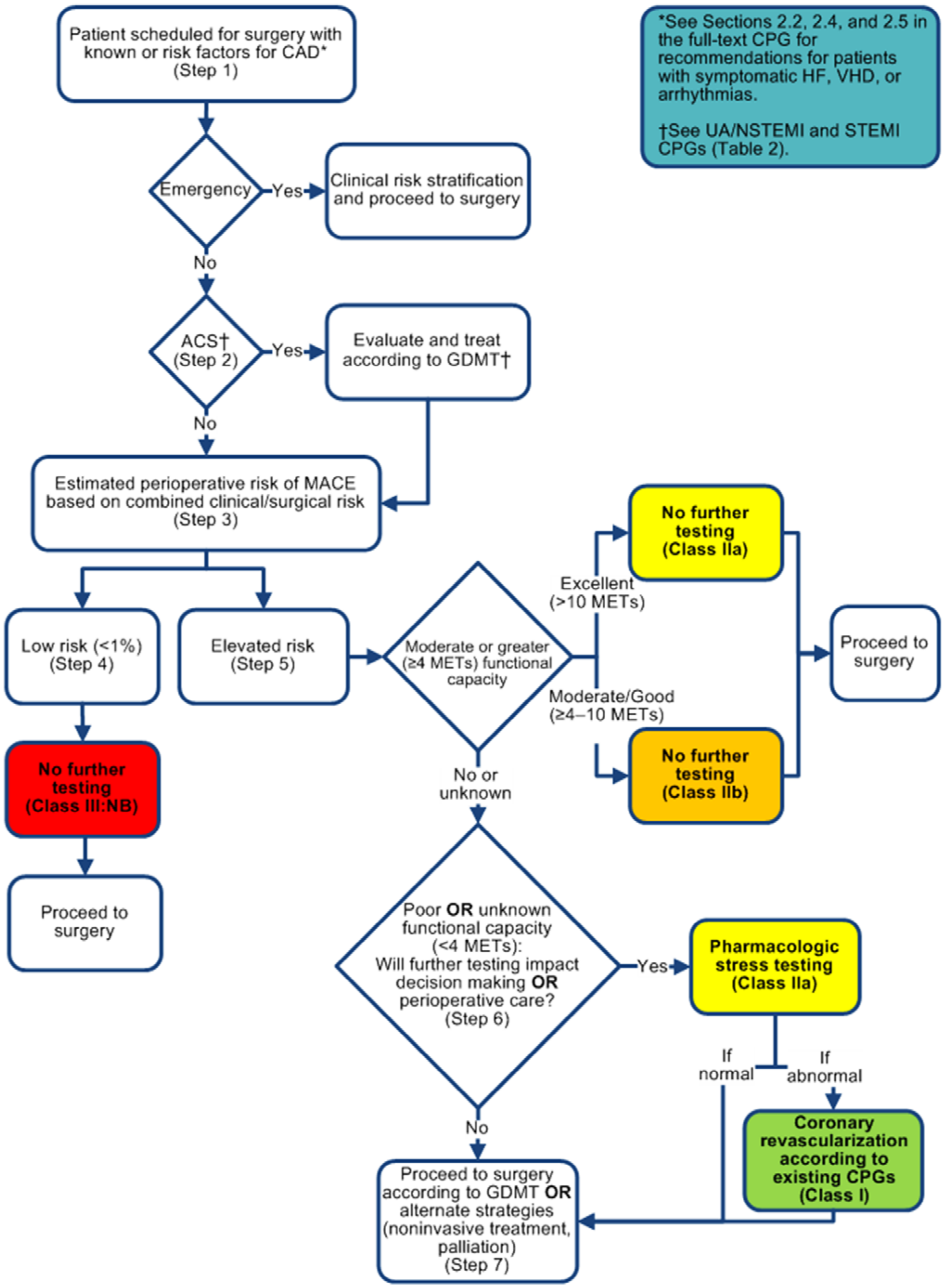


Figure 1. Stepwise approach to perioperative cardiac assessment for CAD. Colors correspond to the Classes of Recommendations in Table 1. **Step 1:** In patients scheduled for surgery with risk factors for or known CAD, determine the urgency of surgery. If an emergency, then determine the clinical risk factors that may influence perioperative management and proceed to surgery with appropriate monitoring and management strategies based on the clinical assessment (see Section 2.1 for more information on CAD). (For patients with symptomatic HF, VHD, or arrhythmias, see Sections 2.2, 2.4, and 2.5 for information on evaluation and management.) **Step 2:** If the surgery is urgent or elective, determine if the patient has an ACS. If yes, then refer patient for cardiology evaluation and management according to GDMT according to the UA/NSTEMI and STEMI CPGs.[18,20] **Step 3:** If the patient has risk factors for stable CAD, then estimate the perioperative risk of MACE on the basis of the combined clinical/surgical risk. This estimate can use the American College of Surgeons NSQIP risk calculator (http://www.riskcalculator.facs.org) or incorporate the RCRI[131] with an estimation of surgical risk. For example, a patient undergoing very low-risk surgery (eg, ophthalmologic surgery), even with multiple risk factors, would have a low risk of MACE, whereas a patient undergoing major vascular surgery with few risk factors would have an elevated risk of MACE (Section 3). **Step 4:** If the patient has a low risk of MACE (<1%), then no further testing is needed, and the patient may proceed to surgery (Section 3). **Step 5:** If the patient is at elevated risk of MACE, then determine functional capacity with an objective measure or scale such as the DASI.[133] If the patient has moderate, good, or excellent functional capacity (≥4 METs), then proceed to surgery without further evaluation (Section 4.1). **Step 6:** If the patient has poor (<4 METs) or unknown functional capacity, then the clinician should consult with the patient and perioperative team to determine whether further testing will impact patient decision making (eg, decision to perform original surgery or willingness to undergo CABG or PCI, depending on the results of the test) or perioperative care. If yes, then pharmacological stress testing is appropriate. In those patients with unknown functional capacity, exercise stress testing may be reasonable to perform. If the stress test is abnormal, consider coronary angiography and revascularization depending on the extent of the abnormal test. The patient can then proceed to surgery with GDMT or consider alternative strategies, such as noninvasive treatment of the indication for surgery (eg, radiation therapy for cancer) or palliation. If the test is normal, proceed to surgery according to GDMT (Section 5.3). **Step 7:** If testing will not impact decision making or care, then proceed to surgery according to GDMT or consider alternative strategies, such as noninvasive treatment of the indication for surgery (eg, radiation therapy for cancer) or palliation. ACS indicates acute coronary syndrome; CABG, coronary artery bypass graft; CAD, coronary artery disease; CPG, clinical practice guideline; DASI, Duke Activity Status Index; GDMT, guideline-directed medical therapy; HF, heart failure; MACE, major adverse cardiac event; MET, metabolic equivalent; NB, No Benefit; NSQIP, National Surgical Quality Improvement Program; PCI, percutaneous coronary intervention; RCRI, Revised Cardiac Risk Index; STEMI, ST-elevation myocardial infarction; UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction; and VHD, valvular heart disease.

Table 5. Summary of Recommendations for Supplemental Preoperative Evaluation

Recommendations	COR	LOE	References
The 12-lead ECG			
Preoperative resting 12-lead ECG is reasonable for patients with known coronary heart disease or other significant structural heart disease, except for low-risk surgery	IIa	B	137–139
Preoperative resting 12-lead ECG may be considered for asymptomatic patients, except for low-risk surgery	IIb	B	37, 138–140
Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures	III: No Benefit	B	35, 141
Assessment of LV function			
It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function	IIa	C	N/A
It is reasonable for patients with HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function	IIa	C	N/A
Reassessment of LV function in clinically stable patients may be considered	IIb	C	N/A
Routine preoperative evaluation of LV function is not recommended	III: No Benefit	B	146–148
Exercise stress testing for myocardial ischemia and functional capacity			
For patients with elevated risk and excellent functional capacity, it is reasonable to forgo further exercise testing and proceed to surgery	IIa	B	132, 135, 136, 162, 163
For patients with elevated risk and unknown functional capacity it may be reasonable to perform exercise testing to assess for functional capacity if it will change management	IIb	B	162–164
For patients with elevated risk and moderate to good functional capacity, it may be reasonable to forgo further exercise testing and proceed to surgery	IIb	B	132, 135, 136
For patients with elevated risk and poor or unknown functional capacity it may be reasonable to perform exercise testing with cardiac imaging to assess for myocardial ischemia	IIb	C	N/A
Routine screening with noninvasive stress testing is not useful for low-risk noncardiac surgery	III: No Benefit	B	165, 166
Cardiopulmonary exercise testing			
Cardiopulmonary exercise testing may be considered for patients undergoing elevated risk procedures	IIb	B	171–179
Noninvasive pharmacological stress testing before noncardiac surgery			
It is reasonable for patients at elevated risk for noncardiac surgery with poor functional capacity to undergo either DSE or MPI if it will change management	IIa	B	183–187
Routine screening with noninvasive stress testing is not useful for low-risk noncardiac surgery	III: No Benefit	B	165, 166
Preoperative coronary angiography			
Routine preoperative coronary angiography is not recommended	III: No Benefit	C	N/A

COR indicates Class of Recommendation; DSE, dobutamine stress echocardiogram; ECG, electrocardiogram; HF, heart failure; LOE, Level of Evidence; LV, left ventricular; MPI, myocardial perfusion imaging; and N/A, not applicable.

heart disease, except for those undergoing low-risk surgery.[37,138–140] ***(Level of Evidence: B)***

Class III: No Benefit

1. **Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures.**[35,141] ***(Level of Evidence: B)***

In patients with established coronary heart disease, the resting 12-lead ECG contains prognostic information relating to short- and long-term morbidity and mortality. In addition, the preoperative ECG may provide a useful baseline standard against which to measure changes in the postoperative period. For both reasons, particularly the latter, the value of the preoperative 12-lead ECG is likely to increase with the risk of the surgical procedure, particularly for patients with known coronary heart disease, arrhythmias, peripheral arterial disease, cerebrovascular disease, or other significant structural heart disease.[137,138]

The prognostic significance of numerous electrocardiographic abnormalities has been identified in observational studies, including arrhythmias,[48,142] pathological Q-waves,[37,142] LV hypertrophy,[139,142] ST depressions,[137,139,142] QTc interval prolongation,[138,143] and bundle-branch blocks.[140,142] However, there is poor concordance across different observational studies as to which abnormalities have prognostic significance and which do not; a minority of studies found no prognostic significance in the preoperative ECG.[141,144,145] The implications of abnormalities on the preoperative 12-lead ECG increase with patient age and with risk factors for coronary heart disease. However, a standard age or risk factor cutoff for use of preoperative electrocardiographic testing has not been defined. Likewise, the optimal time interval between obtaining a 12-lead ECG and elective surgery is unknown. General consensus suggests that an interval of 1 to 3 months is adequate for stable patients.

See Online Data Supplement 9 for additional information on the 12-lead ECG.

5.2. Assessment of LV Function: Recommendations

Class IIa

1. **It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function. *(Level of Evidence: C)***
2. **It is reasonable for patients with HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function. *(Level of Evidence: C)***

Class IIb

1. **Reassessment of LV function in clinically stable patients with previously documented LV dysfunction may be considered if there has been no assessment within a year. *(Level of Evidence: C)***

Class III: No Benefit

1. **Routine preoperative evaluation of LV function is not recommended.[146–148] *(Level of Evidence: B)***

The relationship between measures of resting LV systolic function (most commonly LVEF) and perioperative events has been evaluated in several studies of subjects before noncardiac surgery.[56,58,146–161] These studies demonstrate an association between reduced LV systolic function and perioperative complications, particularly postoperative HF. The association is strongest in patients at high risk for death. Complication risk is associated with the degree of systolic dysfunction, with the greatest risk seen in patients with an LVEF at rest <35%. A preoperatively assessed low EF has a low sensitivity but a relatively high specificity for the prediction of perioperative cardiac events. However, it has only modest incremental predictive power over clinical risk factors. The role of echocardiography in the prediction of risk in patients with clinical HF is less well studied. A cohort of patients with a history of HF demonstrated that preoperative LVEF <30% was associated with an increased risk of perioperative complications.[55] Data are sparse on the value of preoperative diastolic function assessment and the risk of cardiac events.[58,59]

In patients who are candidates for potential solid organ transplantation, a transplantation-specific CPG has suggested it is appropriate to perform preoperative LV function assessment by echocardiography.[31]

See Online Data Supplement 10 for additional information on assessment of LV function.

5.3. Exercise Stress Testing for Myocardial Ischemia and Functional Capacity: Recommendations

Class IIa

1. **For patients with elevated risk and excellent (>10 METs) functional capacity, it is reasonable to forgo further exercise testing with cardiac imaging and proceed to surgery.[132,135,136,162,163] *(Level of Evidence: B)***

Class IIb

1. **For patients with elevated risk and unknown functional capacity, it may be reasonable to perform exercise testing to assess for functional capacity if it will change management.[162–164] *(Level of Evidence: B)***
2. **For patients with elevated risk and moderate to good (≥4 METs to 10 METs) functional capacity, it may be reasonable to forgo further exercise testing with cardiac imaging and proceed to surgery.[132,135,136] *(Level of Evidence: B)***
3. **For patients with elevated risk and poor (<4 METs) or unknown functional capacity, it may be reasonable to perform exercise testing with cardiac imaging to assess for myocardial ischemia if it will change management. *(Level of Evidence: C)***

Class III: No Benefit

1. **Routine screening with noninvasive stress testing is not useful for patients at low risk for noncardiac surgery.[165,166] *(Level of Evidence: B)***

Several studies have examined the role of exercise testing to identify patients at risk for perioperative complications.[162–164,167–170] Almost all of these studies were conducted in patients undergoing peripheral vascular surgery, because these patients are generally considered to be at the highest risk.[162,164,167–169] Although they were important contributions at the time, the outcomes in most of these studies are not reflective of contemporary perioperative event rates, nor was the patient management consistent with current standards of preventive and perioperative cardiac care. Furthermore, many used stress protocols that are not commonly used today, such as non–Bruce protocol treadmill tests or arm ergometry. However, from the available data, patients able to achieve approximately 7 METs to 10 METs have a low risk of perioperative cardiovascular events,[162,164] and those achieving <4 METs to 5 METs have an increased risk of perioperative cardiovascular events.[163,164] Electrocardiographic changes with exercise are not as predictive.[162–164,169]

The vast majority of data on the impact of inducible myocardial ischemia on perioperative outcomes are based on pharmacological stress testing (Sections 5.5.1–5.5.3), but it seems reasonable that exercise stress echocardiography or radionuclide myocardial perfusion imaging (MPI) would perform similarly to pharmacological stress testing in patients who are able to exercise adequately.

See Online Data Supplement 11 for additional information on exercise stress testing for myocardial ischemia and functional capacity.

5.4. Cardiopulmonary Exercise Testing: Recommendation

Class IIb

1. **Cardiopulmonary exercise testing may be considered for patients undergoing elevated risk procedures in**

whom functional capacity is unknown.[171–179] ***(Level of Evidence: B)***

Cardiopulmonary exercise testing has been studied in different settings, including before abdominal aortic aneurysm surgery[172–174,180]; major abdominal surgery (including abdominal aortic aneurysm resection)[175–177]; hepatobiliary surgery[178]; complex hepatic resection[171]; lung resection[181]; and colorectal, bladder, or kidney cancer surgery.[179] These studies varied in patient population, definition of perioperative complications, and what was done with the results of preoperative testing, including decisions about the appropriateness of proceeding with surgery. However, a consistent finding among the studies was that a low anaerobic threshold was predictive of perioperative cardiovascular complications,[171,173,177] postoperative death,[172,174,175] or midterm and late death after surgery.[174,179,180] An anaerobic threshold of approximately 10 mL O_2/kg/min was proposed as the optimal discrimination point, with a range in these studies of 9.9 mL O_2/kg/min to 11 mL O_2/kg/min. Although exercise tolerance can be estimated from instruments such as the DASI[133] or the incremental shuttle walk test, in 1 study, a significant number of patients with poor performance by these measures had satisfactory peak oxygen consumption and anaerobic threshold on cardiopulmonary exercise testing.[182] That particular study was not powered to look at postoperative outcomes.

See Online Data Supplement 12 for additional information on cardiopulmonary exercise testing.

5.5. Pharmacological Stress Testing

5.5.1. Noninvasive Pharmacological Stress Testing Before Noncardiac Surgery: Recommendations

Class IIa

1. **It is reasonable for patients who are at an elevated risk for noncardiac surgery and have poor functional capacity (<4 METs) to undergo noninvasive pharmacological stress testing (either dobutamine stress echocardiogram [DSE] or pharmacological stress MPI) if it will change management.**[183–187] ***(Level of Evidence: B)***

Class III: No Benefit

1. **Routine screening with noninvasive stress testing is not useful for patients undergoing low-risk noncardiac surgery.**[165,166] ***(Level of Evidence: B)***

Pharmacological stress testing with DSE, dipyridamole/adenosine/regadenoson MPI with thallium-201, and/or technetium-99m and rubidium-82 can be used in patients undergoing noncardiac surgery who cannot perform exercise to detect stress-induced myocardial ischemia and CAD. At the time of GWC deliberations, publications in this area confirmed findings of previous studies rather than providing new insight as to the optimal noninvasive pharmacological preoperative stress testing strategy.†

Despite the lack of RCTs on the use of preoperative stress testing, a large number of single-site studies using either DSE or MPI have shown consistent findings. These findings can be summarized as follows:

- The presence of moderate to large areas of myocardial ischemia is associated with increased risk of perioperative MI and/or death.
- A normal study for perioperative MI and/or cardiac death has a very high negative predictive value.
- The presence of an old MI identified on rest imaging is of little predictive value for perioperative MI or cardiac death.
- Several meta-analyses have shown the clinical utility of pharmacological stress testing in the preoperative evaluation of patients undergoing noncardiac surgery.

In terms of which pharmacological test to use, there are no RCTs comparing DSE with pharmacological MPI perioperatively. A retrospective meta-analysis comparing MPI (thallium imaging) and stress echocardiography in patients scheduled for elective noncardiac surgery showed that a moderate to large defect (present in 14% of the population) detected by either method predicted postoperative cardiac events. The authors identified a slight superiority of stress echocardiography relative to nongated MPI with thallium in predicting postoperative cardiac events.[204] However, in light of the lack of RCT data, local expertise in performing pharmacological stress testing should be considered in decisions about which pharmacological stress test to use.

The recommendations in this CPG do not specifically address the preoperative evaluation of patients for kidney or liver transplantation because the indications for stress testing may reflect both perioperative and long-term outcomes in this population. The reader is directed to the AHA/ACC scientific statement titled "Cardiac disease evaluation and management among kidney and liver transplantation candidates" for further recommendations.[31]

See Online Data Supplement 13 for additional information on noninvasive pharmacological stress testing before noncardiac surgery.

5.5.2. Radionuclide MPI

The role of MPI in preoperative risk assessment in patients undergoing noncardiac surgery has been evaluated in several studies.‡ The majority of MPI studies show that moderate to large reversible perfusion defects, which reflect myocardial ischemia, carry the greatest risk of perioperative cardiac death or MI. In general, an abnormal MPI test is associated with very high sensitivity for detecting patients at risk for perioperative cardiac events. The negative predictive value of a normal MPI study is high for MI or cardiac death, although postoperative cardiac events do occur in this population.[204] Most studies have shown that a fixed perfusion defect, which reflects infarcted myocardium, has a low positive predictive value for perioperative cardiac events. However, patients with fixed defects have shown increased risk for long-term events relative to patients with a normal MPI test, which likely reflects

†References 31, 60, 149, 165, 183–185, 188–204.

‡References 166, 190, 193, 195, 197, 199, 202–206.

the fact that they have CAD. Overall, a reversible myocardial perfusion defect predicts perioperative events, whereas a fixed perfusion defect predicts long-term cardiac events.

See Online Data Supplement 14 for additional information on radionuclide MPI.

5.5.3. Dobutamine Stress Echocardiography

The role of DSE in preoperative risk assessment in patients undergoing noncardiac surgery has been evaluated in several studies.[186,187,207–220] The definition of an abnormal stress echocardiogram in some studies was restricted to the presence of new wall motion abnormalities with stress, indicative of myocardial ischemia, but in others also included the presence of akinetic segments at baseline, indicative of MI. These studies have predominantly evaluated the role of DSE in patients with an increased perioperative cardiovascular risk, particularly those undergoing abdominal aortic or peripheral vascular surgery. In many studies, the results of the DSE were available to the managing clinicians and surgeons, which influenced perioperative management, including the preoperative use of diagnostic coronary angiography and coronary revascularization, and which intensified medical management, including beta blockade.

Overall, the data suggest that DSE appears safe and feasible as part of a preoperative assessment. Safety and feasibility have been demonstrated specifically in patients with abdominal aortic aneurysms, peripheral vascular disease, morbid obesity, and severe chronic obstructive pulmonary disease—populations in which there had previously been safety concerns.[186,187,213,214,220–222] Overall, a positive test result for DSE was reported in the range of 5% to 50%. In these studies, with event rates of 0% to 15%, the ability of a positive test result to predict an event (nonfatal MI or death) ranged from 0% to 37%. The negative predictive value is invariably high, typically in the range of 90% to 100%. In interpreting these values, one must consider the overall perioperative risk of the population and the potential results stress imaging had on patient management. Several large studies reporting the value of DSE in the prediction of cardiac events during noncardiac surgery for which Poldermans was the senior author are not included in the corresponding data supplement table[223–225]; however, regardless of whether the evidence includes these studies, conclusions are similar.

See Online Data Supplement 15 for additional information on DSE.

5.6. Stress Testing—Special Situations

In most ambulatory patients, exercise electrocardiographic testing can provide both an estimate of functional capacity and detection of myocardial ischemia through changes in the electrocardiographic and hemodynamic response. In many settings, an exercise stress ECG is combined with either echocardiography or MPI. In the perioperative period, most patients undergo pharmacological stress testing with either MPI or DSE.

In patients undergoing stress testing with abnormalities on their resting ECG that impair diagnostic interpretation (eg, left bundle-branch block, LV hypertrophy with “strain” pattern, digitalis effect), concomitant stress imaging with echocardiography or MPI may be an appropriate alternative. In patients with left bundle-branch block, exercise MPI has an unacceptably low specificity because of septal perfusion defects that are not related to CAD. For these patients, pharmacological stress MPI, particularly with adenosine, dipyridamole, or regadenoson, is suggested over exercise stress imaging.

In patients with indications for stress testing who are unable to perform adequate exercise, pharmacological stress testing with either DSE or MPI may be appropriate. There are insufficient data to support the use of dobutamine stress magnetic resonance imaging in preoperative risk assessment.[221]

Intravenous dipyridamole and adenosine should be avoided in patients with significant heart block, bronchospasm, critical carotid occlusive disease, or a condition that prevents their being withdrawn from theophylline preparations or other adenosine antagonists; regadenoson has a more favorable side-effect profile and appears safe for use in patients with bronchospasm. Dobutamine should be avoided in patients with serious arrhythmias or severe hypertension. All stress agents should be avoided in unstable patients. In patients in whom echocardiographic image quality is inadequate for wall motion assessment, such as those with morbid obesity or severe chronic obstructive lung disease, intravenous echocardiography contrast[187,222] or alternative methods, such as MPI, may be appropriate. An echocardiographic stress test is favored if an assessment of valvular function or pulmonary hypertension is clinically important. In many instances, either exercise stress echocardiography/DSE or MPI may be appropriate, and local expertise may help dictate the choice of test.

At the time of publication, evidence did not support the use of an ambulatory ECG as the only diagnostic test to refer patients for coronary angiography, but it may be appropriate in rare circumstances to direct medical therapy.

5.7. Preoperative Coronary Angiography: Recommendation

Class III: No Benefit

1. **Routine preoperative coronary angiography is not recommended.** ***(Level of Evidence: C)***

Data are insufficient to recommend the use of coronary angiography in all patients (ie, routine testing), including for those patients undergoing any specific elevated-risk surgery. In general, indications for preoperative coronary angiography are similar to those identified for the nonoperative setting. The decreased risk of coronary computerized tomography angiography compared with invasive angiography may encourage its use to determine preoperatively the presence and extent of CAD. However, any additive value in decision making of coronary computed tomography angiography and calcium scoring is uncertain, given that data are limited and involve patients undergoing noncardiac surgery.[226]

The recommendations in this CPG do not specifically address the preoperative evaluation of patients for kidney or liver transplantation because the indications for angiography may be different. The reader is directed to the AHA/ACC scientific statement titled “Cardiac disease evaluation and management among kidney and liver transplantation candidates” for further recommendations.[31]

See Online Data Supplement 16 for additional information on preoperative coronary angiography.

6. Perioperative Therapy

See Table 6 for a summary of recommendations for perioperative therapy.

6.1. Coronary Revascularization Before Noncardiac Surgery: Recommendations

Class I

1. **Revascularization before noncardiac surgery is recommended in circumstances in which revascularization is indicated according to existing CPGs.[25,26] (*Level of Evidence: C*)** (See Table A in Appendix 3 for related recommendations.)

Class III: No Benefit

1. **It is not recommended that routine coronary revascularization be performed before noncardiac surgery exclusively to reduce perioperative cardiac events.[116] *(Level of Evidence: B)***

Patients undergoing risk stratification before elective noncardiac procedures and whose evaluation recommends CABG surgery should undergo coronary revascularization before an elevated-risk surgical procedure.[227] The cumulative mortality and morbidity risks of both the coronary revascularization procedure and the noncardiac surgery should be weighed carefully in light of the individual patient's overall health, functional status, and prognosis. The indications for preoperative surgical coronary revascularization are identical to those recommended in the 2011 CABG CPG and the 2011 PCI CPG and the accumulated data on which those conclusions were based[25,26] (See Table A in Appendix 3 for the related recommendations).

The role of preoperative PCI in reducing untoward perioperative cardiac complications is uncertain given the available data. Performing PCI before noncardiac surgery should be limited to 1) patients with left main disease whose comorbidities preclude bypass surgery without undue risk and 2) patients with unstable CAD who would be appropriate candidates for emergency or urgent revascularization.[25,26] Patients with ST-elevation MI or non–ST-elevation acute coronary syndrome benefit from early invasive management.[26] In such patients, in whom noncardiac surgery is time sensitive despite an increased risk in the perioperative period, a strategy of balloon angioplasty or bare-metal stent (BMS) implantation should be considered.

There are no prospective RCTs supporting coronary revascularization, either CABG or PCI, before noncardiac surgery to decrease intraoperative and postoperative cardiac events. In the largest RCT, CARP (Coronary Artery Revascularization Prophylaxis), there were no differences in perioperative and long-term cardiac outcomes with or without preoperative coronary revascularization by CABG or PCI in patients with documented CAD, with the exclusion of those with left main disease, a LVEF <20%, and severe AS.[116] A follow-up analysis reported improved outcomes in the subset who underwent CABG compared with those who underwent PCI.[228] In an additional analysis of the database of patients who underwent coronary angiography in both the randomized and nonrandomized portion of the CARP trial, only the subset of patients with unprotected left main disease showed a benefit from preoperative coronary artery revascularization.[229] A second RCT also demonstrated no benefit from preoperative testing and directed coronary revascularization in patients with 1 to 2 risk factors for CAD,[230] but the conduct of the trial was questioned at the time of the GWC's discussions.[9]

See Online Data Supplement 17 for additional information on coronary revascularization before noncardiac surgery.

6.1.1. Timing of Elective Noncardiac Surgery in Patients With Previous PCI: Recommendations

Class I

1. **Elective noncardiac surgery should be delayed 14 days after balloon angioplasty *(Level of Evidence: C)* and 30 days after BMS implantation.[231–233] *(Level of Evidence B)***
2. **Elective noncardiac surgery should optimally be delayed 365 days after drug-eluting stent (DES) implantation.[234–237] *(Level of Evidence: B)***

Class IIa

1. **In patients in whom noncardiac surgery is required, a consensus decision among treating clinicians as to the relative risks of surgery and discontinuation or continuation of antiplatelet therapy can be useful. *(Level of Evidence: C)***

Class IIb§

1. **Elective noncardiac surgery after DES implantation may be considered after 180 days if the risk of further delay is greater than the expected risks of ischemia and stent thrombosis.[234,238] *(Level of Evidence: B)***

Class III: Harm

1. **Elective noncardiac surgery should not be performed within 30 days after BMS implantation or within 12 months after DES implantation in patients in whom dual antiplatelet therapy (DAPT) will need to be discontinued perioperatively.[231–237,239] *(Level of Evidence: B)***
2. **Elective noncardiac surgery should not be performed within 14 days of balloon angioplasty in patients in whom aspirin will need to be discontinued perioperatively. *(Level of Evidence: C)***

Patients who require both PCI and noncardiac surgery merit special consideration. PCI should not be performed as a prerequisite in patients who need noncardiac surgery unless it is clearly indicated for high-risk coronary anatomy (eg, left main disease), unstable angina, MI, or life-threatening arrhythmias due to active ischemia amenable to PCI. If PCI is necessary, then the urgency of the noncardiac surgery and the risk of bleeding and ischemic events, including stent thrombosis, associated with the surgery in a patient taking DAPT need to

§Because of new evidence, this is a new recommendation since the publication of the 2011 PCI CPG.[26]

Table 6. Summary of Recommendations for Perioperative Therapy

Recommendations	COR	LOE	References
Coronary revascularization before noncardiac surgery			
Revascularization before noncardiac surgery is recommended when indicated by existing CPGs	I	C	25, 26
Coronary revascularization is not recommended before noncardiac surgery exclusively to reduce perioperative cardiac events	III: No Benefit	B	116
Timing of elective noncardiac surgery in patients with previous PCI			
Noncardiac surgery should be delayed after PCI	I	C: 14 d after balloon angioplasty	N/A
		B: 30 d after BMS implantation	231–233
Noncardiac surgery should optimally be delayed 365 d after DES implantation	I	B	234–237
A consensus decision as to the relative risks of discontinuation or continuation of antiplatelet therapy can be useful	IIa	C	N/A
Elective noncardiac surgery after DES implantation may be considered after 180 d	IIb*	B	234, 238
Elective noncardiac surgery should not be performed in patients in whom DAPT will need to be discontinued perioperatively within 30 d after BMS implantation or within 12 mo after DES implantation	III: Harm	B	231–237, 239
Elective noncardiac surgery should not be performed within 14 d of balloon angioplasty in patients in whom aspirin will need to be discontinued perioperatively	III: Harm	C	N/A
Perioperative beta-blocker therapy			
Continue beta blockers in patients who are on beta blockers chronically	I	B SR†	242–248
Guide management of beta blockers after surgery by clinical circumstances	IIa	B SR†	241, 248, 251
In patients with intermediate- or high-risk preoperative tests, it may be reasonable to begin beta blockers	IIb	C SR†	225
In patients with ≥3 RCRI factors, it may be reasonable to begin beta blockers before surgery	IIb	B SR†	248
Initiating beta blockers in the perioperative setting as an approach to reduce perioperative risk is of uncertain benefit in those with a long-term indication but no other RCRI risk factors	IIb	B SR†	242, 248, 257
It may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably >1 d before surgery	IIb	B SR†	241, 258–260
Beta-blocker therapy should not be started on the d of surgery	III: Harm	B SR†	241
Perioperative statin therapy			
Continue statins in patients currently taking statins	I	B	283–286
Perioperative initiation of statin use is reasonable in patients undergoing vascular surgery	IIa	B	287
Perioperative initiation of statins may be considered in patients with a clinical risk factor who are undergoing elevated-risk procedures	IIb	C	N/A
Alpha-2 agonists			
Alpha-2 agonists are not recommended for prevention of cardiac events	III: No Benefit	B	291–295
ACE inhibitors			
Continuation of ACE inhibitors or ARBs is reasonable perioperatively	IIa	B	300, 301
If ACE inhibitors or ARBs are held before surgery, it is reasonable to restart as soon as clinically feasible postoperatively	IIa	C	N/A
Antiplatelet agents			
Continue DAPT in patients undergoing urgent noncardiac surgery during the first 4 to 6 wk after BMS or DES implantation, unless the risk of bleeding outweighs the benefit of stent thrombosis prevention	I	C	N/A
In patients with stents undergoing surgery that requires discontinuation $P2Y_{12}$ inhibitors, continue aspirin and restart the $P2Y_{12}$ platelet receptor–inhibitor as soon as possible after surgery	I	C	N/A
Management of perioperative antiplatelet therapy should be determined by consensus of treating clinicians and the patient	I	C	N/A

(*Continued*)

Table 6. Continued

Recommendations	COR	LOE	References
In patients undergoing nonemergency/nonurgent noncardiac surgery without prior coronary stenting, it may be reasonable to continue aspirin when the risk of increased cardiac events outweighs the risk of increased bleeding	IIb	B	298, 306
Initiation or continuation of aspirin is not beneficial in patients undergoing elective noncardiac noncarotid surgery who have not had previous coronary stenting	III: No Benefit	B	298
		C: If risk of ischemic events outweighs risk of surgical bleeding	N/A
Perioperative management of patients with CIEDs			
Patients with ICDs should be on a cardiac monitor continuously during the entire period of inactivation, and external defibrillation equipment should be available. Ensure that ICDs are reprogrammed to active therapy	I	C	336

*Because of new evidence, this is a new recommendation since the publication of the 2011 PCI CPG.[26]

†These recommendations have been designated with a SR to emphasize the rigor of support from the ERC's systematic review.

ACE indicates angiotensin-converting-enzyme; ARB, angiotensin-receptor blocker; BMS, bare-metal stent; CIED, cardiovascular implantable electronic device; COR, Class of Recommendation; CPG, clinical practice guideline; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; ERC, Evidence Review Committee; ICD, implantable cardioverter-defibrillator; LOE, Level of Evidence; N/A, not applicable; PCI, percutaneous coronary intervention; RCRI, Revised Cardiac Risk Index; and SR, systematic review.

be considered (see Section 6.2.6 for more information on antiplatelet management). If there is little risk of bleeding or if the noncardiac surgery can be delayed ≥12 months, then PCI with DES and prolonged aspirin and $P2Y_{12}$ platelet receptor–inhibitor therapy is an option. Some data suggest that in newer-generation DESs, the risk of stent thrombosis is stabilized by 6 months after DES implantation and that noncardiac surgery after 6 months may be possible without increased risk.[234,238] If the elective noncardiac surgery is likely to occur within 1 to 12 months, then a strategy of BMS and 4 to 6 weeks of aspirin and $P2Y_{12}$ platelet receptor–inhibitor therapy with continuation of aspirin perioperatively may be an appropriate option. Although the risk of restenosis is higher with BMS than with DES, restenotic lesions are usually not life threatening, even though they may present as an acute coronary syndrome, and they can usually be dealt with by repeat PCI if necessary. If the noncardiac surgery is time sensitive (within 2 to 6 weeks) or the risk of bleeding is high, then consideration should be given to balloon angioplasty with provisional BMS implantation. If the noncardiac surgery is urgent or an emergency, then the risks of ischemia and bleeding, and the long-term benefit of coronary revascularization must be weighed. If coronary revascularization is absolutely necessary, CABG combined with the noncardiac surgery may be considered.

See Online Data Supplement 18 for additional information on the strategy of percutaneous revascularization in patients needing elective noncardiac surgery.

6.2. Perioperative Medical Therapy

6.2.1. Perioperative Beta-Blocker Therapy: Recommendations

See the ERC systematic review report, "Perioperative beta blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery" for the complete evidence review on perioperative beta-blocker therapy,[8] and see Online Data Supplement 19 for more information about beta blockers. The tables in Data Supplement 19 were reproduced directly from the ERC's systematic review for your convenience. These recommendations have been designated with an SR to emphasize the rigor of support from the ERC's systematic review.

As noted in the Scope of this CPG (Section 1.4), the recommendations in Section 6.2.1 are based on a separately commissioned review of the available evidence, the results of which were used to frame our decision making. Full details are provided in the ERC's systematic review report[8] and data supplements. However, 3 key findings were powerful influences on this CPG's recommendations:

1. The systematic review suggests that preoperative use of beta blockers was associated with a reduction in cardiac events in the studies examined, but few data support the effectiveness of preoperative administration of beta blockers to reduce risk of surgical death.
2. Consistent and clear associations exist between beta-blocker administration and adverse outcomes, such as bradycardia and stroke.
3. These findings were quite consistent even when the DECREASE studies[230,240] in question or POISE (Perioperative Ischemic Evaluation Study)[241] were excluded. Stated alternatively, exclusion of these studies did not substantially affect estimates of risk or benefit.

Class I

1. **Beta blockers should be continued in patients undergoing surgery who have been on beta blockers chronically.[242–248]** ***(Level of Evidence: B)*** **SR**

If well tolerated, continuing beta blockers in patients who are currently receiving them for longitudinal reasons, particularly when longitudinal treatment is provided according to GDMT, such as for MI, is recommended (See Table B in Appendix 3 for applicable recommendations from the 2011 secondary prevention CPG).[249] Multiple observational studies support the benefits of continuing beta blockers in patients who are undergoing surgery and who are on these agents for longitudinal indications.[242–248] However, these studies vary in their robustness in terms of their ability to deal with confounding due to the indications for beta blockade or ability to discern whether the reasons for discontinuation are in themselves associated with higher risk (independent of beta-blocker discontinuation), which led to the Level of Evidence B determination. This recommendation is consistent with the Surgical Care Improvement Project National Measures (CARD-2) as of November 2013.[250]

Class IIa

1. **It is reasonable for the management of beta blockers after surgery to be guided by clinical circumstances, independent of when the agent was started.[241,248,251] *(Level of Evidence: B)* SR**

This recommendation requires active management of patients on beta blockers during and after surgery. Particular attention should be paid to the need to modify or temporarily discontinue beta blockers as clinical circumstances (eg, hypotension, bradycardia,[252] bleeding)[251] dictate. Although clinical judgment will remain a mainstay of this approach, evidence suggests that implementation of and adherence to local practice guidelines can play a role in achieving this recommendation.[253]

Class IIb

1. **In patients with intermediate- or high-risk myocardial ischemia noted in preoperative risk stratification tests, it may be reasonable to begin perioperative beta blockers.[225] *(Level of Evidence: C)* SR**

The risks and benefits of perioperative beta blocker use appear to be favorable in patients who have intermediate- or high-risk myocardial ischemia noted on preoperative stress testing.[225,254] The decision to begin beta blockers should be influenced by whether a patient is at risk for stroke[46,255,256] and whether the patient has other relative contraindications (such as uncompensated HF).

Class IIb

2. **In patients with 3 or more RCRI risk factors (eg, diabetes mellitus, HF, CAD, renal insufficiency, cerebrovascular accident), it may be reasonable to begin beta blockers before surgery.[248] *(Level of Evidence: B)* SR**

Observational data suggest that patients appear to benefit from use of beta blockers in the perioperative setting if they have ≥3 RCRI risk factors. In the absence of multiple risk factors, it is unclear whether preoperative administration is safe or effective; again, it is important to gauge the risk related to perioperative stroke or contraindications in choosing to begin beta blockers.

Class IIb

3. **In patients with a compelling long-term indication for beta-blocker therapy but no other RCRI risk factors, initiating beta blockers in the perioperative setting as an approach to reduce perioperative risk is of uncertain benefit.[242,248,257] *(Level of Evidence: B)* SR**

Although beta blockers improve long-term outcomes when used in patients according to GDMT, it is unclear whether beginning beta blockers before surgery is efficacious or safe if a long-term indication is not accompanied by additional RCRI criteria. Rather, a preferable approach might be to ensure beta blockers are initiated as soon as feasible after the surgical procedure.

Class IIb

4. **In patients in whom beta-blocker therapy is initiated, it may be reasonable to begin perioperative beta blockers long enough in advance to assess safety and tolerability, preferably more than 1 day before surgery.[241,258–260] *(Level of Evidence: B)* SR**

It may be reasonable to begin beta blockers long enough in advance of the operative date that clinical effectiveness and tolerability can be assessed.[241,258–260]

Beginning beta blockers ≤1 day before surgery is at a minimum ineffective and may in fact be harmful.[8,241,248,261] Starting the medication 2 to 7 days before surgery may be preferred, but few data support the need to start beta blockers >30 days beforehand.[258–260] It is important to note that even in studies that included preoperative dose titration as an element of their algorithm, patients' drug doses rarely changed after an initial dose was chosen.[254,262] In addition, the data supporting "tight" heart rate control is weak,[262] suggesting that clinical assessments for tolerability are a key element of preoperative strategies.[258–260]

Class III: Harm

1. **Beta-blocker therapy should not be started on the day of surgery.[241] *(Level of Evidence: B)* SR**

The GWC specifically recommends against starting beta blockers on the day of surgery in beta–blocker-naïve patients,[241] particularly at high initial doses, in long-acting form, and if there no plans for dose titration or monitoring for adverse events.

6.2.1.1. Evidence on Efficacy of Beta-Blocker Therapy

Initial interest in using beta blockers to prevent postoperative cardiac complications was supported by a small number of RCTs and reviews.[225,254,263,264] Perioperative beta blockade was quickly adopted because the potential benefit of perioperative beta blockers was large[265] in the absence of other therapies, initial RCTs did not suggest adverse effects, and the effects of beta blockers in surgical patients were consistent with effects in patients with MI (eg, reducing mortality rate from coronary ischemia).

However, these initial data were derived primarily from small trials, with minimum power, of highly screened patient populations undergoing specific procedures (eg, vascular surgery) and using agents (eg, intravenous atenolol, oral bisoprolol) not widely available in the United States. Limitations of initial studies provided the rationale for studies that followed,[241,266] of which 3 showed no cardiac outcome or mortality difference between beta–blocker-treated and -untreated patients.[257,267,268] Additional information was provided by a meta-analysis of all published studies that suggested potential harm as well as a lower protective effect[269]; a robust observational study also suggested an association between use of beta blockers in low-risk patients and higher surgical mortality rate.[242]

Publication of POISE, a multicenter study of adequate size and scope to address sample size, generalizability, and limitations of previous studies, added further complexity to the evidence base by suggesting that use of beta blockers reduced risks for cardiac events (eg, ischemia, AF, need for coronary interventions) but produced a higher overall risk—largely related to stroke and higher rate of death resulting from noncardiac complications.[241] However, POISE was criticized for its use of a high dose of long-acting beta blocker and for initiation of the dose immediately before noncardiac surgery. In fact, a lower starting dose was used in the 3 studies that saw both no harm and no benefit.[257,267,270] Moreover, POISE did not include a titration protocol before or after surgery.

The evidence to this point was summarized in a series of meta-analyses suggesting a mixed picture of the safety and efficacy of beta blockers in the perioperative setting.[269,271–273] These evidence summaries were relatively consistent in showing that use of perioperative beta blockers could reduce perioperative cardiac risk but that they had significant deleterious associations with bradycardia, stroke, and hypotension.

Adding further complexity to the perioperative beta-blocker picture, concern was expressed by Erasmus University about the scientific integrity of studies led by Poldermans[9]; see Section 1.4 for further discussion. For transparency, we included the nonretracted publications in the text of this document if they were relevant to the topic. However, the nonretracted publications were not used as evidence to support the recommendations and were not included in the corresponding data supplement.

6.2.1.2. Titration of Beta Blockers

There are limited trial data on whether or how to titrate beta blockers in the perioperative setting or whether this approach is more efficacious than fixed-dose regimens. Although several studies[254,263] included dose titration to heart rate goal in their protocol, and separate studies suggested that titration is important to achieving appropriate anti-ischemic effects,[274] it appears that many patients in the original trials remained on their starting medication dose at the time of surgery, even if on a research protocol.

Studies that titrated beta blockers, many of which are now under question, also tended to begin therapy >1 day before surgery, making it difficult to discern whether dose titration or preoperative timing was more important to producing any potential benefits of beta blockade.

Several studies have evaluated the intraclass differences in beta blockers (according to duration of action and beta-1 selectivity),[261,275–278] but few comparative trials exist at the time of publication, and it is difficult to make broad recommendations on the basis of evidence available at this time. Moreover, some intraclass differences may be influenced more by differences in beta-adrenoceptor type than by the medication itself.[279] However, data from POISE suggest that initiating long-acting beta blockers on the day of surgery may not be a preferable approach.

6.2.1.3. Withdrawal of Beta Blockers

Although few studies describe risks of withdrawing beta blockers in the perioperative time period,[243,246] longstanding evidence from other settings suggests that abrupt withdrawal of long-term beta blockers is harmful,[280–282] providing the major rationale for the ACC/AHA Class I recommendation. There are fewer data to describe whether short-term (1 to 2 days) perioperative use of beta blockers, followed by rapid discontinuation, is harmful.

6.2.1.4. Risks and Caveats

The evidence for perioperative beta blockers—even excluding the DECREASE studies under question and POISE—supports the idea that their use can reduce perioperative cardiac events. However, this benefit is offset by a higher relative risk for perioperative strokes and uncertain mortality benefit or risk.[242,248,254] Moreover, the time horizon for benefit in some cases may be farther in the future than the time horizon for adverse effects of the drugs.

In practice, the risk–benefit analysis of perioperative beta blockers should also take into account the frequency and severity of the events the therapy may prevent or produce. That is, although stroke is a highly morbid condition, it tends to be far less common than MACE. There may be situations in which the risk of perioperative stroke is lower, but the concern for cardiac events is elevated; in these situations, beta blocker use may have benefit, though little direct evidence exists to guide clinical decision making in specific scenarios.

6.2.2. Perioperative Statin Therapy: Recommendations

Class I

1. **Statins should be continued in patients currently taking statins and scheduled for noncardiac surgery.[283–286]** ***(Level of Evidence: B)***

Class IIa

1. **Perioperative initiation of statin use is reasonable in patients undergoing vascular surgery.[287]** ***(Level of Evidence: B)***

Class IIb

1. **Perioperative initiation of statins may be considered in patients with clinical indications according to GDMT who are undergoing elevated-risk procedures.** ***(Level of Evidence: C)***

Lipid lowering with statin agents is highly effective for primary and secondary prevention of cardiac events.[288] Data from statin trials are now robust enough to allow the GWC to directly answer the critical questions of what works and in whom without estimating cardiovascular risk. The effectiveness of this class of agents in reducing cardiovascular events in high-risk patients has suggested that they may improve perioperative cardiovascular outcomes. A placebo-controlled randomized trial followed patients on atorvastatin for 6 months (50 patients on atorvastatin and 50 patients on placebo) who were undergoing vascular surgery and found a significant decrease in MACE in the treated group.[287] In a Cochrane analysis, pooled results from 3 studies, with a total of 178 participants, were evaluated.[289] In the statin group, 7 of

105 (6.7%) participants died within 30 days of surgery, as did 10 of 73 (13.7%) participants in the control group. However, all deaths occurred in a single study population, and estimates were therefore derived from only 1 study. Two additional RCTs from Poldermans also evaluated the efficacy of fluvastatin compared with placebo and demonstrated a significant reduction in MACE in patients at high risk, with a trend toward improvement in patients at intermediate risk.[240,290]

Most of the data on the impact of statin use in the perioperative period come from observational trials. The largest observational trial used data from hospital administrative databases.[283] Patients who received statins had a lower crude mortality rate and a lower mortality rate when propensity matched. An administrative database from 4 Canadian provinces was used to evaluate the relationship between statin use and outcomes in patients undergoing carotid endarterectomy for symptomatic carotid disease[284]; this study found an inverse correlation between statin use and in-hospital mortality, stroke or death, or cardiovascular outcomes. A retrospective cohort of 752 patients undergoing intermediate-risk, noncardiac, nonvascular surgery was evaluated for all-cause mortality rate.[285] Compared with nonusers, patients on statin therapy had a 5-fold reduced risk of 30-day all-cause death. Another observational trial of 577 patients revealed that patients undergoing noncardiac vascular surgery treated with statins had a 57% lower chance of having perioperative MI or death at 2-year follow-up, after controlling for other variables.[286]

The accumulated evidence to date suggests a protective effect of perioperative statin use on cardiac complications during noncardiac surgery. RCTs are limited in patient numbers and types of noncardiac surgery. The time of initiation of statin therapy and the duration of therapy are often unclear in the observational trials. The mechanism of benefit of statin therapy prescribed perioperatively to lower cardiac events is unclear and may be related to pleiotropic as well as cholesterol-lowering effects. In patients meeting indications for statin therapy, starting statin therapy perioperatively may also be an opportunity to impact long-term health.[288]

See Online Data Supplement 20 for additional information on perioperative statin therapy.

6.2.3. Alpha-2 Agonists: Recommendation

Class III: No Benefit

1. **Alpha-2 agonists for prevention of cardiac events are not recommended in patients who are undergoing noncardiac surgery.[291–295]** ***(Level of Evidence: B)***

Several studies examined the role of alpha-agonists (clonidine and mivazerol) for perioperative cardiac protection.[291,293,294,296]

In a meta-analysis of perioperative alpha-2 agonist administration through 2008, comprising 31 trials enrolling 4578 patients, alpha-2 agonists overall reduced death and myocardial ischemia.[295] The most notable effects were with vascular surgery. Importantly, sudden discontinuation of long-term alpha-agonist treatment can result in hypertension, headache, agitation, and tremor.

A 2004 prospective, double-blinded, clinical trial on patients with or at risk for CAD investigated whether prophylactic clonidine reduced perioperative myocardial ischemia and long-term death in patients undergoing noncardiac surgery.[297] Patients were randomized to clonidine (n=125) or placebo (n=65). Prophylactic clonidine administered perioperatively significantly reduced myocardial ischemia during the intraoperative and postoperative period (clonidine: 18 of 125 patients or 14%; placebo: 20 of 65 patients or 31%; P=0.01). Moreover, administration of clonidine had minimal hemodynamic effects and reduced the postoperative mortality rate for up to 2 years (clonidine: 19 of 125 patients or 15%; placebo: 19 of 65 patients or 29%; relative risk: 0.43; 95% CI: 0.21 to 0.89; P=0.035).

POISE-2 enrolled patients in a large multicenter, international, blinded, 2 × 2 factorial RCT of acetyl-salicylic acid and clonidine.[298] The primary objective was to determine the impact of clonidine compared with placebo and acetyl-salicylic acid compared with placebo on the 30-day risk of all-cause death or nonfatal MI in patients with or at risk of atherosclerotic disease who were undergoing noncardiac surgery. Patients in the POISE-2 trial were randomly assigned to 1 of 4 groups: acetyl-salicylic acid and clonidine together, acetyl-salicylic acid and clonidine placebo, an acetyl-salicylic acid placebo and clonidine, or an acetyl-salicylic acid placebo and a clonidine placebo. Clonidine did not reduce the rate of death or nonfatal MI. Clonidine did increase the rate of nonfatal cardiac arrest and clinically important hypotension.

See Online Data Supplement 21 for additional information on alpha-2 agonists.

6.2.4. Perioperative Calcium Channel Blockers

A 2003 meta-analysis of perioperative calcium channel blockers in noncardiac surgery identified 11 studies involving 1007 patients.[299] Calcium channel blockers significantly reduced ischemia (relative risk: 0.49; 95% CI: 0.30 to 0.80; P=0.004) and supraventricular tachycardia (relative risk: 0.52; 95% CI: 0.37 to 0.72; P<0.0001). Calcium channel blockers were associated with trends toward reduced death and MI. In post hoc analyses, calcium channel blockers significantly reduced death/MI (relative risk: 0.35; 95% CI: 0.15 to 0.86; P=0.02). The majority of these benefits were attributable to diltiazem. Dihydropyridines and verapamil did not decrease the incidence of myocardial ischemia, although verapamil decreased the incidence of supraventricular tachycardia. A large-scale trial is needed to define the value of these agents. Of note, calcium blockers with substantial negative inotropic effects, such as diltiazem and verapamil, may precipitate or worsen HF in patients with depressed EF and clinical HF.

See Online Data Supplement 22 for additional information on perioperative calcium channel blockers.

6.2.5. Angiotensin-Converting Enzyme Inhibitors: Recommendations

Class IIa

1. **Continuation of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) perioperatively is reasonable.[300,301]** ***(Level of Evidence: B)***
2. **If ACE inhibitors or ARBs are held before surgery, it is reasonable to restart as soon as clinically feasible postoperatively.** ***(Level of Evidence: C)***

ACE inhibitors are among the most prescribed drugs in the United States, but data on their potential risk and benefit in the perioperative setting are limited to observational analysis. One large retrospective study evaluated 79 228 patients (9905 patients on ACE inhibitors [13%] and 66 620 patients not on ACE inhibitors [87%]) who had noncardiac surgery.[300] Among a matched, nested cohort in this study, intraoperative ACE inhibitor users had more frequent transient intraoperative hypotension but no difference in other outcomes. A meta-analysis of available trials similarly demonstrated hypotension in 50% of patients taking ACE inhibitors or ARBs on the day of surgery but no change in important cardiovascular outcomes (ie, death, MI, stroke, kidney failure).[301] One study evaluated the benefits of the addition of aspirin to beta blockers and statins, with or without ACE inhibitors, for postoperative outcome in high-risk consecutive patients undergoing major vascular surgery.[302] The combination of aspirin, beta blockers, and statin therapy was associated with better 30-day and 12-month risk reduction for MI, stroke, and death than any of the 3 medications independently. The addition of an ACE inhibitor to the 3 medications did not demonstrate additional risk-reduction benefits. There is similarly limited evidence on the impact of discontinuing ACE inhibitors before noncardiac surgery.[303,304] In these and other small trials, no harm was demonstrated with holding ACE inhibitors and ARBs before surgery,[303,304] but all studies were underpowered and did not target any particular clinical group. Consequently, there are few data to direct clinicians about whether specific surgery types or patient subgroups are most likely to benefit from holding ACE inhibitors in the perioperative time period.

Although there is similarly sparse evidence to support the degree of harm represented by inappropriate discontinuation of ACE inhibitors after surgery (eg, ACE inhibitors held but not restarted), there is reasonable evidence from nonsurgical settings to support worse outcomes in patients whose ACE inhibitors are discontinued inappropriately. Maintaining continuity of ACE inhibitors in the setting of treatment for HF or hypertension is supported by CPGs.[16,305] Data describing harms of ARBs are sparse, but treating such drugs as equivalent to ACE inhibitors is reasonable.

See Online Data Supplement 23 for additional information on ACE inhibitors.

6.2.6. Antiplatelet Agents: Recommendations

Please see Figure 2 for an algorithm for antiplatelet management in patients with PCI and noncardiac surgery.

Class I

1. **In patients undergoing urgent noncardiac surgery during the first 4 to 6 weeks after BMS or DES implantation, DAPT should be continued unless the relative risk of bleeding outweighs the benefit of the prevention of stent thrombosis. *(Level of Evidence: C)***
2. **In patients who have received coronary stents and must undergo surgical procedures that mandate the discontinuation of $P2Y_{12}$ platelet receptor–inhibitor therapy, it is recommended that aspirin be continued if possible and the $P2Y_{12}$ platelet receptor–inhibitor be restarted as soon as possible after surgery. *(Level of Evidence: C)***
3. **Management of the perioperative antiplatelet therapy should be determined by a consensus of the surgeon, anesthesiologist, cardiologist, and patient, who should weigh the relative risk of bleeding with that of stent thrombosis. *(Level of Evidence: C)***

Class IIb

1. **In patients undergoing nonemergency/nonurgent noncardiac surgery who have not had previous coronary stenting, it may be reasonable to continue aspirin when the risk of potential increased cardiac events outweighs the risk of increased bleeding.[298,306] *(Level of Evidence: B)***

Class III: No Benefit

1. **Initiation or continuation of aspirin is not beneficial in patients undergoing elective noncardiac noncarotid surgery who have not had previous coronary stenting[298] *(Level of Evidence: B)*, unless the risk of ischemic events outweighs the risk of surgical bleeding. *(Level of Evidence: C)***

The risk of stent thrombosis in the perioperative period for both BMS and DES is highest in the first 4 to 6 weeks after stent implantation.[231–239,307–309] Discontinuation of DAPT, particularly in this early period, is a strong risk factor for stent thrombosis.[310,311] Should urgent or emergency noncardiac surgery be required, a decision to continue aspirin or DAPT should be individualized, with the risk weighed against the benefits of continuing therapy.

The risk of DES thrombosis during noncardiac surgery more than 4 to 6 weeks after stent implantation is low but is higher than in the absence of surgery, although the relative increased risk varies from study to study. This risk decreases with time and may be at a stable level by 6 months after DES implantation.[234,238] The value of continuing aspirin alone or DAPT to prevent stent thrombosis or other ischemic events during noncardiac surgery is uncertain given the lack of prospective trials. The risk of bleeding is likely higher with DAPT than with aspirin alone or no antiplatelet therapy, but the magnitude of the increase is uncertain.[231,232,307–309,312] As such, use of DAPT or aspirin alone should be individualized on the basis of the considered potential benefits and risks, albeit in the absence of secure data. An algorithm for DAPT use based on expert opinion is suggested in Figure 2. There is no convincing evidence that warfarin, antithrombotics, cangrelor, or glycoprotein IIb/IIIa agents will reduce the risk of stent thrombosis after discontinuation of oral antiplatelet agents.

The value of aspirin in nonstented patients in preventing ischemic complications is uncertain. Observational data suggest that preoperative withdrawal of aspirin increases thrombotic complications[306]; the PEP (Pulmonary Embolism Prevention) trial, which randomized 13 356 patients undergoing hip surgery to 160 mg aspirin or placebo, did not show benefit of aspirin.[313] The POISE-2 trial randomized 10 010 patients who were undergoing noncardiac surgery and were at risk for vascular complications to aspirin 200 mg or placebo. Aspirin did not have a protective effect for MACE or death in patients either continuing aspirin or starting aspirin

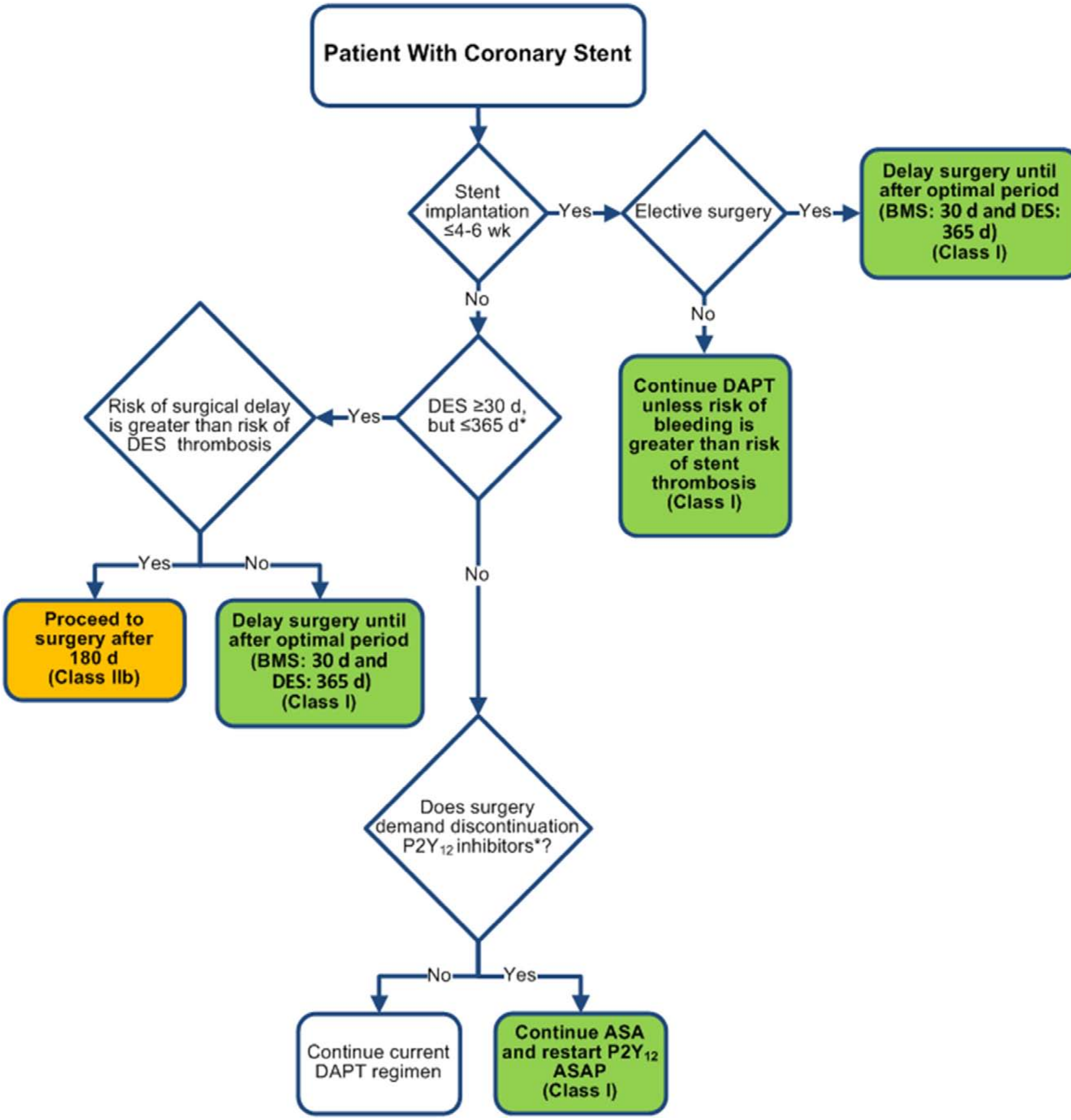


Figure 2. Algorithm for antiplatelet management in patients with PCI and noncardiac surgery. Colors correspond to the Classes of Recommendations in Table 1. *Assuming patient is currently on DAPT. ASA indicates aspirin; ASAP, as soon as possible; BMS, bare-metal stent; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; and PCI, percutaneous coronary intervention.

during the perioperative period.[298] Aspirin use was associated with an increased risk of major bleeding. In the POISE-2 trial, aspirin was stopped at least 3 days (but usually 7 days) preoperatively. Patients within 6 weeks of placement of a BMS or within 1 year of placement of a DES were excluded from the trial, and the number of stented patients outside these time intervals was too small to make firm conclusions as to the risk–benefit ratio. Additionally, only 23% of the study population had known prior CAD, and the population excluded patients undergoing carotid endarterectomy surgery. Thus, continuation may still be reasonable in patients with high-risk CAD or cerebrovascular disease, where the risks of potential increased cardiovascular events outweigh the risks of increased bleeding.

See Online Data Supplement 24 for additional information on antiplatelet agents.

6.2.7. Anticoagulants

Use of therapeutic or full-dose anticoagulants (as opposed to the lower-dose anticoagulation often used for prevention of deep venous thrombosis) is generally discouraged because of their harmful effect on the ability to control and contain surgical blood loss. This section refers to the vitamin K antagonists and novel oral anticoagulant agents but excludes discussion of the antiplatelet agents addressed in Section 6.2.6. Factor Xa inhibitors and direct thrombin inhibitors are examples of alternative anticoagulants now available for oral administration. Vitamin K antagonists (warfarin) are prescribed for stroke prevention in patients with AF, for prevention of thrombotic and thromboembolic complications in patients with prosthetic valves, and in patients requiring deep venous thrombosis prophylaxis and treatment. Factor Xa inhibitors are prescribed for prevention of stroke in the management of AF. Factor Xa inhibitors are not recommended for long-term anticoagulation of prosthetic valves because of an increased risk of thrombosis when compared with warfarin. The role of anticoagulants other than platelet inhibitors in the secondary prevention of myocardial ischemia or MI has not been elucidated.

The risks of bleeding for any surgical procedure must be weighed against the benefit of remaining on anticoagulants on a case-by-case basis. In some instances in which there is minimal to no risk of bleeding, such as cataract surgery or minor dermatologic procedures, it may be reasonable to continue anticoagulation perioperatively. Two published CPGs address the management of perioperative anticoagulation in patients with prosthetic valves and patients with AF.[14,15] Although research with newer agents (eg, prothrombin complex concentrates for reversal of direct factor Xa inhibitor effect) is ongoing, the novel oral anticoagulant agents do not appear to be acutely reversible. Patients with prosthetic valves taking vitamin K antagonists may require bridging therapy with either unfractionated heparin or low-molecular-weight heparin, depending on the location of the prosthetic valve and associated risk factors for thrombotic and thromboembolic events. For patients with a mechanical mitral valve, regardless of the absence of additional risk factors for thromboembolism, or patients with an aortic valve and ≥1 additional risk factor (such as AF, previous thromboembolism, LV dysfunction, hypercoagulable condition, or an older-generation prosthetic aortic valve), bridging anticoagulation may be appropriate when interruption of anticoagulation for perioperative procedures is required and control of hemostasis is essential.[15] For patients requiring urgent reversal of vitamin K antagonists, vitamin K and fresh frozen plasma or the newer prothrombin complex concentrates are options; however, vitamin K is not routinely recommended for reversal because the effect is not immediate and the administration of vitamin K can significantly delay the return to a therapeutic level of anticoagulation once vitamin K antagonists have been restarted.

Factor Xa inhibitors do not have a reversible agent available at this time. For patients with AF and normal renal function undergoing elective procedures during which hemostatic control is essential, such as major surgery, spine surgery, and epidural catheterization, discontinuation of anticoagulants for ≥48 hours is suggested. Monitoring activated partial thromboplastin time for dabigatran and prothrombin time for apixaban and rivaroxaban may be helpful; a level consistent with control levels suggests a low serum concentration of the anticoagulant.[14]

There have been no studies on the benefit of anticoagulants on the prevention of perioperative myocardial ischemia or MI.

6.3. Management of Postoperative Arrhythmias and Conduction Disorders

AF and atrial flutter are the most common sustained arrhythmias that occur in the postoperative setting. However, clinicians must differentiate between atrial flutter, which is common in the postoperative setting (especially with underlying structural heart disease), and other supraventricular tachycardias that may respond to vagal maneuvers or nodal agents. The incidence of postoperative AF after noncardiac surgery varies widely in the literature, ranging from 0.37% in 1 large population-based study in noncardiothoracic surgery to 30% after major noncardiac thoracic surgery, such as esophagectomy and pneumonectomy.[314–324] Peak incidence occurs 1 to 3 days postoperatively and is positively correlated with patient age, preoperative heart rate, and male sex.[315,317,322,325] Treatment of postoperative AF is similar to that for other forms of new-onset AF, except that the potential benefit of anticoagulation needs to be balanced against the risk of postoperative bleeding.

Ventricular rate control in the acute setting is generally accomplished with beta blockers or nondihydropyridine calcium channel blockers (ie, diltiazem or verapamil), with digoxin reserved for patients with systolic HF or with contraindications or inadequate response to other agents. Of note, beta blockers and calcium channel blockers with substantial negative inotropic effects, such as diltiazem or verapamil, may precipitate or worsen HF in patients with depressed EF or clinical HF. An additional benefit of beta blockers is that, compared with diltiazem, they may accelerate the conversion of postoperative supraventricular arrhythmias to sinus rhythm.[326,327] Cardioversion of minimally symptomatic AF/atrial flutter is generally not required until correction of the underlying problems has occurred, which may lead to a return to normal sinus rhythm. Intravenous amiodarone may also be used to aid in restoring or maintaining sinus rhythm if its benefits outweigh the risk of hypotension and other side effects. As with patients outside the perioperative setting, cardioversion of postoperative AF should be performed when hemodynamic compromise is present.

Whereas numerous studies have been performed for prophylaxis of AF in the setting of cardiac surgery, comparatively few data exist in the setting of noncardiac surgery. One RCT of 130 patients undergoing lung resection surgery showed that perioperative amiodarone reduced the incidence of postoperative AF and reduced length of stay compared with placebo.[328] However, the incidence of postoperative AF in the control group (32.3%) was higher than that seen in a large national database (12.6%).[321] Another RCT of 254 patients undergoing lung cancer surgery also showed a significant reduction in postoperative AF with amiodarone but no difference in length of stay or resource utilization.[329,330] An RCT of 80 patients undergoing esophagectomy also showed a reduction in postoperative AF but not in length of stay.[331] Recommendations for prophylaxis and management of postoperative AF after cardiac and thoracic surgery are provided in the 2014 AF CPG.[14]

If the patient develops a sustained, regular, narrow-complex tachycardia (supraventricular tachycardia), which is likely due to atrioventricular nodal reentrant tachycardia or atrioventricular reciprocating tachycardia, the supraventricular tachycardia frequently can be terminated with vagal maneuvers or with intravenous medications (adenosine or verapamil). Most antiarrhythmic agents (especially beta blockers, calcium channel blockers, and class IC antiarrhythmic agents) can be used to prevent further recurrences in the postoperative setting. Digoxin and calcium channel blockers should be avoided in the setting of pre-excited AF. The choice of individual agent will depend on the nature of the arrhythmia and whether the patient has associated structural heart disease. Recurrent supraventricular tachycardia is generally well treated with catheter ablation therapy.[92]

Asymptomatic premature ventricular contractions generally do not require perioperative therapy or further evaluation. Very frequent ventricular ectopy or runs of nonsustained ventricular tachycardia may require antiarrhythmic therapy if they are symptomatic or result in hemodynamic compromise.[332] Patients with new-onset postoperative complex ventricular ectopy, particularly polymorphic ventricular tachycardia, should be evaluated for myocardial ischemia, electrolyte abnormalities, or drug effects. Ventricular arrhythmias may respond to intravenous beta blockers, lidocaine, procainamide, or amiodarone. Electrical cardioversion should be used for sustained supraventricular or ventricular arrhythmias that cause hemodynamic compromise. Patients with ventricular arrhythmias in the setting of chronic cardiomyopathy or inherited arrhythmia syndromes despite GDMT should be evaluated for ICD therapy consistent with existing CPGs.[332–334]

Bradyarrhythmias that occur in the postoperative period are usually sinus bradycardia secondary to some other cause, such as medication, electrolyte or acid-base disturbance, hypoxemia, or ischemia. Pain can also heighten vagal tone, leading to sinus bradycardia and even heart block, despite baseline normal conduction. New atrioventricular block after noncardiac surgery is rare. Sleep apnea may manifest as nocturnal bradycardia in the postoperative setting. Acutely, bradycardia may respond to atropine or aminophylline. Persistent symptomatic bradyarrhythmias due to sinus node dysfunction and atrioventricular block will respond to temporary transvenous pacing. Indications for permanent pacing are similar to those outside the perioperative setting.[333,335] Management of patients with pre-existing pacemakers or ICDs is focused on restoring preoperative settings for those patients who had preoperative reprogramming. It is particularly important to ensure that tachytherapy in patients with ICDs has been restored before discharge from the facility.[336]

See Online Data Supplement 25 for additional information on management of postoperative arrhythmias and conduction disorders.

6.4. Perioperative Management of Patients With CIEDs: Recommendation

Class I

1. **Patients with ICDs who have preoperative reprogramming to inactivate tachytherapy should be on cardiac monitoring continuously during the entire period of inactivation, and external defibrillation equipment should be readily available. Systems should be in place to ensure that ICDs are reprogrammed to active therapy before discontinuation of cardiac monitoring and discharge from the facility.[336]** ***(Level of Evidence: C)***

To assist clinicians with the perioperative evaluation and management of patients with pacemakers and ICDs, the HRS and the American Society of Anesthesiologists together developed an expert consensus statement that was published in July 2011 and endorsed by the ACC and the AHA.[33] Clinicians caring for patients with CIEDs in the perioperative setting should be familiar with that document and the consensus recommendations contained within.

A central concern in perioperative management of patients with CIEDs is the potential for interaction between the CIED and EMI, usually produced by monopolar electrocautery.[337] If the procedure involves only bipolar electrocautery or harmonic scalpel or does not involve electrocautery, then interaction with the CIED is extremely unlikely, unless energy is applied directly to the CIED generator or leads in the operative field. With monopolar electrocautery, the principal concern is that EMI may cause transient inhibition of pacing in pacemaker-dependent patients (usually those with complete atrioventricular block) and/or inappropriate triggering of shocks in patients with ICDs. With technological advances in CIED hardware and filtering, the potential for more permanent adverse effects, such as electrical reset, inadvertent reprogramming, or damage to the CIED hardware or lead–tissue interface, has been largely eliminated.

In advance of elective surgical procedures, a perioperative CIED prescription should be developed by the clinician or team that follows the patient in the outpatient setting and communicated to the surgical/procedure team (Section 2.6). Depending on the patient's underlying cardiac rhythm, the type of CIED (pacemaker versus ICD), the location of the operative procedure, and the potential for EMI from electrocautery, the CIED prescription may involve reprogramming a pacemaker or ICD to an asynchronous pacing mode (ie, VOO or DOO), reprogramming an ICD to inactivate tachytherapies, applying a magnet over the CIED, or no perioperative intervention.[98,99]

Regardless of the CIED prescription, through advance communication with the CIED follow-up outpatient clinician/team, the surgical/procedure team should be familiar with the type of CIED (pacemaker versus ICD), its manufacturer, the response of the CIED to magnet application, and the patient's underlying cardiac rhythm. External defibrillation equipment with transcutaneous pacing capability should be readily available in the operating room for patients with pacemakers or ICDs who are having surgical procedures during which EMI or physical disruption to the CIED system could occur. It is reasonable to have a magnet available for all patients with a CIED who are undergoing a procedure that could involve EMI. All patients with CIEDs should have plethysmographic or arterial pressure monitoring during the procedure, because electrocautery may interfere with electrocardiographic recording and determination of the patient's cardiac rhythm.

A final point concerns patients with ICDs who have tachytherapies inactivated preoperatively. Such patients are intrinsically more susceptible to perioperative ventricular arrhythmias and should have continuous cardiac monitoring during the entire period of ICD inactivation, with external defibrillation immediately available, if needed. In addition, at least 3 deaths have been reported to have been caused by failure to reactivate ICD tachytherapies in patients who had ICD therapy inactivated preoperatively, and this problem is likely to be underreported.[336] It is therefore imperative that surgical services have systems in place to ensure that inactivated ICDs are reprogrammed to active therapy before discontinuation of cardiac monitoring and discharge from the facility.

See Online Data Supplement 26 for additional information on perioperative management of patients with CIEDs.

7. Anesthetic Consideration and Intraoperative Management

See Table 7 for a summary of recommendations for anesthetic consideration and intraoperative management.

7.1. Choice of Anesthetic Technique and Agent

See Online Data Supplement 27 for additional information on choice of anesthetic technique and agent.

There are 4 main classifications of anesthesia: local anesthesia, regional anesthesia (including peripheral nerve blockade and neuraxial blockade), monitored anesthesia care (typically using intravenous sedation with or without local anesthesia), and general anesthesia (which includes volatile-agent anesthesia, total intravenous anesthesia, or a combination of volatile and intravenous anesthesia). The majority of the literature in this field focuses on 1 of 3 areas with regard to preventing perioperative myocardial adverse cardiac events.

7.1.1. Neuraxial Versus General Anesthesia

In patients for whom neuraxial anesthesia (epidural or spinal anesthesia) is an option as the primary anesthetic or as a supplement to general anesthesia, several factors, such as the type of surgery, patient comorbidities, and patient preferences, are crucial in determining risk versus benefits. A 2011 Cochrane review meta-analysis of 4 studies examining neuraxial anesthesia versus general anesthesia for lower-limb revascularization found an overall 4% MI rate in both groups.[338] In 2001, an RCT of abdominal aortic surgery patients comparing a thoracic epidural/light general anesthesia technique with a general anesthetic technique alone demonstrated no significant difference in myocardial ischemia and MI rates between the groups.[339] Therefore, in patients who are eligible for an intraoperative neuraxial anesthetic, there is no evidence to suggest a cardioprotective benefit from the use or addition of neuraxial anesthesia for intraoperative anesthetic management. The evidence relating to neuraxial anesthesia/analgesia for postoperative pain control is discussed in Section 7.2.

7.1.2. Volatile General Anesthesia Versus Total Intravenous Anesthesia: Recommendation

Class IIa

1. **Use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients**

Table 7. Summary of Recommendations for Anesthetic Consideration and Intraoperative Management

Recommendations	COR	LOE	References
Volatile general anesthesia versus total intravenous anesthesia			
Use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients undergoing noncardiac surgery	IIa	A	340, 341
Perioperative pain management			
Neuraxial anesthesia for *postoperative* pain relief can be effective to reduce MI in patients undergoing abdominal aortic surgery	IIa	B	348
Preoperative epidural analgesia may be considered to decrease the incidence of *preoperative* cardiac events in patients with hip fracture	IIb	B	349
Prophylactic intraoperative nitroglycerin			
Prophylactic intravenous nitroglycerin is not effective in reducing myocardial ischemia in patients undergoing noncardiac surgery	III: No Benefit	B	292, 355, 356
Intraoperative monitoring techniques			
Emergency use of perioperative TEE in patients with hemodynamic instability is reasonable in patients undergoing noncardiac surgery if expertise is readily available	IIa	C	N/A
Routine use of intraoperative TEE during noncardiac surgery is not recommended	III: No Benefit	C	N/A
Maintenance of body temperature			
Maintenance of normothermia may be reasonable to reduce perioperative cardiac events	IIb	B	364, 365
Hemodynamic assist devices			
Use of hemodynamic assist devices may be considered when urgent or emergency noncardiac surgery is required in the setting of acute severe cardiac dysfunction	IIb	C	N/A
Perioperative use of pulmonary artery catheters			
Use of pulmonary artery catheterization may be considered when underlying medical conditions that significantly affect hemodynamics cannot be corrected before surgery	IIb	C	N/A
Routine use of pulmonary artery catheterization is not recommended	III: No Benefit	A	380–382

COR indicates Class of Recommendation; LOE, Level of Evidence; MI, myocardial infarction; N/A, not applicable; and TEE, transesophageal echocardiogram.

undergoing noncardiac surgery, and the choice is determined by factors other than the prevention of myocardial ischemia and MI.[340,341] ***(Level of Evidence: A)***

Several studies have attempted to examine whether there is a myocardial protective benefit of volatile anesthetic use in general anesthesia when compared with total intravenous anesthesia.[342] There is no evidence to suggest a difference in myocardial ischemia/MI rates between the use of volatile anesthesia and total intravenous anesthesia in patients undergoing noncardiac surgery. Although the benefit of using volatile anesthetic agents has been demonstrated in cardiac surgery, a reduction in myocardial ischemia or MI has not been demonstrated in noncardiac surgery.[343–347] A meta-analysis of >6000 patients undergoing noncardiac surgery failed to demonstrate a difference in MI rates between patients who received volatile anesthesia and patients who received total intravenous anesthesia.[340] However, the event MI rate in the meta-analysis of >79 studies was 0 for both groups. A randomized comparison of volatile anesthetic administration versus total intravenous administration in patients undergoing noncardiac surgery demonstrated no difference in either myocardial ischemia or MI between the 2 groups.[341]

7.1.3. Monitored Anesthesia Care Versus General Anesthesia

There are no RCTs to suggest a preference for monitored anesthesia care over general anesthesia for reducing myocardial ischemia and MI.

7.2. Perioperative Pain Management: Recommendations

Class IIa

1. **Neuraxial anesthesia for postoperative pain relief can be effective in patients undergoing abdominal aortic surgery to decrease the incidence of perioperative MI.[348]** ***(Level of Evidence: B)***

Class IIb

1. **Perioperative epidural analgesia may be considered to decrease the incidence of preoperative cardiac events in patients with a hip fracture.[349]** ***(Level of Evidence: B)***

Pain management is fundamental to the care of the surgical patient, and pain is one of many factors that can contribute to the development of postoperative myocardial ischemia and MI. Postoperative pain is associated with myocardial ischemia; however, the best practices for perioperative pain management have not been completely elucidated.[90,350–352] Most of the literature focusing on perioperative myocardial events compares epidural analgesia with intravenous analgesia. Importantly, the potential efficacy of epidural analgesia depends on the local system of care. A 2003 review of a large billing registry comparing epidural analgesia with other forms of analgesia failed to show a reduction in perioperative myocardial events[353]; however, other studies, including a meta-analysis of RCTs, concluded that patients receiving epidural analgesia experienced a reduction in postoperative myocardial ischemia and MI.[348,354] An RCT in 2001 examining the use of epidural anesthesia in patients undergoing abdominal surgery found no difference between epidural and intravenous analgesia in the prevention of perioperative MI, although a subgroup analysis demonstrated a reduction in MI in patients undergoing abdominal aortic procedures.[354] In 2012, a Cochrane review of 15 RCTs comparing epidural analgesia with opioids for patients undergoing abdominal aortic surgery reported a decrease in MIs in the patients who received epidural analgesia.[348] There is a paucity of studies on perioperative cardiac events with regard to various methods of pain control in the general surgical population.

Although the majority of perioperative MIs occur during the postoperative period, 1 RCT examined the incidence of preoperative cardiac events in elderly patients with hip fractures. The 64-patient study concluded that preoperative pain control with epidural analgesia reduced the incidence of preoperative myocardial ischemia and preoperative MI, as well as HF and AF.[349]

See Online Data Supplement 28 for additional information on perioperative pain management.

7.3. Prophylactic Perioperative Nitroglycerin: Recommendation

Class III: No Benefit

1. **Prophylactic intravenous nitroglycerin is not effective in reducing myocardial ischemia in patients undergoing noncardiac surgery.[292,355,356]** ***(Level of Evidence: B)***

There are no significant studies within the past 10 years examining the effect of prophylactic nitroglycerin on perioperative myocardial ischemia. Prior RCTs yielded conflicting results and were small (<50 patients) and unblinded.[292,355,356]

See Online Data Supplement 29 for additional information on prophylactic intraoperative nitroglycerin.

7.4. Intraoperative Monitoring Techniques: Recommendations

Class IIa

1. **The emergency use of perioperative transesophageal echocardiogram (TEE) is reasonable in patients with hemodynamic instability undergoing noncardiac surgery to determine the cause of hemodynamic instability when it persists despite attempted corrective therapy, if expertise is readily available.** ***(Level of Evidence: C)***

Class III: No Benefit

1. **The routine use of intraoperative TEE during noncardiac surgery to screen for cardiac abnormalities or to monitor for myocardial ischemia is not recommended in patients without risk factors or procedural risks for significant hemodynamic, pulmonary, or neurological compromise.** ***(Level of Evidence: C)***

TEE is widely available and commonly used perioperatively in patients undergoing cardiac surgery. TEE has the capacity to assess biventricular and valvular function, intracardiac structures, the pericardial space, and the thoracic aorta.[17,357,358] The use of TEE intraoperatively in a patient undergoing noncardiac surgery is less clear.

There are limited data evaluating intraoperative TEE in the assessment of regional myocardial function and any association with cardiac outcomes.[359,360] Moreover, the data are insufficient in terms of predictive accuracy or cost-effectiveness to recommend routine TEE monitoring. In contrast, emergency use of perioperative TEE in patients with hemodynamic instability, to determine the cause of an unexplained, severe hemodynamic instability that persists despite attempted corrective therapy, is appropriate where available.[27,29,361–363] CPGs for the appropriate use of TEE have been developed by the American Society of Anesthesiologists, the Society of Cardiovascular Anesthesiologists, and the American Society of Echocardiography.[17,27,29] Many anesthesiologists are experts in TEE; the use of TEE by those with limited or no training should be avoided.[27]

7.5. Maintenance of Body Temperature: Recommendation

Class IIb

1. **Maintenance of normothermia may be reasonable to reduce perioperative cardiac events in patients undergoing noncardiac surgery.[364,365]** ***(Level of Evidence: B)***

Hypothermia has been associated with several perioperative complications, including wound infection, MACE, immune dysfunction, coagulopathy, increased blood loss, death, and transfusion requirements.[365–372] However, interest is emerging in the therapeutic benefit of hypothermia in preservation of neurological function after head trauma, stroke, and cardiac arrest. Balancing the risks and benefits to determine the appropriate use of hypothermia in the perioperative and inpatient hospital setting is an area of active research.

There are 2 conflicting studies on hypothermia in relation to perioperative cardiac events. They were conducted in very different patient populations and with different goals. In a 1997 study, 300 patients with known cardiovascular disease or risk factors for cardiovascular disease were randomized to forced air warmers or ambient temperature. This study demonstrated a significantly higher incidence of a MACE (eg, ischemia, infarction, cardiac arrest) or an electrocardiographic event, particularly ventricular tachycardia,[365] in the ambient-temperature group.

A large multicenter trial published in 2010 randomized 1000 patients with subarachnoid hemorrhage to either normothermia or perioperative hypothermia to assess the efficacy of hypothermia in brain protection. This large study demonstrated no increased incidence of cardiovascular events either intraoperatively or postoperatively in the hypothermia-treated patients.[364]

See Online Data Supplement 30 for additional information on maintenance of body temperature.

7.6. Hemodynamic Assist Devices: Recommendation

Class IIb

1. **Use of hemodynamic assist devices may be considered when urgent or emergency noncardiac surgery is required in the setting of acute severe cardiac dysfunction (ie, acute MI, cardiogenic shock) that cannot be corrected before surgery.** ***(Level of Evidence: C)***

Rare case reports have noted the use of and complications associated with hemodynamic assist device therapy during noncardiac surgery. There are no published RCTs, retrospective reviews, meta-analyses, or case series of >10 patients. Therefore, there is no evidence for the routine use of hemodynamic assist devices in patients at surgical risk, and it is not recommended. That being said, the number of patients chronically supported with long-term implantable devices, including left, right, or biventricular assist devices or total artificial heart, for advanced HF is steadily increasing. While on mechanical circulatory support, patients may face medical problems requiring emergency or nonemergency noncardiac surgery with varying degrees of risk to the patient and mortality outcomes. Several series have been published reporting outcomes in patients with mechanical circulatory support undergoing noncardiac procedures, with the 30-day mortality rate ranging from 9% to 25%.[373–379]

For perioperative management, a multidisciplinary approach and expert guidance on anticoagulation strategies, pump flow control, hemodynamic monitoring, infection, and bleeding prevention strategies are considered important. Specific recommendations on perioperative management of these patients are addressed in the International Society for Heart and Lung Transplantation CPGs for mechanical circulatory support.[379]

7.7. Perioperative Use of Pulmonary Artery Catheters: Recommendations

Class IIb

1. **The use of pulmonary artery catheterization may be considered when underlying medical conditions that significantly affect hemodynamics (ie, HF, severe valvular disease, combined shock states) cannot be corrected before surgery.** ***(Level of Evidence: C)***

Class III: No Benefit

1. **Routine use of pulmonary artery catheterization in patients, even those with elevated risk, is not recommended.[380–382]** ***(Level of Evidence: A)***

The theoretical basis for better outcomes with the routine use of pulmonary artery catheterization in noncardiac surgery derives from clinicians' improved understanding of perioperative hemodynamics. Unfortunately, the clinical trial data on which recommendations are made are sparse. Of the 3 main trials, 2 are underpowered.[380–382] The largest trial randomly allocated the use of pulmonary artery catheters in 1994 patients at high surgical risk, defined by an American Society of Anesthesiologists risk score of III or IV.[380] In this trial, there were no differences in mortality or morbidity, save for an increase in pulmonary embolism noted in the pulmonary artery catheter arm. Therefore, routine use of pulmonary artery catheterization in patients at elevated surgical risk does not improve outcomes and is not recommended.

See Online Data Supplement 31 for additional information on perioperative use of pulmonary artery catheters.

7.8. Perioperative Anemia Management

Anemia can contribute to myocardial ischemia, particularly in patients with CAD. In patients with CAD who are also anemic, ischemia can be triggered by both the lack of adequate oxygen delivery to poststenotic myocardium and a demand for increased cardiac output to supply oxygen to other vascular beds throughout the body. Transfusions to treat anemia are not without economic costs and individual health costs, in the form of an increased risk of infectious and noninfectious complications. Transfusion practices vary widely, and much of the literature attempts to address the clinical question of when to transfuse an asymptomatic patient below a preset hemoglobin level and when to transfuse patients experiencing symptoms of ischemia. The 2012 American Association of Blood Banks CPG and a 2011 RCT provide some additional information and guidance to clinicians navigating the complex interplay among anemia, transfusions, and attribution of symptoms to anemia.[21,383]

In 2011, a RCT compared 2000 patients with either CAD or known CAD risk factors and a hemoglobin level <10 g/dL after hip fracture surgery who were treated with either a liberal transfusion strategy (hemoglobin <10 g/dL) or a conservative transfusion strategy (hemoglobin <8 g/dL or symptoms of anemia).[383] The endpoints of death and inability to walk at the 60-day follow-up were not found to be significantly different in either the liberal or conservative transfusion group. Additionally, although the study found no difference in MI, unstable angina, or in-hospital death between the 2 groups, it was not sufficiently powered to show a difference in the aforementioned areas if a difference existed.[383]

The 2012 American Association of Blood Banks CPG, which is based on expert opinion and studies, recommends a restricted transfusion strategy (hemoglobin <7 g/dL to 8 g/dL) in asymptomatic, hemodynamically stable patients without CAD.[21] The CPG also recommends adherence to a restrictive transfusion strategy in hospitalized patients with cardiovascular disease and consideration of transfusion for patients with symptoms (eg, chest pain, orthostasis, congestive HF) or hemoglobin <8 g/dL.[21] In postoperative patients, the recommended maintenance hemoglobin concentration is ≥8 g/dL, unless the patient exhibits symptoms. There were no specific recommendations for hemodynamically stable patients with acute coronary syndrome because of the lack of high-quality evidence for either a liberal or a restrictive transfusion strategy in these patients. The consensus of those experts recommended a symptom-guided approach to evaluating a hemoglobin level to determine whether to transfuse a patient with anemia.

8. Perioperative Surveillance

8.1. Surveillance and Management for Perioperative MI: Recommendations

Class I

1. **Measurement of troponin levels is recommended in the setting of signs or symptoms suggestive of myocardial ischemia or MI.[40,384]** ***(Level of Evidence: A)***
2. **Obtaining an ECG is recommended in the setting of signs or symptoms suggestive of myocardial ischemia, MI, or arrhythmia.[384,385]** ***(Level of Evidence: B)***

Class IIb

1. **The usefulness of postoperative screening with troponin levels in patients at high risk for perioperative MI but without signs or symptoms suggestive of myocardial ischemia or MI, is uncertain in the absence of established risks and benefits of a defined management strategy.[386–392]** ***(Level of Evidence: B)***
2. **The usefulness of postoperative screening with ECGs in patients at high risk for perioperative MI but without signs or symptoms suggestive of myocardial ischemia, MI, or arrhythmia, is uncertain in the absence of established risks and benefits of a defined management strategy.[384,385,393–395]** ***(Level of Evidence: B)***

Class III: No Benefit

1. **Routine postoperative screening with troponin levels in unselected patients without signs or symptoms suggestive of myocardial ischemia or MI is not useful for guiding perioperative management.[40,384]** ***(Level of Evidence: B)***

Improvements in surgical outcomes and increasing difficulty in accurately predicting adverse cardiovascular events and death in patients before surgery have fostered efforts to improve early detection of myocardial injury and MI to prevent more serious complications. Routine screening with troponin for cardiac injury has been proposed as a method of early detection to ensure early intervention to avoid more serious complications. Among the studies, elevations of troponin of any level associate directly and consistently with increases in 30-day mortality rates.[40,384,396] In the largest of the studies, the VISION (Vascular Events in Noncardiac Surgery Patients Cohort Evaluation) trial,[40] troponin elevations predicted vascular and nonvascular mortality rates equally. Type 1 MI (ie, related to ischemia from a primary coronary event, such as plaque rupture or thrombotic occlusion) causes <5% of troponin elevation postoperatively[384,396] and therefore constitutes a small minority of the vascular causes of troponin elevation. In a subsequent publication, the authors defined myocardial injury after noncardiac surgery as troponin elevation with or without symptoms of myocardial ischemia.[38] Myocardial injury after noncardiac surgery is a novel classification that predicted 30-day mortality rate but diverges from the Third Universal Definition of MI[397] by combining type 1 and type 2 events (ie, type 2 is secondary to ischemia from a supply-and-demand mismatch), despite their different pathophysiological origin. In a study of 2232 consecutive patients undergoing noncardiac surgery, 315 patients had elevation of troponin I, 9.5% had attendant ECG changes suggestive of cardiac ischemia, and 3.2% had typical chest pain, showing that a small minority of troponin elevation results from type 1 MI.[396] Additionally, none of these studies accounts for patients with troponin elevations before surgery, which may be seen in as many as 21% of high-risk patients[398] and may be even more common if high-sensitivity troponin assays are used. Finally, the median time between troponin elevation and death is >7 days after measurement, and none of the studies clarifies the specific cause of death. In the absence of a description of the specific cause of death and evidence for the use of the biomarker to prevent these events, the use of routine postoperative troponin measurement remains uncertain, even in patients at high risk for perioperative MI. Therefore, routine screening with troponin provides a nonspecific assessment of risk, does not indicate a specific course of therapy, and is not clinically useful outside of the patient with signs or symptoms of myocardial ischemia or MI. The value of postoperative troponin surveillance may be clarified after completion of MANAGE (Management of Myocardial Injury After Noncardiac Surgery Trial), which is testing the effects of 2 drugs (dabigatran and omeprazole) that may prevent death, major cardiovascular complications, and major upper gastrointestinal bleeding in patients who have had myocardial injury after noncardiac surgery.[399] Of note, elevation in the MB fraction of creatine kinase may also be used to detect myocardial necrosis and possible MI, although its interpretation in the perioperative period is often complicated by the significant rise in overall creatine kinase seen with noncardiac surgery.

The role of postoperative electrocardiography remains difficult to define. As noted in in previous versions of this CPG, older studies have demonstrated that changes in the ECG, particularly ST-segment changes, are associated with increases in major cardiac complications—more than 2-fold compared with those without electrocardiographic changes.[400] More recently, however, it has become clear that electrocardiography may not provide information sufficient for routine use. One study involved 337 vascular surgery patients in whom troponin I levels were collected within 48 hours of surgery and 12-lead ECGs were performed daily for 3 postoperative days.[385] Forty percent of the subjects had elevated troponin levels, but ischemic changes on the ECG were noted in 6%. Whereas elevations in troponin predicted death at 1 year, electrocardiographic changes did not. Several large surgical trials have demonstrated the superiority of troponin testing to ECG in identifying patients with types 1 and 2 MI[384,394] and suggest that troponin testing may be a superior initial test in the diagnosis of MI. There are no prospective randomized trials examining the value of adding ECGs to routine postoperative care. In addition, the interpretation of ECGs in the setting of critical illness is only moderately reliable among expert readers.[401] The current use of ECGs may have developed as a method to screen for MI when little else was routinely available. In the absence of clinical trial data, a recommendation for routine postoperative ECGs cannot be made.

See Online Data Supplement 32 for additional information on surveillance and management for perioperative MI.

9. Future Research Directions

Current recommendations for perioperative cardiovascular evaluation and management for noncardiac surgery are based largely on clinical experience and observational studies, with few prospective RCTs. The GWC recommends that future research on perioperative evaluation and management span the spectrum from RCTs to regional and national registries to focus on patient outcomes. Development and participation in registries (such as the American College of Surgeons NSQIP, American Society of Anesthesiologists, and NACOR [National Anesthesia Clinical Outcomes Registry]) for patients undergoing noncardiac surgery will advance knowledge in the following areas:

1. *Surveillance*: How are we doing across different practices? What are the significant gaps in care?
2. *Discovery*: What new information can be learned? What new strategies or interventions can improve these gaps in care?
3. *Translation*: How can we best apply these strategies or interventions to practice?
4. *Dissemination*: How can we spread what works?

The US healthcare system must focus on achieving the triple aim of better patient care and experience, better population health, and lower cost per capita over time. The use of perioperative tests and treatments improves patient outcomes only when targeted at specific patient subsets. Implementation of ACC/AHA CPGs for perioperative cardiovascular evaluation and management has been demonstrated to improve patient outcomes and reduce costs.[402–405] For example, routine perioperative stress testing in patients at low risk for cardiac events undergoing low-risk elective noncardiac surgery has no benefit, but it could have harm by exposing the patient to unnecessary treatments, such as medications or revascularization procedures. Alternatively, the interruption of perioperative medications such as statins and warfarin in situations not supported by evidence/perioperative CPGs can worsen patient outcomes.[406]

Diagnostic cardiovascular testing continues to evolve, with newer imaging modalities being developed, such as coronary calcium scores, computed tomography angiography, and cardiac magnetic resonance imaging. The value of these modalities in preoperative screening is uncertain and warrants further study.

The use of perioperative beta blockers in beta–blocker-naïve patients undergoing noncardiac surgery remains controversial because of uncertainty about the following issues: 1) optimal duration for the initiation of beta blockers before elective noncardiac surgery; 2) optimal dosing and titration protocol perioperatively to avoid hemodynamic instability, including hypotension and bradycardia; and 3) which elevated-risk patient subsets would benefit the most from initiation of perioperative beta blocker. Although there is sufficient evidence that patients who are receiving long-term beta-blocker therapy should continue beta blockers perioperatively, their use in beta–blocker-naïve patients needs additional research to illuminate the benefit (avoidance of MI) versus harm (stroke). RCTs are needed to demonstrate when to start beta-blocker therapy before noncardiac surgery, the optimal type and dose, and titration protocol.

The risk-adjusted mortality rates after noncardiac surgery have declined significantly in the past decade (relative reductions of 11% to 19% for major cancer surgery and 36% for abdominal aortic aneurysm repair), a development that has been attributed to higher volumes, consolidation of high-risk surgery at high-volume hospitals, and implementation of CPGs and local risk-reducing strategies.[407] Research also suggests that additional factors at the practice, clinician, and patient levels can impact patient outcomes after noncardiac surgery. For bariatric surgery, the technical skill of practicing surgeons assessed by peer ratings varied widely, and greater skill was associated with better patient outcomes. The bottom quartile of surgical skill was associated with higher complication rates than was the top quartile (14.5% versus 5.2%; $P<0.001$).[408]

As outlined in Section 8, the evidence base for the predictive value of biomarkers in the perioperative period has grown. However, the utility of this information in influencing management and outcome is unknown and is currently undergoing investigation. The results of these investigations could lead to changes in recommendations in the future.

To implement the recommendations of the current perioperative CPGs effectively, a "perioperative team approach" is needed. The perioperative team is intended to engage clinicians with appropriate expertise; enhance communication of the benefits, risks, and alternatives; and include the patient's preferences, values, and goals. Members of the perioperative team would include the patient and family, surgeon, anesthesiologist, cardiologist, hospitalist, primary care clinician, and additional clinicians (eg, a congenital heart disease specialist) depending on the unique circumstances of the patient. Shared decision making aims to take into account the patient's preferences, values, and goals and is useful for treatment decisions where there are alternatives with comparable outcomes or where patient action is needed, such as medication adherence. Future research will also be needed to understand how information on perioperative risk is incorporated into patient decision making.

Presidents and Staff

American College of Cardiology

Patrick T. O'Gara, MD, MACC, President

Shalom Jacobovitz, Chief Executive Officer

William J. Oetgen, MD, MBA, FACC, Executive Vice President, Science, Education, and Quality

Amelia Scholtz, PhD, Publications Manager, Science and Clinical Policy

American College of Cardiology/American Heart Association

Lisa Bradfield, CAE, Director, Science and Clinical Policy

Emily Cottrell, MA, Quality Assurance Specialist, Science and Clinical Policy

American Heart Association

Elliott Antman, MD, FAHA, President

Nancy Brown, Chief Executive Officer

Rose Marie Robertson, MD, FAHA, Chief Science Officer

Gayle R. Whitman, PhD, RN, FAHA, FAAN, Senior Vice President, Office of Science Operations

Anne Leonard, MPH, RN, FAHA, Science and Medicine Advisor, Office of Science Operations

Jody Hundley, Production Manager, Scientific Publications, Office of Science Operations

References

1. Institute of Medicine (US). *Clinical Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011.
2. Institute of Medicine (US). *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington, DC: National Academies Press; 2011.
3. Jacobs AK, Kushner FG, Ettinger SM, et al. ACCF/AHA clinical practice guideline methodology summit report: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:268–310.
4. Jacobs AK, Anderson JL, Halperin JL. The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey. Circulation. 2014;130:1208–17.
5. Anderson JL, Heidenreich PA, Barnett PG, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. Circulation. 2014;129:2329–45.
6. ACC/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology and American Heart Association. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf. Accessed May 9, 2014.
7. Arnett DK, Goodman R, Halperin JL, et al. AHA/ACC/HHS integrating comorbidities into cardiovascular practice guidelines: a call for comprehensive clinical relevance. Circulation. 2014;130:1662–67.
8. Wijeysundera DN, Duncan D, Nkonde-Price C, et al. Perioperative beta-blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:2246–64.
9. Erasmus MC Follow-up Investigation Committee. *Report on the 2012 Follow-Up Investigation of Possible Breaches of Academic Integrity*. September 30, 2012.
10. Erasmus MC Follow-up Investigation Committee. *Investigation Into Possible Violation of Scientific Integrity-Report Summary*. November 16, 2011.
11. Lüscher TF. The codex of science: honesty, precision, and truth-and its violations. Eur Heart J. 2013;34:1018–23.
12. Chopra V, Eagle KA. Perioperative mischief: the price of academic misconduct. Am J Med. 2012;125:953–5.
13. Chopra V, Eagle KA. The reply. Am J Med. 2013;126:e7.
14. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014;130:e199–267.
15. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:e521–643.
16. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240–327.
17. Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr. 2013;26:921–64.
18. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:e362–425.

18a. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2012;126:e354–471.

19. Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2014;130:1749–67.
20. Jneid H, Anderson JL, Wright RS, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2012;126:875–910.
21. Carson JL, Grossman BJ, Kleinman S, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. Ann Intern Med. 2012;157:49–58.
22. Rooke TW, Hirsch AT, Misra S, et al. 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College

of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124:2020–45.
23. Hirsch AT, Haskal ZJ, Hertzer NR, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary: a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease). Circulation. 2006;113:e463–654.
24. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124:e783–831.
25. Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124:e652–735.
26. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation. 2011;124:e574–651.
27. American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on TRansesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography: an updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Anesthesiology. 2010;112:1084–96.
28. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Circulation. 2008;118:e714–833.
29. Reeves ST, Finley AC, Skubas NJ, et al. Basic perioperative transesophageal echocardiography examination: a consensus statement of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr. 2013;26:443–56.
30. Apfelbaum JL, Connis RT, Nickinovich DG, et al. Practice advisory for preanesthesia evaluation: an updated report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Anesthesiology. 2012;116:522–38.
31. Lentine KL, Costa SP, Weir MR, et al. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. Circulation. 2012;126:617–63.
32. Lackland DT, Elkind MSV, D'Agostino R, et al. Inclusion of stroke in cardiovascular risk prediction instruments: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012;43:1998–2027.
33. Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management. Developed as a joint project with the American Society of Anesthesiologists (ASA), and in collaboration with the American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). Heart Rhythm. 2011;8:1114–54.
34. Jordan SW, Mioton LM, Smetona J, et al. Resident involvement and plastic surgery outcomes: an analysis of 10,356 patients from the American College of Surgeons National Surgical Quality Improvement Program database. Plast Reconstr Surg. 2013;131:763–73.
35. Schein OD, Katz J, Bass EB, et al. The value of routine preoperative medical testing before cataract surgery. Study of Medical Testing for Cataract Surgery. N Engl J Med. 2000;342:168–75.
36. Bilimoria KY, Liu Y, Paruch JL, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg. 2013;217:833–42.e1-3.
37. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100:1043–9.
38. Botto F, Alonso-Coello P, Chan MTV, et al. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. Anesthesiology. 2014;120:564–78.
39. Archan S, Fleisher LA. From creatine kinase-MB to troponin: the adoption of a new standard. Anesthesiology. 2010;112:1005–12.
40. Devereaux PJ, Chan MT, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. JAMA. 2012;307:2295–304.
41. Shah KB, Kleinman BS, Rao TL, et al. Angina and other risk factors in patients with cardiac diseases undergoing noncardiac operations. Anesth Analg. 1990;70:240–7.
42. Livhits M, Ko CY, Leonardi MJ, et al. Risk of surgery following recent myocardial infarction. Ann Surg. 2011;253:857–64.
43. Livhits M, Gibbons MM, de VC, et al. Coronary revascularization after myocardial infarction can reduce risks of noncardiac surgery. J Am Coll Surg. 2011;212:1018–26.
44. Mashour GA, Shanks AM, Kheterpal S. Perioperative stroke and associated mortality after noncardiac, nonneurologic surgery. Anesthesiology. 2011;114:1289–96.
45. Schoenborn CA, Heyman KM. Health characteristics of adults aged 55 years and over: United States, 2004–2007. Natl Health Stat Report. 2009:1–31.
46. Bateman BT, Schumacher HC, Wang S, et al. Perioperative acute ischemic stroke in noncardiac and nonvascular surgery: incidence, risk factors, and outcomes. Anesthesiology. 2009;110:231–8.
47. Dasgupta M, Rolfson DB, Stolee P, et al. Frailty is associated with postoperative complications in older adults with medical problems. Arch Gerontol Geriatr. 2009;48:78–83.
48. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med. 1977;297:845–50.
49. Detsky AS, Abrams HB, McLaughlin JR, et al. Predicting cardiac complications in patients undergoing non-cardiac surgery. J Gen Intern Med. 1986;1:211–9.
50. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009;119:e21–181.
51. Hammill BG, Curtis LH, Bennett-Guerrero E, et al. Impact of heart failure on patients undergoing major noncardiac surgery. Anesthesiology. 2008;108:559–67.
52. Hernandez AF, Whellan DJ, Stroud S, et al. Outcomes in heart failure patients after major noncardiac surgery. J Am Coll Cardiol. 2004;44:1446–53.
53. Van Diepen S., Bakal JA, McAlister FA, et al. Mortality and readmission of patients with heart failure, atrial fibrillation, or coronary artery disease undergoing noncardiac surgery: an analysis of 38 047 patients. Circulation. 2011;124:289–96.
54. Xu-Cai YO, Brotman DJ, Phillips CO, et al. Outcomes of patients with stable heart failure undergoing elective noncardiac surgery. Mayo Clin Proc. 2008;83:280–8.
55. Healy KO, Waksmonski CA, Altman RK, et al. Perioperative outcome and long-term mortality for heart failure patients undergoing intermediate- and high-risk noncardiac surgery: impact of left ventricular ejection fraction. Congest Heart Fail. 2010;16:45–9.
56. Kazmers A, Cerqueira MD, Zierler RE. Perioperative and late outcome in patients with left ventricular ejection fraction of 35% or less who require major vascular surgery. J Vasc Surg. 1988;8:307–15.
57. Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. Eur Heart J. 2012;33:1750–7.
58. Flu W-J, van Kuijk J-P, Hoeks SE, et al. Prognostic implications of asymptomatic left ventricular dysfunction in patients undergoing vascular surgery. Anesthesiology. 2010;112:1316–24.
59. Matyal R, Hess PE, Subramaniam B, et al. Perioperative diastolic dysfunction during vascular surgery and its association with postoperative outcome. J Vasc Surg. 2009;50:70–6.
60. Douglas PS, Garcia MJ, Haines DE, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 appropriate use criteria for echocardiography: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2011;57:1126–66.
61. Rodseth RN, Lurati Buse GA, Bolliger D, et al. The predictive ability of pre-operative B-type natriuretic peptide in vascular patients for major

adverse cardiac events: an individual patient data meta-analysis. J Am Coll Cardiol. 2011;58:522–9.
62. Karthikeyan G, Moncur RA, Levine O, et al. Is a pre-operative brain natriuretic peptide or N-terminal pro-B-type natriuretic peptide measurement an independent predictor of adverse cardiovascular outcomes within 30 days of noncardiac surgery? A systematic review and meta-analysis of observational studies. J Am Coll Cardiol. 2009;54:1599–606.
63. Ryding ADS, Kumar S, Worthington AM, et al. Prognostic value of brain natriuretic peptide in noncardiac surgery: a meta-analysis. Anesthesiology. 2009;111:311–9.
64. Rajagopalan S, Croal BL, Bachoo P, et al. N-terminal pro B-type natriuretic peptide is an independent predictor of postoperative myocardial injury in patients undergoing major vascular surgery. J Vasc Surg. 2008;48:912–7.
65. Leibowitz D, Planer D, Rott D, et al. Brain natriuretic peptide levels predict perioperative events in cardiac patients undergoing noncardiac surgery: a prospective study. Cardiology. 2008;110:266–70.
66. Rodseth RN, Biccard BM, Le MY, et al. The prognostic value of preoperative and post-operative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. J Am Coll Cardiol. 2014;63:170–80.
67. Haering JM, Comunale ME, Parker RA, et al. Cardiac risk of noncardiac surgery in patients with asymmetric septal hypertrophy. Anesthesiology. 1996;85:254–9.
68. Xuan T, Zeng Y, Zhu W. Risk of patients with hypertrophic cardiomyopathy undergoing noncardiac surgery. Chin Med Sci J. 2007;22:211–5.
69. Hreybe H, Zahid M, Sonel A, et al. Noncardiac surgery and the risk of death and other cardiovascular events in patients with hypertrophic cardiomyopathy. Clin Cardiol. 2006;29:65–8.
70. Tabib A, Loire R, Chalabreysse L, et al. Circumstances of death and gross and microscopic observations in a series of 200 cases of sudden death associated with arrhythmogenic right ventricular cardiomyopathy and/or dysplasia. Circulation. 2003;108:3000–5.
71. Tabib A, Loire R, Miras A, et al. Unsuspected cardiac lesions associated with sudden unexpected perioperative death. Eur J Anaesthesiol. 2000;17:230–5.
72. Elkayam U. Clinical characteristics of peripartum cardiomyopathy in the United States: diagnosis, prognosis, and management. J Am Coll Cardiol. 2011;58:659–70.
73. Tiwari AK, Agrawal J, Tayal S, et al. Anaesthetic management of peripartum cardiomyopathy using “epidural volume extension” technique: a case series. Ann Card Anaesth. 2012;15:44–6.
74. Gevaert S, Van BY, Bouchez S, et al. Acute and critically ill peripartum cardiomyopathy and “bridge to” therapeutic options: a single center experience with intra-aortic balloon pump, extra corporeal membrane oxygenation and continuous-flow left ventricular assist devices. Crit Care. 2011;15:R93.
75. Agarwal S, Rajamanickam A, Bajaj NS, et al. Impact of aortic stenosis on postoperative outcomes after noncardiac surgeries. Circ Cardiovasc Qual Outcomes. 2013;6:193–200.
76. Ben-Dor I, Pichard AD, Satler LF, et al. Complications and outcome of balloon aortic valvuloplasty in high-risk or inoperable patients. JACC Cardiovasc Interv. 2010;3:1150–6.
77. Khawaja MZ, Sohal M, Valli H, et al. Standalone balloon aortic valvuloplasty: indications and outcomes from the UK in the transcatheter valve era. Catheter Cardiovasc Interv. 2013;81:366–73.
78. Feldman T. Balloon aortic valvuloplasty: still under-developed after two decades of use. Catheter Cardiovasc Interv. 2013;81:374–5.
79. Hayes SN, Holmes DR, Nishimura RA, et al. Palliative percutaneous aortic balloon valvuloplasty before noncardiac operations and invasive diagnostic procedures. Mayo Clin Proc. 1989;64:753–7.
80. Roth RB, Palacios IF, Block PC. Percutaneous aortic balloon valvuloplasty: its role in the management of patients with aortic stenosis requiring major noncardiac surgery. J Am Coll Cardiol. 1989;13:1039–41.
81. Levine MJ, Berman AD, Safian RD, et al. Palliation of valvular aortic stenosis by balloon valvuloplasty as preoperative preparation for noncardiac surgery. Am J Cardiol. 1988;62:1309–10.
82. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010;363:1597–607.
83. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011;364:2187–98.
84. Ben-Dor I, Maluenda G, Dvir D, et al. Balloon aortic valvuloplasty for severe aortic stenosis as a bridge to transcatheter/surgical aortic valve replacement. Catheter Cardiovasc Interv. 2013;82:632–7.
85. Reyes VP, Raju BS, Wynne J, et al. Percutaneous balloon valvuloplasty compared with open surgical commissurotomy for mitral stenosis. N Engl J Med. 1994;331:961–7.
86. Esteves CA, Munoz JS, Braga S, et al. Immediate and long-term follow-up of percutaneous balloon mitral valvuloplasty in pregnant patients with rheumatic mitral stenosis. Am J Cardiol. 2006;98:812–6.
87. Nercolini DC, da Rocha Loures Bueno R, Eduardo Guérios E, et al. Percutaneous mitral balloon valvuloplasty in pregnant women with mitral stenosis. Catheter Cardiovasc Interv. 2002;57:318–22.
88. Lai H-C, Lai H-C, Lee W-L, et al. Impact of chronic advanced aortic regurgitation on the perioperative outcome of noncardiac surgery. Acta Anaesthesiol Scand. 2010;54:580–8.
89. Bajaj NS, Agarwal S, Rajamanickam A, et al. Impact of severe mitral regurgitation on postoperative outcomes after noncardiac surgery. Am J Med. 2013;126:529–35.
90. Hollenberg M, Mangano DT, Browner WS, et al. Predictors of postoperative myocardial ischemia in patients undergoing noncardiac surgery. The Study of Perioperative Ischemia Research Group. JAMA. 1992;268:205–9.
91. Dorman T, Breslow MJ, Pronovost PJ, et al. Bundle-branch block as a risk factor in noncardiac surgery. Arch Intern Med. 2000;160:1149–52.
92. Blomström-Lundqvist C, Scheinman MM, Aliot EM, et al. ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias-executive summary. a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop guidelines for the management of patients with supraventricular arrhythmias). Circulation. 2003;108:1871–909.
93. Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2012;126:1784–800.
94. Mahla E, Rotman B, Rehak P, et al. Perioperative ventricular dysrhythmias in patients with structural heart disease undergoing noncardiac surgery. Anesth Analg. 1998;86:16–21.
95. O'Kelly B, Browner WS, Massie B, et al. Ventricular arrhythmias in patients undergoing noncardiac surgery. The Study of Perioperative Ischemia Research Group. JAMA. 1992;268:217–21.
96. Gregoratos G, Abrams J, Epstein AE, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). Circulation. 2002;106:2145–61.
97. Pastore JO, Yurchak PM, Janis KM, et al. The risk of advanced heart block in surgical patients with right bundle branch block and left axis deviation. Circulation. 1978;57:677–80.
98. Stone ME, Salter B, Fischer A. Perioperative management of patients with cardiac implantable electronic devices. Br J Anaesth. 2011;107 Suppl 1:i16–26.
99. Mahlow WJ, Craft RM, Misulia NL, et al. A perioperative management algorithm for cardiac rhythm management devices: the PACED-OP protocol. Pacing Clin Electrophysiol. 2013;36:238–48.
100. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association. Circulation. 2009;119:2250–94.
101. Ramakrishna G, Sprung J, Ravi BS, et al. Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. J Am Coll Cardiol. 2005;45:1691–9.
102. Minai OA, Venkateshiah SB, Arroliga AC. Surgical intervention in patients with moderate to severe pulmonary arterial hypertension. Conn Med. 2006;70:239–43.
103. Lai H-C, Lai H-C, Wang K-Y, et al. Severe pulmonary hypertension complicates postoperative outcome of non-cardiac surgery. Br J Anaesth. 2007;99:184–90.
104. Kaw R, Pasupuleti V, Deshpande A, et al. Pulmonary hypertension: an important predictor of outcomes in patients undergoing non-cardiac surgery. Respir Med. 2011;105:619–24.
105. Price LC, Montani D, Jaïs X, et al. Noncardiothoracic nonobstetric surgery in mild-to-moderate pulmonary hypertension. Eur Respir J. 2010;35:1294–302.
106. Meyer S, McLaughlin VV, Seyfarth H-J, et al. Outcomes of noncardiac, nonobstetric surgery in patients with PAH: an international prospective survey. Eur Respir J. 2013;41:1302–7.
107. Minai OA, Yared J-P, Kaw R, et al. Perioperative risk and management in patients with pulmonary hypertension. Chest. 2013;144:329–40.
108. Warner MA, Lunn RJ, O'Leary PW, et al. Outcomes of noncardiac surgical procedures in children and adults with congenital heart disease. Mayo Perioperative Outcomes Group. Mayo Clin Proc. 1998;73:728–34.

109. Ammash NM, Connolly HM, Abel MD, et al. Noncardiac surgery in Eisenmenger syndrome. J Am Coll Cardiol. 1999;33:222–7.
110. Christensen RE, Reynolds PI, Bukowski BK, et al. Anaesthetic management and outcomes in patients with surgically corrected D-transposition of the great arteries undergoing non-cardiac surgery. Br J Anaesth. 2010;104:12–5.
111. Christensen RE, Gholami AS, Reynolds PI, et al. Anaesthetic management and outcomes after noncardiac surgery in patients with hypoplastic left heart syndrome: a retrospective review. Eur J Anaesthesiol. 2012;29:425–30.
112. Maxwell BG, Wong JK, Kin C, et al. Perioperative outcomes of major noncardiac surgery in adults with congenital heart disease. Anesthesiology. 2013;119:762–9.
113. Rabbitts JA, Groenewald CB, Mauermann WJ, et al. Outcomes of general anesthesia for noncardiac surgery in a series of patients with Fontan palliation. Paediatr Anaesth. 2013;23:180–7.
114. Cohen ME, Ko CY, Bilimoria KY, et al. Optimizing ACS NSQIP modeling for evaluation of surgical quality and risk: patient risk adjustment, procedure mix adjustment, shrinkage adjustment, and surgical focus. J Am Coll Surg. 2013;217:336–46.e1.
115. Gupta PK, Gupta H, Sundaram A, et al. Development and validation of a risk calculator for prediction of cardiac risk after surgery. Circulation. 2011;124:381–7.
116. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med. 2004;351:2795–804.
117. Davenport DL, O'Keeffe SD, Minion DJ, et al. Thirty-day NSQIP database outcomes of open versus endoluminal repair of ruptured abdominal aortic aneurysms. J Vasc Surg. 2010;51:305–9.e1.
118. ACS NSQIP Surgical Risk Calculator. 2013.
119. Aronson WL, McAuliffe MS, Miller K. Variability in the American Society of Anesthesiologists Physical Status Classification Scale. AANA J. 2003;71:265–74.
120. Mak PHK, Campbell RCH, Irwin MG, et al. The ASA Physical Status Classification: inter-observer consistency. American Society of Anesthesiologists. Anaesth Intensive Care. 2002;30:633–40.
121. Goei D, Hoeks SE, Boersma E, et al. Incremental value of high-sensitivity C-reactive protein and N-terminal pro-B-type natriuretic peptide for the prediction of postoperative cardiac events in noncardiac vascular surgery patients. Coron Artery Dis. 2009;20:219–24.
122. Choi J-H, Cho DK, Song Y-B, et al. Preoperative NT-proBNP and CRP predict perioperative major cardiovascular events in non-cardiac surgery. Heart. 2010;96:56–62.
123. Weber M, Luchner A, Seeberger M, et al. Incremental value of high-sensitive troponin T in addition to the revised cardiac index for peri-operative risk stratification in non-cardiac surgery. Eur Heart J. 2013;34:853–62.
124. Farzi S, Stojakovic T, Marko T, et al. Role of N-terminal pro B-type natriuretic peptide in identifying patients at high risk for adverse outcome after emergent non-cardiac surgery. Br J Anaesth. 2013;110:554–60.
125. Yun KH, Jeong MH, Oh SK, et al. Preoperative plasma N-terminal pro-brain natriuretic peptide concentration and perioperative cardiovascular risk in elderly patients. Circ J. 2008;72:195–9.
126. Feringa HHH, Bax JJ, Elhendy A, et al. Association of plasma N-terminal pro-B-type natriuretic peptide with postoperative cardiac events in patients undergoing surgery for abdominal aortic aneurysm or leg bypass. Am J Cardiol. 2006;98:111–5.
127. Feringa HHH, Schouten O, Dunkelgrun M, et al. Plasma N-terminal pro-B-type natriuretic peptide as long-term prognostic marker after major vascular surgery. Heart. 2007;93:226–31.
128. Goei D, Schouten O, Boersma E, et al. Influence of renal function on the usefulness of N-terminal pro-B-type natriuretic peptide as a prognostic cardiac risk marker in patients undergoing noncardiac vascular surgery. Am J Cardiol. 2008;101:122–6.
129. Schouten O, Hoeks SE, Goei D, et al. Plasma N-terminal pro-B-type natriuretic peptide as a predictor of perioperative and long-term outcome after vascular surgery. J Vasc Surg. 2009;49:435–41.
130. Goei D, van Kuijk JP, Flu W-J, et al. Usefulness of repeated N-terminal pro-B-type natriuretic peptide measurements as incremental predictor for long-term cardiovascular outcome after vascular surgery. Am J Cardiol. 2011;107:609–14.
131. Ford MK, Beattie WS, Wijeysundera DN. Systematic review: prediction of perioperative cardiac complications and mortality by the revised cardiac risk index. Ann Intern Med. 2010;152:26–35.
132. Reilly DF, McNeely MJ, Doerner D, et al. Self-reported exercise tolerance and the risk of serious perioperative complications. Arch Intern Med. 1999;159:2185–92.
133. Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). Am J Cardiol. 1989;64:651–4.
134. Goldman L, Hashimoto B, Cook EF, et al. Comparative reproducibility and validity of systems for assessing cardiovascular functional class: advantages of a new specific activity scale. Circulation. 1981;64:1227–34.
135. Goswami S, Brady JE, Jordan DA, et al. Intraoperative cardiac arrests in adults undergoing noncardiac surgery: incidence, risk factors, and survival outcome. Anesthesiology. 2012;117:1018–26.
136. Tsiouris A, Horst HM, Paone G, et al. Preoperative risk stratification for thoracic surgery using the American College of Surgeons National Surgical Quality Improvement Program data set: functional status predicts morbidity and mortality. J Surg Res. 2012;177:1–6.
137. Jeger RV, Probst C, Arsenic R, et al. Long-term prognostic value of the preoperative 12-lead electrocardiogram before major noncardiac surgery in coronary artery disease. Am Heart J. 2006;151:508–13.
138. Payne CJ, Payne AR, Gibson SC, et al. Is there still a role for preoperative 12-lead electrocardiography? World J Surg. 2011;35:2611–6.
139. Landesberg G, Einav S, Christopherson R, et al. Perioperative ischemia and cardiac complications in major vascular surgery: importance of the preoperative twelve-lead electrocardiogram. J Vasc Surg. 1997;26:570–8.
140. Van Klei WA, Bryson GL, Yang H, et al. The value of routine preoperative electrocardiography in predicting myocardial infarction after noncardiac surgery. Ann Surg. 2007;246:165–70.
141. Gold BS, Young ML, Kinman JL, et al. The utility of preoperative electrocardiograms in the ambulatory surgical patient. Arch Intern Med. 1992;152:301–5.
142. Noordzij PG, Boersma E, Bax JJ, et al. Prognostic value of routine preoperative electrocardiography in patients undergoing noncardiac surgery. Am J Cardiol. 2006;97:1103–6.
143. Biteker M, Duman D, Tekkesin AI. Predictive value of preoperative electrocardiography for perioperative cardiovascular outcomes in patients undergoing noncardiac, nonvascular surgery. Clin Cardiol. 2012;35:494–9.
144. Liu LL, Dzankic S, Leung JM. Preoperative electrocardiogram abnormalities do not predict postoperative cardiac complications in geriatric surgical patients. J Am Geriatr Soc. 2002;50:1186–91.
145. Turnbull JM, Buck C. The value of preoperative screening investigations in otherwise healthy individuals. Arch Intern Med. 1987;147:1101–5.
146. Kontos MC, Brath LK, Akosah KO, et al. Cardiac complications in noncardiac surgery: relative value of resting two-dimensional echocardiography and dipyridamole thallium imaging. Am Heart J. 1996;132:559–66.
147. Rohde LE, Polanczyk CA, Goldman L, et al. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. Am J Cardiol. 2001;87:505–9.
148. Halm EA, Browner WS, Tubau JF, et al. Echocardiography for assessing cardiac risk in patients having noncardiac surgery. Study of Perioperative Ischemia Research Group. Ann Intern Med. 1996;125:433–41.
149. Baron JF, Mundler O, Bertrand M, et al. Dipyridamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. N Engl J Med. 1994;330:663–9.
150. Foster ED, Davis KB, Carpenter JA, et al. Risk of noncardiac operation in patients with defined coronary disease: The Coronary Artery Surgery Study (CASS) registry experience. Ann Thorac Surg. 1986;41:42–50.
151. Fletcher JP, Antico VF, Gruenewald S, et al. Risk of aortic aneurysm surgery as assessed by preoperative gated heart pool scan. Br J Surg. 1989;76:26–8.
152. Pedersen T, Kelbaek H, Munck O. Cardiopulmonary complications in high-risk surgical patients: the value of preoperative radionuclide cardiography. Acta Anaesthesiol Scand. 1990;34:183–9.
153. Lazor L, Russell JC, DaSilva J, et al. Use of the multiple uptake gated acquisition scan for the preoperative assessment of cardiac risk. Surg Gynecol Obstet. 1988;167:234–8.
154. Pasternack PF, Imparato AM, Riles TS, et al. The value of the radionuclide angiogram in the prediction of perioperative myocardial infarction in patients undergoing lower extremity revascularization procedures. Circulation. 1985;72:II13–7.
155. Pasternack PF, Imparato AM, Bear G, et al. The value of radionuclide angiography as a predictor of perioperative myocardial infarction in patients undergoing abdominal aortic aneurysm resection. J Vasc Surg. 1984;1:320–5.
156. Kazmers A, Moneta GL, Cerqueira MD, et al. The role of preoperative radionuclide ventriculography in defining outcome after revascularization of the extremity. Surg Gynecol Obstet. 1990;171:481–8.
157. Kazmers A, Cerqueira MD, Zierler RE. The role of preoperative radionuclide ejection fraction in direct abdominal aortic aneurysm repair. J Vasc Surg. 1988;8:128–36.
158. Kazmers A, Cerqueira MD, Zierler RE. The role of preoperative radionuclide left ventricular ejection fraction for risk assessment in carotid surgery. Arch Surg. 1988;123:416–9.
159. Fiser WP, Thompson BW, Thompson AR, et al. Nuclear cardiac ejection fraction and cardiac index in abdominal aortic surgery. Surgery. 1983;94:736–9.

160. Poldermans D, Fioretti PM, Forster T, et al. Dobutamine stress echocardiography for assessment of perioperative cardiac risk in patients undergoing major vascular surgery. Circulation. 1993;87:1506–12.
161. Kertai MD, Boersma E, Bax JJ, et al. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. Heart. 2003;89:1327–34.
162. Leppo J, Plaja J, Gionet M, et al. Noninvasive evaluation of cardiac risk before elective vascular surgery. J Am Coll Cardiol. 1987;9:269–76.
163. Carliner NH, Fisher ML, Plotnick GD, et al. Routine preoperative exercise testing in patients undergoing major noncardiac surgery. Am J Cardiol. 1985;56:51–8.
164. Sgura FA, Kopecky SL, Grill JP, et al. Supine exercise capacity identifies patients at low risk for perioperative cardiovascular events and predicts long-term survival. Am J Med. 2000;108:334–6.
165. Mangano DT, London MJ, Tubau JF, et al. Dipyridamole thallium-201 scintigraphy as a preoperative screening test: a reexamination of its predictive potential. Study of Perioperative Ischemia Research Group. Circulation. 1991;84:493–502.
166. Eagle KA, Coley CM, Newell JB, et al. Combining clinical and thallium data optimizes preoperative assessment of cardiac risk before major vascular surgery. Ann Intern Med. 1989;110:859–66.
167. Cutler BS, Wheeler HB, Paraskos JA, et al. Applicability and interpretation of electrocardiographic stress testing in patients with peripheral vascular disease. Am J Surg. 1981;141:501–6.
168. Arous EJ, Baum PL, Cutler BS. The ischemic exercise test in patients with peripheral vascular disease: implications for management. Arch Surg. 1984;119:780–3.
169. McPhail N, Calvin JE, Shariatmadar A, et al. The use of preoperative exercise testing to predict cardiac complications after arterial reconstruction. J Vasc Surg. 1988;7:60–8.
170. Gerson MC, Hurst JM, Hertzberg VS, et al. Cardiac prognosis in noncardiac geriatric surgery. Ann Intern Med. 1985;103:832–7.
171. Junejo MA, Mason JM, Sheen AJ, et al. Cardiopulmonary exercise testing for preoperative risk assessment before hepatic resection. Br J Surg. 2012;99:1097–104.
172. Hartley RA, Pichel AC, Grant SW, et al. Preoperative cardiopulmonary exercise testing and risk of early mortality following abdominal aortic aneurysm repair. Br J Surg. 2012;99:1539–46.
173. Prentis JM, Trenell MI, Jones DJ, et al. Submaximal exercise testing predicts perioperative hospitalization after aortic aneurysm repair. J Vasc Surg. 2012;56:1564–70.
174. Carlisle J, Swart M. Mid-term survival after abdominal aortic aneurysm surgery predicted by cardiopulmonary exercise testing. Br J Surg. 2007;94:966–9.
175. Older P, Smith R, Courtney P, et al. Preoperative evaluation of cardiac failure and ischemia in elderly patients by cardiopulmonary exercise testing. Chest. 1993;104:701–4.
176. Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. Chest. 1999;116:355–62.
177. Snowden CP, Prentis JM, Anderson HL, et al. Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery. Ann Surg. 2010;251:535–41.
178. Snowden CP, Prentis J, Jacques B, et al. Cardiorespiratory fitness predicts mortality and hospital length of stay after major elective surgery in older people. Ann Surg. 2013;257:999–1004.
179. Wilson RJT, Davies S, Yates D, et al. Impaired functional capacity is associated with all-cause mortality after major elective intra-abdominal surgery. Br J Anaesth. 2010;105:297–303.
180. Thompson AR, Peters N, Lovegrove RE, et al. Cardiopulmonary exercise testing provides a predictive tool for early and late outcomes in abdominal aortic aneurysm patients. Ann R Coll Surg Engl. 2011;93:474–81.
181. Brunelli A, Belardinelli R, Pompili C, et al. Minute ventilation-to-carbon dioxide output (Ve/Vco_2) slope is the strongest predictor of respiratory complications and death after pulmonary resection. Ann Thorac Surg. 2012;93:1802–6.
182. Struthers R, Erasmus P, Holmes K, et al. Assessing fitness for surgery: a comparison of questionnaire, incremental shuttle walk, and cardiopulmonary exercise testing in general surgical patients. Br J Anaesth. 2008;101:774–80.
183. Boucher CA, Brewster DC, Darling RC, et al. Determination of cardiac risk by dipyridamole-thallium imaging before peripheral vascular surgery. N Engl J Med. 1985;312:389–94.
184. Cutler BS, Leppo JA. Dipyridamole thallium 201 scintigraphy to detect coronary artery disease before abdominal aortic surgery. J Vasc Surg. 1987;5:91–100.
185. McEnroe CS, O'Donnell TF, Yeager A, et al. Comparison of ejection fraction and Goldman risk factor analysis to dipyridamole-thallium 201 studies in the evaluation of cardiac morbidity after aortic aneurysm surgery. J Vasc Surg. 1990;11:497–504.
186. Das MK, Pellikka PA, Mahoney DW, et al. Assessment of cardiac risk before nonvascular surgery: dobutamine stress echocardiography in 530 patients. J Am Coll Cardiol. 2000;35:1647–53.
187. Morgan PB, Panomitros GE, Nelson AC, et al. Low utility of dobutamine stress echocardiograms in the preoperative evaluation of patients scheduled for noncardiac surgery. Anesth Analg. 2002;95:512–6.
188. Fletcher JP, Kershaw LZ. Outcome in patients with failed percutaneous transluminal angioplasty for peripheral vascular disease. J Cardiovasc Surg (Torino). 1988;29:733–5.
189. Sachs RN, Tellier P, Larmignat P, et al. Assessment by dipyridamole-thallium-201 myocardial scintigraphy of coronary risk before peripheral vascular surgery. Surgery. 1988;103:584–7.
190. Younis LT, Aguirre F, Byers S, et al. Perioperative and long-term prognostic value of intravenous dipyridamole thallium scintigraphy in patients with peripheral vascular disease. Am Heart J. 1990;119:1287–92.
191. Strawn DJ, Guernsey JM. Dipyridamole thallium scanning in the evaluation of coronary artery disease in elective abdominal aortic surgery. Arch Surg. 1991;126:880–4.
192. Watters TA, Botvinick EH, Dae MW, et al. Comparison of the findings on preoperative dipyridamole perfusion scintigraphy and intraoperative transesophageal echocardiography: implications regarding the identification of myocardium at ischemic risk. J Am Coll Cardiol. 1991;18:93–100.
193. Hendel RC, Whitfield SS, Villegas BJ, et al. Prediction of late cardiac events by dipyridamole thallium imaging in patients undergoing elective vascular surgery. Am J Cardiol. 1992;70:1243–9.
194. Madsen PV, Vissing M, Munck O, et al. A comparison of dipyridamole thallium 201 scintigraphy and clinical examination in the determination of cardiac risk before arterial reconstruction. Angiology. 1992;43:306–11.
195. Brown KA, Rowen M. Extent of jeopardized viable myocardium determined by myocardial perfusion imaging best predicts perioperative cardiac events in patients undergoing noncardiac surgery. J Am Coll Cardiol. 1993;21:325–30.
196. Kresowik TF, Bower TR, Garner SA, et al. Dipyridamole thallium imaging in patients being considered for vascular procedures. Arch Surg. 1993;128:299–302.
197. Bry JD, Belkin M, O'Donnell TF, et al. An assessment of the positive predictive value and cost-effectiveness of dipyridamole myocardial scintigraphy in patients undergoing vascular surgery. J Vasc Surg. 1994;19:112–21.
198. Koutelou MG, Asimacopoulos PJ, Mahmarian JJ, et al. Preoperative risk stratification by adenosine thallium 201 single-photon emission computed tomography in patients undergoing vascular surgery. J Nucl Cardiol. 1995;2:389–94.
199. Marshall ES, Raichlen JS, Forman S, et al. Adenosine radionuclide perfusion imaging in the preoperative evaluation of patients undergoing peripheral vascular surgery. Am J Cardiol. 1995;76:817–21.
200. Van Damme H, Piérard L, Gillain D, et al. Cardiac risk assessment before vascular surgery: a prospective study comparing clinical evaluation, dobutamine stress echocardiography, and dobutamine Tc-99m sestamibi tomoscintigraphy. Cardiovasc Surg. 1997;5:54–64.
201. Huang Z, Komori S, Sawanobori T, et al. Dipyridamole thallium-201 single-photon emission computed tomography for prediction of perioperative cardiac events in patients with arteriosclerosis obliterans undergoing vascular surgery. Jpn Circ J. 1998;62:274–8.
202. Cohen MC, Siewers AE, Dickens JD, et al. Perioperative and long-term prognostic value of dipyridamole Tc-99m sestamibi myocardial tomography in patients evaluated for elective vascular surgery. J Nucl Cardiol. 2003;10:464–72.
203. Harafuji K, Chikamori T, Kawaguchi S, et al. Value of pharmacologic stress myocardial perfusion imaging for preoperative risk stratification for aortic surgery. Circ J. 2005;69:558–63.
204. Beattie WS, Abdelnaem E, Wijeysundera DN, et al. A meta-analytic comparison of preoperative stress echocardiography and nuclear scintigraphy imaging. Anesth Analg. 2006;102:8–16.
205. Lette J, Waters D, Cerino M, et al. Preoperative coronary artery disease risk stratification based on dipyridamole imaging and a simple three-step, three-segment model for patients undergoing noncardiac vascular surgery or major general surgery. Am J Cardiol. 1992;69:1553–8.
206. Stratmann HG, Younis LT, Wittry MD, et al. Dipyridamole technetium-99m sestamibi myocardial tomography in patients evaluated for elective vascular surgery: prognostic value for perioperative and late cardiac events. Am Heart J. 1996;131:923–9.
207. Lane RT, Sawada SG, Segar DS, et al. Dobutamine stress echocardiography for assessment of cardiac risk before noncardiac surgery. Am J Cardiol. 1991;68:976–7.

208. Lalka SG, Sawada SG, Dalsing MC, et al. Dobutamine stress echocardiography as a predictor of cardiac events associated with aortic surgery. J Vasc Surg. 1992;15:831–40.
209. Eichelberger JP, Schwarz KQ, Black ER, et al. Predictive value of dobutamine echocardiography just before noncardiac vascular surgery. Am J Cardiol. 1993;72:602–7.
210. Langan EM, Youkey JR, Franklin DP, et al. Dobutamine stress echocardiography for cardiac risk assessment before aortic surgery. J Vasc Surg. 1993;18:905–11.
211. Dávila-Román VG, Waggoner AD, Sicard GA, et al. Dobutamine stress echocardiography predicts surgical outcome in patients with an aortic aneurysm and peripheral vascular disease. J Am Coll Cardiol. 1993;21:957–63.
212. Shafritz R, Ciocca RG, Gosin JS, et al. The utility of dobutamine echocardiography in preoperative evaluation for elective aortic surgery. Am J Surg. 1997;174:121–5.
213. Ballal RS, Kapadia S, Secknus MA, et al. Prognosis of patients with vascular disease after clinical evaluation and dobutamine stress echocardiography. Am Heart J. 1999;137:469–75.
214. Torres MR, Short L, Baglin T, et al. Usefulness of clinical risk markers and ischemic threshold to stratify risk in patients undergoing major noncardiac surgery. Am J Cardiol. 2002;90:238–42.
215. Labib SB, Goldstein M, Kinnunen PM, et al. Cardiac events in patients with negative maximal versus negative submaximal dobutamine echocardiograms undergoing noncardiac surgery: importance of resting wall motion abnormalities. J Am Coll Cardiol. 2004;44:82–7.
216. Raux M, Godet G, Isnard R, et al. Low negative predictive value of dobutamine stress echocardiography before abdominal aortic surgery. Br J Anaesth. 2006;97:770–6.
217. Umphrey LG, Hurst RT, Eleid MF, et al. Preoperative dobutamine stress echocardiographic findings and subsequent short-term adverse cardiac events after orthotopic liver transplantation. Liver Transpl. 2008;14:886–92.
218. Lerakis S, Kalogeropoulos AP, El-Chami MF, et al. Transthoracic dobutamine stress echocardiography in patients undergoing bariatric surgery. Obes Surg. 2007;17:1475–81.
219. Nguyen P, Plotkin J, Fishbein TM, et al. Dobutamine stress echocardiography in patients undergoing orthotopic liver transplantation: a pooled analysis of accuracy, perioperative and long term cardiovascular prognosis. Int J Cardiovasc Imaging. 2013;29:1741–8.
220. Bossone E, Martinez FJ, Whyte RI, et al. Dobutamine stress echocardiography for the preoperative evaluation of patients undergoing lung volume reduction surgery. J Thorac Cardiovasc Surg. 1999;118:542–6.
221. Rerkpattanapipat P, Morgan TM, Neagle CM, et al. Assessment of preoperative cardiac risk with magnetic resonance imaging. Am J Cardiol. 2002;90:416–9.
222. Pellikka PA, Roger VL, Oh JK, et al. Safety of performing dobutamine stress echocardiography in patients with abdominal aortic aneurysm > or = 4 cm in diameter. Am J Cardiol. 1996;77:413–6.
223. Poldermans D, Arnese M, Fioretti PM, et al. Improved cardiac risk stratification in major vascular surgery with dobutamine-atropine stress echocardiography. J Am Coll Cardiol. 1995;26:648–53.
224. Poldermans D, Arnese M, Fioretti PM, et al. Sustained prognostic value of dobutamine stress echocardiography for late cardiac events after major noncardiac vascular surgery. Circulation. 1997;95:53–8.
225. Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: Role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. JAMA. 2001;285:1865–73.
226. Ahn J-H, Park JR, Min JH, et al. Risk stratification using computed tomography coronary angiography in patients undergoing intermediate-risk noncardiac surgery. J Am Coll Cardiol. 2013;61:661–8.
227. Guidelines and indications for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Coronary Artery Bypass Graft Surgery). J Am Coll Cardiol. 1991;17:543–89.
228. Ward HB, Kelly RF, Thottapurathu L, et al. Coronary artery bypass grafting is superior to percutaneous coronary intervention in prevention of perioperative myocardial infarctions during subsequent vascular surgery. Ann Thorac Surg. 2006;82:795–800.
229. Garcia S, Moritz TE, Ward HB, et al. Usefulness of revascularization of patients with multivessel coronary artery disease before elective vascular surgery for abdominal aortic and peripheral occlusive disease. Am J Cardiol. 2008;102:809–13.
230. Poldermans D, Schouten O, Vidakovic R, et al. A clinical randomized trial to evaluate the safety of a noninvasive approach in high-risk patients undergoing major vascular surgery: the DECREASE-V Pilot Study. J Am Coll Cardiol. 2007;49:1763–9.
231. Kaluza GL, Joseph J, Lee JR, et al. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol. 2000;35:1288–94.
232. Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. J Am Coll Cardiol. 2003;42:234–40.
233. Nuttall GA, Brown MJ, Stombaugh JW, et al. Time and cardiac risk of surgery after bare-metal stent percutaneous coronary intervention. Anesthesiology. 2008;109:588–95.
234. Wijeysundera DN, Wijeysundera HC, Yun L, et al. Risk of elective major noncardiac surgery after coronary stent insertion: a population-based study. Circulation. 2012;126:1355–62.
235. Berger PB, Kleiman NS, Pencina MJ, et al. Frequency of major noncardiac surgery and subsequent adverse events in the year after drug-eluting stent placement results from the EVENT (Evaluation of Drug-Eluting Stents and Ischemic Events) Registry. JACC Cardiovasc Interv. 2010;3:920–7.
236. Van Kuijk J-P, Flu W-J, Schouten O, et al. Timing of noncardiac surgery after coronary artery stenting with bare metal or drug-eluting stents. Am J Cardiol. 2009;104:1229–34.
237. Cruden NLM, Harding SA, Flapan AD, et al. Previous coronary stent implantation and cardiac events in patients undergoing noncardiac surgery. Circ Cardiovasc Interv. 2010;3:236–42.
238. Hawn MT, Graham LA, Richman JS, et al. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. JAMA. 2013;310:1462–72.
239. Grines CL, Bonow RO, Casey DE, et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. Circulation. 2007;115:813–8.
240. Dunkelgrun M, Boersma E, Schouten O, et al. Bisoprolol and fluvastatin for the reduction of perioperative cardiac mortality and myocardial infarction in intermediate-risk patients undergoing noncardiovascular surgery: a randomized controlled trial (DECREASE-IV). Ann Surg. 2009;249:921–6.
241. Devereaux PJ, Yang H, Guyatt GH, et al. Rationale, design, and organization of the PeriOperative ISchemic Evaluation (POISE) trial: a randomised controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. Am Heart J. 2006;152:223–30.
242. Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. N Engl J Med. 2005;353:349–61.
243. Shammash JB, Trost JC, Gold JM, et al. Perioperative beta-blocker withdrawal and mortality in vascular surgical patients. Am Heart J. 2001;141:148–53.
244. Wallace AW, Au S, Cason BA. Association of the pattern of use of perioperative beta-blockade and postoperative mortality. Anesthesiology. 2010;113:794–805.
245. Andersson C, Mérie C, Jørgensen M, et al. Association of beta-blocker therapy with risks of adverse cardiovascular events and deaths in patients with ischemic heart disease undergoing noncardiac surgery: a Danish nationwide cohort study. JAMA Intern Med. 2014;174:336–44.
246. Hoeks SE, Scholte Op Reimer WJM, van Urk H, et al. Increase of 1-year mortality after perioperative beta-blocker withdrawal in endovascular and vascular surgery patients. Eur J Vasc Endovasc Surg. 2007;33:13–9.
247. Barrett TW, Mori M, De Boer D. Association of ambulatory use of statins and beta-blockers with long-term mortality after vascular surgery. J Hosp Med. 2007;2:241–52.
248. London MJ, Hur K, Schwartz GG, et al. Association of perioperative beta-blockade with mortality and cardiovascular morbidity following major noncardiac surgery. JAMA. 2013;309:1704–13.
249. Smith SC, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011;124:2458–73.
250. Surgical Care Improvement Project. SCIP-Card-2: surgery patients on beta blocker therapy prior to admission who received a beta blocker during the perioperative period. 2013;
251. Le Manach Y, Collins GS, Ibanez C, et al. Impact of perioperative bleeding on the protective effect of beta-blockers during infrarenal aortic reconstruction. Anesthesiology. 2012;117:1203–11.
252. Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomized controlled trial. Lancet. 2008;371:1839–47.

253. Brooke BS, Dominici F, Makary MA, et al. Use of beta-blockers during aortic aneurysm repair: bridging the gap between evidence and effective practice. Health Aff (Millwood). 2009;28:1199–209.
254. Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. N Engl J Med. 1999;341:1789–94.
255. Ng JLW, Chan MTV, Gelb AW. Perioperative stroke in noncardiac, nonneurosurgical surgery. Anesthesiology. 2011;115:879–90.
256. Sharifpour M, Moore LE, Shanks AM, et al. Incidence, predictors, and outcomes of perioperative stroke in noncarotid major vascular surgery. Anesth Analg. 2013;116:424–34.
257. Brady AR, Gibbs JSR, Greenhalgh RM, et al. Perioperative beta-blockade (POBBLE) for patients undergoing infrarenal vascular surgery: results of a randomized double-blind controlled trial. J Vasc Surg. 2005;41:602–9.
258. Wijeysundera DN, Beattie WS, Wijeysundera HC, et al. Duration of preoperative beta-blockade and outcomes after major elective non-cardiac surgery. Can J Cardiol. 2014;30:217–23.
259. Ellenberger C, Tait G, Beattie WS. Chronic beta-blockade is associated with a better outcome after elective noncardiac surgery than acute beta-blockade: a single-center propensity-matched cohort study. Anesthesiology. 2011;114:817–23.
260. Flu W-J, van Kuijk J-P, Chonchol M, et al. Timing of pre-operative beta-blocker treatment in vascular surgery patients: influence on post-operative outcome. J Am Coll Cardiol. 2010;56:1922–9.
261. Dai N, Xu D, Zhang J, et al. Different beta-blockers and initiation time in patients undergoing noncardiac surgery: a meta-analysis. Am J Med Sci. 2014;347:235–44.
262. Biccard BM, Sear JW, Foëx P. Meta-analysis of the effect of heart rate achieved by perioperative beta-adrenergic blockade on cardiovascular outcomes. Br J Anaesth. 2008;100:23–8.
263. Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. N Engl J Med. 1996;335:1713–20.
264. Auerbach AD, Goldman L. Beta-blockers and reduction of cardiac events in noncardiac surgery: scientific review. JAMA. 2002;287:1435–44.
265. Lindenauer PK, Fitzgerald J, Hoople N, et al. The potential preventability of postoperative myocardial infarction: underuse of perioperative beta-adrenergic blockade. Arch Intern Med. 2004;164:762–6.
266. Auerbach A, Goldman L. Assessing and reducing the cardiac risk of noncardiac surgery. Circulation. 2006;113:1361–76.
267. Yang H, Raymer K, Butler R, et al. The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 2006;152:983–90.
268. Juul AB, Wetterslev J, Gluud C, et al. Effect of perioperative beta-blockade in patients with diabetes undergoing major non-cardiac surgery: randomised placebo controlled, blinded multicentre trial. BMJ. 2006;332:1482.
269. Devereaux PJ, Beattie WS, Choi PT-L, et al. How strong is the evidence for the use of perioperative beta blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials. BMJ. 2005;331:313–21.
270. Juul AB, Wetterslev J, Kofoed-Enevoldsen A, et al. The Diabetic Postoperative Mortality and Morbidity (DIPOM) trial: rationale and design of a multicenter, randomized, placebo-controlled, clinical trial of metoprolol for patients with diabetes mellitus who are undergoing major noncardiac surgery. Am Heart J. 2004;147:677–83.
271. Schouten O, Shaw LJ, Boersma E, et al. A meta-analysis of safety and effectiveness of perioperative beta-blocker use for the prevention of cardiac events in different types of noncardiac surgery. Coron Artery Dis. 2006;17:173–9.
272. Talati R, Reinhart KM, White CM, et al. Outcomes of perioperative beta-blockade in patients undergoing noncardiac surgery: a meta-analysis. Ann Pharmacother. 2009;43:1181–8.
273. Bouri S, Shun-Shin MJ, Cole GD, et al. Meta-analysis of secure randomised controlled trials of beta-blockade to prevent perioperative death in non-cardiac surgery. Heart. 2014;100:456–64.
274. Beattie WS, Wijeysundera DN, Karkouti K, et al. Does tight heart rate control improve beta-blocker efficacy? An updated analysis of the noncardiac surgical randomized trials. Anesth Analg. 2008;106:1039–48.
275. Ashes C, Judelman S, Wijeysundera DN, et al. Selective beta1-antagonism with bisoprolol is associated with fewer postoperative strokes than atenolol or metoprolol: a single-center cohort study of 44,092 consecutive patients. Anesthesiology. 2013;119:777–87.
276. Wallace AW, Au S, Cason BA. Perioperative beta-blockade: atenolol is associated with reduced mortality when compared to metoprolol. Anesthesiology. 2011;114:824–36.
277. Redelmeier D, Scales D, Kopp A. Beta blockers for elective surgery in elderly patients: population based, retrospective cohort study. BMJ. 2005;331:932.
278. Badgett RG, Lawrence VA, Cohn SL. Variations in pharmacology of beta-blockers may contribute to heterogeneous results in trials of perioperative beta-blockade. Anesthesiology. 2010;113:585–92.
279. Zaugg M, Bestmann L, Wacker J, et al. Adrenergic receptor genotype but not perioperative bisoprolol therapy may determine cardiovascular outcome in at-risk patients undergoing surgery with spinal block: the Swiss Beta Blocker in Spinal Anesthesia (BBSA) study: a double-blinded, placebo-controlled, multicenter trial with 1-year follow-up. Anesthesiology. 2007;107:33–44.
280. Rangno RE, Langlois S. Comparison of withdrawal phenomena after propranolol, metoprolol, and pindolol. Am Heart J. 1982;104:473–8.
281. Swedberg K, Hjalmarson A, Waagstein F, et al. Adverse effects of beta-blockade withdrawal in patients with congestive cardiomyopathy. Br Heart J. 1980;44:134–42.
282. Walker PR, Marshall AJ, Farr S, et al. Abrupt withdrawal of atenolol in patients with severe angina: comparison with the effects of treatment. Br Heart J. 1985;53:276–82.
283. Lindenauer PK, Pekow P, Wang K, et al. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. JAMA. 2004;291:2092–9.
284. Kennedy J, Quan H, Buchan AM, et al. Statins are associated with better outcomes after carotid endarterectomy in symptomatic patients. Stroke. 2005;36:2072–6.
285. Raju MG, Pachika A, Punnam SR, et al. Statin therapy in the reduction of cardiovascular events in patients undergoing intermediate-risk noncardiac, nonvascular surgery. Clin Cardiol. 2013;36:456–61.
286. Desai H, Aronow WS, Ahn C, et al. Incidence of perioperative myocardial infarction and of 2-year mortality in 577 elderly patients undergoing noncardiac vascular surgery treated with and without statins. Arch Gerontol Geriatr. 2010;51:149–51.
287. Durazzo AES, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. J Vasc Surg. 2004;39:967–75.
288. Ridker PM, Wilson PWF. A trial-based approach to statin guidelines. JAMA. 2013;310:1123–4.
289. Sanders RD, Nicholson A, Lewis SR, et al. Perioperative statin therapy for improving outcomes during and after noncardiac vascular surgery. Cochrane Database Syst Rev. 2013;7:CD009971.
290. Schouten O, Boersma E, Hoeks SE, et al. Fluvastatin and perioperative events in patients undergoing vascular surgery. N Engl J Med. 2009;361:980–9.
291. Oliver MF, Goldman L, Julian DG, et al. Effect of mivazerol on perioperative cardiac complications during non-cardiac surgery in patients with coronary heart disease: the European Mivazerol Trial (EMIT). Anesthesiology. 1999;91:951–61.
292. Thomson IR, Mutch WA, Culligan JD. Failure of intravenous nitroglycerin to prevent intraoperative myocardial ischemia during fentanyl-pancuronium anesthesia. Anesthesiology. 1984;61:385–93.
293. Stühmeier KD, Mainzer B, Cierpka J, et al. Small, oral dose of clonidine reduces the incidence of intraoperative myocardial ischemia in patients having vascular surgery. Anesthesiology. 1996;85:706–12.
294. Ellis JE, Drijvers G, Pedlow S, et al. Premedication with oral and transdermal clonidine provides safe and efficacious postoperative sympatholysis. Anesth Analg. 1994;79:1133–40.
295. Wijeysundera DN, Naik JS, Beattie WS. Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: a meta-analysis. Am J Med. 2003;114:742–52.
296. Perioperative sympatholysis: beneficial effects of the alpha 2-adrenoceptor agonist mivazerol on hemodynamic stability and myocardial ischemia. McSPI-Europe Research Group. Anesthesiology. 1997;86:346–63.
297. Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. Anesthesiology. 2004;101:284–93.
298. Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370:1494–503.
299. Wijeysundera DN, Beattie WS. Calcium channel blockers for reducing cardiac morbidity after noncardiac surgery: a meta-analysis. Anesth Analg. 2003;97:634–41.
300. Turan A, You J, Shiba A, et al. Angiotensin converting enzyme inhibitors are not associated with respiratory complications or mortality after noncardiac surgery. Anesth Analg. 2012;114:552–60.
301. Rosenman DJ, McDonald FS, Ebbert JO, et al. Clinical consequences of withholding versus administering renin-angiotensin-aldosterone system antagonists in the preoperative period. J Hosp Med. 2008;3:319–25.

302. Lau WC, Froehlich JB, Jewell ES, et al. Impact of adding aspirin to beta-blocker and statin in high-risk patients undergoing major vascular surgery. Ann Vasc Surg. 2013;27:537–45.
303. Brabant SM, Bertrand M, Eyraud D, et al. The hemodynamic effects of anesthetic induction in vascular surgical patients chronically treated with angiotensin II receptor antagonists. Anesth Analg. 1999;89:1388–92.
304. Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg. 2001;92:26–30.
305. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(suppl 2):S1–45.
306. Burger W, Chemnitius J-M, Kneissl GD, et al. Low-dose aspirin for secondary cardiovascular prevention - cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation - review and meta-analysis. J Intern Med. 2005;257:399–414.
307. Tokushige A, Shiomi H, Morimoto T, et al. Incidence and outcome of surgical procedures after coronary bare-metal and drug-eluting stent implantation: a report from the CREDO-Kyoto PCI/CABG registry cohort-2. Circ Cardiovasc Interv. 2012;5:237–46.
308. Sharma AK, Ajani AE, Hamwi SM, et al. Major noncardiac surgery following coronary stenting: when is it safe to operate? Catheter Cardiovasc Interv. 2004;63:141–5.
309. Reddy PR, Vaitkus PT. Risks of noncardiac surgery after coronary stenting. Am J Cardiol. 2005;95:755–7.
310. Van Werkum JW, Heestermans AA, Zomer AC, et al. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. J Am Coll Cardiol. 2009;53:1399–409.
311. Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA. 2005;293:2126–30.
312. Gandhi NK, Abdel-Karim A-RR, Banerjee S, et al. Frequency and risk of noncardiac surgery after drug-eluting stent implantation. Catheter Cardiovasc Interv. 2011;77:972–6.
313. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet. 2000;355:1295–302.
314. Amar D, Burt ME, Bains MS, et al. Symptomatic tachydysrhythmias after esophagectomy: incidence and outcome measures. Ann Thorac Surg. 1996;61:1506–9.
315. Amar D, Zhang H, Leung DHY, et al. Older age is the strongest predictor of postoperative atrial fibrillation. Anesthesiology. 2002;96:352–6.
316. Amar D, Zhang H, Shi W, et al. Brain natriuretic peptide and risk of atrial fibrillation after thoracic surgery. J Thorac Cardiovasc Surg. 2012;144:1249–53.
317. Bhave PD, Goldman LE, Vittinghoff E, et al. Incidence, predictors, and outcomes associated with postoperative atrial fibrillation after major noncardiac surgery. Am Heart J. 2012;164:918–24.
318. Cardinale D, Martinoni A, Cipolla CM, et al. Atrial fibrillation after operation for lung cancer: clinical and prognostic significance. Ann Thorac Surg. 1999;68:1827–31.
319. Christians KK, Wu B, Quebbeman EJ, et al. Postoperative atrial fibrillation in noncardiothoracic surgical patients. Am J Surg. 2001;182:713–5.
320. Ojima T, Iwahashi M, Nakamori M, et al. Atrial fibrillation after esophageal cancer surgery: an analysis of 207 consecutive patients. Surg Today. 2014;44:839–47.
321. Onaitis M, D'Amico T, Zhao Y, et al. Risk factors for atrial fibrillation after lung cancer surgery: analysis of the Society of Thoracic Surgeons general thoracic surgery database. Ann Thorac Surg. 2010;90:368–74.
322. Passman RS, Gingold DS, Amar D, et al. Prediction rule for atrial fibrillation after major noncardiac thoracic surgery. Ann Thorac Surg. 2005;79:1698–703.
323. Polanczyk CA, Goldman L, Marcantonio ER, et al. Supraventricular arrhythmia in patients having noncardiac surgery: clinical correlates and effect on length of stay. Ann Intern Med. 1998;129:279–85.
324. Vaporciyan AA, Correa AM, Rice DC, et al. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. J Thorac Cardiovasc Surg. 2004;127:779–86.
325. Rao VP, Addae-Boateng E, Barua A, et al. Age and neo-adjuvant chemotherapy increase the risk of atrial fibrillation following oesophagectomy. Eur J Cardiothorac Surg. 2012;42:438–43.
326. Balser JR, Martinez EA, Winters BD, et al. Beta-adrenergic blockade accelerates conversion of postoperative supraventricular tachyarrhythmias. Anesthesiology. 1998;89:1052–9.
327. Bayliff CD, Massel DR, Inculet RI, et al. Propranolol for the prevention of postoperative arrhythmias in general thoracic surgery. Ann Thorac Surg. 1999;67:182–6.
328. Tisdale JE, Wroblewski HA, Wall DS, et al. A randomized trial evaluating amiodarone for prevention of atrial fibrillation after pulmonary resection. Ann Thorac Surg. 2009;88:886–93.
329. Riber LP, Christensen TD, Jensen HK, et al. Amiodarone significantly decreases atrial fibrillation in patients undergoing surgery for lung cancer. Ann Thorac Surg. 2012;94:339–44.
330. Riber LP, Christensen TD, Pilegaard HK. Amiodarone is a cost-neutral way of preventing atrial fibrillation after surgery for lung cancer. Eur J Cardiothorac Surg. 2014;45:120–5.
331. Tisdale JE, Wroblewski HA, Wall DS, et al. A randomized, controlled study of amiodarone for prevention of atrial fibrillation after transthoracic esophagectomy. J Thorac Cardiovasc Surg. 2010;140:45–51.
332. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). Circulation. 2006;114:1088–132.
333. Epstein AE, Dimarco JP, Ellenbogen KA, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2013;127:e283–352.
334. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document. Heart Rhythm. 2013;10:1932–63.
335. Gillis AM, Russo AM, Ellenbogen KA, et al. HRS/ACCF expert consensus statement on pacemaker device and mode selection. J Am Coll Cardiol. 2012;60:682–703.
336. Hauser RG, Kallinen L. Deaths associated with implantable cardioverter defibrillator failure and deactivation reported in the United States Food and Drug Administration Manufacturer and User Facility Device Experience Database. Heart Rhythm. 2004;1:399–405.
337. Cheng A, Nazarian S, Spragg DD, et al. Effects of surgical and endoscopic electrocautery on modern-day permanent pacemaker and implantable cardioverter-defibrillator systems. Pacing Clin Electrophysiol. 2008;31:344–50.
338. Barbosa FT, Jucá MJ, astro AA, et al. Neuraxial anaesthesia for lower-limb revascularization. Cochrane Database Syst Rev. 2013;7:CD007083.
339. Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. Anesthesiology. 2001;95:1054–67.
340. Landoni G, Fochi O, Bignami E, et al. Cardiac protection by volatile anesthetics in non-cardiac surgery? A meta-analysis of randomized controlled studies on clinically relevant endpoints. HSR Proc Intensive Care Cardiovasc Anesth. 2009;1:34–43.
341. Lurati Buse GAL, Schumacher P, Seeberger E, et al. Randomized comparison of sevoflurane versus propofol to reduce perioperative myocardial ischemia in patients undergoing noncardiac surgery. Circulation. 2012;126:2696–704.
342. Landoni G, Bignami E, Oliviero F, et al. Halogenated anaesthetics and cardiac protection in cardiac and non-cardiac anaesthesia. Ann Card Anaesth. 2009;12:4–9.
343. Guarracino F, Landoni G, Tritapepe L, et al. Myocardial damage prevented by volatile anesthetics: a multicenter randomized controlled study. J Cardiothorac Vasc Anesth. 2006;20:477–83.
344. Nader ND, Li CM, Khadra WZ, et al. Anesthetic myocardial protection with sevoflurane. J Cardiothorac Vasc Anesth. 2004;18:269–74.
345. Bignami E, Biondi-Zoccai G, Landoni G, et al. Volatile anesthetics reduce mortality in cardiac surgery. J Cardiothorac Vasc Anesth. 2009;23:594–9.
346. Tritapepe L, Landoni G, Guarracino F, et al. Cardiac protection by volatile anaesthetics: a multicentre randomized controlled study in patients undergoing coronary artery bypass grafting with cardiopulmonary bypass. Eur J Anaesthesiol. 2007;24:323–31.
347. Conzen PF, Fischer S, Detter C, et al. Sevoflurane provides greater protection of the myocardium than propofol in patients undergoing off-pump coronary artery bypass surgery. Anesthesiology. 2003;99:826–33.
348. Nishimori M, Low JHS, Zheng H, et al. Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery. Cochrane Database Syst Rev. 2012;7:CD005059.
349. Matot I, Oppenheim-Eden A, Ratrot R, et al. Preoperative cardiac events in elderly patients with hip fracture randomized to epidural or conventional analgesia. Anesthesiology. 2003;98:156–63.
350. Beattie WS, Buckley DN, Forrest JB. Epidural morphine reduces the risk of postoperative myocardial ischaemia in patients with cardiac risk factors. Can J Anaesth. 1993;40:532–41.

351. Beattie WS, Badner NH, Choi P. Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis. Anesth Analg. 2001;93:853–8.
352. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ. 2000;321:1493.
353. Wu CL, Anderson GF, Herbert R, et al. Effect of postoperative epidural analgesia on morbidity and mortality after total hip replacement surgery in medicare patients. Reg Anesth Pain Med. 2003;28:271–8.
354. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: a randomized, controlled Veterans Affairs cooperative study. Ann Surg. 2001;234:560–9.
355. Dodds TM, Stone JG, Coromilas J, et al. Prophylactic nitroglycerin infusion during noncardiac surgery does not reduce perioperative ischemia. Anesth Analg. 1993;76:705–13.
356. Zvara DA, Groban L, Rogers AT, et al. Prophylactic nitroglycerin did not reduce myocardial ischemia during accelerated recovery management of coronary artery bypass graft surgery patients. J Cardiothorac Vasc Anesth. 2000;14:571–5.
357. Kallmeyer IJ, Collard CD, Fox JA, et al. The safety of intraoperative transesophageal echocardiography: a case series of 7200 cardiac surgical patients. Anesth Analg. 2001;92:1126–30.
358. Michelena HI, Abel MD, Suri RM, et al. Intraoperative echocardiography in valvular heart disease: an evidence-based appraisal. Mayo Clin Proc. 2010;85:646–55.
359. Eisenberg MJ, London MJ, Leung JM, et al. Monitoring for myocardial ischemia during noncardiac surgery: a technology assessment of transesophageal echocardiography and 12-lead electrocardiography. The Study of Perioperative Ischemia Research Group. JAMA. 1992;268:210–6.
360. London MJ, Tubau JF, Wong MG, et al. The "natural history" of segmental wall motion abnormalities in patients undergoing noncardiac surgery. S.P.I. Research Group. Anesthesiology. 1990;73:644–55.
361. Bilotta F, Tempe DK, Giovannini F, et al. Perioperative transoesophageal echocardiography in noncardiac surgery. Ann Card Anaesth. 2006;9:108–13.
362. Memtsoudis SG, Rosenberger P, Loffler M, et al. The usefulness of transesophageal echocardiography during intraoperative cardiac arrest in noncardiac surgery. Anesth Analg. 2006;102:1653–7.
363. Shillcutt SK, Markin NW, Montzingo CR, et al. Use of rapid "rescue" perioperative echocardiography to improve outcomes after hemodynamic instability in noncardiac surgical patients. J Cardiothorac Vasc Anesth. 2012;26:362–70.
364. Nguyen HP, Zaroff JG, Bayman EO, et al. Perioperative hypothermia (33 degrees C) does not increase the occurrence of cardiovascular events in patients undergoing cerebral aneurysm surgery: findings from the Intraoperative Hypothermia for Aneurysm Surgery Trial. Anesthesiology. 2010;113:327–42.
365. Frank SM, Fleisher LA, Breslow MJ, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. JAMA. 1997;277:1127–34.
366. Karalapillai D, Story D, Hart GK, et al. Postoperative hypothermia and patient outcomes after major elective non-cardiac surgery. Anaesthesia. 2013;68:605–11.
367. Rajagopalan S, Mascha E, Na J, et al. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. Anesthesiology. 2008;108:71–7.
368. Wenisch C, Narzt E, Sessler DI, et al. Mild intraoperative hypothermia reduces production of reactive oxygen intermediates by polymorphonuclear leukocytes. Anesth Analg. 1996;82:810–6.
369. Hannan EL, Samadashvili Z, Wechsler A, et al. The relationship between perioperative temperature and adverse outcomes after off-pump coronary artery bypass graft surgery. J Thorac Cardiovasc Surg. 2010;139:1568–75.e1.
370. Karalapillai D, Story DA, Calzavacca P, et al. Inadvertent hypothermia and mortality in postoperative intensive care patients: retrospective audit of 5050 patients. Anaesthesia. 2009;64:968–72.
371. Schmied H, Kurz A, Sessler DI, et al. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet. 1996;347:289–92.
372. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med. 1996;334:1209–15.
373. Chestovich PJ, Kwon MH, Cryer HG, et al. Surgical procedures for patients receiving mechanical cardiac support. Am Surg. 2011;77:1314–7.
374. Eckhauser AE, Melvin WV, Sharp KW. Management of general surgical problems in patients with left ventricular assist devices. Am Surg. 2006;72:158–61.
375. Garatti A, Bruschi G, Colombo T, et al. Noncardiac surgical procedures in patient supported with long-term implantable left ventricular assist device. Am J Surg. 2009;197:710–4.
376. Schmid C, Wilhelm M, Dietl KH, et al. Noncardiac surgery in patients with left ventricular assist devices. Surgery. 2001;129:440–4.
377. Stehlik J, Nelson DM, Kfoury AG, et al. Outcome of noncardiac surgery in patients with ventricular assist devices. Am J Cardiol. 2009;103:709–12.
378. Goldstein DJ, Mullis SL, Delphin ES, et al. Noncardiac surgery in long-term implantable left ventricular assist-device recipients. Ann Surg. 1995;222:203–7.
379. Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant. 2013;32:157–87.
380. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med. 2003;348:5–14.
381. Valentine RJ, Duke ML, Inman MH, et al. Effectiveness of pulmonary artery catheters in aortic surgery: a randomized trial. J Vasc Surg. 1998;27:203–11.
382. Bender JS, Smith-Meek MA, Jones CE. Routine pulmonary artery catheterization does not reduce morbidity and mortality of elective vascular surgery: results of a prospective, randomized trial. Ann Surg. 1997;226:229–36.
383. Carson JL, Terrin ML, Noveck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med. 2011;365:2453–62.
384. Devereaux PJ, Xavier D, Pogue J, et al. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. Ann Intern Med. 2011;154:523–8.
385. Garcia S, Marston N, Sandoval Y, et al. Prognostic value of 12-lead electrocardiogram and peak troponin I level after vascular surgery. J Vasc Surg. 2013;57:166–72.
386. Keller T, Zeller T, Ojeda F, et al. Serial changes in highly sensitive troponin I assay and early diagnosis of myocardial infarction. JAMA. 2011;306:2684–93.
387. D'Costa M, Fleming E, Patterson MC. Cardiac troponin I for the diagnosis of acute myocardial infarction in the emergency department. Am J Clin Pathol. 1997;108:550–5.
388. Brogan GX, Hollander JE, McCuskey CF, et al. Evaluation of a new assay for cardiac troponin I vs creatine kinase-MB for the diagnosis of acute myocardial infarction. Biochemical Markers for Acute Myocardial Ischemia (BAMI) Study Group. Acad Emerg Med. 1997;4:6–12.
389. Wu AH, Feng YJ, Contois JH, et al. Comparison of myoglobin, creatine kinase-MB, and cardiac troponin I for diagnosis of acute myocardial infarction. Ann Clin Lab Sci. 1996;26:291–300.
390. Nagele P, Brown F, Gage BF, et al. High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. Am Heart J. 2013;166:325–32.
391. Adams JE, Sicard GA, Allen BT, et al. Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I. N Engl J Med. 1994;330:670–4.
392. Apple FS, Maturen AJ, Mullins RE, et al. Multicenter clinical and analytical evaluation of the AxSYM troponin-I immunoassay to assist in the diagnosis of myocardial infarction. Clin Chem. 1999;45:206–12.
393. Rinfret S, Goldman L, Polanczyk CA, et al. Value of immediate postoperative electrocardiogram to update risk stratification after major noncardiac surgery. Am J Cardiol. 2004;94:1017–22.
394. Blackshear JL, Cutlip DE, Roubin GS, et al. Myocardial infarction after carotid stenting and endarterectomy: results from the carotid revascularization endarterectomy versus stenting trial. Circulation. 2011;123:2571–8.
395. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42:1206–52.
396. Van Waes JAR, Nathoe HM, de Graaff JC, et al. Myocardial injury after noncardiac surgery and its association with short-term mortality. Circulation. 2013;127:2264–71.
397. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol. 2012;60:1581–98.
398. Linnemann B, Sutter T, Herrmann E, et al. Elevated cardiac troponin T is associated with higher mortality and amputation rates in patients with peripheral arterial disease. J Am Coll Cardiol. 2014;63:1529–38.
399. Management of Myocardial Injury After Noncardiac Surgery Trial (MANAGE). clinicaltrials.gov. 2014. Available at: http://clinicaltrials.gov/show/NCT01661101. Accessed May 5, 2014.
400. Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society,

Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine, and Society for Vascular Surgery. Circulation. 2009;120:e169–276.
401. Lim W, Tkaczyk A, Holinski P, et al. The diagnosis of myocardial infarction in critically ill patients: an agreement study. J Crit Care. 2009;24:447–52.
402. Chopra V, Flanders SA, Froehlich JB, et al. Perioperative practice: time to throttle back. Ann Intern Med. 2010;152:47–51.
403. Skolarus LE, Morgenstern LB, Froehlich JB, et al. Guideline-discordant periprocedural interruptions in warfarin therapy. Circ Cardiovasc Qual Outcomes. 2011;4:206–10.
404. Chopra V, Wesorick DH, Sussman JB, et al. Effect of perioperative statins on death, myocardial infarction, atrial fibrillation, and length of stay: a systematic review and meta-analysis. Arch Surg. 2012;147:181–9.
405. Sheffield KM, McAdams PS, Benarroch-Gampel J, et al. Overuse of preoperative cardiac stress testing in medicare patients undergoing elective noncardiac surgery. Ann Surg. 2013;257:73–80.
406. Holbrook A, Schulman S, Witt DM, et al. Evidence-based management of anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141:e152S–84S.
407. Finks JF, Osborne NH, Birkmeyer JD. Trends in hospital volume and operative mortality for high-risk surgery. N Engl J Med. 2011;364:2128–37.
408. Birkmeyer JD, Finks JF, O'Reilly A, et al. Surgical skill and complication rates after bariatric surgery. N Engl J Med. 2013;369:1434–42.
409. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360:961–72.
410. Feit F, Brooks MM, Sopko G, et al. Long-term clinical outcome in the Bypass Angioplasty Revascularization Investigation Registry: comparison with the randomized trial. BARI Investigators. Circulation. 2000;101:2795–802.
411. King SB, Barnhart HX, Kosinski AS, et al. Angioplasty or surgery for multivessel coronary artery disease: comparison of eligible registry and randomized patients in the EAST trial and influence of treatment selection on outcomes. Emory Angioplasty versus Surgery Trial Investigators. Am J Cardiol. 1997;79:1453–9.
412. Morice MC, Serruys PW, Kappetein AP, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. Circulation. 2010;121:2645–53.
413. Grover FL, Shroyer AL, Hammermeister K, et al. A decade's experience with quality improvement in cardiac surgery using the Veterans Affairs and Society of Thoracic Surgeons national databases. Ann Surg. 2001;234:464–72.
414. Kim Y-H, Park D-W, Kim W-J, et al. Validation of SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score for prediction of outcomes after unprotected left main coronary revascularization. JACC Cardiovasc Interv. 2010;3:612–23.
415. Shahian DM, O'Brien SM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1-coronary artery bypass grafting surgery. Ann Thorac Surg. 2009;88:S2–22.
416. Shahian DM, O'Brien SM, Normand SLT, et al. Association of hospital coronary artery bypass volume with processes of care, mortality, morbidity, and the Society of Thoracic Surgeons composite quality score. J Thorac Cardiovasc Surg. 2010;139:273–82.
417. Welke KF, Peterson ED, Vaughan-Sarrazin MS, et al. Comparison of cardiac surgery volumes and mortality rates between the Society of Thoracic Surgeons and Medicare databases from 1993 through 2001. Ann Thorac Surg. 2007;84:1538–46.
418. Chakravarty T, Buch MH, Naik H, et al. Predictive accuracy of SYNTAX score for predicting long-term outcomes of unprotected left main coronary artery revascularization. Am J Cardiol. 2011;107:360–6.
419. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main coronary artery disease. Long-term CASS experience. Circulation. 1995;91:2325–34.
420. Chaitman BR, Fisher LD, Bourassa MG, et al. Effect of coronary bypass surgery on survival patterns in subsets of patients with left main coronary artery disease. Report of the Collaborative Study in Coronary Artery Surgery (CASS). Am J Cardiol. 1981;48:765–77.
421. Dzavik V, Ghali WA, Norris C, et al. Long-term survival in 11,661 patients with multivessel coronary artery disease in the era of stenting: a report from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) Investigators. Am Heart J. 2001;142:119–26.
422. Takaro T, Hultgren HN, Lipton MJ, et al. The VA Cooperative Randomized Study of Surgery for Coronary Arterial Occlusive Disease, II: subgroup with significant left main lesions. Circulation. 1976;54:III107–17.
423. Takaro T, Peduzzi P, Detre KM, et al. Survival in subgroups of patients with left main coronary artery disease. Veterans Administration Cooperative Study of Surgery for Coronary Arterial Occlusive Disease. Circulation. 1982;66:14–22.
424. Taylor HA, Deumite NJ, Chaitman BR, et al. Asymptomatic left main coronary artery disease in the Coronary Artery Surgery Study (CASS) registry. Circulation. 1989;79:1171–9.
425. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet. 1994;344:563–70.
426. Buszman PE, Kiesz SR, Bochenek A, et al. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. J Am Coll Cardiol. 2008;51:538–45.
427. Capodanno D, Caggegi A, Miano M, et al. Global risk classification and clinical SYNTAX (synergy between percutaneous coronary intervention with TAXUS and cardiac surgery) score in patients undergoing percutaneous or surgical left main revascularization. JACC Cardiovasc Interv. 2011;4:287–97.
428. Hannan EL, Wu C, Walford G, et al. Drug-eluting stents vs. coronary-artery bypass grafting in multivessel coronary disease. N Engl J Med. 2008;358:331–41.
429. Ellis SG, Tamai H, Nobuyoshi M, et al. Contemporary percutaneous treatment of unprotected left main coronary stenoses: initial results from a multicenter registry analysis 1994–1996. Circulation. 1997;96:3867–72.
430. Biondi-Zoccai GGL, Lotrionte M, Moretti C, et al. A collaborative systematic review and meta-analysis on 1278 patients undergoing percutaneous drug-eluting stenting for unprotected left main coronary artery disease. Am Heart J. 2008;155:274–83.
431. Boudriot E, Thiele H, Walther T, et al. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. J Am Coll Cardiol. 2011;57:538–45.
432. Brener SJ, Galla JM, Bryant R, et al. Comparison of percutaneous versus surgical revascularization of severe unprotected left main coronary stenosis in matched patients. Am J Cardiol. 2008;101:169–72.
433. Chieffo A, Morici N, Maisano F, et al. Percutaneous treatment with drug-eluting stent implantation versus bypass surgery for unprotected left main stenosis: a single-center experience. Circulation. 2006;113:2542–7.
434. Chieffo A, Magni V, Latib A, et al. 5-year outcomes following percutaneous coronary intervention with drug-eluting stent implantation versus coronary artery bypass graft for unprotected left main coronary artery lesions the Milan experience. JACC Cardiovasc Interv. 2010;3:595–601.
435. Lee MS, Kapoor N, Jamal F, et al. Comparison of coronary artery bypass surgery with percutaneous coronary intervention with drug-eluting stents for unprotected left main coronary artery disease. J Am Coll Cardiol. 2006;47:864–70.
436. Mäkikallio TH, Niemelä M, Kervinen K, et al. Coronary angioplasty in drug eluting stent era for the treatment of unprotected left main stenosis compared to coronary artery bypass grafting. Ann Med. 2008;40:437–43.
437. Naik H, White AJ, Chakravarty T, et al. A meta-analysis of 3,773 patients treated with percutaneous coronary intervention or surgery for unprotected left main coronary artery stenosis. JACC Cardiovasc Interv. 2009;2:739–47.
438. Palmerini T, Marzocchi A, Marrozzini C, et al. Comparison between coronary angioplasty and coronary artery bypass surgery for the treatment of unprotected left main coronary artery stenosis (the Bologna Registry). Am J Cardiol. 2006;98:54–9.
439. Park D-W, Seung KB, Kim Y-H, et al. Long-term safety and efficacy of stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: 5-year results from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry. J Am Coll Cardiol. 2010;56:117–24.
440. Rodés-Cabau J, Deblois J, Bertrand OF, et al. Nonrandomized comparison of coronary artery bypass surgery and percutaneous coronary intervention for the treatment of unprotected left main coronary artery disease in octogenarians. Circulation. 2008;118:2374–81.
441. Sanmartín M, Baz JA, Claro R, et al. Comparison of drug-eluting stents versus surgery for unprotected left main coronary artery disease. Am J Cardiol. 2007;100:970–3.
442. Kappetein AP, Feldman TE, Mack MJ, et al. Comparison of coronary bypass surgery with drug-eluting stenting for the treatment of left main and/or three-vessel disease: 3-year follow-up of the SYNTAX trial. Eur Heart J. 2011;32:2125–34.
443. Seung KB, Park D-W, Kim Y-H, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. N Engl J Med. 2008;358:1781–92.

444. White AJ, Kedia G, Mirocha JM, et al. Comparison of coronary artery bypass surgery and percutaneous drug-eluting stent implantation for treatment of left main coronary artery stenosis. JACC Cardiovasc Interv. 2008;1:236–45.
445. Montalescot G, Brieger D, Eagle KA, et al. Unprotected left main revascularization in patients with acute coronary syndromes. Eur Heart J. 2009;30:2308–17.
446. Lee MS, Tseng C-H, Barker CM, et al. Outcome after surgery and percutaneous intervention for cardiogenic shock and left main disease. Ann Thorac Surg. 2008;86:29–34.
447. Lee MS, Bokhoor P, Park S-J, et al. Unprotected left main coronary disease and ST-segment elevation myocardial infarction: a contemporary review and argument for percutaneous coronary intervention. JACC Cardiovasc Interv. 2010;3:791–5.
448. Park S-J, Kim Y-H, Park D-W, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med. 2011;364:1718–27.
449. Jones RH, Kesler K, Phillips HR, et al. Long-term survival benefits of coronary artery bypass grafting and percutaneous transluminal angioplasty in patients with coronary artery disease. J Thorac Cardiovasc Surg. 1996;111:1013–25.
450. Myers WO, Schaff HV, Gersh BJ, et al. Improved survival of surgically treated patients with triple vessel coronary artery disease and severe angina pectoris: a report from the Coronary Artery Surgery Study (CASS) registry. J Thorac Cardiovasc Surg. 1989;97:487–95.
451. Smith PK, Califf RM, Tuttle RH, et al. Selection of surgical or percutaneous coronary intervention provides differential longevity benefit. Ann Thorac Surg. 2006;82:1420–8.
452. Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med. 1988;319:332–7.
453. Brener SJ, Lytle BW, Casserly IP, et al. Propensity analysis of long-term survival after surgical or percutaneous revascularization in patients with multivessel coronary artery disease and high-risk features. Circulation. 2004;109:2290–5.
454. Hannan EL, Racz MJ, Walford G, et al. Long-term outcomes of coronary-artery bypass grafting versus stent implantation. N Engl J Med. 2005;352:2174–83.
455. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007;356:1503–16.
456. Di Carli MF, Maddahi J, Rokhsar S, et al. Long-term survival of patients with coronary artery disease and left ventricular dysfunction: implications for the role of myocardial viability assessment in management decisions. J Thorac Cardiovasc Surg. 1998;116:997–1004.
457. Hachamovitch R, Hayes SW, Friedman JD, et al. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation. 2003;107:2900–7.
458. Sorajja P, Chareonthaitawee P, Rajagopalan N, et al. Improved survival in asymptomatic diabetic patients with high-risk SPECT imaging treated with coronary artery bypass grafting. Circulation. 2005;112:I311–6.
459. Davies RF, Goldberg AD, Forman S, et al. Asymptomatic Cardiac Ischemia Pilot (ACIP) study two-year follow-up: outcomes of patients randomized to initial strategies of medical therapy versus revascularization. Circulation. 1997;95:2037–43.
460. Cameron A, Davis KB, Green G, et al. Coronary bypass surgery with internal-thoracic-artery grafts-effects on survival over a 15-year period. N Engl J Med. 1996;334:216–9.
461. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. N Engl J Med. 1986;314:1–6.
462. Shaw LJ, Berman DS, Maron DJ, et al. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. Circulation. 2008;117:1283–91.
463. Pijls NH, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. N Engl J Med. 1996;334:1703–8.
464. Tonino PA, De Bruyne B, Pijls NHJ, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009;360:213–24.
465. Sawada S, Bapat A, Vaz D, et al. Incremental value of myocardial viability for prediction of long-term prognosis in surgically revascularized patients with left ventricular dysfunction. J Am Coll Cardiol. 2003;42:2099–105.
466. Alderman EL, Fisher LD, Litwin P, et al. Results of coronary artery surgery in patients with poor left ventricular function (CASS). Circulation. 1983;68:785–95.
467. O'Connor CM, Velazquez EJ, Gardner LH, et al. Comparison of coronary artery bypass grafting versus medical therapy on long-term outcome in patients with ischemic cardiomyopathy (a 25-year experience from the Duke Cardiovascular Disease Databank). Am J Cardiol. 2002;90:101–7.
468. Phillips HR, O'Connor CM, Rogers J. Revascularization for heart failure. Am Heart J. 2007;153:65–73.
469. Tarakji KG, Brunken R, McCarthy PM, et al. Myocardial viability testing and the effect of early intervention in patients with advanced left ventricular systolic dysfunction. Circulation. 2006;113:230–7.
470. Tsuyuki RT, Shrive FM, Galbraith PD, et al. Revascularization in patients with heart failure. CMAJ. 2006;175:361–5.
471. Bonow RO, Maurer G, Lee KL, et al. Myocardial viability and survival in ischemic left ventricular dysfunction. N Engl J Med. 2011;364:1617–25.
472. Velazquez EJ, Lee KL, Deja MA, et al. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med. 2011;364:1607–16.
473. Every NR, Fahrenbruch CE, Hallstrom AP, et al. Influence of coronary bypass surgery on subsequent outcome of patients resuscitated from out of hospital cardiac arrest. J Am Coll Cardiol. 1992;19:1435–9.
474. Borger van der Burg AE, Bax JJ, Boersma E, et al. Impact of percutaneous coronary intervention or coronary artery bypass grafting on outcome after nonfatal cardiac arrest outside the hospital. Am J Cardiol. 2003;91:785–9.
475. Kaiser GA, Ghahramani A, Bolooki H, et al. Role of coronary artery surgery in patients surviving unexpected cardiac arrest. Surgery. 1975;78:749–54.
476. Cashin WL, Sanmarco ME, Nessim SA, et al. Accelerated progression of atherosclerosis in coronary vessels with minimal lesions that are bypassed. N Engl J Med. 1984;311:824–8.
477. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: the Bypass Angioplasty Revascularization Investigation (BARI). Circulation. 1997;96:1761–9.
478. BARI Investigaors. The final 10-year follow-up results from the BARI randomized trial. J Am Coll Cardiol. 2007;49:1600–6.
479. Banning AP, Westaby S, Morice M-C, et al. Diabetic and nondiabetic patients with left main and/or 3-vessel coronary artery disease: comparison of outcomes with cardiac surgery and paclitaxel-eluting stents. J Am Coll Cardiol. 2010;55:1067–75.
480. Hoffman SN, TenBrook JA, Wolf MP, et al. A meta-analysis of randomized controlled trials comparing coronary artery bypass graft with percutaneous transluminal coronary angioplasty: one- to eight-year outcomes. J Am Coll Cardiol. 2003;41:1293–304.
481. Hueb W, Lopes NH, Gersh BJ, et al. Five-year follow-up of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation. 2007;115:1082–9.
482. Malenka DJ, Leavitt BJ, Hearne MJ, et al. Comparing long-term survival of patients with multivessel coronary disease after CABG or PCI: analysis of BARI-like patients in northern New England. Circulation. 2005;112:I371–6.
483. Niles NW, McGrath PD, Malenka D, et al. Survival of patients with diabetes and multivessel coronary artery disease after surgical or percutaneous coronary revascularization: results of a large regional prospective study. Northern New England Cardiovascular Disease Study Group. J Am Coll Cardiol. 2001;37:1008–15.
484. Weintraub WS, Stein B, Kosinski A, et al. Outcome of coronary bypass surgery versus coronary angioplasty in diabetic patients with multivessel coronary artery disease. J Am Coll Cardiol. 1998;31:10–9.
485. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. US Carvedilol Heart Failure Study Group. N Engl J Med. 1996;334:1349–55.
486. Poole-Wilson PA, Swedberg K, Cleland JGF, et al. Comparison of carvedilol and metoprolol on clinical outcomes in patients with chronic heart failure in the Carvedilol Or Metoprolol European Trial (COMET): randomised controlled trial. Lancet. 2003;362:7–13.
487. Domanski MJ, Krause-Steinrauf H, Massie BM, et al. A comparative analysis of the results from 4 trials of beta-blocker therapy for heart failure: BEST, CIBIS-II, MERIT-HF, and COPERNICUS. J Card Fail. 2003;9:354–63.
488. Freemantle N, Cleland J, Young P, et al. Beta blockade after myocardial infarction: systematic review and meta regression analysis. BMJ. 1999;318:1730–7.
489. De Peuter OR, Lussana F, Peters RJG, et al. A systematic review of selective and non-selective beta blockers for prevention of vascular events in patients with acute coronary syndrome or heart failure. Neth J Med. 2009;67:284–94.
490. De Lima LG, Soares BGO, Saconato H, et al. Beta-blockers for preventing stroke recurrence. Cochrane Database Syst Rev. 2013:5:CD007890.

KEY WORDS: AHA Scientific Statements ■ adrenergic beta-antagonists ■ anesthesia and analgesia ■ diagnostic techniques, cardiovascular ■ monitoring, intraoperative ■ perioperative care ■ troponin ■ platelet aggregation inhibitors ■ referral and consultation

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery (March 2013)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Lee A. Fleisher (Chair)	University of Pennsylvania Health System Department of Anesthesiology and Critical Care—Chair	None	None	None	None	None	None	None
Kirsten E. Fleischmann (Vice Chair)	UCSF School of Medicine, Division of Cardiology—Professor of Clinical Medicine	None	None	None	None	None	None	None
Andrew D. Auerbach	UCSF Division of Hospital Medicine—Professor of Medicine in Residence	None	None	None	None	None	None	None
Susan A. Barnason	University of Nebraska Medical Center, College of Nursing—Professor and Director of the Doctor of Nursing Practice Program	None	None	None	None	None	None	None
Joshua A. Beckman	Harvard Medical School—Associate Professor of Medicine; Brigham and Women's Hospital Cardiovascular Fellowship Program—Director	• AstraZeneca • Bristol-Myers Squibb† • Novartis† • Merck	None	None	None	• Boston Scientific	None	6.1, 6.1.1, 6.2.1, 6.2.2, 6.2.4, 6.2.5, 6.2.6, 6.3, 6.4, 7.3, 7.4, and 7.7
Biykem Bozkurt	Winters Center for Heart Failure Research, Baylor College of Medicine—The Mary and Gordon Cain Chair, Professor of Medicine, and Director; Michael E. DeBakey VA Medical Center Cardiology Section—Chief	None	None	None	• Forest Pharmaceuticals (PI)†	• Novartis	None	6.2.1, 6.2.2, and 6.2.5
Victor G. Davila-Roman	Washington University School of Medicine Anesthesiology and Radiology Cardio-vascular Division—Professor of Medicine	• Valve Xchange† • Boston Scientific† • St. Jude Medical†	None	None	None	None	None	2.4, 2.4.1, 2.4.2, 2.4.3, 5.7, 6.1, 6.1.1, 6.3, 6.4, 7.4, and 7.7
Marie D. Gerhard-Herman	Harvard Medical School—Associate Professor	None	None	None	None	None	None	None
Thomas A. Holly	Northwestern University Feinberg School of Medicine—Medical Director, Nuclear Cardiology; Associate Professor of Medicine and Radiology; Program Director, Cardiovascular Disease Fellowship	None	None	None	None	Astellas‡	None	5.5.1 and 5.7
Garvan C. Kane	Mayo Clinic, Division of Cardiovascular Diseases—Codirector and Echocardiography Laboratory Consultant; Associate Professor of Medicine	None	None	None	None	None	None	None

(Continued)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Joseph E. Marine	Johns Hopkins University School of Medicine—Associate Professor of Medicine; Associate Director of Electrophysiology; Associate Division Chief of Cardiology	None	None	None	None	None	None	None
M. Timothy Nelson	University of New Mexico—Professor; Program Director and Vice Chair of Education, Department of Surgery; Executive Medical Director, Adult Inpatient Services		None	None	None	None	None	None
Crystal C. Spencer	Spencer Meador Johnson—Lawyer	None	None	None	None	None	None	None
Annemarie Thompson	Duke University School of Medicine—Professor of Anesthesiology	None	None	None	None	None	None	None
Henry H. Ting	Mayo Clinic—Professor of Medicine; Mayo Clinic Quality Academy—Director; Mayo School for Continuous Professional Development—Associate Dean	None	None	None	None	None	None	None
Barry F. Uretsky	University of Arkansas for Medical Sciences—Clinical Professor of Medicine, Director of Interventional Cardiology	None	None	None	None	• St. Jude Medical†§	None	None
Duminda N. Wijeysundera (ERC Chair)	Li Ka Shing Knowledge Institute of St. Michael's Hospital—Scientist; Toronto General Hospital—Staff, Department of Anesthesia and Pain Management; University of Toronto—Assistant Professor, Department of Anesthesia and Institute of Health Policy Management and Evaluation; Institute for Clinical Evaluative Sciences—Adjunct Scientist	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$10 000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACC/AHA, a person has a *relevant* relationship IF: a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) the *person or a member of the person's household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply.

†Significant relationship.

‡No financial benefit.

§Dr. Uretsky's relationship with St. Jude Medical began just before balloting of the recommendations and was not relevant during the writing stage.

ACC indicates American College of Cardiology; AHA, American Heart Association; ERC, Evidence Review Committee; PI, principal investigator; UCSF, University of California, San Francisco; and VA, Veterans Affairs.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Relevant)—2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery (June 2014)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Kim Eagle	Official Reviewer—AHA	University of Michigan Health System—Albion Walter Hewlett Professor of Internal Medicine	None	None	None	• GORE • Medtronic	None	None
Dipti Itchhaporia	Official Reviewer—ACC Board of Trustees	Hoag Memorial Hospital Presbyterian—Robert and Georgia Roth Chair for Excellence in Cardiac Care; Director of Disease Management	None	None	None	None	None	None
Mary Lough	Official Reviewer—AHA	Stanford Hospital and Clinics—Critical Care Clinical Nurse Specialist	None	None	None	None	None	None
G. B. John Mancini	Official Reviewer—ACC Board of Governors	Vancouver Hospital Research Pavilion—Professor of Medicine	• Merck • Pfizer • Servier	None	None	• Merck*	• Miraculins*	None
Frank W. Sellke	Official Reviewer—ACC/AHA Task Force on Practice Guidelines	Brown Medical School, Rhode Island Hospital—Professor; Chief of Cardiothoracic Surgery	None	None	None	None	• CSL Behring • The Medicines Company	None
Michael Baker	Organizational Reviewer—ASE	Vanderbilt University—Assistant Professor of Medicine	None	None	None	None	• Medtronic†	None
Michael England	Organizational Reviewer—ASA	Tufts University School of Medicine—Division Chief, Cardiac Anesthesiology; Assistant Professor	None	• Hospira	None	None	None	None
Leonard Feldman	Organizational Reviewer—SHM	Johns Hopkins School of Medicine–Director, Medicine-Pediatrics Urban Health Residency Program; Assistant Professor of Pediatrics; Assistant Professor of Medicine	None	None	None	None	None	• Defendant, pulmonary embolism, 2013 • Defendant, aortic dissection, 2013 • Defendant, stroke, 2013 • Defendant, sudden cardiac death, 2013
Jason Kovacic	Organizational Reviewer—SCAI	Mount Sinai School of Medicine—Assistant Professor of Medicine	• AstraZeneca*	• AstraZeneca	None	None	None	None
Martin London	Organizational Reviewer—SCA	University of California, San Francisco Medical Center—Professor of Clinical Anesthesia	None	None	None	None	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Rupa Mehta Sanghani	Organizational Reviewer—ASNC	University of Chicago Medicine—Director, Cardiac Rehabilitation; Assistant Professor of Medicine	• Astellas	• Astellas	None	None	None	None
Reena Pande	Organizational Reviewer—SVM	Brigham and Women's Hospital, Prevention Brigham and Women's Hospital—Associate Physician; Harvard Medical School, Professor	None	None	None	None	None	None
Jeanne Poole	Organizational Reviewer—HRS	University of Washington—Professor of Medicine, Division of Cardiology	• Biotronik • Boston Scientific* • Medtronic • St. Jude Medical	None	None	None	• Boston Scientific • Medtronic	None
Russell Postier	Organizational Reviewer—ACS	University of Oklahoma Health Sciences Center—John A. Schilling Professor and Chairman, Department of Surgery	None	None	None	None	None	None
M. Obadah N. Al-Chekakie	Content Reviewer—ACC Board of Governors	Cheyenne Regional Medical Group—Physician	None	None	None	None	None	None
Jeffrey L. Anderson	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Intermountain Medical Center—Associate Chief of Cardiology	• Sanofi-aventis • The Medicines Company	None	None	None	None	None
H. Vernon Anderson	Content Reviewer—ACC Interventional Section Leadership Council	University of Texas Cardiology Division—Professor of Medicine	None	None	None	None	• MedPlace Medical Devices (DSMB)	None
Hugh Calkins	Content Reviewer	Johns Hopkins Hospital—Professor of Medicine; Director of Electrophysiology	None	None	None	• St. Jude Medical*	None	None
Steven Cohn	Content Reviewer	University of Miami—Professor of Clinical Medicine; University of Miami Hospital— Director, Medical Consultation Service; University Health Preoperative Assessment Center—Medical Director	None	None	• AstraZeneca* • Bristol-Myers Squibb* • GlaxoSmithKline* • Merck* • Pfizer*	None	None	• Defendant, venous thromboemboli pulmonary embolism, 2013 • Defendant, preoperative evaluation, 2013

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
George Crossley	Content Reviewer—ACC Electrophysiology Section Leadership Council	St. Thomas Heart—Medical Director, Cardiac Services	• Boston Scientific • Medtronic*	• Medtronic* • Sanofi-aventis	None	None	None	• Defendant, pacemaker complication, 2012 • Defendant, EP procedure complication, 2013
P.J. Devereaux	Content Reviewer	McMaster University—Associate Professor, Departments of Clinical Epidemiology and Biostatistics; Juravinski Hospital and Cancer Centre—Head of Cardiology and the Perioperative Cardiovascular Service	None	None	None	• Abbott Diagnostics* • Bayer* • Boehringer Ingelheim* • Roche Diagnostics* • Stryker*	• Canadian Perioperative Guideline Chair	None
Richard Lange	Content Reviewer	University of Texas Health Science Center at San Antonio—Professor of Medicine	None	None	None	None	None	None
Maria Lantin-Hermoso	Content Reviewer—ACC Congenital and Pediatric Cardiology Section Leadership Council	Baylor College of Medicine—Associate Professor, Department of Pediatrics, Section of Cardiology; Texas Children's Hospital—Attending Physician	None	None	None	None	None	None
Srinivas Murali	Content Reviewer—ACC Board of Governors	Temple University School of Medicine—Professor of Medicine; Director, Division of Cardiovascular Medicine; Cardiovascular Institute Medical—Medical director	• Actelion • Bayer • Gilead • Lung Biotechnology	• Actelion	None	• Cardiokinetics • CVRx • Gilead • Ikaria • Medtronic • St. Jude Medical	None	None
E. Magnus Ohman	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Duke University Medical Center—Professor of Medicine; Director, Program for Advanced Coronary Disease	• Abiomed* • AstraZeneca • Daiichi-Sankyo* • Gilead Sciences • Janssen Pharmaceuticals* • Pozen • Sanofi-aventis* • The Medicines Company	None	None	• Eli Lilly* • Gilead Sciences*	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Gurusher Panjrath	Content Reviewer—ACC Heart Failure and Transplant Section Leadership Council	George Washington Heart and Vascular Institute—Assistant Professor of Medicine; Director, Heart Failure and Mechanical Support Program	None	None	None	None	None	None
Susan J. Pressler	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	University of Michigan School of Nursing—Professor	None	None	None	None	• Pfizer†	None
Pasala Ravichandran	Content Reviewer—ACC Surgeons' Council	Oregon Health and Science University—Associate Professor	None	None	None	None	None	None
Ezra Amsterdam	Content Reviewer	University of California Davis Medical Center Division of Cardiology—Professor	None	None	None	None	None	None
John Erwin	Content Reviewer	Scott and White Hospital and Clinic—Senior Staff Cardiologist, Associate Professor of Medicine	None	None	None	• Eli Lilly (PI)*	None	None
Samuel Gidding	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Nemours/Alfred I. DuPont Hospital for Children—Chief, Division of Pediatric Cardiology	None	None	None	• GlaxoSmithKline*	None	None
Robert Hendel	Content Reviewer	University of Miami School of Medicine—Director Cardiac Imaging and Outpatient Services	• Adenosine Therapeutics • Astellas • Bayer	None	None	None	None	None
Glenn Levine	Content Reviewer	Baylor College of Medicine—Associate Professor of Medicine	None	None	None	None	None	None
Karen Mauck	Content Reviewer	Mayo Clinic Minnesota—Associate Professor of Medicine	None	None	None	None	None	None
Win-Kuang Shen	Content Reviewer—ACC/AHA Task Force on Practice Guidelines	Mayo Clinic Arizona—Professor of Medicine	None	None	None	None	None	None

(Continued)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Ralph Verdino	Content Reviewer	Hospital of the University of Pennsylvania—Associate Professor of Medicine; Director, Cardiology Electrophysiology Fellowship Program	• Biotronik • Medtronic • St. Jude Medical*	None	None	None	• LifeWatch*	None
L. Samuel Wann	Content Reviewer	Columbia St. Mary's Cardiovascular Physicians—Clinical Cardiologist	None	None	None	None	None	None
Clyde W. Yancy	Content Reviewer	Northwestern University, Feinberg School of Medicine—Magerstadt Professor of Medicine; Chief, Division of Cardiology	None	None	None	None	None	None

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review and determined to be relevant to this document. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$10 000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review.

According to the ACC/AHA, a person has a *relevant* relationship IF: a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document*; or b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the *document*; or c) the *person or a member of the person's household* has a reasonable potential for financial, professional, or other personal gain or loss as a result of the issues/content addressed in the *document*.

*Significant relationship.

†No financial benefit.

ACC indicates American College of Cardiology; ACS, American College of Surgeons; AHA, American Heart Association; ASA, American Society of Anesthesiologists; ASE, American Society of Echocardiography; ASNC, American Society of Nuclear Cardiology; DSMB, data safety monitoring board; EP, electrophysiology; HRS, Heart Rhythm Society; PI, principal investigator; SCA, Society of Cardiovascular Anesthesiologists; SCAI, Society for Cardiovascular Angiography and Interventions; SHM, Society of Hospital Medicine; and SVM, Society for Vascular Medicine.

Appendix 3. Related Recommendations From Other CPGs

Table A. Left Main CAD Revascularization Recommendations From the 2011 CABG and PCI CPGs

Anatomic Setting	COR	LOE	References
UPLM or complex CAD			
CABG and PCI	I—Heart Team approach recommended	C	409–411
CABG and PCI	IIa—Calculation of the STS and SYNTAX scores	B	296, 409, 412–418
UPLM*			
CABG	I	B	419–425
PCI	IIa—For SIHD when both of the following are present: 2. Anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of good long-term outcome (eg, a low SYNTAX score of ≤22, ostial, or trunk left main CAD) 3. Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (eg, STS-predicted risk of operative mortality ≥5%)	B	412, 414, 418, 426–444
	IIa—For UA/NSTEMI if not a CABG candidate	B	412, 432–435, 440, 441, 443–445
	IIa—For STEMI when distal coronary flow is TIMI flow grade <3 and PCI can be performed more rapidly and safely than CABG	C	429, 446, 447
	IIb—For SIHD when *both* of the following are present: 2. Anatomic conditions associated with a low-to-intermediate risk of PCI procedural complications and intermediate-to-high likelihood of good long-term outcome (eg, low–intermediate SYNTAX score of <33, bifurcation left main CAD) 3. Clinical characteristics that predict an increased risk of adverse surgical outcomes (eg, moderate–severe COPD, disability from prior stroke, or prior cardiac surgery; STS-predicted risk of operative mortality >2%)	B	412, 414, 418, 426–444, 448
	III: Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	B	412, 414, 418–425, 427, 428
3-vessel disease with or without proximal LAD artery disease*			
CABG	I	B	421, 425, 449–452
	IIa—It is reasonable to choose CABG over PCI in patients with complex 3-vessel CAD (eg, SYNTAX >22) who are good candidates for CABG	B	428, 443, 451, 453, 454
PCI	IIb—Of uncertain benefit	B	421, 442, 449, 451, 455
2-vessel disease with proximal LAD artery disease*			
CABG	I	B	421, 425, 449–452
PCI	IIb—Of uncertain benefit	B	421, 449, 451, 455
2-vessel disease without proximal LAD artery disease*			
CABG	IIa—With extensive ischemia	B	456–459
	IIb—Of uncertain benefit without extensive ischemia	C	451
PCI	IIb—Of uncertain benefit	B	421, 449, 451, 455
1-vessel proximal LAD artery disease			
CABG	IIa—With LIMA for long-term benefit	B	425, 451, 460, 461
PCI	IIb—Of uncertain benefit	B	421, 449, 451, 455
1-vessel disease without proximal LAD artery involvement			
CABG	III: Harm	B	425, 449 ,456, 457, 462–465
PCI	III: Harm	B	425, 449, 456, 457, 462–465

(Continued)

Table A. Continued

Anatomic Setting	COR	LOE	References
LV dysfunction			
CABG	IIa—EF 35% to 50%	B	425, 466–470
CABG	IIb—EF <35% without significant left main CAD	B	425, 466–472
PCI	Insufficient data		N/A
Survivors of sudden cardiac death with presumed ischemia-mediated VT			
CABG	I	B	473–475
PCI	I	C	474
No anatomic or physiological criteria for revascularization			
CABG	III: Harm	B	425, 449, 456, 457, 462–465, 476
PCI	III: Harm	B	425, 449, 456, 457, 462–465, 476

*In patients with multivessel disease who also have diabetes mellitus, it is reasonable to choose CABG (with LIMA) over PCI[458,477–484] (*Class IIa; LOE: B*).

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COR, Class of Recommendation; CPG, clinical practice guideline; EF, ejection fraction; LAD, left anterior descending; LIMA, left internal mammary artery; LOE, Level of Evidence; LV, left ventricular; N/A, not applicable; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease; STEMI, ST-elevation myocardial infarction; STS, Society of Thoracic Surgeons; SYNTAX, Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery; TIMI, Thrombolysis In Myocardial Infarction; UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction; UPLM, unprotected left main disease; and VT, ventricular tachycardia.

Reproduced from Levine et al[26] and Hillis et al.[25]

Table B. GDMT Recommendations for Beta Blockers From 2011 Secondary Prevention CPG

Beta Blockers	**Class I** 1. Beta-blocker therapy should be used in all patients with LV systolic dysfunction (EF ≤40%) with HF or prior MI, unless contraindicated. (Use should be limited to carvedilol, metoprolol succinate, or bisoprolol, which have been shown to reduce mortality.).[485–487] ***(Level of Evidence: A)*** 2. Beta-blocker therapy should be started and continued for 3 years in all patients with normal LV function who have had MI or ACS.[488–490] ***(Level of Evidence: B)*** **Class IIa** 1. It is reasonable to continue beta blockers >3 years as chronic therapy in all patients with normal LV function who have had MI or ACS.[488–490] ***(Level of Evidence: B)*** 2. It is reasonable to give beta-blocker therapy in patients with LV systolic dysfunction (EF ≤40%) without HF or prior MI. ***(Level of Evidence: C)***

ACS indicates acute coronary syndrome; CPG, clinical practice guideline; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; LV, left ventricular; and MI, myocardial infarction.

Reproduced from Smith Jr et al.[249]

Appendix 4. Abbreviations

ACE = angiotensin-converting enzyme
ACHD = adult congenital heart disease
AF = atrial fibrillation
AR = aortic regurgitation
ARB = angiotensin-receptor blocker
AS = aortic stenosis
AVR = aortic valve replacement
BMS = bare-metal stent
CABG = coronary artery bypass graft
CAD = coronary artery disease
CI = confidence interval
CIED = cardiovascular implantable electronic device
CPG = clinical practice guideline
DAPT = dual antiplatelet therapy
DES = drug-eluting stent
DSE = dobutamine stress echocardiogram
ECG = electrocardiogram
EF = ejection fraction
EMI = electromagnetic interference
ERC = Evidence Review Committee
GDMT = guideline-directed medical therapy
GWC = guideline writing committee
HF = heart failure
ICD = implantable cardioverter-defibrillator
LV = left ventricular
LVEF = left ventricular ejection fraction
MACE = major adverse cardiac event
MET = metabolic equivalent
MI = myocardial infarction
MPI = myocardial perfusion imaging
MR = mitral regurgitation
OR = odds ratio
PCI = percutaneous coronary intervention
RCT = randomized controlled trial
RV = right ventricular
TAVR = transcatheter aortic valve replacement
TEE = transesophageal echocardiogram

Circulation

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Lee A. Fleisher, Kirsten E. Fleischmann, Andrew D. Auerbach, Susan A. Barnason, Joshua A. Beckman, Biykem Bozkurt, Victor G. Davila-Roman, Marie D. Gerhard-Herman, Thomas A. Holly, Garvan C. Kane, Joseph E. Marine, M. Timothy Nelson, Crystal C. Spencer, Annemarie Thompson, Henry H. Ting, Barry F. Uretsky and Duminda N. Wijeysundera

Circulation. 2014;130:e278-e333; originally published online August 1, 2014;
doi: 10.1161/CIR.0000000000000106
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Author Relationships With Industry and Other Entities (Comprehensive)—2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery **(March 2013)**

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership /Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Lee A. Fleisher (*Chair)*	University of Pennsylvania Health System Department of Anesthesiology and Critical Care—Chair	None	None	None	• Johns Hopkins Medical Institutions (DSMB)† • Foundation For Anesthesia Education and Research • NIH*	• AAAHC Institute for Quality Improvement† • Accreditation Association for Ambulatory Care Quality Institute† • Association of University Anesthesiologists† • Foundation for Anesthesia Education and Research† • National Quality Forum†	None
Kirsten E. Fleischmann (*Vice Chair)*	UCSF School of Medicine, Division of Cardiology—Professor of Clinical Medicine	None	None	None	• NHLBI* • The Bluefield Project to Cure Frontotemporal Dementia	• Massachusetts Medical Society	None
Andrew D. Auerbach	UCSF Division of Hospital Medicine—Professor of Medicine in Residence	None	None	None	None	• AHRQ Choice Grant • American Board of Internal Medicine • Journal of Hospital Medicine (Editor-in-Chief)* • NIH/NHLBI K24 grant*	• Plaintiff, hospitalist failure to recognize and treat sepsis, 2012
Susan A. Barnason	University of Nebraska Medical Center, College of Nursing—Professor and Director of the Doctor of Nursing Practice Program	None	None	None	None	None	None

Joshua A. Beckman	Harvard Medical School—Associate Professor of Medicine; Brigham and Women's Hospital Cardiovascular Fellowship Program—Director	• AstraZeneca • Bristol-Myers Squibb* • Ferring Pharmaceuticals • Novartis* • Merck	None	None	None	• Boston Scientific • Vascular Interventional Advances*	None
Biykem Bozkurt	Winters Center for Heart Failure Research, Baylor College of Medicine—The Mary and Gordon Cain Chair, Professor of Medicine, and Director; Michael E. DeBakey VA Med Center Cardiology Section—Chief	None	None	None	• Forest Pharmaceuticals (PI)* • NIH (PI and CI)*	• NIH (CI)* • Novartis	None
Victor G. Davila-Roman	Washington University School of Medicine Anesthesiology and Radiology Cardiovascular Division—Professor of Medicine	• Boston Scientific* • St. Jude Medical* • ValveXchange*	None	None	• NIH*	• Cardiovascular Imaging and Clinical Research Core Laboratory†	None
Marie D. Gerhard-Herman	Harvard Medical School—Associate Professor	None	None	None	• Progeria Research Foundation	• American Board of Internal Medicine	None
Thomas A. Holly	Northwestern University Feinberg School of Medicine—Medical Director, Nuclear Cardiology; Associate Professor of Medicine and Radiology; Program Director, Cardiovascular Disease Fellowship	None	None	None	None	• Astellas†	None
Garvan C. Kane	Mayo Clinic, Division of Cardiovascular Diseases—Codirector and Echocardiography Laboratory Consultant; Associate Professor of Medicine	None	None	None	None	None	None
Joseph E. Marine	Johns Hopkins University School of Medicine—Associate Professor of Medicine; Associate	None	None	None	None	None	None

	Director of Electrophysiology; Associate Division Chief of Cardiology						
M. Timothy Nelson	University of New Mexico—Professor; Program Director and Vice Chair of Education, Department of Surgery; Executive Medical Director, Adult Inpatient Services	None	None	None	None	None	None
Crystal C. Spencer	Spencer Meador Johnson—Lawyer	None	None	None	None	• AHA† • Dermatologic Surgery Associates* • Hospital Corporation of America*	None
Annemarie Thompson	Duke University School of Medicine—Professor of Anesthesiology	None	None	None	None	None	None
Henry H. Ting	Mayo Clinic—Professor of Medicine; Mayo Clinic Quality Academy—Director; Mayo School for Continuous Professional Development—Associate Dean	None	None	None	None	None	None
Barry F. Uretsky	University of Arkansas for Medical Sciences—Clinical Professor of Medicine, Director of Interventional Cardiology	None	None	None	• St. Jude Medical*‡	None	None
Duminda N. Wijeysundera (*ERC Chair)*	Li Ka Shing Knowledge Institute of St. Michael's Hospital—Scientist; Toronto General Hospital—Staff, Department of Anesthesia and Pain Management; University of Toronto—Assistant Professor, Department of Anesthesia and Institute of Health Policy Management and Evaluation; Institute for Clinical Evaluative Sciences—Adjunct Scientist	None	None	None	• Anesthesia Patient Safety Foundation† • Canadian Institutes of Health Research (DSMB)† • Canadian Institutes of Health Research* • Heart and Stroke Foundation of Canada* • Ministry of Health and Long-Term Care of Ontario*	None	None

This table represents all relationships of committee members with industry and other entities that were reported by authors, including those not deemed to be relevant to this document, at the time this document was under development. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$10,000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Please refer to http://www.cardiosource.org/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/Relationships-With-Industry-Policy.aspx for definitions of disclosure categories or additional information about the ACC/AHA Disclosure Policy for Writing Committees.

*Significant relationship.
†No financial benefit.
‡Dr. Uretsky's relationship with St. Jude Medical began just before balloting of the recommendations and was not relevant during the writing stage.

AAAHC indicates Accreditation Association for Ambulatory Health Care; ACC, American College of Cardiology; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; CI, coinvestigator; DSMB, data safety monitoring board; NIH, National Institutes of Health; NHLBI, National Heart, Lung, and Blood Institute; PI, primary investigator; and VA, Veterans Affairs.

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery

Data Supplement

(Section numbers correspond to the full-text guideline.)

Data Supplement 1. Coronary Artery Disease (Section 2.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Wijeysundera DN, et al., 2012 (1) 22893606	To evaluate the outcomes of pts who underwent elective intermediate- to high-risk noncardiac surgery after stent implantation	Cohort study, secondary analysis of prospective clinical registry (2003–2009)	8,116 stent pts, who had stents within 10 y prior to noncardiac surgery	N/A	N/A	Surgeries included: AAA repair, carotid endarterectomy, peripheral bypass, total hip or knee replacement, large bowel resection, partial liver resection, Whipple, pneumonectomy, pulmonary lobectomy, gastrectomy, esophagectomy, total abdominal hysterectomy, radical prostatectomy, nephrectomy, and cystectomy	N/A	N/A	Stent pts <2 y after stent compared to those pts >2 y after stent at time of noncardiac surgery	Overall mortality for pts who previously had stent was 1.2% (n=100) at 30 d and 5.2% (n=419) at 1 y	N/A	The overall risk of MACE at 30 d was 2.1% (n=170) and at 1 y was 9.8% (n=798). MACE was highest when major elective noncardiac surgery was performed within 45 d after coronary stent.	N/A	Event rates are low, limiting statistical power. Administrative databases may not adequately capture all in-hospital complications.
Mashour GA, et al., 2011 (2) 21478735	Assess the incidence and predicators of periop stroke and its role in mortality in noncardiac, non-neurosurgical surgery	Secondary analysis of ACS NSQIP	523,059 pt data sets (deidentified from NSQIP database)	NSQIP participants from 250 participating U.S. medical centers for 4 y (2005–2008)	N/A	General surgery, orthopedic, urology, otolaryngology, plastics, thoracic, minor vascular, and gynecology cases	Cardiac, major vascular, and neurosurgical cases	N/A	N/A	The incidence of periop stroke was 0.1%	N/A	1. Multivariate analyses indicated MI within 6 mo of surgery and was an independent risk factor for periop stroke. 2. Multivariate analyses indicated HTN (requiring medication) and was an	MI within 6 mo of surgery was an independent risk factor for periop stroke (OR: 13.2; CI: 8.9–19.7; p<0.001). HTN was an independent risk factor for periop stroke (OR: 3.8; CI:	Observational study does not allow for additional data collection for pts exhibiting primary outcome. In addition, the data definitions are clinically relevant, but could not be modified for purposes of

												independent risk factor for periop stroke.	3.1–4.7; p<0.001).	this study.
Healy KO, et al., 2010 (3) [20412467](20412467)	To evaluate the impact of LVEF on periop outcomes and long-term mortality in pts with HF undergoing intermediate- to high-risk surgery	Retrospective chart review	174 pts	Pts diagnosed with HF who underwent intermediate- or high-risk noncardiac surgery from 2001–2004	N/A	Diagnosis with HF; intermediate- or high-risk noncardiac surgery (including PVD surgery, aortic repair, carotid endarterectomy, head & neck, intraperitoneal, noncardiac intrathoracic, orthopedic or prostate surgery)	N/A	N/A	Pts with HF compared by LVEF (>50% normal; 40%–50% mildly reduced; 30%≥40% moderately reduced; <30% severely reduced)	1. 30.5% (n=53) had ≥1 periop events: death (n=14, 8.1%); MI (n=26, 14.9%); HF exacerbation (n=44, 25.3%) 2. Severely reduced LVEF (<30%) independently associated with adverse events.	N/A	N/A	1. Multivariate analyses for LVEF was an independent predictor of periop events including mortality (OR: 4.88; CI: 1.78–14.40).	Small, retrospective chart review from single institution.
Ferket BS, et al., 2011 (4) [21474039](21474039)	To critically appraise guidelines on imaging of asymptomatic CAD	Systematic review	14 guidelines included in the review (published between 2003–2010)	N/A	N/A	1. Used IOM definition of clinical practice guidelines. 2. Contained recommendations on imaging of asymptomatic CAD aimed to prevent first coronary event. 3. Involved healthy persons (adults). 4. Produced on behalf of national or international medical specialty society.	N/A	N/A	N/A	1. 8 of 14 studies recommended against or concluded that there was insufficient evidence to recommend testing of asymptomatic CAD. 2. In 6 of the guidelines testing was indicated for pts with a priori elevated risk level based on absolute CAD risk or multiple risk factors (e.g., Framingham risk score).	N/A	1. 1 guideline recommended CT calcium scoring solely in an intermediate CAD risk population. 2. Guidelines unanimously did not advocate CT calcium scoring for low or high CAD risk pts.	N/A	Only guidelines developed by national or international medical specialty organizations were reviewed
Wijeysundera	To determine	Cohort study	Adult pts	Pts who had	Pts who did	Adults >40 y of	N/A	N/A	N/A	1. Hospital	1. Preop	Effects of	Mortality:	1. Did not

DN, et al., 2010 (5) 20110306	the association of noninvasive cardiac stress testing before elective intermediate- to high-risk noncardiac surgery with survival and hospital stay		from acute care hospitals in Ontario, Canada	noninvasive stress testing before surgical procedure (n=23,060)	not undergo stress testing before surgical procedure (n=247,090)	age, who had elective surgery from 1994–2004. Surgical procedures that had intermediate- to high-risk for periop cardiac complications.				mortality reduced among pts who had stress testing. 2. Hospital LOS reduced for pts who had stress testing prior to surgery.	stress testing was associated with harm in low-risk pts (RCRI: 0 points; HR: 1.35; 95% CI: 1.05–1.74). 2. Improved survival in intermediate-risk pts (RCRI: 1–2 points; HR: 0.92; 95% CI: 0.85–0.99) and high-risk pts (RCRI: 3–6 points; HR: 0.80; 95% CI: 0.67–0.97).	testing on mortality varied with RCRI class (p=0.005).	RR: 0.85; 95% CI: 0.73–0.98; p<0.03. Hospital LOS: difference of -0.24 d; 95% CI: 0.07–0.43; p<0.001.	compare outcomes form different stress tests (e.g., exercise treadmill, nuclear perfusion). 2. Observational design demonstrates association between preop testing and survival cannot determine causation.

AAA indicates abdominal aortic aneurysm; ACS, American College of Surgeons; CAD, coronary artery disease; CI: confidence interval; CT, computed tomography; HF, heart failure; HR, hazard ratio; HTN, hypertension; IOM, Institute of Medicine; LOS, length of stay; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac event; MI, myocardial infarction; n, subgroup from N; N/A, not applicable; NSQIP, National Surgical Quality Improvement Program; OR: odds ratio; periop, perioperative; preop, preoperative; pt, patient; pts, patients; PVD, peripheral vascular disease; RCRI, Revised Cardiac Risk Index; and RR, relative risk.

Data Supplement 2. Influence of Age and Sex (Section 2.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Bateman BT, et al., 2009 (6) 19194149	To conduct an analysis of AIS to determine incidence, risk factors, and effect of outcome on periop AIS in	Secondary analysis of NIS database	n=131,067 hemicolectomy surgical pts; n=201,235 total hip replacement surgical pts; n=39,339	N/A	N/A	Common noncardiac surgeries: hemicolectomy, total hip replacements, and segmental/ lobar lung	N/A	N/A	N/A	AIS incidence: hemicolectomy 935 cases—0.7% (95% CI: 0.7%–0.8%); total hip replacement 420 cases—	N/A	1. Higher incidence of AIS among pts ≥65 y of age. 2. Higher incidence of AIS among	1. Among pts >65 y of age, AIS incidence: hemicolectomy 1.0% (95% CI: 0.9%–1.0%); total hip replacement	Limited by range of variables that could be explored as risk factors for AIS. Use of database may

	noncardiac surgical pts		pulmonary lobectomy/ segment resection surgical pts			resection				0.2% (95% CI: 0.2%–0.2%); lobectomy/ segmental lung resection 242 cases—0.6% (95% CI: 0.7%–0.9%)		female pts and female sex was an independent risk factor for AIS.	0.3% (95% CI: 0.3%–0.3%); lobectomy/ segmental lung resection 0.8% (95% CI: 0.7%–0.9); 2. Female sex independent risk factor (OR: 1.21; CI: 1.07–1.36; p<0.001).	underestimate morbidity and mortality.
Mashour GA, et al., 2011 (2) 21478735	Assess the incidence and predicators of periop stroke and its role in mortality in noncardiac, non-neurosurgical surgery	Secondary analysis of ACS NSQIP	523,059 pt data sets (deidentified from NSQIP database)	NSQIP participants from 250 participating U.S. medical center for 4 y (2005–2008)	N/A	General surgery, orthopedic, urology, otolaryngology, plastics, thoracic, minor vascular, and gynecology cases	Cardiac, major vascular, and neurosurgical cases	N/A	Age dichotomized into 62 y of age and ≥62 y of age	The incidence of periop stroke was 0.1%	N/A	1. Multivariate analyses indicated age ≥62 y of age was an independent risk factor for periop stroke. 2. Multivariate analyses indicated male sex was an independent risk factor for periop stroke.	1. Older age was an independent risk factor for periop stroke (OR: 6.6; CI: 5.4–8.2; p<0.001). 2. Male sex was an independent risk factor for periop stroke (OR: 1.2; CI: 1.0–1.5; p=0.02).	Observational study does not allow for additional data collection for pts exhibiting primary outcome. In addition the data definitions are clinically relevant, but could not be modified for purposes of this study.
Rogers SO, et al., 2007 (7) 17544079	To develop and test a risk model for venous thromboembolic events. To develop and validate a risk index for VTE.	Secondary analysis of the PSS	183,069 pt records	Records from 128 VA and 14 private sector academic medical centers in general and peripheral vascular surgery subspecialties from 2002–	None	VTE defined as either PE or DVT	N/A	N/A	N/A	VTE occurred in 1,162 pts	N/A	Female sex was 1 of 15 independent factors associated with an increased risk of VTE compared to males	Female sex as independent risk factor for VTE (OR: 1.370; CI: 1.118–1.680).	Models limited by variables that are not part of NSQIP database that might impact the rates of VTE

				2004										
Dasgupta M, et al., 2009 (8) 18068828	To examine if frailty is associated with an increased risk of postop complications	Exploratory, prospective, descriptive	125	N/A	N/A	≥70 y of age, undergoing elective noncardiac surgery	Day surgery procedures, active cancer	N/A	N/A	Occurrence of an in-hospital, postop complication (unrelated to surgical technique). Adverse events occurred in 31/125 pts (25%). Both age (p<0.0074) and EFS scores (p<0.00042), indicators of frailty, were independently associated with being discharge to an institution and having a prolonged LOS.	N/A	N/A	OR was 1.14 for age (95% CI: 1.05–1.24) and 1.22 for EFS score (95% CI: 1.02–1.6)	Method of outcome identification using chart review. Single center study. Limited sample size.
Healy KO, et al., 2010 (3) 20412467	To evaluate the impact of LVEF on periop outcomes and long-term mortality in pts with HF undergoing intermediate- to high-risk noncardiac surgery	Retrospective chart review	174 pts	Pts diagnosed with HF who underwent intermediate- or high-risk noncardiac surgery from 2001–2004	N/A	Diagnosis with HF; intermediate- or high-risk noncardiac surgery (including PVD surgery, aortic repair, carotid endarterectomy, head & neck, intraperitoneal, noncardiac intrathoracic, orthopedic or prostate surgery)	N/A	N/A	Pts with HF compared by LVEF (>50% normal, 40%–50% mildly reduced, 30%–40% moderately reduced, <30% severely reduced)	N/A	≥80 y of age independently associated with adverse events	N/A	Multivariate analyses for older age as an independent predictor of periop events (OR: 3.84; CI: 1.70–8.17)	Small, retrospective chart review from single institution

ACS indicates American College of Surgeons; AIS, acute ischemic stroke; CI, confidence interval; DVT, deep vein thrombosis; EFS, Edmonton Frail Scale; HF, heart failure; HR, hazard ratio; LOS, length of stay; LVEF, left ventricular ejection fraction; n, subgroup from N; N/A, not applicable; NIS, Nationwide Inpatient Sample; NSQIP, National Surgical Quality Improvement Program; OR, odds ratio; PE, pulmonary embolism; periop, perioperative; postop, postoperative; PSS, protein secondary structure; pts, patients; PVD, peripheral vascular disease; RR, relative risk; VA, Veterans Affairs; and VTE, venous thromboembolism.

Data Supplement 3. HF and Cardiomyopathy (Sections 2.2 and 2.3)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:
						Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (Efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*	
Impact of HF on Periop and Postop Outcomes													
Hammill BG, et al., 2008 (9) 18362586	To determine operative mortality and 30-d all-cause readmission among pts with HF, CAD, or neither who underwent major noncardiac surgery	Retrospective	159,327 procedures	N/A	N/A	Pts >65 y of age with Medicare FFS coverage, and underwent major noncardiac procedures from 2000–2004	Pts with end-stage renal disease and pts who did not have at least 1 y of Medicare FFS eligibility before surgery	N/A	Pts with HF or CAD against neither	Operative mortality and 30-d all-cause readmission	N/A	Pts with HF were at significantly higher risk for both outcomes compared with pts with CAD	Adjusted HR of mortality and readmission for pts with HF, compared with pts with neither HF nor CAD, were 1.63 (95% CI: 1.52–1.74) and 1.51 (95% CI: 1.45–1.58), respectively
Hernandez AF, et al., 2004 (10) 15464326	To evaluate mortality and readmission rates of pts with HF after major noncardiac surgery	Retrospective	1,532 pts with HF and 1,757 pts with CAD who underwent major noncardiac surgery. 44,512 pts in control group with major noncardiac surgery.	N/A	N/A	>65 y of age; 1997–1998 5% sample of Medicare beneficiaries, pts with HF who underwent major noncardiac surgery	?	N/A	Pts with HF or CAD against neither	Operative mortality (death before discharge or within 30 d of surgery)	?	Risk-adjusted 30-d readmission rate 0	The risk-adjusted operative mortality (death before discharge or within 30 d of surgery) for HF 11.7%, CAD 6.6%, and control 6.2% (HF vs. CAD, p<0.001; CAD vs. control; p=0.518). The risk-adjusted 30-d readmission rate for was HF 20.0%, CAD 14.2%, and control 11.0% (p<0.001).
van Diepen S, et al., 2011 (11) 21709059	To compare the postop mortality of pts with HF, AF, or CAD undergoing major and minor noncardiac	Retrospective	Nonischemic HF (n=7,700), ischemic HF (n=12,249), CAD (n=13,786), or AF (n=4,312)	N/A	N/A	Pts who underwent noncardiac surgery between April 1, 1999–September 31, 2006, in Alberta, Canada	?	N/A	?	The main outcome was 30-d postop mortality.	?	Among pts undergoing minor surgical procedures, the 30-d postop mortality was 8.5% in NIHF, 8.1% in IHF, 2.3% in CAD,	Unadjusted 30-d postop mortality was 9.3% in NIHF, 9.2% in IHF, 2.9% in CAD, and 6.4% in AF (each vs. CAD, p<0.0001). After multivariable

	surgery											and 5.7% in AF (p<0.0001)	adjustment, postop mortality remained higher in pts with NIHF, IHF, and AF than in those with CAD (NIHF vs. CAD, OR: 2.92; 95% CI: 2.44–3.48; IHF vs. CAD, OR: 1.98; 95% CI: 1.70–2.31; AF vs. CAD, OR: 1.69; 95% CI: 1.34–2.14).
Xu-Cai YO, et al., 2008 (12) 18315993	To evaluate modern surgical outcomes in pts with stable HF undergoing elective major noncardiac surgery and to compare the experience of pts with HF who have reduced vs. preserved LVEF	Retrospective	557 pts with HF (192 LVEF ≤40% and 365 LVEF>40%) and 10,583 controls	N/A	N/A	Pts who underwent systematic evaluation by hospitalists in a preop clinic before having major elective noncardiac surgery between January 1, 2003–March 31, 2006	?	N/A	Mortality in HF with reduced EF or preserved EF vs. control pts	1-mo postop mortality and1-y mortality	?	Unadjusted differences in mean hospital LOS among pts with HF vs. controls (5.7 vs. 4.3 d; p<0.001) and 1-mo readmission (17.8% vs. 8.5%; p<0.001) were also markedly attenuated in propensity-matched groups	Unadjusted 1-mo postop mortality in pts with both types of HF vs. controls was 1.3% vs. 0.4% (p=0.009), but NS in propensity-matched groups (p=0.09). Crude 1-y HR (p<0.01) for mortality were 1.71 (95% CI: 1.5–2.0) for both types of HF, 2.1 (95% CI: 1.7–2.6) in pts with HF who had LVEF ≤40%, and 1.4 (95% CI: 1.2–1.8) in those who had LVEF >40%; however, the differences were NS in propensity-matched groups (p=0.43).
Impact of LVEF on Periop and Postop Outcomes													
Meta-analysis Global Group in Chronic Heart Failure (MAGGIC), 2012 (13)	To determine whether survival in pts with HF-PEF is similar to those pts with HF-REF	Meta-analysis using individual pt data	41,972 pts (10,347 with HF-PEF and 31,625 with HF-REF)	N/A	N/A	31 studies including pts with HF	?	N/A	Deaths per 1,000-pt y	Mortality in HF-PEF vs. HF-REF	?	The risk of death did not increase notably until EF fell below 40%.	Pts with HF-PEF had lower mortality than those with HF-REF (adjusted for age, sex, etiology, and Hx of HTN, diabetes mellitus, and AF; HR: 0.68; 95% CI: 0.64–0.71)

21821849													
Kazmers A., et al., 1988 (14) 3047443	To determine periop (30-d) and subsequent outcome after major vascular surgery in those with severe cardiac dysfunction, defined by LVEF ≤35%	Retrospective	35 pts who required 47 major vascular procedures	N/A	N/A	From August 1, 1984–January 1, 1988, pts with LVEF ≤35% who required vascular surgery	?	N/A	Mortality according to LVEF	Cumulative mortality	?	?	Survival for those with an LVEF ≤29% was significantly worse than for those with an LVEF >29% (p<0.012). The cumulative mortality rate was 59% LVEF ≤29% and 18% in those with LVEF >29% (p<0.029)
Kazmers A., et al., 1988 (15) 3348731	To determine periop and long-term mortality according to LVEF in pts undergoing carotid endarterectomy	Retrospective	73 pts before 82 carotid operations	N/A	N/A	Pts who had radionuclide ventriocculography before carotid endarterectomy	?	N/A	Periop and long-term mortality in pts with LVEF <35% vs. LVEF >35%	Periop and cumulative1-y mortality	Periop cardiac complications were more frequent with LVEF ≤35% , occurring in 43% vs.9% in pts with LVEF >35%	?	There was no statistical difference in periop mortality, but cumulative mortality differed, being 57% (4/7) in those with EF of ≤35% vs. 11% (7/66) in pts with LVEF >35%
McCann RL, Wolfe WG, 1989 2778886	To evaluate the influence of LVEF on both periop and long-term morbidity and mortality	Retrospective	104	N/A	N/A	Preop LVEF measured in 104 of 208 pts undergoing elective AAA	?	N/A	19 pts with LVEF <35% was compared to 85 pts with LVEF >35%	Periop and cumulative mortality	?	?	The periop mortality was not significantly different (low EF, 5%; high EF, 2%). The cumulative life-table survival of the 2 groups was not statistically different. 4-y actuarial survival 0.74 in low EF compared to 0.63 (p=NS) in the high EF group
Healy KO, et al., 2010 (3) 20412467	To determine impact of LVEF on outcome in pts with HF undergoing noncardiac surgery	Retrospective	174	?	?	174 subjects who underwent intermediate- or high-risk noncardiac surgery	?	?	?	30-d and long-term mortality	Adverse periop events occurred in 53 (30.5%) of subjects, including 14 (8.1%) deaths within 30 d, 26 (14.9%) MI, and 44 (25.3%) HF exacerbations	Among the factors associated with adverse periop outcomes in the first 30-d were advanced age (e.g., >80 y), diabetes mellitus, and a severely decreased EF (e.g., <30%)	Long-term mortality was high and Cox proportional hazards analysis demonstrated that EF was an independent risk factor for long term mortality

Role of HF in CV Risk Indices													
Goldman L, et al., 1977 (15, 16) 904659	To determine which preop factors affect the development of cardiac complications after major noncardiac operations	Prospective cohort	1,001 pts	N/A	N/A	?	?	?	?	Postop fatality and life-threatening complication	?	36 of the 39 pts manifesting ≥1 life-threatening cardiac complications had pulmonary edema. 9 independent significant correlates of life-threatening and fatal cardiac complications: preop S3 or JVD; MI in the preceding 6 mo; >5 PVC/min; rhythm other than sinus or presence of PACs on preop ECG; >70 y of age; intraperitoneal, intrathoracic or aortic operation; emergency operation; important valvular AS; and poor general medical condition.	Clinical signs of HF including an S3 gallop or JVD were the most significant predictors of postop life-threatening or fatal cardiac complications. In the final analysis, signs of HF carried the highest weight in the original CRI. 10 of the 19 postop cardiac fatalities occurred in the 18 pts at highest risk.
Detsky AS, et al., 1986 (15, 17) 3772593	To validate a previously derived multifactorial index in their clinical setting and to test a modified version of the index	Prospective cohort	455	?	?	455 consecutive pts referred to the general medical consultation service for cardiac risk assessment prior to noncardiac surgery	?	?	?	Major cardiac complications	?		The interobserver agreement for S3 and JVD was poor (κ statistic, 0.42 and 0.50, respectively). Therefore, to make the diagnosis of HF more objective and reproducible preoperatively, grouped HF into 2 categories as the presence of alveolar pulmonary edema within 1 wk or ever. Definition was stricter; HF still had a major role in predicting events and being a

													major outcome. Of the 43 serious events, there were 10 new or worsened episodes of HF without alveolar pulmonary edema, and 5 episodes of alveolar pulmonary edema.
Lee TH, et al., 1999 (15, 18) 10477528	To develop and validate an index for risk of cardiac complications	Prospective cohort	4,315	N/A	N/A	4,315 pts ≥50 y of age undergoing elective major noncardiac procedures in a tertiary-care teaching hospital	?	?	?	The main outcome measures were major cardiac complications	?	?	HF was both an important predictor and a key complication. Outcome required a formal reading of pulmonary edema on the chest x-ray. In the validation set, it provided the highest OR (4.3) for major cardiac complications. 6 independent predictors of complications were identified in RCRI: high-risk type of surgery, Hx of ischemic heart disease, Hx of CHF, Hx of cerebrovascular disease, preop treatment with insulin, and preop serum creatinine >2.0 mg/dL.

AAA indicates abdominal aortic aneurysm; AF, atrial fibrillation; AS, aortic stenosis; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; CRI, Cardiac Risk Index; CV, cardiovascular; ECG, electrocardiogram; EF, ejection fraction; FFS, fee-for-service; HF, heart failure; HF-PEF, heart failure with preserved ejection fraction; HF-REF, heart failure with reduced ejection fraction; HR, hazard ratio; HTN, hypertension; Hx, history; IHF, ischemic heart failure; JVD, jugular venous distention; LOS, length of stay; LVEF, left ventricular ejection fraction; MI, myocardial infarction; n, subgroup of N; N/A, not applicable; NIHF, nonischemic heart failure; NS, nonsignificant; OR, odds ratio; PAC, pulmonary artery catheterization; periop, perioperative; postop, postoperative; pts, patients; PVC, premature ventricular contraction; preop, preoperative; RCRI, Revised Cardiac Risk Index; RR, relative risk; and S3, third heart sound.

Data Supplement 4. Valvular Heart Disease (Section 2.4)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (Efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*	*Primary Endpoint*	
Agarwal S, et al., 2013 (19) 23481524	Postop outcomes after nonemergent noncardiac surgery in pts with moderate or severe AS	Retrospective cohort; age, sex, and propensity score matched control	3,170	634	2,536	Moderate AS (AVA=1.0–1.5 cm^2) or severe AS (AVA<1.0 cm^2)	Emergent surgery	N/A	Pts without AS	Composite of 30-d mortality and postop MI	N/A	30-d mortality, long-term mortality, postop MI, HF, stroke, and LOS	Moderate AS 4.4% vs. control 1.7% (OR: 2.6; p=0.002); Severe AS 5.7% vs. control 2.7% (OR: 2.1; p=0.02)	Retrospective, single center
Calleja AM, et al., 2010 (20) 20381670	Postop outcomes after noncardiac surgery in pts with asymptomatic, severe AS	Retrospective; age- and sex-matched control	90	30	60	Severe AS (AVA<1.0 cm^2)	Symptomatic AS, moderate or severe AR	N/A	Pts with mild-to-moderate AS	Composite of in-hospital death, MI, HF, ventricular arrhythmias, and intraoperative hypotension requiring vasopressor	N/A	Intraoperative hypotension requiring vasopressor	AS 33% vs. control 23% (OR: 1.4; p=0.06)	Retrospective, single center, small sample size
Leibowitz D, et al., 2009 (21) 19287130	Postop outcomes after hip fracture surgery in pts with severe AS	Retrospective; age-matched control	120	32	88	Severe AS (AVA<1.0 cm^2)	N/A	N/A	Pts without AS	30-d mortality	N/A	Composite of 30-d mortality, ACS, and pulmonary edema	AS 6.2% vs. control 6.8% (OR: 0.9; p=NS)	Retrospective, single center, small sample size
Zahid M, et al., 2005 (22) 16054477	Postop outcomes after noncardiac surgery in pts with AS from NHDS database	Retrospective; age and surgical risk-matched control	15,433	5,149	10,284	AS	N/A	N/A	Pts without AS	Composite of in-hospital mortality and MI	N/A	In-hospital MI	AS 8.3% vs. control 7.2%, (OR: 1.2; p=0.01)	Retrospective, claims database
Torsher LC, et al., 1998 (23) 9485135	Postop outcomes after noncardiac surgery in pts with severe AS	Retrospective; no control	19	19	N/A	Severe AS (mean gradient >50 mm Hg)	N/A	N/A	N/A	In-hospital mortality	N/A	N/A	AS 10.5%	Retrospective, no control group, single center, small sample size
Lai HC, et al., 2010	Postop outcomes after noncardiac	Retrospective; age, sex, and	334	167	167	Moderate-to-severe AR or	Pt is already intubated,	N/A	Pts without AR	In-hospital mortality	NA	Postop MI, stroke,	AR 9.0% vs. control 1.8%	Retrospective, single center,

(24) 19930243	surgery in pts with moderate-severe or severe chronic AR	surgical risk-matched control				severe AR	surgery performed with local anesthesia					pulmonary edema, intubation >24 h, and major arrhythmia	(OR: 5.0; p=0.008)	small sample size
Bajaj NS, et al., 2013 (25) 23587300	Postop outcomes after nonemergent noncardiac surgery in pts with moderate-to-severe or severe MR	Retrospective; age, sex, and propensity score matched control	1,470	298	1,172	Moderate-to-severe MR or severe MR	Emergent surgery	N/A	Pts without MR	Composite of 30-d mortality and postop MI, HF, and stroke	N/A	30-d mortality, postop MI, HF, stroke, and AF	MR 22.2% vs. control 16.4% (OR: 1.4; p=0.02)	Retrospective, single center
Lai HC, et al., 2007 (26) 17576968	Postop outcomes after noncardiac surgery in pts with moderate-to-severe or severe MR	Retrospective; no control	84	84	N/A	Moderate-to-severe MR or severe MR	Pt is already intubated, surgery performed with local anesthesia	N/A	N/A	In-hospital mortality	N/A	Postop MI, stroke, pulmonary edema, intubation >24 h, and major arrhythmia	MR 11.9%	Retrospective, no control group, single center, small sample size

ACS, acute coronary syndrome; AF, atrial fibrillation; AR, aortic regurgitation; AS, aortic stenosis; AVA, aortic valve area; CI, confidence interval; HF, heart failure; HR, hazard ratio; LOS, length of stay; MI, myocardial infarction; MR, mitral regurgitation; NHDS, National Hospital Discharge Survey; N/A, not applicable; NS, nonsignificant; OR, odds ratio; pts, patients; postop, postoperative, and RR, relative risk.

Data Supplement 5. Arrhythmias and Conduction Disorders (Section 2.5)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Biteker M, et al., 2012 (27) 22057953	To determine ECG predictors of periop cardiac events in pts undergoing noncardiac/ nonvascular surgery	Prospective observational cohort	660	660	N/A	660 pts scheduled for elective noncardiac nonvascular surgery expected to stay ≥2 d	Cardiac or vascular surgery, day surgery, emergent surgery, ASA=5	None	None	Abnormal ECG (p=0.019) and AF (p<0.001) predicted PCE on univariate analysis but not multivariate	N/A	Pts with PCEs had longer QTc (437 ms) that those without (413 ms) (OR: 1.043/ms; CI: 1.028/ms–1.058/ms)	N/A	N/A
Goldman L, et al., 1977	To develop risk score for cardiac events	Prospective observational cohort	1,001	N/A	N/A	All pts >40 y of age undergoing general,	Cardiac or thoracic surgery, no consent	None	None	Rhythm other than sinus (MDFC 0.283)	N/A	N/A	p<0.001	N/A

(16) 904659	after noncardiac surgery					orthopedic, or urologic surgery at MGH over a 7 mo period				and PVCs >5/min (MDFC 0.279) both predictive of risk of MACE				
Lee TH, et al., 1999 (18) 10477528	To develop revised risk score for cardiac events after noncardiac surgery	Prospective observational cohort	4,315	2,893 derivation	1,422 validation	All pts >50 y of age undergoing noncardiac surgery at 1 center over 5 y	Cardiac surgery, no consent	None	None	Abnormal rhythm not predictive of risk	N/A	N/A	RR 0.8; CI: 0.3–2.6; p=NS	No validation cohort
Mahla E, et al., 1998 (28) 9428844	To evaluate whether frequency of periop ventricular dysrhythmia independently predicts risk of noncardiac surgery	Prospective observational cohort	70	70	N/A	70 pts scheduled for noncardiac surgery with ventricular couplets or NSVT	10 pts excluded for poor Holter quality	None	None	Frequency of VPBs not predictive of outcome	N/A	AF did predict worse outcome (p=0.05)	p=NS	N/A
Mangano DT, et al., 1992 (29) 1608143	To determine predictors of long-term adverse cardiac events after noncardiac surgery	Prospective observational cohort	444	444	N/A	Consecutive pts at high-risk for CAD undergoing noncardiac surgery at SFVAMC who survived initial hospitalization	Cardiac surgery	None	None	Preop dysrhythmia did not predict adverse outcome	N/A	Preop NSVT did not predict risk	Dysrhythmia RR:1.4 (p=0.08); NSVT HR: 0.7 (CI: 0.2–1.9; p=0.40)	Small study, no control group
O'Kelly B, et al., 1992 (30) 1608140	To determine incidence and clinical predictors of periop ventricular arrhythmias during noncardiac surgery	Prospective observational cohort	230	230	N/A	Consecutive males with CAD or high risk for CAD undergoing noncardiac surgery at SFVAMC	N/A	None	None	Preop ventricular arrhythmia predicted periop and postop VA, but not MACE	N/A	N/A	Periop ventricular arrhythmias OR: 7.3 (95% CI: 3.3–16.0); postop ventricular arrhythmias OR: 6.4 (95% CI: 2.7–15.0), nonfatal MI/cardiac death OR :1.6 (95% CI: 0.4–	No validation cohort

													6.2)	

AF indicates atrial fibrillation; ASA, aspirin; CAD, coronary artery disease; ECG, electrocardiogram; MACE, major adverse cardiac event; MGH, Massachusetts General Hospital; MI, myocardial infarction; N/A, not applicable; NS, nonsignificant; NSVT, non-sustained ventricular tachycardia; PCE, perioperative cardiovascular events; periop, perioperative; preop, preoperative; pts; patients; PVC, premature ventricular contraction; QTc, corrected QT interval; RR, relative risk; SFVAMC, San Francisco Veterans Affairs Medical Center; VA, ventricular arrhythmia; and VPB, ventricular premature beat.

Data Supplement 6. Pulmonary Vascular Disease (Section 2.6)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Ramakrishna G, et al., 2005 (31) [15893189](15893189)	Determine predictors of poor outcome after noncardiac surgery in pts with PH	Retrospective review, single center	145 (all with PH)	None	None	Adults with Group 1, 3, or 4 PH; general anesthesia (100%); intermediate-/high-risk surgery (79%)	Cardiac, obstetric surgery	None	1) pts who died and 2) pts who had morbid event (HF, cardiac ischemia, stroke, respiratory failure, hepatic dysfunction, renal failure, sepsis, dysrhythmia) vs. those who did not	Death in 7% associated with 1) Hx of PE, 2) RAD on ECG, 3) RVH or RV dysfunction on echo, 4) RVSP/systolic BP ratio, 5) vasopressor use intraoperatively, 6) absence of iNO use intraoperatively	N/A	Morbidity in 42% associated with 1) functional class, 2) prior PE, 3) obstructive sleep apnea, 4) 5) vasopressor use intraoperatively	Independent multivariate predictors of postop morbidity: Hx of PE (OR: 7.3; CI: 1.9–38.3; p=0.01); PH symptoms (OR: 2.9; CI: 1.2–7.7; p=0.02); intermediate/high-risk vs. low-risk surgery (OR: 3.03; CI: 1.1–9.4; p=0.04); anesthesia duration >3 h (OR: 2.9; CI: 1.03–4.6; p=0.04)	Retrospective, single center, no comparison group
Minai OA, et al., 2006 (32) [16768070](16768070)	Determine frequency of poor outcome after noncardiac surgery in pts with PH	Retrospective review, single center	28 (all with PH)	None	None	Adults with Group 1 PH; general anesthesia (79%); intermediate-/high-risk surgery (86%)	Cardiac, obstetric surgery	None	1) pts who died and 2) pts who had morbid event vs. those who did not	Death in 18%	N/A	Morbidity in 19%	N/A	Retrospective, single center, no comparison group
Lai HC, et al.,	Determine	Retrospective	124 (62	None	Controls	Adults with	Cardiac,	None	1) pts who	Death in 10% vs.	N/A	Morbidity in	Independent	Retrospective,

2007 (26) 17576968	predictors of poor outcome after noncardiac surgery in pts with PH	case control study, single center	PH and 62 non–PH controls)		matched for age, sex, anesthesia, LVEF, surgical risk, and urgency	Group 1, 2, 3, or 4 PH; general anesthesia (58%); intermediate-/high-risk surgery (65%)	obstetric surgery		died and 2) pts who had morbid event vs. those who did not	0% in controls		24% vs. 3% in controls	multivariate predictors of postop mortality: emergency surgery (OR: 45; CI: 1.5–1,315; p=0.03); CAD (OR: 9.9; CI: 1.1–91; p=0.04); PASP (OR: 1.1; CI: 1.0–1.2; p=0.03). Independent multivariate predictors of postop morbidity: Cardiac risk level (OR: 6.8; CI: 1.2–39; p=0.03); CAD (OR: 6.5; CI: 1.4–30; p=0.02).	single center
Kaw R, et al., 2011 (32, 33) 21195595	Determine association of PH with periop outcomes	Retrospective cohort study, single center	173 (96 PH and 77 non–PH controls)	None	Controls who underwent RHC but had normal PA pressures, otherwise unmatched	Adults with Group 1,2,3, or 4 PH; general anesthesia (100%); intermediate-/high-risk surgery (100%); RHC	Minor procedures, cardiac, obstetric surgery	None	1) pts who died and 2) pts who had morbid event vs. those who did not	Morbidity/mortality (HF, respiratory failure, sepsis, MI) in 26% vs. 3% in controls	N/A	N/A	Mortality/morbidity OR: 13.1 (p<0.0001). Independent multivariate predictors of postop morbidity: PH (OR: 15.2; p=0.001); CKD (OR: 3.2; p=0.03); age (OR: 1.04; p=0.09); ASA Class >2 (OR: 4.2; p=0.02); surgical risk class	Retrospective, single center
Price LC, et al., 2010 (34) 19897552	Discuss the anesthetic management and follow-up of well-characterized pts with PAH presenting for noncardiothoracic nonobstetric	N/A	28 (all with PH)	None	None	Adults with Group 1 or 4 PH; general anesthesia (50%); intermediate-/high-risk surgery (75%)	Cardiac, obstetric surgery	None	1) pts who died and 2) pts who had morbid event vs. those who did not	Death in 7%	N/A	Morbidity (HF, respiratory failure) in 29%	Periop complications more likely in FC 3–4 (p=0.14) and with lower 6-min walk distance (p=0.06)	Retrospective, single center, no comparison group

	surgery													
Meyer S, et al., 2013 (35) [23143546](https://www.ncbi.nlm.nih.gov/pubmed/23143546)	Assess periop outcomes in pts with PAH undergoing noncardiac surgery	Prospective, multicenter registry	114 (all with PH)	None	None	Adults with Group 1 PH; general anesthesia (82%)	Minor, cardiac or obstetric surgery	None	1) pts who died and 2) pts who had morbid event vs. those who did not	Death in 3.5%	N/A	Morbidity in 6.1%	Predictors of postop events: emergency surgery (OR: 2.4; 95% CI: 1.4–3.6; p=0.01); use of vasopressors (OR: 1.5; 95% CI: 1.2–2.7; p=0.03); surgery performed in PH center (OR: 0.2; CI: 0.05–1.0; p=0.06); mRA pressure (OR: 1.1; 95% CI: 1.0–1.3; p=0.01)	No comparison group

ASA indicates American Society of Anesthesiologists; BP, blood pressure; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; ECG, electrocardiogram; FC, functional class; HF, heart failure; HR, hazard ratio; Hx, history; iNO, inhaled nitric oxide; LVEF, left ventricular ejection fraction; MI, myocardial infarction; N/A, not applicable; mRA, mean right atrial; OR, odds ratio; PA, pulmonary artery; PAH, pulmonary arterial hypertension; PASP, pulmonary artery systolic pressure; PE, pulmonary embolism; periop, perioperative; PH, pulmonary hypertension; postop, postoperative; pts, patients; RAD, right-axis deviation; RHC, right heart catheterization; RR, relative risk; RVH, right ventricular hypertrophy; and RVSP, right ventricular systolic pressure.

Data Supplement 7. Multivariate Risk Indices (Section 3.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
McFalls EO, et al., 2004 (36) [15625331](https://www.ncbi.nlm.nih.gov/pubmed/15625331)	Compare rates of morbidity and mortality with/without coronary artery revascularization before cardiovascular operations	RCT, multicenter	510	258	252	Elective vascular procedure, increased risk of cardiac complications, ≥1 major coronary arteries with >70% stenosis	Urgent or emergent vascular procedure, severe coexisting illness, prior revascularization without evidence of recurrent ischemia	CABG or coronary angioplasty	No coronary revascularization	Long-term mortality	N/A	Periop MI: 7.1% in intervention group vs. 5.0% in control group	NS	Only looked at rate of periop MI in vascular surgery pts
Davenport	Compare	Retrospective	427	99	328	ACS NSQIP	Pts who died	EVAR	Open AAA repair	Mortality: 22.2%	None	Cardiac	p=0.003	Retrospective

DL, et al., 2010 (37) 19939609	outcomes of open vs. endovascular repair of ruptured AAA	cohort study using prospectively collected national database NSQIP				database from 2005–2007 at 173 hospitals. Pts were selected who had ruptured AAA	before having operation			EVAR vs. 37.2% open		arrest or infarction: 4.0% in EVAR vs. 8.2% in open	for mortality; p=0.159 for cardiac arrest or infarction	and not randomized.
Jordan SW, et al., 2013 (38) 23249982	Comparing outcomes of plastic surgery operations with and without resident involvement	Retrospective cohort study using prospectively collected national database NSQIP	10,356	4,453	5,903	ACS NSQIP database from 2006–2010 with "plastics" listed as primary service to include pts with reconstructive procedures	Cosmetic procedures	Resident involvement	No resident involvement	Overall complication, wound infection, graft/prosthesis/flap failure, mortality rates	N/A	Cardiac arrest: 0.13% with resident; 0.14% no resident: MI: 0.11% with resident; 0.08% no resident	NS	Retrospective and not randomized.

AAA indicates abdominal aortic aneurysm; ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; CI, confidence interval; EVAR, endovascular aneurysm repair; CABG, coronary artery bypass graft; HR, hazard ratio; MI, myocardial infarction; N/A, not applicable; NS, nonsignificant; OR, odds ratio; periop, perioperative; pts, patients; RCT, randomized controlled trial, and RR, relative risk.

Data Supplement 8. Exercise Capacity and Functional Capacity (Section 4.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Patient Population		Study Intervention	Endpoints	P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
				Inclusion Criteria	***Exclusion Criteria***		***Primary Endpoint (Efficacy) and Results***		
Leung JM, et al., 2001 (39) 11555070	To determine prevalence and predictors of adverse postop outcomes in older surgical pts undergoing noncardiac surgery	Prospective cohort	544	Pts ≥70 y of age undergoing noncardiac surgery at an academic medical center	Local anesthesia or MAC	N/A	3.7% of pts died and 21% experienced postop complications. Decreased functional status preop was an important predictor of adverse neurological outcomes (OR: 3)	OR: 3 (95% CI: 1.4–6.4) for adverse neurological outcome	N/A
Reilly DF, et al., 1999 (40) 10527296	To determine the relationship between self-reported exercise tolerance and serious periop complications	Cohort	600	Consecutive outpts referred to a medical consultation clinic at a tertiary care medical center	N/A	Pts were asked to estimate the number of blocks they could walk and stairs they could climb without symptoms	All pts were monitored for 26 serious periop complications. Pts with poor exercise tolerance (<4 blocks or <2 flights) had more complications (20.4% vs. 10.4%).	Likelihood of serious complications was inversely related to the number of blocks that could be walked (p=0.006) or flights of stairs climbed (p=0.01).	N/A
Older P, et al., 1999 (41) 10453862	To develop an integrated strategy for the identification and subsequent management	Cohort	548	>60 y of age (or younger with known cardiopulmonary disease) scheduled for	N/A	All pts underwent cardiopulmonary exercise testing. Anaerobic threshold results and hemic ECG	Mortality was 3.9%. There were no deaths in those assigned to a ward strategy based on their cardiopulmonary parameters.	N/A	N/A

	of high-risk pts in order to reduce both morbidity and mortality			major intra-abdominal surgery		changes with exercise were used to triage to ICU, HCU, and ward.			
Wiklund RA, et al., 2001 (42) [11393264](https://pubmed.ncbi.nlm.nih.gov/11393264)	To evaluate METs as a predictor of cardiac complications following elective noncardiac surgery	Retrospective cohort	5,939	Pts undergoing preanesthetic assessment within 2 mo of elective noncardiac surgery	N/A	N/A	94 pts (1.6%) had cardiac complications, 38% occurred after vascular surgery. Age and ASA Physical Status Class were independent predictors of complications but METs were not once ASA Physical Status Class was included.	N/A	ASA Physical Status Class and METs were colinear
Crawford RS, et al., 2010 (43) [20141958](https://pubmed.ncbi.nlm.nih.gov/20141958)	To relate preop functional status to periop morbidity and mortality	Cohort	5,639	Vascular surgery pts undergoing infrainguinal surgical bypass	N/A	N/A	Dependent pts (18.4%) were older and had more diabetes mellitus, COPD ESRD on dialysis, and critical limb ischemia. Dependent pts had higher mortality (6.1% vs. 1.5%) and complication rates (30.3% vs. 14.2%). Dependent status was an independent predictor of death and major complications.	Serious complications OR: 2 (95% CI: 1.7–2.4) and death OR: 2.3 (95% CI: 1.6–3.4)	N/A
Goswami S, et al., 2012 (44) [23042223](https://pubmed.ncbi.nlm.nih.gov/23042223)	To determine incidence and risk factors for intraoperative cardiac arrest	Cohort	362, 767	Noncardiac surgeries in the ACS NSQIP database	N/A	N/A	Incidence of intraoperative CA was 7.22 per 10,000. Predictors included being functionally dependent (OR: 2.3) as well as emergency surgery and the amount of transfusions needed.	Adjusted OR:2.33 (95% CI: 1.69–3.22) for being functionally dependent	Definition of dependent in NSQIP database based on need for assistance with ADLs rather than METs values.
Tsiouris A, et al., 2012 (45) [22484381](https://pubmed.ncbi.nlm.nih.gov/22484381)	To assess the effect of functional status on morbidity or mortality	Cohort	6,373	Thoracic surgery pts in 2005-2009 NSQIP database	N/A	N/A	812 pts had dependent functional status preoperatively. Mortality was 7.7 times higher in them than in those with nondependent functional status. Complications were also increased.	OR: 7.7 for mortality in dependent pts preop as compared with nondependent pts ($p<0.001$). OR: 9.3 for prolonged ventilation and OR: 3.1 for reintubation.	N/A

ACS indicates American College of Surgeons; ADLs, activities of daily living; ASA, American Society of Anesthesiologists; CA, cardiac arrest; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; ESRD, end-stage renal disease; HCU, high care unit; HR, hazard ratio; ICU, intensive care unit; MAC, monitored anesthesia care; METs, metabolic equivalent; N/A, nonapplicable; NSQIP; National Surgical Quality Improvement Program; OR, odds ratio; periop, perioperative; postop, postoperative, preop, preoperative; pts, patients; and RR, relative risk.

Data Supplement 9. The 12-Lead ECG (Section 5.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints		P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Secondary Endpoint and Results***		
Biteker M, et al., 2012 (27) 22057953	To examine the association of preop ECG abnormalities and periop cardiovascular outcomes in pts undergoing noncardiac, nonvascular surgery	Prospective observational single-center cohort	660	N/A	N/A	Pts >18 y of age undergoing nonday case open surgery	Emergent cases and day-case surgery, ASA5	None	None	PCE 12.1%—Only QTc predicted periop CV events on MVA	Other ECG abnormalities did not predict CV events	N/A	Small sample size
Carliner NH, et al., 1986 (46) 3719447	To determine which ECG abnormalities were most predictive of high-risk surgical pts	Prospective observational single-center cohort	198	N/A	N/A	Pts >40 y of age undergoing elective thoracic, abdominal, or vascular surgery under GA	Recent MI, UA, CHF, AS, high-grade VE, uncontrolled HTN	None	None	Death/MI (3%)—Not reported due to small number of endpoints	All cardiac events including ischemia (17%)—Only abnormal ECG predicted	Sensitivity 85%, specificity 41%, PPV 22%; p<0.01	Small sample size, few primary hard endpoints. Individual ECG abnormalities did not predict events.
Gold BS, et al., 1992 (47) 1739358	To determine the value of preop ECG in an ambulatory surgical population	Retrospective single-center cohort	751	N/A	N/A	All ambulatory surgical pts with preop ECG undergoing surgery	Local anesthesia only	None	None	Any adverse CV event (1.6%)—no ECG abnormality predictive	N/A	No ECG abnormality predicted adverse CV events	Small sample size, few CV events (12/751= 1.6%)
Goldman L, et al., 1977 (16) 904659	To develop multifactorial risk score for cardiac events after noncardiac surgery	Prospective observational single-center cohort	1,001	N/A	N/A	All pts >40 y of age undergoing general, orthopedic, or urologic surgery at MGH over 7-mo period	Cardiac or thoracic surgery, local anesthesia only, endoscopy, TURP, no consent	None	None	Cardiac death (1.9%) or MACE (MI, pulmonary edema, VT–3.9%)-Rhythm other than sinus or PACs predicted cardiac death	N/A	Death—OR: 9 (p<0.001); nonfatal MACE—OR: 3.3 (p<0.001)	No validation cohort, older study, ECGs abnormalities not well-classified

										and MACE			
Jeger RV, et al., 2006 (48) [16442922](16442922)	To determine whether preop ECG abnormalities predict death/MACE 2 y postop in pts with CAD or high CAD risk	Prospective observational single-center cohort	172	N/A	N/A	Clinically stable adult pts with documented or suspected CAD undergoing noncardiac surgery	None stated	None	None	Death (23%) or MACE (18%) at 2 y-ST depressions and faster HR predicted mortality	N/A	ST depression—OR: 4.5 (95% CI: 1.9–10.5); faster heart rate–OR: 1.6 (95% CI: 1.1–2.4)	Small sample size
Landesberg G, et al.,1997 (49) 9357456	To examine the association between preop ECG abnormalities, periop MI, and postop cardiac complications	Prospective observational 2-center cohort	405	N/A	N/A	Adult pts undergoing vascular surgery under GA or epidural	LBBB, LVH with strain	None	None	Cardiac death (0.5%) or MI (4.2%)—Only LVH and ST depression >0.5 mm predicted endpoint	N/A	OR: 5.8 (p=0.004)	Small sample size, limited to vascular surgery
Lee TH, et al., 1999 (15, 18) 10477528	To derive and validate a simple index for the prediction of the risk of cardiac complications in major elective noncardiac surgery	Prospective observational single-center cohort	4,315	N/A	N/A	Pts ≥50 undergoing nonemergent noncardiac procedures with expected LOS ≥2 d	Pt unwilling to consent to full study protocol	None	None	Major cardiac complications-MI, pulmonary edema, VF/SCA, complete AV block (2%)—Pathologic Q-waves (present in 17%) predictive in derivation set, but not ST-T changes	N/A	Pathologic Q-waves: RR: 2.4 (CI: 1.3–4.2; p<0.05)	Pt consent required, and pts who did not give consent had much higher event rate (4.8% vs. 1.7%)
Liu LL., et al., 2002 (50) 12133011	To determine whether abnormalities on preop ECGs were predictive of postop cardiac complications	Prospective observational single-center cohort	513	N/A	N/A	Pts ≥70 undergoing noncardiac surgery	Local anesthesia or MAC	None	None	Death (3.7%) and combined cardiac complications (MI, ischemia, arrhythmia, CHF: 10.1%)–No association between ECG abnormalities and postop cardiac	Other noncardiac adverse events	OR: 0.63 (95% CI: 0.28–1.40; p=0.26)	Small sample size, only age ≥70

										complications			
Payne CJ, et al., 2011 (51) 21989644	To assess the predictive value of a preop 12-lead ECG in pts undergoing major surgery in a population with a high prevalence of cardiovascular disease	Prospective observational single-center cohort	345	N/A	N/A	Consecutive adult pts undergoing major vascular surgery or laparotomy	None stated	None	None	MACE (MI and cardiac death:13.3%) and all-cause mortality (7.8%) within 6 wk—LV strain and prolonged QTc predictive of MACE on MVA	N/A	LV strain—HR: 3.93 (CI: 2.14–7.20; p<0.001); Prolonged QTc—HR: 2.38 (CI: 1.32–4.31; p=0.004)	Small sample size; other ECG abnormalities not predictive on MVA
Schein OD, et al., 2000 (52) 10639542	To determine whether routine testing helps reduce the incidence of intraop and postop medical complications	Prospective randomized multicenter controlled trial	18,189	9,411	9,408	Pts ≥50 scheduled to undergo cataract surgery	General anesthesia, MI within 3 mo, any preop testing within 28 d	Routine preop testing=12-lead ECG, CBC, SMA-7	No preop testing	Adverse medical events (3.1%)—No difference between groups	Individual cardiac endpoints	RR: 1.00 (CI: 0.9–1.2)	Limited to single type of low-risk surgery, cardiac events not specifically studied, unable to exclude testing done >28 d
Seymour DG, et al., 1983 (53) 6869118	To examine the role of the routine preop ECG in the elderly surgical pt	Prospective observational single-center cohort	222	N/A	N/A	Pts ≥65 undergoing general surgery	None stated	None	None	MI or CHF (12.2%–9.6% in men and 16.1% in women)—Major ECG abnormalities (LVH, Q-waves, ST depression, T-wave abnormalities) predicted events in women but not men	N/A	Women: X^2=4.0 (p<0.05); Men: X^2=0.17 (p=NS)	Small sample size, unusual statistical analysis, included emergency cases (24.3%)
Turnbull JM, et al., 1987 (54) 3592875	To investigate the value of traditionally accepted preop investigations in otherwise healthy pts admitted to hospital for open	Retrospective 2-center cohort	1,010	N/A	N/A	Adult pts admitted for cholecystectomy and no major medical conditions	Active or ongoing disease on admission, morbid obesity	None	None	Any adverse medical event—ECG not predictive	N/A	PPV=0.040 (p=NS)	Retrospective, ECG criteria not well-defined, statistical comparisons not rigorous

	cholecystectomy												
Van Klei WA, et al., 2007 (55) [17667491](https://www.ncbi.nlm.nih.gov/pubmed/17667491)	To estimate the value of a preop ECG in addition to pt Hx in the prediction of MI and death during postop stay	Retrospective analysis of a prospective 2-center cohort study	2,967	N/A	N/A	Pts ≥50 undergoing noncardiac surgery with expected length of stay >24 h	Lung or liver transplant operation	None	None	Postop MI (2.3%) or death (2.5%)—RBBB predictive of postop MI, LBBB predictive of postop MI and death, other ECG abnormalities not predictive	N/A	RBBB/postop MI—OR: 2.1 (CI: 1.0–4.5; p=0.06); LBBB/postop MI—OR: 3.1 (CI: 1.0–9.9; p=0.05); LBBB/death—OR: 3.5 (CI: 1.3–10; p=0.02)	Retrospective, 20% did not get ECG. In ROC analysis, BBB not additive to risk prediction

AS indicates aortic stenosis; ASA, American Society of Anesthesiologists; AV, atrioventricular; BBB, bundle branch block; CAD, coronary artery disease; CBC, complete blood count; CHF, congestive heart failure; CI, confidence interval; CV, cardiovascular; ECG, electrocardiogram; GA, general anesthesia; HR, hazard ratio; HTN, hypertension; LBBB, left bundle-branch block; LOS, length of stay; LV, left ventricular; LVH, left ventricular hypertrophy; MACE, major adverse cardiac event; MGH, Massachusetts General Hospital; MI, myocardial infarction; MAC, monitored anesthesia care; MVA, multivariable analysis; N/A, not applicable; NS, nonsignificant; OR, odds ratio; PAC, pulmonary artery catheterization; PCE, perioperative cardiovascular event; periop, perioperative; postop, postoperative; PPV, positive predictive value; preop, preoperative; pts, patients; QTc, corrected QT interval; ROC, receiver operating characteristic; RBBB, right bundle-branch block; RR, relative risk; SCA, sudden cardiac arrest; SMA, sequential multiple analysis; TURP, transurethral resection of the prostate; UA, unstable angina; VE, ventricular ectopy; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Data Supplement 10. Assessment of LV Function (Section 5.2)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Baron JF, et al., 1994 (56) [8107716](https://www.ncbi.nlm.nih.gov/pubmed/8107716)	Ability of LVEF (and ischemia by dipyridamole thallium stress) by MUGA to predict periop MACE	Prospective	457	None	N/A	LVEF by MUGA undergoing elective abdominal aortic surgery	N/A	None	Pts with reduced LVEF vs. preserved LVEF	An LVEF <50% predicted cardiac complications (OR 2.1; 95% CI: 1.2–3.7)	N/A	EF<50% associated with postop HF (OR 4.6; 95% CI: 1.8–11.8) but not death (OR 1.3; 95% CI: 0.4–4.1), MI (OR 1.5; 95% CI: 0.5–4.4).Sensitivity of low EF to detech HF 25%; specificity 86%	N/A	N/A
Kontos MC, et al., 1996	Ability of LVEF by TTE to predict	Prospective	96 procedures in 87 pts	None	N/A	LVEF by TTE undergoing moderate- or	N/A	None	Pts with reduced LVEF (or	Major cardiac complications (MI, HF, arrhythmia) occurred	N/A	N/A	Sensitivity of low LVEF by ECG to predict MACE	N/A

(57) 8800025	periop MACE and compare to dypramidole thallium stress		(56 vascular, 40 general)			high-risk noncardiac surgery			ischemia on thallium stress) vs. preserved LVEF	in 10 pts. Reduced LVEF preoperatively present in 29%.			86% (95% CI: 60%–96%) and specificity 81% (95% CI: 70%–88%). LVEF by echo more specific than dipyridamole thallium stress for prediction of events.	
Halm EA, et al., 1996 (58) 8779454	Ability of LVEF by TTE to predict periop MACE	Prospective	339	N/A	N/A	Known or suspected CAD, major noncardiac surgery	N/A	N/A	N/A	Postop IEs (cardiac-related death, nonfatal MI, and UA), CHF, and VT. 10 pts (3%) had IEs; 26 (8%) had CHF; and 29 (8%) had VT. In univariate analyses, an EF<40% was associated with all cardiac outcomes combined (OR: 3.5; 95% CI: 1.8–6.7), CHF (OR: 3.0; CI: 1.2–7.4), and VT (OR: 2.6; CI: 1.1–6.2). In multivariable analyses that adjusted for known clinical risk factors, an EF<40% was a significant predictor of all outcomes combined (OR: 2.5; CI: 1.2–5.0) but not CHF (OR: 2.1; CI: 0.7–6.0) or VT [corrected] (OR: 1.8; CI: 0.7–4.7).	N/A	An EF <40% had a sensitivity of 28%-31% and a specificity of 87%-89% for all categories of adverse outcomes.	N/A	N/A
Rohde LE, et al., 2001 (59) 11230829	Ability of LVEF by TTE to predict periop MACE	Prospective	570	None	N/A	LVEF by TTE undergoing major noncardiac surgery	N/A	None	Pts with reduced LVEF vs. preserved LVEF	Preop systolic dysfunction was associated with postop MI, cardiogenic pulmonary edema (and major cardiac	N/A	ECG data added significant information for pts at increased risk for cardiac complications by clinical criteria,	With low LVEF: MI (OR: 2.8; 95% CI: 1.1–7.0), cardiogenic pulmonary edema (OR: 3.2; 95% CI: 1.4–7.0),	N/A

										complications		but not in otherwise low-risk pts	and major cardiac complications (OR: 2.4; 95% CI: 1.3–4.5).	
Healy KO, et al., 2010 (3) [20412467](https://pubmed.ncbi.nlm.nih.gov/20412467)	Determine the impact of LVEF on outcome in pts with HF undergoing noncardiac surgery	Retrospective	174	N/A	N/A	LVEF assessment in pts with HF undergoing intermediate or high risk noncardiac surgery.	N/A	N/A	N/A	Mortality	MACE in 53 (31%), including 14 (8%) deaths within 30 d, 26 (14.9%) MI, and 44 (25.3%) HF exacerbations	Among the factors associated with adverse periop outcomes in the first 30 d were advanced age (e.g., >80 y), diabetes and a severely decreased EF (e.g., <30%)	Long-term mortality was high and Cox proportional hazards analysis demonstrated that EF was an independent risk factor for long term mortality	N/A

CAD indicates coronary artery disease; CHF, congestive heart failure; CI, confidence interval; ECG, echocardiogram; EF, ejection fraction; HF, heart failure; HR, hazard ratio; IE, ischemic event; LV, left ventricular; LVEF, left ventricular ejection fraction; MACE, major adverse cardiac event; MI, myocardial infarction; MUGA, Multigated Acquisition Scan; N/A, not applicable; NS, nonsignificant; OR, odds ratio; periop, perioperative; postop, postoperative; preop, preoperative; pts; patients; RR, relative risk; TTE, transthoracic echocardiogram; UA, unstable angina; and VT, ventricular tachycardia.

Data Supplement 11. Exercise Stress Testing for Myocardial Ischemia and Functional Capacity (Section 5.3)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Cutler BS, et al., 1981 (60) [7223937](https://pubmed.ncbi.nlm.nih.gov/7223937)	Report of continuing experience with the electrocardiographically monitored arterial stress test in pts with peripheral vascular disease	Observational	130	N/A	N/A	Pts undergoing peripheral vascular reconstructive surgery	N/A	N/A	N/A	Lowest risk group was pts who achieved 75% maximum predicted heart rate without MI and no cardiac complications. Highest risk group was 26 pts who had an ischemic response at <75% maximum predicted heart	None	None	N/A	No stats. Event rates we don't see today.

										rate, 10 cardiac complications including 7 MIs (5 of which were fatal).				
Gerson MC, et al., 1985 (61) 4062085	To test whether objective assessment of rest and exercise LV function before elective noncardiac surgery is a more sensitive predictor of periop cardiac complications than data from pt Hx, physical exam, X-ray, lab ECG, and stress-rest radionuclide ventriculography	Consecutive series	Preliminary study: 100 (50 men and 50 women); prospective study: 54 pts (25 men and 29 women)	N/A	N/A	Pts aged ≥65 y scheduled for major elective abdominal or noncardiac thoracic surgery	N/A	N/A	N/A	Preliminary study: 13 pts (of 100) had a total of 22 major periop complications (cardiac death, VT or VF, MI, CHF) including 6 deaths. When radionuclide variables and clinical variables were entered into multivariate analysis that included preop Hx, physical examination, and x-ray, ECG, and chemical laboratory variables, individually and in combination, only resting radionuclide LV regional wall motion abnormality (p=0.002) and inability to exercise for 2 min to raise the heart rate above 99 bpm (p=0.006) were independent predictors of periop cardiac risk.	None	None	Preliminary study: Pts unable to bicycle at least 2 min to a heart rate >99 bpm had an 11-fold increase in the risk of developing a periop cardiac complication. Prospective study: 10 pts (out of 54) had a total of 12 periop complications including 2 deaths. The inability to bicycle 2 min to a heart rate >99 bpm was the only significant predictor of a periop cardiac complication (p<0.05). Inability to exercise had a sensitivity of 80% and specificity of 53% for prediction of periop cardiac complications.	Small sample size.
Arous EJ, et al., 1984 (62)	To determine the safest treatment option for the pt with	Retrospective analysis	Out of 808 pts with AAA or peripheral occlusive	135 pts with ischemia on stress test: Group 1 (56	37 pts with no Hx of MI or symptoms of CAD with	Pts with AAA or peripheral occlusive disease of the	None mentioned	Treadmill exercise (Bruce protocol) to	Pts with no Hx of MI or symptoms of CAD with	Positive exercise test (135): Group 1 (56) standard operation: MI in 15	None	None	In the positive stress test group, the total incidence of MI,	High rate of events compared with today's

6610402	combined coronary and PVD through a retrospective analysis of the postop course of pts with an ischemic response to treadmill exercise		disease of the lower extremities who underwent ECG monitored stress tests, this study concerns 135 with an ischemic response to exercise and 37 pts with no Hx of MI or symptoms of CAD with normal ECGs at rest	pts) standard operation, Group 2 (23 pts) extra-anatomic bypass, Group 3 (10 pts) CABG and standard operation, and Group 4 (46 pts) no operation	normal ECGs at rest: Group 1 (21), Group 2 (2), Group 3 (4), and Group 4 (10)	lower extremities		at least 75% max predicted heart rate; arm ergometer for those whose claudication precluded adequate treadmill exercise. Ischemia defined as new or additional ST segment depression of at least 1 mm.	normal ECGs at rest	(27%), fatal in 11; Group 2 (23) extra-anatomic bypass: 4 MI (17%), 3 fatal; Group 3 (10) CABG and standard operation: 0 MI; and Group 4 (46) no operation: 10 (22%) late fatal MI (1–5 y). No known CAD: Group 1 (21) 5 MI (24%), 4 fatal; Group 2 (2) 1 nonfatal MI (50%); Group 3 (4) 0 MI; and Group 4 (10) 1 late fatal MI (10%)			including both the postop and follow-up periods, was significantly reduced when Group 3 was compared with Group 1 (p=0.05).	standards. Decision on type of surgery influenced by stress test results. Arm ergometry used for some pts, but how many is unclear. Not really a study of ischemia vs. no ischemia on stress test.
Carliner NH, et al., 1985 (63) 4014040	To determine if preop exercise testing would be useful for predicting risk in pts undergoing a wide variety of major surgical procedures01078	Prospective	200	N/A	N/A	Pts over 40 y of age scheduled to undergo elective major noncardiac surgery under general anesthesia.	Documented MI within 6 mo, UA, decompensated HF, hemodynamically significant AS, low-grade 4A and 4B ventricular arrhythmias at rest, uncontrolled HTN, physical disability and mental incompetence	Treadmill (134), bicycle (21), arm ergometer (43). Treadmill was modified Balke or modified Bruce protocol.	N/A	2 pts with markedly positive stress tests were excluded from further analysis. 6 pts (3%) had a primary endpoint (death or MI). Only 1 of these 6 pts had a positive ST segment response to exercise, 5 of the 6 pts had a maximal exercise capacity of <5 METs.	None	On multivariate analysis, the preop ECG was the only factor that was a statistically significant predictor of postop outcome. A pt with an abnormal ECG was 3.2 times more likely to die postoperatively or MI or suspected myocardial ischemia/injury than was a pt with a normal ECG.	Postop death, MI, and suspected myocardial ischemia/injury occurred more frequently in pts who had an abnormal electrocardiographic response to exercise and/or an exercise capacity of <5 METs than in pts with neither of these findings; however, none of the exercise variables was statistically significant as an independent	Small number of primary events limits analysis. Mix of treadmill (67.7%), bike (10.6%), and arm (21.7%) exercise.

													predictor of risk.	
Leppo J, et al., 1987 (64) [3805515](3805515)	It was hypothesized that the presence of thallium redistribution would be of prime importance in detecting those pts having coronary disease who have potentially jeopardized myocardium	Prospective	100 underwent dipyridamole thallium scintigraphy; 69 underwent exercise testing (56, Bruce protocol), 13 arm ergometry). 27 didn't undergo exercise because of physical limitations and 4 because of scheduling conflicts.	N/A	N/A	Consecutive pts admitted for elective aortic or limb vascular surgery.	New or medically UA, recent (4-6 mo) MI.	N/A	N/A	Of the 89 pts who underwent vascular surgery without cardiac catheterization, 15 had a periop MI (1 fatal and 10 non-Q wave infarctions). Only the presence of either an abnormal scan (p=0.001) or thallium redistribution (p=0.001) demonstrated a significant difference.	None	Although pts with ST depression and shorter total exercise time tended to have more events, these differences were not statistically significant. No events occurred in the 12 pts who were able to perform >9 min of exercise.	From the regression analysis, the predicted probability of a cardiac event in pts not having redistribution was 2±2% (1 of 47), but in pts with redistribution it was 33±7% (14 of 42) .In the second regression analysis which included the 60 pts having both exercise and scan studies, only the presence of thallium redistribution was significant at step 0.	Relatively small number of patients undergoing exercise (69, and 13 of these were arm ergometry). High event rates not seen today.
McPhail N, et al., 1988 (65) [3336127](3336127)	To report on their experience with the use of exercise testing in an effort to predict cardiac complications in pts requiring arterial repair	Observational	110, 9 excluded. Treadmill exercise in 61 pts (Bruce protocol) and arm ergometry in 40 pts.	N/A	N/A	Consecutive pts requiring arterial surgery who had clinical evidence of significant CAD were referred for cardiac evaluation	9 pts with recent MI (<6 mo), UA, or CHF were excluded	N/A	N/A	Contingency table analysis showed that maximum heart rate achieved during exercise was a significant predictor of complications (MI, CHF, malignant ventricular arrhythmias and cardiac death). Of 70 pts who achieved <85% of their predicted maximum heart	None	Of 21 pts with a positive stress test (≥1 mm ST depression) who attained <85% of their predicted maximum heart rate, 7 (33.3%) developed cardiac complications. In contrast, no complications occurred among 9 pts	The logistic regression analysis indicates that pts who achieved a high maximal heart rate during exercise had a low probability of developing cardiac complications (p=0.040). A similar result was observed when high METs	Unclear selection of pts ("clinical evidence of significant CAD"). Relatively small number underwent treadmill exercise. High event rates not seen today.

										rate, 17 (24.3%) developed complications. Only 2 (6.6%) of 30 pts who achieved >85% maximum predicted heart rate had complications (p=0.0396). The degree of ST segment depression that occurred with exercise was NS in predicting cardiac complications.		with ST depression of ≥1 mm who were able to achieve 85% of their predicted maximum heart rate.	was present (p=0.033). Note: 4 METs ~25% event rate.	
Sgura FA, et al., 2000 (66) 11014727	To determine the value of preop exercise testing with a supine bicycle in predicting periop cardiovascular events and long-term outcomes in pts scheduled for vascular surgery	Consecutive series	149	N/A	N/A	Underwent supine exercise testing and vascular surgery	Underwent vascular surgery or coronary revascularization before exercise testing	N/A	N/A	Cardiovascular events within 30 d of surgery: death, MI, cardiac arrest; 7% had periop cardiovascular events	None	No significant association between exercise-induced ST depression, radionuclide angiographic factors, or any clinical variable (other than age) and periop cardiovascular events or long-term mortality	The level of peak exercise achieved was associated with periop CV events with 12% occurring in low-capacity pts (<4 METs), 3% occurring in intermediate-capacity pts (4–7 METs), and none in the high capacity pts (>7 METs) (p=0.03). Long-term survival rates were substantially less in the low-workload group than in intermediate- and high-workload groups (p=0.007).	Pts were selected who were felt to be capable of exercising. Selected group of pts for whom exercise radionuclide angiography was ordered.

AAA indicates abdominal aortic aneurysm; CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; CV, cardiovascular; ECG, echocardiogram; HR, hazard ratio; Hx, history; LV, left ventricular; MET; MI, myocardial infarction, N/A, not applicable; NS, nonsignificant; periop, perioperative; preop, preoperative; pts, patients; PVD, peripheral vascular disease; UA, unstable angina; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Data Supplement 12. Cardiopulmonary Exercise Testing (Section 5.4)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Hartley RA, et al., 2012 (67) [23001820](https://pubmed.ncbi.nlm.nih.gov/23001820)	To evaluate whether preop CPET is useful in the prediction of 30- and 90-d mortality in pts undergoing elective open AAA repair and EVAR	Prospective cohort	415	N/A	N/A	Pts undergoing AAA repair and CPET	None given	N/A	N/A	On multivariable analysis, open repair, AT <10.2 mL/kg/min, anemia and inducible cardiac ischemia were associated with 30-d mortality. Anemia, inducible cardiac ischemia and peak VO2 <15 mL/kg/min were associated with 90-d mortality on multivariable analysis. Pts with ≥2 subthreshold CPET values were at increased risk of both 30- and 90-d mortality.	None	None	On multivariable analysis, open repair (OR: 4.92; 95 % CI: 1.55–17.00; p=0.008), AT below 10.2 mL/kg/min (OR: 6.35; 95 % CI: 1.84–29.80; p=0.007), anemia (OR: 3.27; 95 % CI: 1.04–10.50; p=0.041) and inducible cardiac ischemia (OR: 6.16; 95 % CI: 1.48–23.07; p=0.008) were associated with 30-d mortality. Anemia, inducible cardiac ischemia and peak VO2 <15 mL/kg/min (OR: 8.59; 95 % CI: 2.33–55.75;	Observational study, relatively small number of deaths (6 in EVAR group and 8 with open AAA repair at 30 d and 11 EVAR/8 open repair at 90 d), mix of EVAR and open repair

													p=0.005) were associated with 90-d mortality on multivariable analysis. Pts with ≥2 subthreshold CPET values were at increased risk of both 30- and 90-d mortality.	
Thompson AR, et al., 2011 (68) 21929919	To assess the usefulness of CPET and the Detsky score to predict midterm mortality in AAA pts assessed for open repair. Secondary aim to compare ability of CPET and other scores to predict 30-d periop mortality.	Prospective cohort	102	66 (deemed "fit" by CPET variables, comorbidities, and size of AAA)	36 (deemed "unfit" by CPET variables, comorbidities, and size of AAA)	Consecutive pts undergoing AAA repair	None given	N/A	N/A	Midterm (30-mo) survival was predicted by the anaerobic threshold (p=0.02).	None	None of the scoring tools were able to predict 30-d major morbidity or mortality as defined by periop complications (p>0.05)	Midterm (30-mo) survival was predicted by the anaerobic threshold (p=0.02)	Lack of detail on cause of death, relatively small numbers total, and deaths (1 30-day death), not clear what "cardiac events" were
Prentis JM, et al., 2012 (69) 22858436	To assess the use of CPET to predict morbidity in unselected pts scheduled for elective EVAR or open AAA repair	Observational	185 pts (101 EVAR and 84 open repair)	N/A	N/A	"Unselected" pts undergoing EVAR or open AAA repair at a single center	AT not confidently determined from CPET data	N/A	N/A	Open repair: AT was a significant independent predictor of postop complications and hospital LOS. EVAR: No independent variables were significantly predictive of major postop complications on univariate analysis. No multivariate	None	Open repair: The in-hospital mortality rate was 5 of 84 (5.9%). 3 of 27 pts (11.1%) were in the unfit group (AT<10) compared with 2 of 58 (3.4%) in the fit group (AT>10), both of whom had an AT <12 mL/min/kg. Open repair: Cardiac complications (MI, LV failure, major arrhythmias) 18.5% unfit vs. 3.5% fit, p=0.03.	Open repair: ROC curve analysis showed that 10.0 mL/min/kg was the optimal AT level to predict those at risk for increased rates of postop complications. This was sensitive (70%) and specific (86%), with good accuracy (area under the curve, 0.75; 95% CI: 0.63–	Single center. Not consecutive pts although "unselected." No mortality data.

										analysis was performed.			0.83; p=0.001).	
Carlisle J, et al., 2007 (70) 17440956	To review whether preop fitness, measured by CPET, correlated with survival following elective open AAA repair	Observational	130 (37 pts did not undergo CPET and weren't analyzed)	N/A	N/A	Pts undergoing AAA repair	Did not undergo CPET	N/A	N/A	Multivariable analyses indicated that survival, to both 30 d and for the total observation period, correlated best with VE/VCO2. The risk of death was greater with higher values of VE/VCO2. The RCRI was significantly associated with midterm survival, as was the AT, but to a lesser degree.	None	Unfit pts had an RCRI >1 and a VE/VCO2 of >42. Fit pts had an RCRI of 1 (and any VE/VCO2), or an RCRI >1 but a VE/VCO2 lower than 43. There were 30 unfit pts and 100 fit pts.	Multivariable analysis of midterm (median 35 mo) survival: VE/ VCO2 HR: 1.13 (CI: 1.07–1.19; p<0.001); RCRI HR: 1.76 (CI: 1.07–1.19; p=0.006); AT HR: 0.84 (CI: 0.72–0.98; p=0.033). The 2-y survival rate was 55% for unfit pts and 97% for fit pts; the absolute difference was 42% (95% CI: 18%–65%; p<0·001).	Single center, observational, unclear selection of CPET variable cutoffs
Older P, et al., 1993 (71) 8365279	To compare the extent of cardiac failure classified by AT and postop mortality	Prospective cohort	187	N/A	N/A	Pts >60 y of age scheduled for major abdominal surgery ("likely to cause a significant increase in oxygen demand, e.g., AAA resection, anterior resection of the rectum")	Could not complete CPET (4 of 191 pts)	N/A	N/A	10 CV deaths in 55 pts (18%) with AT <11 mL/kg/min vs. 1 CV death in 132 pts (0.8%) with AT of ≥11 mL/kg/min (p<0.001)	None	42% mortality in the 19 pts with an AT of <11 mL/min/kg and preop ischemia (h/o MI, angina or ischemia on CPET) vs. 4% mortality in the 25 pts with AT >11 and ischemia (p<0.01).	10 CV deaths in 55 pts (18%) with AT <11 mL/kg/min vs. 1 CV death in 132 pts (0.8%) with AT of ≥11 mL/kg/min (p<0.001)	Single center, not blinded to results (all pts with ischemic tests admitted to ICU regardless of AT)
Snowden CP, et al., 2010 (72) 20134313	To test the null hypothesis that CPET does not improve preop assessment of pt risk of postop	Prospective, single center cohort study	171 (123 went on for operation and 48 did not; 7	N/A	N/A	Pts planned to undergo major elective surgery (AAA repairs, aortobifem grafts, liver	Emergency and elective colorectal, urological, or orthopedic operations	N/A	N/A	POMS on postop d 7	None	Cardiovascular complication rate was 25% in pts with AT <10.1 mL/kg/min and 3% in those with AT	Receiver operator curve analysis showed an optimal AT threshold level of 10.1	Size and selected nature of the chosen pt cohort. 48 pts did not undergo planned

	complications when compared to a questionnaire-based assessment method		pts did not achieve AT leaving 116 for analysis)			resections, pancreatic and large retroperitoneal intra-abdominal sarcoma surgery) and low subjective functional capacity based on clinical Hx						>10.1 mL/kg/min (p=0.0005). Note POMS definition of CV complication: Diagnostic tests or therapy within the last 24 h for any of the following: new MI or ischemia, hypotension (requiring fluid therapy >200 mL/h or pharmacological therapy), atrial or ventricular arrhythmias, pulmonary edema, thrombotic event (requiring anticoagulation).	mL/kg/min to predict those at risk for increased rates of postop complications. This was highly sensitive (88%) and specific (79%) with high degree of accuracy (area under the curve 0.85; 95% CI: 0.78–0.91; p=0.001).	procedure. No comment on mortality.
Snowden CP, et al., 2013 (73) 23665968	To assess the relationship between cardiopulmonary fitness and age upon mortality and LOS in an unselected group of pts undergoing major hepatobiliary surgery	Single center prospective cohort study	389	N/A	N/A	All pts being considered for major hepatobiliary surgery (liver resection, Whipple, retroperitoneal intra-abdominal sarcoma excision)	Major surgery not performed because of extensive malignancy, laparoscopic rather than open procedure performed, or pts did not exercise enough to reach AT	N/A	N/A	Hospital mortality	None	Critical care and hospital LOS	Multivariate regression identified anaerobic threshold as the most significant independent predictor for postop mortality from the exercise variables in this population of major surgical pts (OR: 0.52; p=0.003; beta=−0.657). ROC analysis demonstrated an optimal anaerobic threshold level of 10 mL/min/kg with good	Limited to hepatobiliary surgery. Single center.

													accuracy (area under curve =0.75; 95% CI: 0.65–0.85; p=0.0001).	
Wilson RJT, et al., 2010 (74) 20573634	To evaluate whether CPET variables and clinical data from Lee's cardiac risk index are useful predictors of all cause hospital and 90-d mortality in pts undergoing nonvascular intra-abdominal surgery	Retrospective analysis of anonymized data	847	N/A	N/A	All pts aged >55 y being considered for colorectal surgery, bladder, or kidney cancer excision who performed or attempted a CPET as part of their routine preop evaluation at the Preassessment Clinic	Pts who did not proceed to planned surgery were excluded from analysis	N/A	N/A	An AT of ≤10.9 mL/kg/min, a VE/VCO2 of ≥34, and a Hx of ischemic heart disease were all associated with an increased relative risk for all-cause hospital mortality. The overall presence of any ≥1 of the Lee's cardiac risk factors was not significantly associated with an increased risk of mortality.	None	None	Nonsurvival: For AT of ≤10.9, RR: 6.8 (95% CI: 1.6–29.5); for VE/VCO2 of ≥34, RR: 4.6 (95% CI: 1.4–14.8). Survival at 90 d was significantly greater in pts with an AT of ≥11 (p=0.034), in pts with VE/VCO2 <34 (p=0.021), and in pts without IHD (p=0.02).	Low incidence of all-cause mortality (2.1% in hospital and 4.1% at 90 d)
Older P, et al., 1999 (41) 10453862	To test a strategy of postop triage based on CPET results	Prospective consecutive series	548 pts	153 to ICU	Pts sent to HDU (115) or ward (280)	Pts over 60 y of age scheduled for major surgery or <60 but had previous diagnosis of myocardial ischemia or cardiac failure	Pts undergoing thoracic surgery	AT <11 to ICU (28% of pts)	Pts with AT >11 with inducible ischemia or VE/VO2 >35 (21%) admitted to HDU; all others (51%) admitted to general ward	4.6% mortality in pts with AT <11	0.5% mortality in pts with AT >11	None	None given	Confounding of CPET results and postop care, but should have improved outcomes in higher risk pts. Lack of stats.
Junejo MA, et al., 2012 (75) 22696424	To evaluate the role of CPET in periop risk assessment in pts undergoing	Single center prospective cohort study	94 with CPET and surgery; 2 could not	94 in CPET group	23 pts deemed low risk	Pts over 65 y, younger pts with comorbidity and those likely to require complex	None given	N/A	N/A	Death within 30 d of operation	None	In-hospital deaths, LOS in ICU and high dependency unit, overall hospital stay and	AT was the only preop marker associated with postop in-hospital	AT cutoff derived from high-risk group; small number of in-hospital

	hepatic resection		attain AT leaving 92 for analysis			resection underwent CPET						longer-term survival (up to 4 y)	mortality (OR: 0.48; 95% CI: 0.25–0.94; p=0.032). ROC curve analysis identified a cut-off at 9.9 mLl/kg/min that provided 100% sensitivity and 76% specificity, with a PPV of 19% (95% CI: 9%–38%) and a NPV of 100% (95% CI: 94–100). Pts with an AT ≥9.9 mL/kg/min had improved long-term survival (median duration 1,067 d) compared with pts with a lower value (p=0.038), but worse survival than those low-risk pts who did not undergo CPET (p=0.038).	deaths (4.2% in whole group); CPET data available to managing clinicians; heterogeneous group in terms of type of resection and tumor histopathology

AAA indicates abdominal aortic aneurysm; AT, anaerobic threshold; CI, confidence interval; CPET, cardiopulmonary exercise stress test; EVAR, endovascular aneurysm repair; HR, hazard ratio; ICU, intensive care unit; LOS, length of stay; LV, left ventricular; MI, myocardial infarction; N/A, not applicable; NPV, net predictive value; OR, odds raio; periop, perioperative; POMS, postoperative morbidity survey; postop, postoperative; PPV, positive predictive value; preop, preoperative; RCRI, Revised Cardiac Risk Index; ROC, receiver operating characteristic; and VE/VO2, ventilatory equivalent of oxygen.

Data Supplement 13. Pharmacological Stress Testing (Section 5.5)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (Efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Beattie WS, et al., 2006 (76) 16368798	Compare SE vs. MPI in preop evaluation prior to noncardiac surgery	Meta-analysis of 68 studies	10,049	N/A	Preop noncardiac surgery	N/A	N/A	MI and/or death	MI and/or death	LR for SE more indicative of postop cardiac event vs. TI (LR: 4.09; 95% CI: 3.21–6.56 vs. LR: 1.83; 1.59–2.10; p<0.001). This difference was attributable to fewer false negative SEs. No difference in ROC curves (SE: 0.80; 95% CI: 0.76–0.84 vs. TI: 0.75; 95% CI: 0.70–0.81).	A moderate-to-large defect, seen in 14% of pts by either method predicts a postop cardiac event (LR: 8.35; 95% CI: 5.6–12.45)	N/A	N/A

CI indicates confidence interval; LR, likelihood ratio; MI, myocardial infarction; MPI, myocardial perfusion imaging; N/A, not applicable; postop, postoperative; preop, preoperative; ROC, receiver operating characteristic; SE, stress echocardiography; and TI, thallium imaging.

Data Supplement 14. Radionuclide MPI (Section 5.5.2)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Patient Population		Ischemia	Endpoints			P Values, OR: HR: RR & 95% CI:
				Inclusion Criteria	*Exclusion Criteria*		*Primary Endpoint (Efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*	
Eagle KA, et al.,1989 (77) 8653858	Periop risk assessment by MPI	Single center, retrospective	200	Vascular surgery	N/A	41%	Periop events: PPV: 16%; NPV: 98%	N/A	N/A	N/A
Younis LT, et al., 1990 (78) 2353615	Periop risk assessment by MPI	Single center, retrospective	111	Peripheral vascular disease	N/A	36%	Periop events: PPV: 15%; NPV: 100%	N/A	N/A	N/A
Hendel RC, et al., 1992 (79) 1442573	Periop risk assessment by MPI	Single center, retrospective	327	N/A	N/A	51%	Periop events: PPV: 14%; NPV: 99%	N/A	N/A	N/A
Lette J, et al., 1992 (80) 1598869	Periop risk assessment by MPI	Single center, retrospective	355	N/A	N/A	45%	Periop events: PPV: 17%; NPV: 99%	N/A	N/A	N/A

Brown KA, et al., 1993 (81) 8425993	Periop risk assessment by MPI	Single center, retrospective	231	N/A	N/A	33%	Periop events: PPV: 13%; NPV: 99%	N/A	N/A	N/A
Bry JD, et al., 1994 (82) 8301724	Periop risk assessment by MPI	Single center, retrospective	237	N/A	N/A	46%	Periop events: PPV: 11%; NPV: 100%	N/A	N/A	N/A
Marshall ES, et al., 1995 (83) 7572662	Periop risk assessment by MPI	Single center, retrospective	117	N/A	N/A	47%	Periop events: PPV: 16%; NPV: 97%	N/A	N/A	N/A
Stratman HG, et al., 1996 (84) 8615311	Periop risk assessment by MPI	Single center, retrospective	229	Nonvascvular surgery	N/A	29%	Periop events: PPV: 6%; NPV: 99%	N/A	N/A	N/A
Cohen MC, et al., 2003 (85) 14569239	Periop risk assessment by MPI	Single center, retrospective	153	N/A	N/A	31%	Periop events: PPV: 4%; NPV: 100%	N/A	N/A	N/A
Harafuji K, et al., 2005 (86) 15849442	Periop risk assessment by MPI	Single center, retrospective	302	N/A	N/A	30%	Periop events: PPV: 2%; NPV: 100%	N/A	N/A	N/A
Beattie WS, et al., 2006 (76) 16368798	Compare SE vs. MPI in preop evaluation prior to noncardiac surgery	Meta-analysis of 68 studies	10,049	Preop noncardiac surgery	N/A	N/A	Outcomes: MI and/or death	There were no differences in ROC curves between SE and TI (SE: 0.80; 95% CI: 0.76–0.84 vs. TI: 0.75; 95% CI: 0.70–0.81)	A moderate-to-large defect, seen in 14% of pts, by either method predicts a postop cardiac event (LR: 8.35; 95% CI: 5.6–12.45).	LR for SE more indicative of postop cardiac event vs. TI (LR: 4.09; 95% CI: 3.21–6.56 vs. TI: 1.83; 95% CI: 1.59–2.10; p<0.001); this difference was attributable to fewer false negative SEs

CI indicates confidence interval; LR, likelihood ratio; MPI, myocardial perfusion imaging; N/A, not available; NPV, net present value; periop, perioperative; postop, postoperative; PPV, positive predictive value; ROC, receiver operating characteristic; SE, stress echocardiography; and TI, thallium imaging.

Data Supplement 15. Dobutamine Stress Echocardiography (Section 5.5.3)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Patient Population	Events (MI/death)	Ischemia, %	Endpoints		P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
				Inclusion Criteria			***Primary Endpoint (Efficacy) and Results***	***Secondary Endpoint and Results***		
Lane RT, et al.,1991 (87) 1927965	Periop risk assessment by DSE	Single center, retrospective	38	Vascular and general surgery	8%	50%	PPV 16%, NPV 100%	N/A	N/A	N/A
Lalka SG. et al., 1992 (88) 1578539	Periop risk assessment by DSE	Single center, retrospective	60	Abdominal aortic surgery	15%	50%	PPV 23%, NPV 93%	N/A	Event rate 29% vs. 4.6%, p=0.025	N/A

Eichelberger JP, et al., 1993 (89) 8362778	Periop risk assessment by DSE	Single center, prospective	75	Major vascular surgery	3%	36%	PPV 7%, NPV 100%	N/A	N/A	N/A
Langan EM, et al., 1993 (90) 8264046	Periop risk assessment by DSE	Single center, retrospective	74	Aortic surgery	4%	24%	PPV 17%, NPV 100%	N/A	N/A	Surgery deferred in 4 highly positive DSE who proceeded with CABG
Davila-Roman V, et al., 1993 (91) 8450165	Periop risk assessment by DSE	Single center, prospective	88	Aortic and LE PVD surgery	2%	23%	PPV 10%, NPV 100%	Abnormal DSE associated with increased long-term event rate also (15% vs. 3%; p=0.038)	N/A	N/A
Shafritz R, et al., 1997 (92) 9293826	Periop risk assessment by DSE, comparison to historical cohort without preop DSE	Single center, retrospective	42	Aortic surgery	2%	0%	NPV 100%	No difference in overall mortality (2.3% vs. 4.4%) or cardiac mortality (0% vs. 2.9%) in those who had preop DSE testing vs. those who did not	N/A	N/A
Bossone, 1999 (93) 10469973	Periop risk assessment by DSE	Single center, prospective	46	Lung-volume reduction surgery	2%	9%	PPV 25%, NPV 100%	N/A	N/A	N/A
Ballal RS, et al., 1999 (94) 10047628	Periop risk assessment by DSE	Single center, prospective	233	Major vascular surgery	3%	17%	PPV 0%, NPV 96%	N/A	N/A	Surgery deferred in 8 highly positive DSE who proceeded with PCI
Das MK, et al., 2000 (95) 10807472	Periop risk assessment by DSE	Single center, prospective	530	Nonvascular surgery	6%	40%	PPV 15%, NPV 100%	High risk study (defined as ischemia before 60% of age-predicted heart rate threshold) associated event rate of 43%. Incremental risk prediction over clinical characteristics	N/A	N/A
Morgan PB, et al., 2002 (96) 12198027	Periop risk assessment by DSE	Single center, retrospective	78	Vascular and general surgery	0%	5%	PPV 0, NPV 100%	N/A	N/A	All 4 pts with ischemia underwent preop coronary angiography +/- PCI.
Torres MR et al., 2002 (97) 12127610	Periop risk assessment by DSE	Single center, prospective	105	Predominantly vascular surgery	10%	47%	PPV 18%, NPV 98%	N/A	N/A	Beta-blocker therapy given on basis of DSE, 4 pts had surgery deferred for PCI/CABG
Labib SB, et al., 2004 (98) 15234412	Periop risk assessment by DSE, comparison of maximal vs. submaximal achieved peak heart rate	Single center, prospective	429	1/3 vascular surgery	2%	7%	PPV 9%, NPV 98%	High NPV even when peak heart rate not achieved	N/A	N/A
Raux M, et al., 2006 (99)	Periop risk assessment by a	Single center, retrospective	143	Abdominal aortic surgery	N/A	N/A	NPV 93% events predominantly were	N/A	N/A	All with abnormal DSE underwent coronary

16973646	negative DSE and incidence of elevated troponin						nonclinical elevated troponin measures			angiogram +/- PCI prior to surgery
Umphrey LG, et al., 2008 (100) 18508373	Periop risk assessment by DSE	Single center, retrospective	157	Orthotropic liver transplantation	3.80%	0%	NPV	Inability during DSE to achieve >80% of targeted heart rate associated with increased cardiac events (22% vs. 6%; p=0.01)	N/A	N/A
Lerakis S, et al., 2007 (101) 18219774	Periop risk assessment by DSE	Single center, retrospective	539	Bariatric surgery	0.05% (all noncardiac death)	1.20%	N/A	N/A	N/A	All with abnormal DSE underwent coronary angiogram +/- PCI prior to surgery
Nguyen P, et al., 2013 23974907	Periop risk assessment by DSE	Pooled analysis of 7 studies	580	Orthotropic liver transplantation	N/A	N/A	PPV 37%, NPV 75%	N/A	N/A	N/A

CABG indicates coronary artery bypass graft; DSE, dobutamine stress echocardiography; N/A, not available; NPV, net predictive value; PCI, percutaneous coronary intervention; periop, perioperative; PPV positive predictive value; preop, preoperative; and PVD, peripheral valvular disease.

Data Supplement 16. Preoperative Coronary Angiography (Section 5.7)

Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints		P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Secondary Endpoint and Results***		
Monaco et al., 2009 (102) 19729114	RCT	208	105	103	Vascular surgery, CRI ≥2	N/A	Routine angiography	Selective angiography	L/T MACE (58±17 mo): p=0.01	MACE by 30 d preop: 11.7% selective vs. 4.8% routine	L/T MACE p=0.003; 30 d MACE p=0.1	Small sample size, unblinded; recruit/random methods unclear

CABG indicates coronary artery bypass graft; CRI, cardiac risk index; DSE, dobutamine stress echocardiography; MACE, major adverse cardiac event; NCS, noncardiac surgery; NPV, net predictive value; PCI, percutaneous coronary intervention; PPV, positive predictive value; preop, preoperative; and RCT, randomized controlled trial.

Data Supplement 17. Coronary Revascularization Prior to Noncardiac Surgery (Section 6.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints		P Values, OR: HR: RR & 95% CI:
						Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (Efficacy) and Results*	*Secondary Endpoint and Results*	
McFalls EO, et al., 2004 (36) 15625331	Revascularization vs. medical therapy before elective major vascular surgery	RCT	510	258	252	Vascular surgery	Urgent/emergency: UA; LM; EF<20%; AS	Revascularization (CABG or PCI)	Medical therapy	Death (30 d) 3.1% (revascularization) vs. 3.4% (medical therapy)	Lost to follow up: death 2.7 y	Primary endpoint p=0.87; secondary endpoint p=0.92 (RR: 0.98; 95% CI: 0.7–1.37)

AS indicates aortic stenosis; CABG, coronary artery bypass graft; CI, confidence interval; EF, ejection fraction; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; RR, relative risk; and UA, unstable angina.

Data Supplement 18. Timing of Elective Noncardiac Surgery in Patients With Previous PCI (Section 6.1.1)

Table 1. Risk of NCS Following PCI With BMS and Risk of NCS Following PCI With DES

Author, Year	Study Type	Study Size (n)	Type of Surgery (%)					PCI to NCS (d)	MACE		APT in Perioperative Period (%)			Major Bleeding		Study Limitations	Risk of NCS in Stented Pt
			Low	*Intermediate*	*High*	*Cardiac*	*Unknown*		*Endpoints*	*(%)*	*ASA*	*$P2Y_{12}$ Inhibitor*	*DAPT*	*Endpoints*	*(%)*		
Risk of NCS following PCI With BMS																	
Kaluza, 2000 (103) 10758971	Retrospective	40	N/A	33	65	2	N/A	13	Death, MI	20, 17.5	5	12.5	2.5	Tx or reoperation	27	SC, small sample size, retrospective, APT status not well described	All MACE <2 wk after PCI, emphasizing high-risk early period
Wilson, 2003 (104) 12875757	Retrospective	207	N/A	36	58	N/A	6	1–60	Death, MI, ST or revascularization	4	51	14	26	"Excessive" surgical site bleed, Tx	2, 33	Retrospective, SC	All events occurred within first 6 wk
Sharma AK, et al., 2004 (105) 15390248	Retrospective	47	N/A	68	30	N/A	2	<21 (n=27); 21–90 (n=20)	Death or MI	25 (<21 d), 15 (21–90 d)	N/A	74 (<21 d), 70 (21–90 d)	N/A	Tx, reoperation	29 (<21 d), 0 (21–90 d)	Small sample size, retrospective, APT status not well described, SC, 6/7 deaths in first 21 d considered probable ST	Study confined to early phase NCS pt. 6/7 IE in pts who discontinued DAPT. This study suggests importance of continuation of DAPT during early period.
Reddy, 2005	Retrospective	56	10	60	20	N/A	10	<42	MI or CVD	14	79*	32*	N/A	Reoperation, Tx >2 PRBC, Hb drop >2 g/dL	5	Small sample size, retrospective, APT status not well described, SC.	All IE occurred within 42 d of PCI, emphasizing

(106) 15757604														or IC, IO or RP bleed		All 3 bleeding episodes were in pts receiving P2Y12 inhibitor.	high risk early period
Brichon, 2006 (107) 16996274	Retrospective	32	N/A	100	N/A	N/A	N/A	<90	ST	9	66	0	0	Hemothorax or RP bleed	10	Small sample size, retrospective. 30% of pts received only heparin	ST rather higher (9%) within 3 mo of stenting and lung surgery
Nuttal, 2008 (108) 18813036	Retrospective	889	21	46	33	N/A	N/A	64	Death, MI, ST, or TLR	Overall 5.2; <30 d 10.5; 30-90 d 3.8; 90-365 d 2.8	64.5†			Need for non–PRBC tx	5	Retrospective, APT status not well described, SC	This study emphasizes that risk is highest very early after PCI
Risk of NCS Following PCI With DES																	
Compton, 2006 (109) 17056330	Retrospective	38	31	35	15	N/A	19	260	MI	0	83	40	*†	Postop Tx	3	Small sample size, retrospective, APT status not well described, SC	MACE is low with NCS performed late after PCI
Brotman, 2007 (110) 18081175	Retrospective	114	52	42	6	N/A	N/A	236	MI, ST, or death	1.8	1.8	0	21	Reoperation, IC or RP bleed	0.9	Retrospective, SC	MACE is low with NCS performed late after PCI
Conroy, 2007 (111) 18084986	Retrospective	24 (42)	N/A	N/A	N/A	N/A	N/A	N/A	Ischemia on ECG, troponin elevation, or ST	7	N/A	50	N/A	Surgical site bleed or reoperation	2.4	Small sample size, retrospective, APT status not well described, SC. MACE and bleeding EP not well defined	IE: 3/14 pts who discontinued DAPT to ASA alone had ST. 4/4 with alternate anticoagulant or IV APT had no ST, suggesting value of DAPT to prevent IE.
Rhee, 2008 (112) 18475013	Retrospective	141	N/A	96	N/A	N/A	N/A	228	ST	5	5	0	0	N/A	N/A	Retrospective, SC, bleeding endpoint not well defined	IE: >7 d of $P2Y_{12}$ inhibitor discontinuation and use of Taxus stent was associated with ST
Godet, 2008 (113) 18310674	Retrospective	96	N/A	26	74	N/A	N/A	425	Troponin elevation, ST	12, 2	70	38	N/A	N/A	N/A	Small sample size, APT status and bleeding endpoints not well described, SC	The risk of a serious complication, i.e., ST, was relatively low (2%)
Rabbitts, 2008 (114) 18813037	Retrospective	520 (400 <1 y, 120 >1 y)	18	56	25	N/A	N/A	204	Death, MI, ST or revascularization	5.4 (6 <1 y, 3.3 >1 y)	70	33	*†	Surgical site, excessive bleed'	1	Retrospective, SC, APT not well described	IE: Trend to lower IE rate if NCS >1 y after PCI
Chia, 2010 (115) 20609638	Retrospective	710	N/A	N/A	N/A	N/A	N/A	348	MI or ST	1.5	14	9	18	N/A	N/A	Retrospective, bleeding endpoint not well defined, questionnaire-based	IE: The low IE rate may have been due to late NCS plus questionnaire method, i.e.,

																	underreporting
Anwarud din, 2009 (116) 19539259	Retrospective	481 (606)	5.6	55.6	20	22	N/A	390	Primary ST (definite and moderate probability); secondary death, nonfatal MI, ST	2; 9	15	1	21	N/A	N/A	Retrospective, bleeding endpoint not well defined, SC	Risk of MACE higher if NCS <30 d after PCI but some level persisted for 2-3 y after PCI
Assali, 2009 (117) 19626693	Retrospective	78	N/A	81	19	N/A	N/A	414	MI, ST, or death	7.7	18	42	21	Hb drop >2 g/dL	16.7	Small sample size, retrospective, SC	Most MACE occurred <1 wk after NCS and there was no difference in MACE between 6–12 mo vs. >12 mo
Berger, 2010 (118) 20850090	Prospective registry, retrospective	206	N/A	76	20	N/A	4	179	Death, MI, or ST	1.9	N/A	N/A	N/A	N/A	N/A	APT status and bleeding endpoint not well described	Most IEs occur within 1st wk after NCS
Gandhi, 2011 (119) 20824750	Retrospective	135 (191)	23	62	15	N/A	N/A	547	Death, ST, or MI	0.5; 2	54	30	N/A	Bleeding with hypotension, blood loss >500cc, or >2 Tx	6	Retrospective, SC, APT status not well defined	Low risk of IE when NCS performed relatively late after PCI
Brilaki, 2011 (120) 21315220	Retrospective	164	100	N/A	N/A	N/A	N/A	<365	Death, MI or ST	0.6	N/A	N/A	N/A	N/A	N/A	Retrospective, APT status and bleeding endpoint not well defined	Low risk of events in low risk NCS

*All studies were retrospective analyses.

†Rates of individual or dual APT not provided.

APT indicates antiplatelet therapy; ASA, aspirin; BMS, bare-metal stent; CVD, cardiovascular disease; DAPT, dual antiplatelet therapy; ECG, echocardiogram; Hb, hemoglobin; IC, intracranial; IE, ischemic events; IO, intraocular; IV, intravenous; MACE, major adverse coronary event; MI, myocardial infarction; N/A, not applicable; NCS, noncardiac surgery; PCI, percutaneous coronary intervention; postop, postoperative; PRBC, packed red blood cell; pt, patient; RP, retroperitoneal; rx, therapy; SC, single center; and ST, stent thrombosis; and Tx, transfusion.

Table 2. Risk of Noncardiac Surgery Following BMS or DES

Author, Year	Study Type	Study Size (n)		Type of Surgery (%)				PCI to NCS (d)	MACE			APT in Periop Period (%)			Major bleeding		Study Limitations	Risk of NCS in Stented Pt
		BMS	*DES*	*Low*	*Intermediate*	*High*	*Unknown*		*Endpoint*	*BMS (%)*	*DES (%)*	*ASA*	*$P2Y_{12}$ Inhibitor*	*DAPT*	*EP*	*(%)*		
Kim, 2008 (121) 17346821	Retrospective	101	138	N/A	N/A	N/A	N/A	N/A	Death, ST, or MI	0	2.2	N/A	N/A	N/A	N/A	N/A	Retrospective, SC, APT status and bleeding definition not well described	Limited study but showed low rate of IE for both BMS and DES
Schouten, 2007 (122)	Retrospective	93	99	12	60	23	5	<730	MI or death	2	3	53 (either single or dual APT)			N/A	N/A	Small SC, retrospective, APT	IE: APT interruption was associated with higher

17207733																	use, IE, and bleeding not well defined	MACE (5.5% vs. 0.0%; p=0.023). No difference in MACE between BMS and DES
Van Kuijk, 2009 (123) 19840567	Retrospective	174	376	33; 31	51; 47	15; 22	N/A	BMS 1314; DES 511	D, MI, ST, or revascularization	6	13	91*; 70*		9†; 30‡	Severe; moderate	10; 8	Retrospective, APT status not well described	Early NCS (<30 d) in either group was associated with increased MACE (overall p<0.001). Bleeding complications significantly higher with DAPT in both groups.
Cruden, 2010 (124) 20442357	Retrospective	1,383	570	19	71	10	N/A	BMS 503; DES 371	Primary in-hospital death + IE; secondary in-hospital death + MI	Primary 13.3; secondary 1.3	Primary 14.6; secondary 1.9	N/A	N/A	N/A	N/A	N/A	Retrospective, APT status and bleeding endpoint not well described	No significant difference in MACE risk in BMS vs. DES. MACE higher if NCS <6 wk
Albaladejo, 2011 (125) 21791513	Prospective registry; retrospective analysis	623	367	20	40	26	14	>80% were after 6 mo	MI, ST, HF, CS, SA, or stroke	10.9†		N/A	N/A	N/A	Major	9.5	APT status not well described	IE and bleeding relatively high despite relatively long time between PCI and NCS
Brancati, 2011 (126) 21297198	Retrospective	70	31	26	65	9	0	288	Death, MI, ST, or revascularization	6		39 (either ASA or $P2Y_{12}$)		49	Need for Tx or surgical hemostasis	BMS 14%, DES 6%	Retrospective, SC	Similar IE and bleeding for both groups
Tokushige, 2012 (127) 22396582	Prospective registry; retrospective analysis	1,103	1295	N/A	N/A	N/A	N/A	<42d BMS 4.4% DES 1.9%	Death, MI, ST 30 d with 2 groups:<42 after PCI; >42 d after PCI	3.5	2.9	17.8	0.6	27	Moderate, severe (GUSTO)	BMS 3.2%, DES 2.1%	Retrospective	IE and bleed risk low for both BMS and DES. >95% in each group had NCS >42 d after stent.
Wijeysundera, 2012 (1) 22893606	Retrospective	1820‡ (<2 y)	905 (<2 y)	0§	85.9	14.1	0	Range: 1–3,650	Death, ACS, revascularization by 30 d after surgery	6.7(<45 d), 2.6 (45–180 d), 2.9 (181–365 d), 1.7 (366–730 d), 0 (731–3,650 d)	20 (<45 d), 3.8 (45–180 d), 1.1 (181–365 d),1.6 (366–730 d), 1.5 (731–3,650 d)	N/A	N/A	N/A	N/A	N/A	Retrospective, administrative data base	First 45 d high-risk period; DES risk low and equal to intermediate risk surgery by 180 d

Small study defined as <100 patients

*Percentage of patients taking both ASA and $P2Y_{12}$ inhibitor not provided.

†Rates of individual or dual APT not provided.

‡Total number of patients in Wijeysundera study was 8116; 2725 patients underwent stenting <2 y.

§Total procedures=7,998; 2,725 <2 y after stent implantation.

ASA indicates aspirin; APT, anti-platelet therapy; BMS, bare-metal stent; DAPT, dual anti-platelet therapy; DES, drug-eluting stent; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; IE, ischemic events; MACE, major adverse cardiac events; MI, myocardial infarction; n, subgroup; N/A, not available; NCS, noncardiac surgery; PCI, percutaneous coronary intervention; periop, perioperative; postop, postoperative; pt, patient; SC, single center; ST, stent thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization; and Tx, transfusion.

Data Supplement 19. Perioperative Beta-Blocker Therapy (Section 6.2.1)

Please see the complete Evidence Review Committee's Systematic Review Report for more information (128). The following few tables/figures are provided for ease of use and may contain data from Poldermans studies which were included in the scope of the systematic review.

Table 1. Summary of Included Studies

Study (Year)	N	Inclusion Criteria	Exclusion Criteria	Types of Surgery	Long-Term Preoperative Beta-Blocker Therapy	Participant Characteristics
Randomized Controlled Trials						
Mangano et al. (1996) (129) 8929262	200	Known CAD or ≥2 risk factors (≥65 y of age, hypertension, current smoker, elevated cholesterol level, diabetes mellitus)	Pacemaker dependency, resting ECG abnormalities (left bundle-branch block, marked ST-T abnormalities)	Elective vascular (41%), intra-abdominal (21%), orthopedic (14%), neurosurgical (9%), or other (16%) procedures	13%	Mean age 67.5 y, 39% with known CAD
Jakobsen et al. (1997) (130) 9327317	100	Pts undergoing thoracotomy for lung resection with no known current or previous cardiovascular disease	NR	Intrathoracic (100%) procedures	NR	66% males, mean age 60.4 y
Bayliff et al. (1999) (131) 10086546	99	Pts >18 y of age undergoing major thoracic operation	Prior beta-blocker use, asthma, HF, heart block, supraventricular tachyarrhythmias, prior specific drug use (digoxin, quinidine, procainamide, amiodarone, diltiazem, verapamil)	Intrathoracic (100%) procedures	0%	62% males, mean age 62.5 y, 6% with prior MI, 5% with current angina
DECREASE-I (1999) (132) 10588963	112	Pts with ≥1 cardiac risk factor (>70 y of age, angina; prior MI, HF, diabetes mellitus, limited exercise capacity, ventricular arrhythmias) and positive result on dobutamine stress echocardiography.	Prior beta-blocker use, asthma, very high-risk dobutamine stress echocardiography result (extensive wall-motion abnormalities, strong evidence of left main or severe 3-vessel CAD)	Major vascular (100%) procedures	0%	87% males, mean age 67.5 y, 100% with known CAD, 52% with prior MI, 32% with current angina
Raby et al. (1999) (133) 10071990	26	Pts with preoperative myocardial ischemia detected by 24-h ECG monitoring performed within 1–12 d before surgery	Baseline ST-T abnormalities on ECG that preclude accurate interpretation of ECG monitoring for ischemia	Major vascular (100%) procedures	35%	46% males, mean age 68.1 y, 38% with prior MI or current angina
Zaugg et al. (1999)* (134) 10598610	43	Pts ≥65 y of age	Prior beta-blocker use, other prior drugs (beta-adrenergic agonists, glucocorticoids, anticonvulsants), heart block, rhythm other than sinus on ECG, HF, bronchospasm, systemic infection, neurological disorders	Intra-abdominal (81%), orthopedic (7%), and other (12%) procedures	0%	40% males, mean age 74.6 y, 37% with known CAD
Urban et al.	107	Pts 50 to 80 y of age undergoing elective	Specific ECG abnormalities (heart block,	Orthopedic (100%) procedures	28%	Mean age 69.5 y, 17% with prior MI, 31% with

(2000) (135) 10825304		total knee arthroplasty with known CAD or ≥1 risk factor (≥65 y of age, hypertension, current smoker, elevated cholesterol level, diabetes mellitus)	bundle-branch block, atrial arrhythmias, LV hypertrophy with repolarization abnormalities), LVEF <30%, symptomatic mitral or aortic valvular disease, bronchospasm			current angina
POBBLE (2005) (136) 15874923	103	Pts undergoing major elective infrarenal vascular surgery under general anesthesia	Prior MI in past 2 y, unstable angina, positive dobutamine stress test, prior beta-blocker use, asthma, aortic stenosis, heart rate ≤45 beats/min, systolic BP <100 mm Hg	Major vascular procedures (100%)	0%	78% males, median age 73 y
DIPOM (2006) (137) 16793810	921	Pts with diabetes mellitus >39 y of age undergoing noncardiac surgery with expected duration >1 h	Long-term beta-blocker use, conditions indicating beta blocker treatment, severe HF, heart block	Orthopedic (33%), intra-abdominal (28%), neurosurgical (8%), vascular (7%), gynecological (5%), and other (19%) procedures	0%	59% males, mean age 64.9 y, 8% with prior MI, 11% with current angina
Lai et al. (2006) (138) 16687084	60	Pts ≥65 y of age undergoing esophagectomy for esophageal cancer with no known prior CAD	Prior beta-blocker use, heart rate ≤55 beats/min, systolic BP ≤100 mm Hg, heart block	Intrathoracic (100%) procedures	0%	82% males, median ages 66 (beta blocker arm) and 67 (control arm),
MaVS (2006) (139) 17070177	496	Pts (ASA-PS Class ≤3) undergoing major vascular (abdominal aortic repair, infra-inguinal, or axillo-femoral bypass) surgery	Long-term beta-blocker use, current amiodarone use, reactive airways disease, HF, heart block	Major vascular (100%) procedures	0%	76% males, mean age 66.1 y, 14% with prior MI, 9% with current angina
Neary et al. (2006) (140) 16764198	38	Pts undergoing emergency surgery with ≥1 of the following criteria: CAD, cerebrovascular disease (prior stroke or TIA), ≥2 minor risk criteria (≥65 y of age, hypertension, smoker, diabetes mellitus, hypercholesterolemia)	Prior beta-blocker use, heart rate <55 beats/min, heart block, chronic obstructive airway disease, asthma, cardiovascular collapse, uncorrected hypovolemia	Intra-abdominal (29%), amputation (24%), major vascular (21%), orthopedic (16%), and other (10%) procedures	0%	NR
BBSA (2007) (141) 17585213	219	Pts undergoing surgery with spinal anesthesia with known CAD or ≥2 risk factors (≥65 y of age, hypertension, current smoker, elevated cholesterol level, diabetes mellitus)	Prior beta-blocker use, significant HF, heart block, severe asthma, left bundle-branch block	Orthopedic (67%), urologic (25%), and other (8%) procedures	0%	55% males, mean age 70.0 y, 8% with prior MI, 6% with current angina
POISE-1 (2008) (142) 18479744	8,351	Pts ≥45 y of age and ≥1 of the following criteria: CAD, PVD, stroke, hospitalization for HF within past 3 y, major vascular surgery, or ≥3 minor risk factors (HF, TIA, diabetes mellitus, renal insufficiency, age >70 y, nonelective surgery, intrathoracic surgery, or intraperitoneal surgery)	Prior beta-blocker use, verapamil use, heart rate <50 beats/min, heart block, asthma, CABG surgery in previous 5 y with no subsequent ischemia, low-risk surgery	Vascular (41%), intraperitoneal (22%), orthopedic (21%), and other (16%) procedures	0%	63% males, mean age 69.0 y, 43% with known CAD
Yang et al. (2008) (143) 18953854	102	Pts ≥45 y of age with ≥1 of the following criteria: CAD, PVD, stroke, hospitalization for HF in prior 3 y, or ≥3 minor risk factors (HF, diabetes mellitus, ≥65 y of age, hypertension, hypercholesterolemia,	Prior beta-blocker use, heart rate <50 beats/min, cardiac pacemaker, heart block, asthma, chronic obstructive pulmonary disease	Intra-abdominal and intrathoracic procedures	0%	59% males, mean age 71.0 y

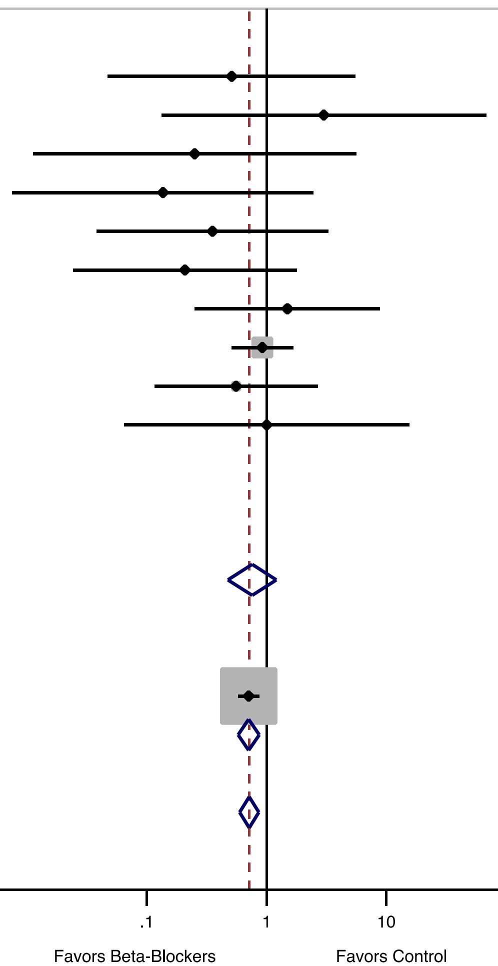
		smoker, intrathoracic surgery, or intraperitoneal surgery)				
DECREASE-IV (2009) (144) 19474688	1,066	Pts ≥40 y of age undergoing elective noncardiovascular surgery with an estimated 1%–6% perioperative cardiovascular risk	Current use, or contraindication to use, of beta blockers or statins	General surgical (39%), urologic (19%), orthopedic (16%), ear-nose-throat (12%), and other surgical (14%) procedures	0%	60% males, mean age 65.4 y, 6% with current angina, 5% with previous MI
Cohort Studies						
Matyal et al. (2008)† (145) 18503921	348	Pts undergoing supra- and infrainguinal vascular surgery	NR	Major vascular (100%) procedures	0%†	60% males

*Information on 2 of the study arms (preoperative/postoperative atenolol *versus* no beta-blocker therapy). The third study arm (intraoperative atenolol) did not meet the review definition for eligible perioperative beta-blockade.
†Only data on the subgroup of 348 pts who were not previously receiving preoperative long-term beta-blocker therapy.

ASA-PS indicates American Society of Anesthesiologists Physical Status; BBSA, Beta Blocker in Spinal Anesthesia; BP, blood pressure; CABG, coronary artery bypass graft; CAD, coronary artery disease; DECREASE, Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography; DIPOM, Diabetic Postoperative Mortality and Morbidity; ECG, electrocardiogram; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; MaVS, Metoprolol After Vascular Surgery; MI, myocardial infarction; NR, not reported; pts, patients; POBBLE, Perioperative Beta Blockage; POISE, Perioperative Ischemic Study Evaluation; PVD, peripheral vascular disease; and TIA, transient ischemic attack.

Figure 1. Effect of Perioperative Beta Blockade on In-Hospital or 30-Day Nonfatal MI in RCTs, With Members of the DECREASE Family of Trials Excluded

Study	Year	Beta Blocker	RR (95% CI)	Events, Beta-Blockers	Events, Control	% Weight
Non POISE Trials						
Mangano 1996	1996	Atenolol	0.51 (0.05, 5.54)	1/99	2/101	0.61
Jakobsen 1997	1997	Metoprolol	3.00 (0.13, 68.26)	1/15	0/15	0.36
Raby 1999	1999	Esmolol	0.25 (0.01, 5.62)	0/15	1/11	0.36
Zaugg 1999	1999	Atenolol	0.14 (0.01, 2.47)	0/20	3/19	0.41
Urban 2000	2000	Esmolol & Metoprolol	0.35 (0.04, 3.28)	1/52	3/55	0.70
POBBLE	2005	Metoprolol	0.21 (0.02, 1.79)	1/53	4/44	0.75
DIPOM	2006	Metoprolol	1.49 (0.25, 8.88)	3/462	2/459	1.09
MaVS	2006	Metoprolol	0.92 (0.51, 1.67)	19/246	21/250	9.80
Neary 2006	2006	Atenolol	0.56 (0.12, 2.68)	2/18	4/20	1.40
Yang 2008	2008	Metoprolol	1.00 (0.06, 15.56)	1/51	1/51	0.46
Bayliff 1999	1999	Propranolol	(Excluded)	0/49	0/50	0.00
Lai 2006	2006	Metoprolol	(Excluded)	0/30	0/30	0.00
BBSA	2007	Bisoprolol	(Excluded)	0/110	0/109	0.00
Subtotal (I-squared = 0.0%, p = 0.772)			0.76 (0.47, 1.21)	29/1220	41/1214	15.94
.						
POISE Trial						
POISE	2008	Metoprolol	0.71 (0.58, 0.87)	152/4174	215/4177	84.06
Subtotal (I-squared = .%, p = .)			0.71 (0.58, 0.87)	152/4174	215/4177	84.06
.						
Overall (I-squared = 0.0%, p = 0.837)			0.72 (0.59, 0.86)	181/5394	256/5391	100.00

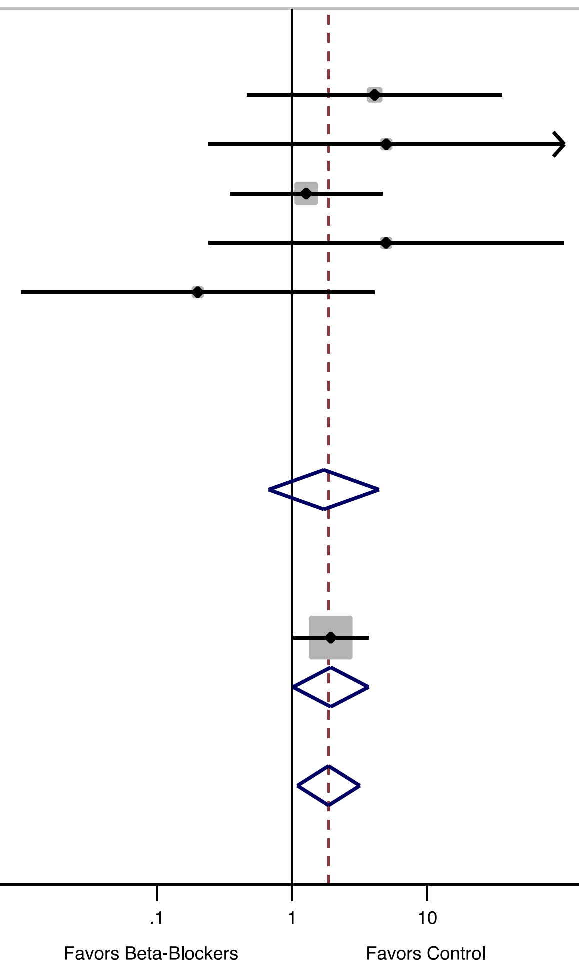


Effect of perioperative beta blockade on in-hospital or 30-day nonfatal MI, within subgroups defined by the POISE-1 trial versus other trials. The pooled effect is expressed as a pooled RR with associated 95% CI. The solid black diamonds represent point estimates in individual RCTs. The area of each gray square correlates with its contribution toward the pooled summary estimates. Horizontal lines denote 95% CIs. Estimates to the left of the line of unity (i.e., RR: 1) indicate superior clinical outcomes (i.e., fewer nonfatal MIs) with beta blockade ("*Favors Beta-Blockers*"), whereas estimates to the right of the line of unity indicate superior clinical outcomes with control ("*Favors Control*"). The blue diamonds represent the pooled estimates for all studies (RR: 0.72; 95% CI: 0.59–0.86), as well as the POISE-1 trial (RR: 0.70; 95% CI: 0.57–0.86) and the subgroup of other trials (RR: 0.76; 95% CI: 0.47–1.21). Statistical heterogeneity, as measured by the I^2 statistic, was 0% for the overall analysis.

BBSA indicates Beta Blocker in Spinal Anesthesia; CI, confidence interval; DECREASE, Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography; DIPOM, Diabetic Postoperative Mortality and Morbidity; MaVS, Metoprolol After Vascular Surgery; MI, myocardial infarction; POBBLE, Perioperative Beta Blockade; POISE, Perioperative Ischemic Evaluation Study; RCT, randomized controlled trial; and RR, relative risk.

Figure 2. Effect of Perioperative Beta Blockade on In-Hospital or 30-Day Nonfatal Stroke in RCTs, With Members of the DECREASE Family of Trials Excluded

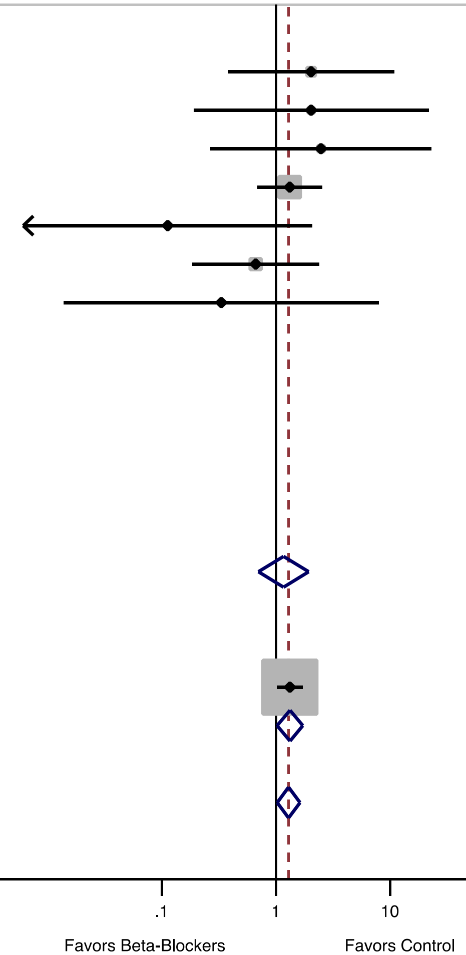
Study	Year	Beta Blocker	RR (95% CI)	Events, Beta-Blockers	Events, Control	% Weight
Non POISE Trials						
Mangano 1996	1996	Atenolol	4.08 (0.46, 35.87)	4/99	1/101	5.98
DIPOM	2006	Metoprolol	4.97 (0.24, 103.19)	2/462	0/459	3.07
MaVS	2006	Metoprolol	1.27 (0.35, 4.67)	5/246	4/250	16.64
BBSA	2007	Bisoprolol	4.95 (0.24, 102.03)	2/110	0/109	3.09
Yang 2008	2008	Metoprolol	0.20 (0.01, 4.07)	0/51	2/51	3.11
Bayliff 1999	1999	Propranolol	(Excluded)	0/49	0/50	0.00
POBBLE	2005	Metoprolol	(Excluded)	0/53	0/44	0.00
Lai 2006	2006	Metoprolol	(Excluded)	0/30	0/30	0.00
Subtotal			1.72 (0.67, 4.40)	13/1100	7/1094	31.89
POISE Trial						
POISE	2008	Metoprolol	1.93 (1.01, 3.68)	27/4174	14/4177	68.11
Subtotal			1.93 (1.01, 3.68)	27/4174	14/4177	68.11
Overall			1.86 (1.09, 3.16)	40/5274	21/5271	100.00



Effect of perioperative beta blockade on in-hospital or 30-day nonfatal stroke, within subgroups defined by the POISE-1 trial versus other trials. The pooled effect is expressed as a pooled RR with associated 95% CI. The solid black diamonds represent point estimates in individual RCTs. The area of each gray square correlates with its contribution toward the pooled summary estimates. Horizontal lines denote 95% CIs. Estimates to the left of the line of unity (i.e., RR: 1) indicate superior clinical outcomes (i.e., fewer nonfatal strokes) with beta blockade ("*Favors Beta-Blockers*"), whereas estimates to the right of the line of unity indicate superior clinical outcomes with control ("*Favors Control*"). The blue diamonds represent the pooled estimates for all studies (RR: 1.86; 95% CI: 1.09–3.16), as well as the POISE-1 trial (RR: 1.93; 95% CI: 1.01–3.68) and the subgroup of other trials (RR: 1.72; 95% CI: 0.67–4.40). Statistical heterogeneity, as measured by the I^2 statistic, was 0% for the overall analysis.

BBSA indicates Beta Blocker in Spinal Anesthesia; CI, confidence interval; DECREASE, Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography; DIPOM, Diabetic Postoperative Mortality and Morbidity; MaVS, Metoprolol After Vascular Surgery; POBBLE, Perioperative Beta Blockade; POISE, Perioperative Ischemic Evaluation Study; RCT, randomized controlled trial; and RR, relative risk.

Figure 3. Effect of Perioperative Beta Blockade on In-Hospital or 30-Day Mortality in RCTs, With Members of the DECREASE Family of Trials Excluded



Study	Year	Beta Blocker	RR (95% CI)	Events, Beta-Blockers	Events, Control	% Weight
Non POISE Trials						
Mangano 1996	1996	Atenolol	2.04 (0.38, 10.89)	4/99	2/101	1.91
Bayliff 1999	1999	Propranolol	2.04 (0.19, 21.79)	2/49	1/50	0.95
POBBLE	2005	Metoprolol	2.49 (0.27, 23.11)	3/53	1/44	1.08
DIPOM	2006	Metoprolol	1.32 (0.69, 2.55)	20/462	15/459	12.40
MaVS	2006	Metoprolol	0.11 (0.01, 2.09)	0/246	4/250	0.63
Neary 2006	2006	Atenolol	0.67 (0.19, 2.40)	3/18	5/20	3.26
Yang 2008	2008	Metoprolol	0.33 (0.01, 8.00)	0/51	1/51	0.53
Jakobsen 1997	1997	Metoprolol	(Excluded)	0/15	0/15	0.00
Raby 1999	1999	Esmolol	(Excluded)	0/15	0/11	0.00
Zaugg 1999	1999	Atenolol	(Excluded)	0/20	0/19	0.00
Urban 2000	2000	Esmolol & Metoprolol	(Excluded)	0/52	0/55	0.00
Lai 2006	2006	Metoprolol	(Excluded)	0/30	0/30	0.00
BBSA	2007	Bisoprolol	(Excluded)	0/110	0/109	0.00
Subtotal			1.17 (0.70, 1.94)	32/1220	29/1214	20.76
POISE Trial						
POISE	2008	Metoprolol	1.33 (1.03, 1.73)	129/4174	97/4177	79.24
Subtotal			1.33 (1.03, 1.73)	129/4174	97/4177	79.24
Overall			1.30 (1.03, 1.63)	161/5394	126/5391	100.00

Effect of perioperative beta blockade on in-hospital or 30-day mortality rate, within subgroups defined by POISE-1 trial versus other trials. The pooled effect is expressed as a pooled RR with associated 95% CI. The solid black diamonds represent point estimates in individual RCTs. The area of each gray square correlates with its contribution toward the pooled summary estimates. Horizontal lines denote 95% CIs. Estimates to the left of the line of unity (i.e., RR: 1) indicate superior clinical outcomes (i.e., fewer deaths) with beta blockade ("*Favors Beta-Blockers*"), whereas estimates to the right of the line of unity indicate superior clinical outcomes with control ("*Favors Control*"). The blue diamonds represent the pooled estimates for all studies (RR: 1.30; 95% CI: 1.03–1.63), as well as the POISE-1 trial (RR: 1.33; 95% CI: 1.03–1.73) and the subgroup of other trials (RR: 1.17; 95% CI: 0.70–1.94). Statistical heterogeneity, as measured by the I^2 statistic, was 0% for the overall analysis.

BBSA indicates Beta Blocker in Spinal Anesthesia; CI, confidence interval; DECREASE, Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography; DIPOM, Diabetic Postoperative Mortality and Morbidity; MaVS, Metoprolol After Vascular Surgery; POBBLE, Perioperative Beta Blockade; POISE, Perioperative Ischemic Evaluation Study; RCT, randomized controlled trial; and RR, relative risk.

Data Supplement 20. Perioperative Statin Therapy (Section 6.2.2)

Study Name, Author, Year	Aim of Study	Study Type	Study Intervention (n)	Study Comparator Group (n)	Patient Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	***Exclusion Criteria***	***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Sanders RD, et al., 2013 (146) 23824754	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis	Meta-analysis
Raju MG, et al., 2013 (147) 23670940	Impact of statin therapy on 0-d all-cause mortality, AF, and nonfatal MI	Retrospective cohort of pts undergoing intermediate-risk noncardiac, nonvascular surgery	Statin use	No statin use	All pts undergoing ACC/AHA intermediate-risk noncardiovascular surgeries during the study period	N/A	Decreased composite endpoint of 30-d all-cause mortality, AF, and nonfatal MI after adjusting for baseline characteristics	N/A	All-cause mortality reduced	OR: 0.54; 95% CI: 0.30–0.97; p=0.039. All-cause mortality p=0.0002.	Retrospective cohort
Lau WC, et al., 2013 (148) 23535525	Evaluated the benefits of adding ASA to beta blocker and statin (ABBS), with/without ACEI on postop outcome in high-risk pts undergoing major vascular surgery	Retrospective review	Statin, beta blocker and ASA use	No recorded use of combination therapy	Consecutive pts undergoing elective vascular surgery	Pts with emergent and traumatic vascular procedures, peripheral digit or distal limb amputation, or venous procedures	30-d and 12-mo mortality and survival status, MI was 3-fold lower in ABBS±ACEI (n=513) as compared with non–ABBS±ACEI (n=306). The 12-mo mortality was 8-fold lower in ABBS±ACEI as compared non–ABBS±ACEI (5.9% vs. 37.5%)	N/A	N/A	MI OR 0.31(95% CI: 0.15–0.61; p=0.001) in ABBS±ACEI (n=513) vs. non-ABBS±ACEI (n=306). 12-mo mortality HR: 0.13 (95% CI: 0.08–0.20; p<0.0001) in ABBS±ACEI vs. non-ABBS±ACEI	Retrospective , but reviews a real world pattern
Durazzo AE, et al., 2004 (149) 15111846	To analyze the effect of atorvastatin compared with placebo on the occurrence of a 6-mo composite of cardiovascular events after vascular surgery	RCT	20 mg by mouth atorvastatin for 45 d (55 pts)	Placebo (50 pts)	Pts scheduled to undergo elective noncardiac arterial vascular surgery, defined as aortic, femoropopliteal and carotid procedures	Severe hepatic or renal disease, pregnancy or breast-feeding; current or previous use of drugs to treat dyslipidemia; recent cardiovascular event, such as stroke, MI, or UA; serious infectious disease, malignancy	Less death from cardiac cause, nonfatal MI, UA, and stroke with active treatment	None	None	0.03	Small size

ACC indicates American College of Cardiology; ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AHA, American Heart Association; ASA, aspirin; BB, beta-blocker; and MI, myocardial infarction; N/A, not available; postop, postoperative; pt, patient; RCT, randomized controlled trial; and UA, unstable angina.

Data Supplement 21. Alpha-2 Agonists (Section 6.2.3)

Study Name, Author, Year	Aim of Study	Study Type	Study Intervention (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Oliver MF, et al., 1999 (150) [10519497](10519497)	To evaluate the impact of the alpha-2 adrenergic agonist, mivazerol, on rates of MI or cardiac death in pts with known CHD undergoing noncardiac surgery	A double-blind randomized placebo-controlled trial was conducted in 61 European centers	Mivazerol, 4.0 mcg/kg, was given during the first 10 min followed by a constant rate infusion. Infusion was started 20 min before the induction of anesthesia and continued for 72 h postoperatively	0.9% saline solution started 20 min before the induction of anesthesia	Pts with known CHD and those at high risk for CHD were eligible for the trial. All were scheduled to have noncardiac surgery estimated to last for at least 1 h and to have postsurgical hospitalization of at least 4 d.	UA, MI in the past 14 d, uninterpretable ECG Q-waves, cardiogenic shock, prescribed alpha agonist, severe hepatic disorders, emergency surgery, pregnant or nursing women or women aged <45 y without adequate contraception	N/A	N/A	Results presented relate to the 1,897 pts with known previous CHD. Preplanned subgroup analysis based on tests of heterogeneity. Primary endpoint was the incidence of acute MI or death during the intra- and postop hospitalization period (up to 30 d after surgery). 10.4% decrease in the primary endpoint (MI or death) and a 37% reduction in all-cause death. Secondary endpoints relate to the period of 30 d (follow-up visit) included HF, life-threatening arrhythmias, and UA	Hypotension was defined as a decrease in systolic BP of ≥20% below the baseline figure. In 10.5% (150) of mivazerol group pts and 9.4% (134) of placebo group pts, the infusion had to be stopped prematurely: of these, 62% were because of adverse events, such as hypotension, brady- or tachycardia, cardiac arrest, or organ failure; 19% (of the 62%) had to be withdrawn from the trial	NS	Cardiac deaths: MI endpoint 95% CI: 0.25–0.96 (p=0.037); for all surgeries 95% CI: 0.67–1.18 (p=NS); for vascular surgery 95% CI: 0.45–0.98 (p=0.03)	Overall study negative, positive results presented from CHD pts (not those pts with only risk factors)
Stuhmeier KD, et al., 1996 (151) [8873539](8873539)	To evaluate the effects clonidine (n=145) or placebo (n=152) on the incidence of periop myocardial ischemic episodes, MI,	Randomized double-blind study design	2 mcg/kg-1 oral clonidine (145 pts)	Oral placebo (15 pts)	Pts undergoing nonemergent vascular surgery who were not taking clonidine	Chronic myocardial ischemia, preop digitalis or chronic clonidine medication, AF, left or right BBB, and second-degree or greater atrioventricular-nodal block in the preop ECG	N/A	N/A	Myocardial IEs reduced, no change in MI and cardiac death	More fluid given to clonidine group to treat hypotension	N/A	Reduced the incidence of periop myocardial IEs from 39% (59 of 152) to 24% (35 of 145) (p<0.01)	Size

	and cardiac death												
Wallace AW, et al., 2004 (152) 15277909	To test the hypothesis that prophylactic clonidine reduces the incidence of periop myocardial ischemia and postop death in pts undergoing noncardiac surgery	Prospective, double-blinded, clinical trial	125 pts with CAD or risk factors	65 pts with CAD or risk factors	Definite CAD, peripheral arterial disease, and previous vascular surgery or 2 cardiac risk factors	UA, uninterpretable ECG, preop alpha blocker use, symptomatic AS; systolic BP <100 mmHg; and refusal or inability to give informed consent	0.2 mg oral tablet of clonidine 1 h before surgery and a 7.0 cm^2 transdermal patch of clonidine	Placebo pill and patch	30-d mortality reduced, 2-y mortality reduced, decreased IEs	N/A	N/A	p=0.035 for 30-d mortality, p=0.048 for 2-y mortality, p=0.01 for IEs	Size

AF indicates atrial fibrillation; AS, aortic stenosis; BBB, bundle branch block; BP, blood pressure; CAD, coronary artery disease; CHD indicates coronary heart disease; ECG, electrocardiogram; IE, ischemic episode; MI, myocardial infarction; N/A, not available; NS, nonsignificant; periop, perioperative; postop, postoperative; preop, preoperative; and UA, unstable angina.

Data Supplement 22. Perioperative Calcium Channel Blockers (Section 6.2.4)

Study Name, Author, Year	Aim of Study	Study Type	Study Intervention	Study Comparator Group	Patient Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	***Exclusion Criteria***	***Primary Endpoint (efficacy and results)***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Wijeysundera DN, et al., 2003 (153) 12933374	To evaluate the impact of CCBs on death, MI, supraventricular tachycardia, and major morbid events	Meta-analysis RCT evaluating CCBs during noncardiac surgery	CCB, 11 studies with 1,107 pts	Placebo	Published RCTs that evaluated CCBs (administered immediately preoperatively, intraoperatively, or postoperatively within 48 h) during noncardiac surgery, and reported any of the following outcomes: death, MI, ischemia, or supraventricular tachycardia	Studies exclusively recruited prior organ transplant recipients, individuals younger than 18 y of age, pts who had already developed supraventricular tachycardia, or pts undergoing surgery for subarachnoid hemorrhage	Mortality not decreased, ischemia and supraventricular tachycardia reduced	Trend toward hypotension	Combined endpoint of MI and death	RR: 0.49 (95% CI: 0.3–0.8) for ischemia; RR: 0.52 (95% CI: 0.37–0.72) for supraventricular tachycardia; RR: 0.35 (95% CI 0.15–0.86)	Meta-analysis, different types of CCBs
Kashimoto S, et al., 2007 (154) 17321926	To assess whether nicorandil reduces the likelihood of cardiac events during and after intermediate risk surgery	Multicenter randomized trial	Nicoradil intraoperatively during surgery	Standard therapy, 237 pts	Intermediate cardiac risk pts having intermediate cardiac risk surgery	N/A	N/A	p=0.02; 95% CI: 0.03–0.76	N/A	95% CI: 0.03–0.76	Size, limited report

CCB indicates calcium channel blocker; MI, myocardial infarction; N/A, not available; pts, patients; RCT, randomized controlled trial; and RR, relative risk.

Data Supplement 23. Angiotensin-Converting Enzyme Inhibitors (Section 6.2.5)

Study Name, Author, Year	Aim of Study	Study Type	Study Intervention	Study Comparator Group	Patient Population		Endpoints			P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
					Inclusion Criteria	*Exclusion Criteria*	*Primary Endpoint (Efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Turan A, et al., 2012 (155) 22253266	To evaluate the association of ACEI therapy with periop respiratory morbidity in adult noncardiac surgical pts, 30-d mortality secondary endpoint	Retrospective, controlled	ACEI	No ACEI	79,228 adult general surgical pts treated at the Cleveland Clinic main campus hospital between 2005 and 2009. Pts who received only general anesthesia were included.	30-d follow up data unavailable	The observed incidence of experiencing ≥1 intraoperative respiratory morbidity was 3.6% (n=360) for pts who took ACEI and 2.7% (n=1814) for pts who did not. The observed incidence of the collapsed postop respiratory morbidity was 4.2% (n=412) and 3.1% (n=2053) in pts who did and did not take ACEIs.	N/A	No significant association was found between ACEI use and any of the secondary outcomes, including 30-d mortality and the composite of in-hospital morbidity and mortality	Secondary endpoint: 30-d mortality (OR: 0.93; 95% CI: 0.73–1.19), ACEI vs. non–ACEI p=0.56; composite of in-hospital morbidity and mortality (OR: 1.06; 95% CI: 0.97–1.15)	Retrospective chart review to obtain data

ACEI indicates angiotensin-converting enzyme inhibitors; N/A, not available; periop, perioperative; and pt, patient.

Data Supplement 24. Antiplatelet Agents (Section 6.2.6)

Table 1. Risk of Bleeding on Single or Dual Antiplatelet Therapy With Noncardiac Surgery

Study Name, Author, Year	Patients on DAPT at Time of NCS	DAPT Patients With Bleeding	DAPT Patients With Bleeding (%)	Patients on Single APT at Time of NCS	Single APT Patients With Bleeding	Single APT Patients With Bleeding (%)	Study Limitations
Kaluza GL, et al., 2000 (103) 10758971	1	1	100	N/A	N/A	N/A	Small*, retrospective, SC, APT status not described
Wilson SH, et al., 2003 (104) 12875757	54	1	1.85	134	1	0.7	Retrospective, SC

Brotman DJ, et al., 2007 (110) 18081175	24	1	4	2	0	0	Retrospective, SC
Assali A, et al., 2009 (117) 19626693	17	3	17.6	47	7	15	Small, retrospective, SC
Van Kuijk JP, et al., 2009 (123) 19840567	128	27	21	421	17	4	Retrospective, APT status not described
Total	224	33	14.7	604	25	4.1	N/A

*Small= <100 patients

APT indicates antiplatelet therapy; DAPT, dual antiplatelet therapy; N/A, not applicable; NCS, noncardiac surgery; pt, patient; and SC, single center.

Table 2. Value of APT during NCS with BMS*

Author, Year	Study Size	Type of Surgery (%)				PCI to NCS (d)	MACE		APT in Periop Period (%)			Major Bleeding		Study Limitations	Value/Risk of APT
		Low	*Intermediate*	*High*	*Unknown*		*Endpoint*	*(%)*	*ASA*	*$P2Y_{12}$ Inhibitor*	*DAPT*	*Endpoint*	*(%)*		
Wilson, 2003 (12) 12875757	207	0	36	58	6	1-60	Death, MI, ST, or revascularization	4	51	14	26	"Excessive" surgical site bleed Tx	2 33 No APT: 38.5% ASA: 31.7% DAPT: 42.6%	Retrospective, SC	IE: unclear Bleeding: no excessive bleeding with ASA or DAPT
Sharma, 2004 (13) 15390248	47	0	68	30	2	<21 (n=27) 21-90 (n=20)	Death or MI	25 (<21 d) Death: ASA 5%, DAPT 85.7% 15 (21-90 d)	N/A	74 70	N/A	Tx Reoperation <21 d after PCI: ASA 43.8%, DAPT 25.0%	29 0	Small, retrospective, SC	IE: Suggestive of need for DAPT <21 d after PCI Bleeding: No excess with DAPT vs. ASA alone
Reddy, 2005 (14) 15757604	56	10	60	20	10	<42	MI or CVD ST	14 8.9 (3/5 on DAPT)	79*	32*	N/A	Reoperation, Tx >2 PRBC, Hb drop >2 g/dL or IC, IO or RP bleed	3 (2 DAPT, 1 $P2Y_{12}$ inhibitor only)	Small, retrospective	IE: unclear Bleeding: unclear
Nuttal,	899	21	46	33	0	64	Death, MI, ST or	Overall 5.2; <30 d	64.5†			Need for	5	SC, retrospective, APT status	IE: APT may be better than no APT,

2008 (16) 18813036							TLR	10.5; 30–90 d 3.8; 90–365 d 2.8 MACE: no APT after PCI 20 (4/20); ASA 3.8 (3/79); $P2Y_{12}$ 2.9 (1/35); DAPT 3.7 (28/752)		nonPRBC tx		not well defined at NCS	but SAPT vs. DAPT no difference Bleeding: unclear

*All studies were retrospective analyses.
†Rates of individual or dual APT not provided.
APT indicates antiplatelet therapy; ASA, aspirin; BMS, bare-metal stent; CVD, cardiovascular disease; DAPT, dual antiplatelet therapy; Hb, hemoglobin; IC, intracranial; IE, ischemic event; IO, intraocular; MACE, major adverse cardiac event; MI, myocardial infarction; N/A, not available; NCS, noncardiac surgery; PCI, percutaneous coronary intervention; periop, perioperative; PRBC, packed red blood cells; RP, retroperitoneal; SAPT, single antiplatelet therapy; SC, single center; ST, stent thrombosis; TLR, target lesion revascularization; and Tx, transfusion.

Table 3. Value of APT during NCS With DES*

Study, Author	Study Size (n)	Type of Surgery (%)				PCI to NCS (d)	MACE		APT in Periop Period (%)			Major Bleeding		Study Limitations	Value/Risk of APT
		Low	*Intermediate*	*High*	*Cardiac*		*Endpoint*	*(%)*	*ASA*	*P2Y12 inhibitor*	*DAPT*	*Endpoint*	*(%)*		
Brotman, 2007 (18) 18081175	114	52	42	6		236	MI, ST, or death	1.8	1.8	0	21	Reoperation or IC or RP bleed	0.9	Retrospective, SC	IE: In low- and intermediate-risk NCS late after PCI, lack of APT does not adversely impact IE
Rhee, 2008 (20) 18475013	141	N/A	96	N/A	4	228	ST	5 for >7 d of $P2Y_{12}$ discontinuation (OR: 12.8; p=0.027)	5	0	0	N/A	N/A	Retrospective, SC, bleeding endpoint not well defined	IE: Suggests value of DAPT or SAPT to prevent IE
Godet, 2008 (21) 18310674	96	N/A	26	74	N/A	425	Troponin elevation ST	12 2	70	38	N/A	N/A 26% of pts received LMWH in periop period	N/A	Retrospective, APT not well described, SC, bleeding not well defined	IE: IE uncommon late after PCI
Rabbitts, 2008 (22) 18813037	520 <1 y=400 >1 y=120	18	56	25	N/A	204	Death, MI, ST, or revascularization	5.4 (<1 y =6, >1 y =3.3)	70	33	*	Surgical site 'excessive bleed'	1	Retrospective, APT not well defined, SC	IE: Continued $P2Y_{12}$ associated with MACE in univariate but not multivariate analysis; time after PCI most important factor
Anwaruddin, 2009 (25) 19539259	481 (606)	5.6	55.6	20	22	390	Primary: ST (definite + moderate probability)	2	15	1	21	N/A	N/A	Retrospective, SC, bleeding endpoint not well defined	IE: At a mean of slightly >1 y use or nonuse of ASA or clopidogrel was not related to MACE

							Secondary: death, non-fatal MI, ST	9							
Assali, 2009 (26) [19626693](https://www.ncbi.nlm.nih.gov/pubmed/19626693)	78	N/A	81	19	N/A	414	MI, ST, or cardiac death	7.7 MACE according to APT use: no APT 10 (2/20); ASA or clopidogrel 3.9 (2/51); DAPT 11.8 (2/17)	18	42	21	Hb drop > 2g/dL	16.7	Retrospective, small, SC	Suggestion that one APT is better than none, but DAPT not better than SAPT

*All studies were retrospective analyses.

APT, antiplatelet therapy; ASA, aspirin; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; Hb, hemoglobin; IC, intracranial; IE, ischemic events; MI, myocardial infarction; LMWH, low-molecular-weight heparin; MACE, major adverse cardiac events; n, subgroup of N; N/A, not available; NCS, noncardiac surgery; OR, odds ratio; PCI, percutaneous coronary intervention; periop, perioperative; RP, retroperitoneal; SAPT, single antiplatelet therapy; SC, single center; and ST, stent thrombosis.

Table 4. Value of APT During NCS With BMS or DES*

Author	Study Size		Type of Surgery (%)				PCI to NCS (d)	MACE			APT in Periop Period (%)			Major Bleeding		Study Limitations	Value/Risk of APT
	BMS	***DES***	***Low***	***Intermediate***	***High***	***Cardiac***		***Endpoint***	***BMS (%)***	***DES (%)***	***ASA***	***P2Y12 inhibitor***	***DAPT***	***Endpoint***	***(%)***		
Van Kuijk, 2009 (31) [19840567](https://www.ncbi.nlm.nih.gov/pubmed/19840567)	174	376	BMS 33; DES 31	BMS 51; DES 47	BMS 15; DES 22	N/A	BMS: 1,314; DES: 511	Death, MI, ST, or revascularization	6	13	BMS 91*; DES 70*		BMS 9†; DES 30†	Severe: death, IC, reoperation, or Tx of >4 units Moderate : Tx of 1–3 units	Severe 10; moderate 8	Retrospective, APT not well described	Bleeding complications significantly higher with DAPT in both groups
Cruden, 2010 (5) [20442357](https://www.ncbi.nlm.nih.gov/pubmed/20442357)	1,383	570	19	71	10	N/A	BMS: 503; DES: 371	Primary: in-hospital death or IE; secondary: in-hospital death or MI	Primary: 13.3; Secondary: 1.3	Primary: 14.6; Secondary 1.9	N/A	N/A	N/A	N/A	N/A	Retrospective, APT not well described, bleeding endpoint not well defined	IE: No difference between SAPT and DAPT for pts with MACE; SAPT 45% and DAPT 55% Bleeding: significantly worse (p<0.001) with DAPT (21%) than

																	SAPT (4%)
Albaladejo, 2011 (32) [21791513]	623	367	20	40	26	14	Π	MI, ST, HF, CS, SA, or stroke	10.9†		N/A	N/A	N/A	Major	9.5‡	Retrospective, APT not well defined	IE: By multivariate analysis, discontinuation of all APT increased MACE risk (OR: 2.11; CI: 1.04–6.55; p=0.04). Bleeding: no difference between APT and no APT during NCS; SAPT vs. DAPT not described.
Tokushige, 2012 (127) [22396582]	1,103	1,295	N/A	N/A	N/A	N/A1	N/A	Death, MI, or ST 30 d after NCS	3.5	2.9	N/A	N/A	N/A	N/A	BMS: 3.2%; DES: 2.1%	Retrospective, use of APT based on hospital charts	IE (p=0.0005): No APT 2.3% (26/1088); SAPT: 1.1% (5/416); DAPT: 4.9% (28/534) Bleeding (p=0.047): no APT 2.4% (27/104); SAPT: 1.6% (7/403); DAPT: 4.0% 22/490)
Hawn, 2013 (156) [24101118]	21,986	20,003	37.5	29.5	33	N/A	730 (52.2% <1 y)	Death, MI, revascularization	5.1	4.3	N/A	N/A	N/A	N/A	N/A	Retrospective, use of administrative database, APT analysis very small (n=369); APT cessation analysis limited to NCS >6 wk after stenting	MACE w/ APT cessation OR: 0.86 (95%CI: 0.6–1.29)

*All studies were retrospective analyses. The Tokushige study used data from a prospective registry. In the Hawn study, surgical risk was classified as “low” for operations of the eye, ear, skin, and other, “intermediate” for genitourinary and musculoskeletal, and “high” for digestive, respiratory, vascular, and nervous system.

†Rates of individual or dual APT not provided.

APT indicates antiplatelet therapy; ASA, aspirin; BMS, bare-metal stent; CABG, coronary artery bypass graft; CI, confidence interval; DES, drug-eluting stent; HF, heart failure; IC, intracranial; IE, ischemic event; MACE, major adverse cardiac event; MI, myocardial infarction; N/A, not available; NCS, noncardiac surgery; OR, odds ratio; PCI, percutaneous coronary intervention; periop, perioperative; pt, patient; SAPT, single antiplatelet therapy; ST, stent thrombosis; and Tx, transfusion.

Data Supplement 25. Management of Postoperative Arrhythmias and Conduction Disorders (Section 6.3)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints		P Values, OR: HR: RR: & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (Efficacy) and Results***	***Secondary Endpoint and Results***		
Polanczyk CA, et al., 1998 (157) 9729180	To determine the incidence, clinical correlates, and effect on LOS of periop SVA in pts having major noncardiac surgery	Prospective SC cohort	4,181	4,181	N/A	Pts ≥50 y of age who had major, nonemergency, noncardiac procedures and were in sinus rhythm at the preop evaluation	N/A	N/A	N/A	Periop SVA occurred in 7.6% of pts (2.0% during surgery)	Male sex (OR: 1.3; 95% CI: 1.0–1.7); age >70 (OR: 1.3; CI: 1.0–1.7), valve disease (OR: 2.1; CI: 1.2–3.6), hx of SVA (OR: 3.4; CI: 2.4–4.8), asthma (OR: 2.0; CI: 1.3–3.1), CHF (OR: 1.7; CI: 1.1–2.7), PACs (OR: 2.1; CI: 1.3–3.4), intrathoracic procedure (OR: 9.2; CI: 6.7–13) were independent predictors of risk of SVA	N/A	Did not separate AF from other SVA, nor break out intrathoracic procedures
Amar D, et al., 2002 (158) 12198031	To determine incidence and outcomes of ventricular arrhythmia after lung resection	Prospective SC cohort	412	412	N/A	Pts undergoing lung resection at a single center 1994-1999	Rhythm other than sinus, receiving AADs, high grade AV block, hemodynamically unstable after	N/A	N/A	NSVT occurred in 15% of pts, no sustained VT or cancer. Postop AF predictive of NSVT (OR: 2.6; CI: 1.4–4.8; p=0.002)	Periop NSVT had no impact on outcome	N/A	Only included lung resection pts

							surgery						
Bayliff CD, et al., 1999 (131) 10086546	To determine whether propranolol decreases risk of postop arrhythmia in noncardiac thoracic surgery pts	Prospective randomized double blind placebo controlled trial	99	49	50	Pts undergoing major noncardiac thoracic surgery	Hx of CHF or asthma	Propranolol 10 mg every 6 h for 5 d	Placebo	Treated arrhythmia occurred in 6% of propranolol treated pts and 20% of placebo pts	N/A	p=0.07	Small size, mixed arrhythmias and included sinus tachycardia in outcome
Roselli EE, et al., 2005 (159) 16077410	To determine incidence and predictors of AF after lung cancer resection	Retrospective observational cohort	604	604	N/A	Consecutive pts undergoing lung cancer resection at CCF 1998–2002	Persistent AF, lung transplant, prior lung resection	N/A	N/A	Postop AF in 19% peaking d 2	Male sex (p=0.009), older age (p<0.0001), Hx PAF (p=0.0004), CHF (p=0.006), and right pneumonectomy predicted postop AF	N/A	Retrospective, outcomes not assessed
Amar D, et al., 2002 (2) (160) 11818768	To determine incidence and predictors of AF after major noncardiac thoracic surgery	Prospective observational SC cohort	527	527	N/A	All pts undergoing major thoracic surgery 1990–1999 in sinus rhythm	AF or on AADs	N/A	N/A	Postop AF occurred in 15%; age, preop heart rate, and postop pneumonia or respiratory failure predicted AF	N/A	Age OR: 2.5 (CI: 1.7–3.4; p<0.0001); heart rate >74, OR: 2.3 (95% CI: 1.4–3.8; p<0.0007); pneumonia OR: 3.2 (95% CI: 1.5–6.7; p<0.0021)	Limited to noncardiac thoracic surgery
Amar D, et al., 2005 (161) 16304294	To determine whether statin use is associated with lower risk of postop AF after noncardiac thoracic surgery	Prospective observational SC cohort	131	131	N/A	Pts undergoing major lung or esophageal surgery age ≥60	AF or taking AADs or steroids	N/A	N/A	Postop AF in 29%, peak at 70 h; statin use associated with lower risk of AF, but unrelated to CRP or IL-6	N/A	Statin use OR: 0.38 (p=0.025)	Small size, limited to noncardiac thoracic surgery
Amar D, et al., 2012 (162) 22841166	To determine whether BNP levels are associated with POAF after noncardiac thoracic surgery	Prospective observational SC cohort	415	415	N/A	Pts undergoing major lung or esophageal surgery age ≥60	AF or taking AADs or steroids	N/A	N/A	POAF in 16%; age, male sex, BNP>30 predicted POAF	N/A	Age OR: 1.28 per 5 y (95% CI: 1.01–1.61; p=0.04); male OR: 2.16 (95% CI: 1.12–4.17; p=0.02); BNP>30	Small size, limited to noncardiac thoracic surgery

												pg/mL OR: 4.52 (95% CI: 2.19–9.32; p<0.0001)	
Balser JR, et al., 1998 (163) 9821992	To compare outcome of post –SVA pts treated with beta blocker vs. CCB	Prospective RCT	63	Esmolol -28	Diltiazem - 27	Pts in ICU with postop SVA	Shock, preop permanent SVA	Esmolol IV	Diltiazem IV	Conversion to sinus: Esmolol 59% vs. Diltiazem 33%	N/A	p<0.05	Small sample size, limited to surgical pts in the ICU
Bhave PD, et al., 2012 (1) (164) 23194493	To define the incidence of POAF and its impact on outcomes after major noncardiac surgery	Retrospective review of administrative data from 375 hospitals over 1 y period	370,447	370,447	N/A	Pts >18 y of age undergoing noncardiac surgery in 1 of 375 hospitals in database in 2008	N/A	N/A	N/A	POAF in 3%. Older age and CHF predictive. Black race, statin. ACE-I/ARB use protective. Mortality, LOS, and cost higher for POAF group	N/A	Mortality adjusted OR: 1.68 (95% CI: 1.52–1.86; p<0.001); LOS +37% (95% CI: 34%–41%; p<0.001); cost +5,900 (95% CI: 5,400–6,400; p<0.001)	Administrative data
Bhave PD, et al., 2012 (165) 21907173	To examine association of statin use with POAF after noncardiac surgery	Retrospective cohort	370,447	79,871 (statin)	290,576 (no statin)	Pts >18 y of age undergoing noncardiac surgery in 1 of 375 hospitals in database in 2008	N/A	Periop statin used	No periop statin	POAF 2.6% in statin users vs. 3.0% in nonstatin users	N/A	Adjusted OR: 0.74 (CI: 0.57–0.95; p=0.021)	Administrative data, retrospective nonrandomized design
Borgeat A, et al., 1991 (166) 1903918	To compare use of IV flecainide vs. IV digoxin to prevent POAF	RCT	30	15	15	Pts undergoing noncardiac thoracic surgery	N/A	IV flecainide periop	IV digoxin periop	POAF 7% (flecainide) vs. 47% (digoxin)	N/A	p<0.05	Very small study, IV use only, digoxin is poor comparator, not blinded
Brathwaite D, et al., 1998 (167) 9726731	To evaluate incidence and outcomes of POAF after noncardiac nonthoracic surgery	Prospective observational SC cohort	462	462	N/A	Consecutive pts admitted to surgical ICU after noncardiac-nonthoracic surgery	Thoracic surgery or chest tube insertion	N/A	N/A	POAF in 10.2%. Mortality with POAF 23% vs. 4% without POAF; LOS 8 d vs. 2 d	N/A	p<0.05 for both	Limited to surgical ICU pts, clustered analysis of atrial arrhythmias
Cardinale D, et al., 1999 (168) 10585066	To evaluate incidence and outcomes of POAF after lung cancer surgery	Prospective observational SC cohort	233	233	N/A	Consecutive pts undergoing surgery for lung cancer	Preop AF or AAD use	N/A	N/A	POAF in 12%. No difference in mortality or LOS	N/A	p=NS	SC, single type of thoracic surgery
Christians KK,	To estimate	Retrospective	13,696	13,696	N/A	All pts	Preop AF,	N/A	N/A	POAF in 0.37%. 30-	N/A	N/A	Retrospective

et al., 2001 (169) 11839344	incidence of POAF in large cohort of pts undergoing noncardiac nonthoracic surgery	SC cohort				undergoing any noncardiac nonthoracic surgery over 2 y period in SC	thoracic surgery, PE			d mortality 12% in POAF Group.			design, use of ICD-9 code for diagnosis of POAF, limited statistical analysis
Ojima T, et al., 2013 (170) 23674202	To evaluate incidence and outcomes of POAF after esophageal surgery	N/A	207	207	N/A	Consecutive pts undergoing transthoracic esophagectomy over 6 y by single surgeon	Preop AF, concomitant lung/laryngeal surgery, palliative surgery	N/A	N/A	POAF in 9.2% associated with use of ileocolon conduit and postop heart rate >100	N/A	Ileocolon use adjusted OR: 13.6 (p=0.0023); heart rate >100 beats/min adjusted OR: 18.4 (p=0.0004)	SC, single surgeon, single type of surgery
Oniatis M, et al., 2010 (171) 20667313	To determine risk factors for POAF in pts undergoing lung cancer surgery	Interrogation of STS database	13,906	13,906	N/A	Consecutive pts entered into STS database 2002–2008 for lung cancer surgery	N/A	N/A	N/A	POAF in 12.6%; predictors include pneumonectomy, older age, bilobectomy, male sex, higher cancer stage; black race protective	30-d mortality higher in POAF (5.6% vs. 1.6%, p<0.0001); LOS longer in POAF (8 d vs. 5 d; p<0.0001)	Pneumonectomy OR: 2.04 (CI: 1.58–2.64; p<0.0001); age OR: 1.81 per 10 y (CI: 1.69–1.93; p<0.0001); bilobectomy OR: 1.67 (CI: 1.30–2.14; p<0.0001); male sex OR: 1.60 (CI: 1.40–1.83; p<0.0001), clinical stage II+ OR: 1.28 (CI: 1.07–1.52; p=0.006), black race OR: 0.62 (CI: 0.45–0.85; p=0.003)	N/A
Polanczyk CA, et al., 1998 (157) 9729180	To determine incidence and predictors of SVA after noncardiac surgery	Prospective SC cohort	4,181	4,181	N/A	Pts ≥50 undergoing nonemergent noncardiac surgery	Rhythm other than sinus	N/A	N/A	SVA in 7.6%	Older age, male sex, valvular disease, CHF, type of surgery were predictors	N/A	N/A
Riber LP, et al., 2012 (172) 22516832	To determine whether periop amiodarone reduces POAF	RCT	254	122	120	Pts >18 y of age undergoing lobectomy for lung cancer	Preop AF, heart rate <40 beats/min, LQT, hypotension	Amio 300 mg IV then 600 mg by mouth twice	Placebo	Time to AF (9% vs. 32)	Time to symptomatic AF (3% vs. 10%)	p=0.001 × 2	N/A

	after lung cancer surgery							daily for 5 d					
Tisdale JE, et al., 2009 (173) 19699916	To determine whether periop amiodarone reduces POAF after pulmonary resection	RCT	130	65	65	Adult pts undergoing lung resection	Preop AF, heart rate <50 beats/min, on AAD, LQT, hypotension	Amio IV load 24 h then 400 mg twice daily for 6 d	Usual care	POAF requiring treatment (13.8% vs. 32.3%)	LOS	p=0.02	No placebo control, not blinded
Tisdale JE, et al., 2010 (174) 20381077	To determine whether periop amiodarone reduces risk of POAF after esophagectomy	RCT	80	40	40	Adult pts undergoing esophagectomy	Preop AF, heart rate <50 beats/min, on AAD, LQT, hypotension	Amio IV for 96 h	Usual care	POAF requiring treatment (15% vs. 40%)	LOS	p=0.02	No placebo control, not blinded
Vaporciyan AA, et al., 2004 (173, 175) 15001907	To determine risk factors for POAF in pts undergoing thoracic surgery	Prospective SC observational cohort	2,588	2,588	N/A	Adult pts undergoing resection of lung, esophagus, chest wall, or mediastinal mass >5-y period at MD Anderson	N/A	N/A	N/A	POAF in 12.3%	Male sex, older age, more extensive resection were significant predictors	N/A	N/A

AAD indicates antiarrhythmic drug; ACE-I/ARB, Angiotensin-converting enzyme/ angiotensin receptor blockers; AF, atrial fibrillation; AV, atrioventricular; BNP, B-type natriuretic peptide; CCB, calcium channel blocker; CCF, congestive cardiac failure; CHF, congestive heart failure; CI, confidence interval; CRP, c-reactive protein; HR, hazard ratio; Hx, history; ICD-9, international classification of diseases ninth revision; ICU, intensive care unit; IL, interleukin; IV, intravenous; LOS, length of stay; LQT, Long QT Syndrome; n, subgroup of N; N/A, not applicable; NS, not significant; NSVT, nonsustained ventricular tachycardia; OR, odds raio; PAC, premature atrial contraction; PAF, paroxysmal atrial fibrillation; PE, pulmonary embolism; STS, Society of Thoracic Surgeons; SVA, supraventricular arrhythmia; SVT, supraventricular tachycardia; periop, perioperative; POAF, post-operative atrial fibrillation; postop, postoperative; preop, preoperative; pts, patients; and PE, pulmonary embolism; RCT, randomized controlled trial; SC, single center; and VT, ventricular tachycardia.

Data Supplement 26. Perioperative Management of Patients With CIEDs (Section 6.4)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Cheng A, et al., 2008 (176) 18307631	To determine the frequency of PPM or ICD malfunction	Prospective observational single-center cohort	92	92	N/A	Adult pts with PPM or ICD >1 mo undergoing	Unwilling to give informed consent	All pts' CIEDs programmed to detect tachyarrhythmia	None	EMI seen in 5 PPMs and no ICDs; no permanent	No major device malfunctions; 1 pacemaker near ERI reset; no	N/A	N/A	Small sample size, observational only

	from periprocedural electrocautery					noncardiac surgery or endoscopy with electrocautery or ultrasound		and interrogated before and after surgery		damage to any device	complications related to CIED			
Fiek M, et al., 2004 (177) 15009852	Evaluate prevalence of EMI in pts with ICD undergoing noncardiac surgery	Prospective observational single-center cohort	33	N/A	N/A	Pts undergoing surgery with ICD	None	None	None	No EMI detected	No adverse effects on ICD	N/A	N/A	Retrospective observational design
Hauser RG, et al., 2004 (178) 15851191	To review reports of deaths to FDA associated with ICD failure to determine cause	Retrospective observational	212	N/A	N/A	Deaths associated with ICD failure reported to FDA database 1996–2003	N/A	N/A	N/A	11 deaths occurred in pts with tachytherapies turned off —3 documented to have been inactivated prior to elective surgery	N/A	N/A	N/A	Study relies upon voluntary reporting of events to FDA, so likely underestimates incidence
Mahlow WJ, et al., 2013 (179) 23252749	To determine whether an institutional protocol for periop CIED management would be associated with a reduction in the amount of device reprogramming without increase in complications	Retrospective single-center cohort	379	197	179	Consecutive pts undergoing surgery requiring anesthesia before and after new PACED-OP protocol	None stated	PACED-OP institutional protocol, which standardized recommendations for periop CIED management	CIED pts undergoing surgery before protocol started	Percent of pts needing preop reprograming—decreased from 42%–16%	No major adverse events in either group. 3% preintervention vs. 2.2% postinterventions required adjusting sensing or output	N/A	OR 0.26 [0.15–0.44]; p<0.001 (efficacy) HR/OR 0.55–1.1; p>0.1 (safety)	No randomization, not performed prospectively
Matzke TJ, et al., 2006 (180) 16970697	Evaluate effect of electrocautery during dermatological surgery on	Retrospective single-center cohort	186	N/A	N/A	Consecutive pts with CIEDs undergoing dermatologic surgery with	None	None	None	No CIED malfunction	No adverse effects related to CIED	N/A	N/A	Retrospective observtional design

	CIEDs					electrocautery 2001–2004								
Pili-Fluory, et al., 2008 (181) 18272014	To evaluate the periop outcome of pacemaker pts undergoing noncardiac surgery	Prospective observational single-center cohort	65	N/A	N/A	All adult pacemaker pts undergoing noncardiac surgery or procedures under general or regional anesthesia	Age <18 y, unwilling to consent	None	None	No EMI described, no adverse events related to PPM	No pacemaker malfunction	11% of pts had some pre-op problem with pacemaker requiring reprogramming	N/A	Small sample size, observational only, not all devices interrogated, not programmed to detect EMI

CIED indicates cardiac implantable electronic device; EMI, Electromagnetic interference; ERI, elective replacement interval; FDA, Food and Drug Administration; ICD, implantable cardioverter-defibrillator; N/A, not available; OR, odds ratio; PACED-OP, Program for All-Inclusive Care of the Elderly-Outpatient; periop, perioperative; PPM, permanent pacemaker; and pts, patients.

Data Supplement 27. Choice of Anesthetic Technique and Agent (Section 7.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Barbosa FT, et al., 2013 (182) 23897485	Effect of epidural /spinal anesthesia for lower limb revascularization compared with other types of anesthesia (general anesthesia)	Meta-analysis of RCTs (Cochrane review)	696	417	279	Adults (≥18 y) undergoing lower limb revascularization with neuraxial anesthesia (spinal or epidural)	N/A	Neuraxial anesthesia	General anesthesia	No definitive difference mortality, stroke, MI, nerve dysfunction, lower limb amputation	N/A	Reduction in pneumonia. Otherwise no difference in-hospital stay, postop cognitive dysfunction, postop wound infection, postop anesthesia recovery room issues (nausea/vomiting/ tremor/supplemental oxygen dependence/ hypotension/HTN/ dysrhythmia), pt satisfaction, pain	OR: 0.37 favoring decrease in pneumonia in pts receiving neuraxial anesthesia (95% CI: 0.15–0.89)	Risk of pneumonia was only analyzed in 2 studies

												score, transfusions, urinary retention, claudication distance, postop rest pain in limb.		
Park WY, et al., 2001 (183) 11573049	Test whether epidural anesthesia and postop epidural analgesia decrease morbidity and mortality after intra-abdominal surgical procedures	Randomized, controlled	984	489	495	≥21 y old and undergoing abdominal aortic surgery, gastric surgery, biliary surgery, or colon surgery	<21 y old, female, ASA Class I/II/V, confused, emergency, MI within past 6 mo, abdominal procedure within past 3 mo, any prior abdominal aortic surgery, receiving chemotherapy or immunosuppressives other than steroids, tracheostomy, preop intubation, hypersensitivity to drugs, contraindication to epidural, surgeon/ anesthesiologist preference for one anesthetic	Epidural and general anesthesia plus postop epidural morphine	General anesthesia plus postop systemic opioids	Death, MI, CHF, persistent VT, complete AV block, severe hypotension, cardiac arrest, PE, respiratory failure, cerebral event, renal failure; Decrease incidence of MI, respiratory failure and stroke in subgroup of pts who underwent abdominal aortic procedures with epidural. Otherwise no difference in primary or secondary endpoints in combined group of abdominal surgery pts.	N/A	Pneumonia, sepsis, GI bleed, new angina, epidural hematoma, respiratory depression, respiratory arrest, reoperation for complications. For results see primary endpoint heading.	p 0.03 for MI favoring aortic surgery pts with epidural	Gender-specific study
Norris EJ, et al.,	Determine effect of epidural	Randomized, controlled	168	Neuraxial intraop +	GA+ PCA postop =37	Pts undergoing abdominal aortic	Procedure requiring aortic	See aforemention	GA + PCA	No difference in	N/A	No difference in medical costs,	N/A	Underpowered study; study

2001 (184) 11684971	anesthesia+ general anesthesia vs. general anesthesia + intravenous opioid			PCA postop =39; Neuraxial + GA+ epidural postop =46, GA + epidural postop =38		reconstructive surgery	cross clamp, contraindication to epidural anesthesia, previous surgery or severe deformity of thoracolumbar spine, opioid dependence, major surgery within 14 d prior, pt refusal, neurologic disease affecting thorax or lower	ed groups		LOS		hospital mortality, major cardiac morbidity		halted due to ethical concerns; monitoring committee terminated pt recruitment
Guarracino F, et al., 2006 (185) 16884976	Determine if volatile anesthetics were associated with a decrease in myocardial damage	Multicenter, randomized, controlled	112	57 who received desflurane (volatile anesthetic)	55 pts who received propofol (total IV anesthetic)	Off-pump coronary artery bypass pts	MI within 6 wk of surgery, valvular insufficiency, acute CHF, additional surgeries during hospitalization, illicit drug use within 1 mo of surgery, unusual response to an anesthetic	Volatile anesthetic administration	Propofol anesthetic administration	Myocardial damage as measured by postop cTnI. Volatile anesthetic was associated with a significant reduction in median peak cTnI (p<0.001)	N/A	Prolonged hospitalization increased in total intravenous anesthesia group (p=0.005)	p<0.001 favoring volatile anesthetics for lower postop cTnI as a surrogate for decreased myocardial damage; p=0.005 favoring volatile anesthetics for reduced hospitalization	Used biomarker release as an indicator for myocardial injury; other data such as incidence of postop AF not collected
Zangrillo A, et al., 2011 (186) 21872490	Compare the effects of total intravenous anesthesia to sevoflurane on postop cTnI after noncardiac	Single center, randomized, controlled. Blinded to all study personnel other than	88	44 pts receiving sevoflurane	44 pts received propofol (TIVA)	Pts undergoing elective lung surgery pts or peripheral revascularization	Unusual prior anesthetic response; current use of sulfonylurea theophylline, or allopurinol	Volatile anesthetic (sevoflurane) administration	TIVA (propofol)	Myocardial damage as measured postop cTnI; no statistical difference between	N/A	N/A	p=0.6	Pt hx was not extensively taken, so may not have looked at a highly "at risk" group for myocardial

	surgery	anesthesiologists who did not participate in the analysis								volatile anesthetic group and TIVA group				ischemia, thus diminishing the potential to detect a difference if it did exist. No pt in the study had a periop MI or ischemia. Small sample of pts. Underpowered.
Landoni G, et al., 2009 (187) 23439516	To evaluate the effects of volatile anesthetics in myocardial protection in noncardiac surgery	Meta-analysis of randomized trials	79 trials, 6,219 pts	3,451 pts receiving either desflurane or sevoflurane (volatile anesthetics)	2,768 pts receiving TIVA	Pts undergoing noncardiac surgery	N/A	Volatile anesthetic (sevoflurane or desflurane) administration	TIVA (propofol)	Periop MI and death; no primary endpoint was observed in any of the studies	N/A	N/A	No infarctions or deaths reported in any of the studies examined in either the volatile anesthetic pts or the TIVA pts	No author reported any postop MI or death in their study populations. No report of any significant cardiac event in any study. Authors of the meta-analysis reported difficulty conducting meta-analysis because no author reported pt outcome. Poor quality studies. All studies were single center design.
Conzen PF, et al., 2003 (188) 14508313	To evaluate the myocardial protective effects of sevoflurane in pts undergoing OFF PUMP CABG	Randomized, controlled	20	10 pts undergoing OPCAB ≤=2 vessel) receiving sevoflurane	10 pts undergoing OPCAB (≤2 vessel) receiving propofol	Pts with unusual anesthetic response, experimental drug use, severe comorbid disease, prior coronary surgery, EF<30%, sulfonylurea use	N/A	Volatile anesthetic (sevoflurane) administration	TIVA (propofol)	cTNI; significantly lower in pts receiving volatile anesthetics vs. TIVA	N/A	N/A	Significantly higher troponin I levels in TIVA pts (p=0.009)	No deaths, no transmural MI in either group; underpowered to detect clinical cardiac events

Landoni G, et al., 2007 (189) 17678775	To evaluate whether or not the cardioprotective effects of volatile anesthetics translate into decreased morbidity and mortality in cardiac surgery pts	Meta-analysis of RCTs	1,922 pts	979 pts with CAB receiving volatile anesthetic (desflurane or sevoflurane)	874 pts with CAB receiving TIVA	N/A	N/A	Volatile anesthetic (sevoflurane or desflurane) administration	TIVA (propofol)	In-hospital MI, in-hospital mortality. Volatile anesthetics were associated with significant reductions in MI (2.4% vs. 5.1%), all-cause mortality (0.4% vs. 1.6%)	N/A	Peak cardiac troponin release, inotrope use, time on mechanical ventilation, ICU LOS, hospital LOS. Volatile anesthetics associated with significant decreased peak troponin release (p=0.001), ICU stay (p=0.001), time to hospital discharge (p=0.005)	Volatile anesthetic reduction in MI p=0.008; volatile anesthetic reduction in mortality p=0.02	Definition of MI as per author; suboptimal RCTs included in the study
Bignami, et al., 2013 (190) 22819469	Investigate the cardioprotective properties of isoflurane vs. any comparator in terms of MI and all-cause mortality	Meta-analysis of 37 RCTs	3,539 pts (both cardiac and noncardiac surgery)	N/A	N/A	N/A	N/A	N/A	N/A	Isoflurane reduced mortality in high-quality studies and showed a trend toward reduction in mortality when compared with propofol. Rates of overall mortality and MI were the same when all studies (high quality and otherwise) were considered.	N/A	N/A	p=0.4 for a reduction in mortality p=0.05 for reduction in mortality for isoflurane when propofol was the control group	Important study to demonstrate isoflurane is comparable to other anesthetic drugs with better pharmacokinetic profiles but higher cost and lower potency in terms of incidence of periop MI and death. The studies included had small sample sizes, marked heterogeneity regarding surgery/MI/ length of follow-up. Only 10 of 37 studies had a low risk of bias.

ASA indicates American Society of Anesthesiologists; AV, atrioventricular; CAB, coronary artery bypass; CHF, congestive heart failure; CI, confidence interval; cTnI, cardiac troponin I; EF, ejection fraction; GA, general anesthesia; GI, gastrointestinal; HTN, hypertension; Hx, history; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; OPCAB, off-pump coronary artery bypass; N/A, not applicable; OR, odds ratio; PCA, patient-controlled analgesia; PE, pulmonary embolism; postop, postoperative; preop, preoperative; pt, patient; pts, patients; RCT, randomized controlled trial; TIVA, total intravenous anesthesia; and VT, ventricular tachycardia.

Data Supplement 28. Perioperative Pain Management (Section 7.2)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Nishimori M, et al., 2012 (191) 22786494	Assess benefits and harms of epidural analgesia compared with opioid-based analgesia for adult pts undergoing elective abdominal aortic surgery	Meta-analysis of RCTs	15 eligible trials out of 53 trials; 1297 pts	633 pts with epidurals	664 pts receiving systemic opioids	RCTs comparing postop epidural analgesia and postop sysemic opioid based analgesia for electiveabdominal aortic surgery	N/A	N/A	N/A	All cause death, cardiac death, MI, angina, ischemia, arrhythmia, CHF, severe hypotension; respiratory, GI, cerebrovascular, renal, DVT/PE	N/A	Extubation time, pain scores, bowel motility, functionality, ICU stay length, hospital stay length	Event rate of MI was reduced by epidural analgesia (RR; 0.52, CI: 0.29–0.93); no difference in angina, ischemia, CHF, arrhythmia, heart block)	N/A
Wu CL, et al., 2003 (192) 12945019	Assess effects of postop epidural analgesia compared with no postop epidural	Retrospective review of random sample of Medicare beneficiaries who underwent total hip arthroplasty	23,136	2,591 with postop epidural	20,545 without epidural	Medicare pts undergoing total hip arthroplasty	N/A	Postop epidural	No postop epidural	No difference between groups regarding mortality and morbidity: Acute MI, angina, dysrhythmias, HF, pneumonia, PE, DVT, sepsis, acute renal failure, acute cerebrovascular events, paralytic ileus.	N/A	N/A	N/A	Database designed for billing and administration, not clinical outcomes research
Matot I, et al., 2003	Assess risk of preop cardiac	Randomized controlled,	68	34	34	≥60 y old with traumatic hip	Pts with contraindication to	Preop epidural	Standard pain relief	Increased preiop cardiac events:	N/A	Postop cardiac	Preop cardiac	Unblinded study; only 1

(193) 12502992	events in pts with hip fracture who receive preop epidural (local anesthetic + opioid) vs. conventional (opioid) treatment	unblinded				fracture, known or high risk CAD	epidural, allergy to study drugs, LBBB, ?10 h from time of injury to presentation to ED; acute coronary syndrome at presentation		with opioids	combined cardiac death, MI, UA, CHF, new onset AF (20 events vs. 0 events in epidural group)		events are higher in the standard care group. No difference in postop PE, pneumonia	events p=0.01	dose of meperidine; used IM opioid instead of PCA (IV administratio n)
Park WY, et al., 2001 (183) 11573049	Test whether epidural anesthesia and postop epidural analgesia decrease morbidity and mortality after intra-abdominal surgical procedures	Randomized, controlled	984	489	495	≥21 y old and undergoing abdominal aortic surgery, gastric surgery, biliary surgery, or colon surgery	<21 y old, female, ASA Class I/II/V, confused, emergency, MI within past 6 mo, abdominal procedure within past 3 mo, any prior abdominal aortic surgery, receiving chemotherapy or immunosuppresses other than steroids, tracheostomy, preop intubation, hypersensitivity to drugs, contraindication to epidural, surgeon/anesthesiologist preference for 1 anesthetic	Epidural and general anesthesia plus postop epidural morphine	General anesthesia plus postop systemic opioids	Death, MI, CHF, persistent Vtach, complete AV block, severe hypotension, cardiac arrest, PE, respiratory failure, cerebral event, renal failure; Decrease incidence of MI, respiratory failure and stroke in subgroup of pts who underwent abdominal aortic procedures with epidural. Otherwise no difference in primary or secondary endpoints in combined group of abdominal surgery pts.	N/A	Pneumonia, sepsis, GI bleed, new angina, epidural hematoma, respiratory depression, respiratory arrest, reoperation for complications. For results see primary endpoint heading.	p0.03 for MI favoring aortic surgery pts with epidural	Gender-specific study
Liu LL, et al., 2012 (50) 12133011	Determine if there is an association between NSAID use and postop MI	Retrospective EMR from large orthopedic hospital (Hospital for Special	10,873	9,831 (NSAIDs)	1,042 (no NSAIDs)	Pts undergoing total hip arthroplasty at a single center	N/A	NSAID administration	No NSAID administratio n	No increase in postop MI with NSAID use	N/A	N/A	RR: 0.95, 95% CI: 0.5–1.8	Single center, healthy population? (mortality 0%)

		Surgery, NY) Propensity-matched controls												

AF indicates atrial fibrillation; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; DVT, deep vein thrombosis; ED, emergency department; EMR, electronic medical records; GI, gastrointestinal; HF, heart failure; ICU, intensive care unit; IV, intravenous; LBBB, left bundle-branch block; MI; myocardial infarction; N/A, not applicable; NSAID, nonsteroidal anti-inflammatory drugs; PCA, patient-controlled analgesia; PE, pulmonary embolism; postop, postoperative; pt, patient; pts, patients; preop, preoperative; RCT, randomized controlled trial; RR, relative risk; and UA, unstable angina.

Data Supplement 29. Prophylactic Intraoperative Nitroglycerin (Section 7.3)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Dodds TM, et al., 1993 (194) 8466005	To determine the effect of prophylactic NTG on the incidence of myocardial ischemia in pts with either documented CAD or a high likelihood of clinically silent CAD who undergo noncardiac surgery	Randomized, placebo-controlled; unblinded to anesthesiologists, blinded to cardiologist reading the Holter monitor	45	23	22	Hx of MI, angina, >70% narrowing of an epicardial artery, those undergoing vascular surgery for atherosclerotic disease	LBBB, WPW, nonsinus rhythm, pre-existing ST depression ≥1mm	NTG 0.9 mcg/kg/min titrated to maintain heart rate and systolic BP within 20% baseline; continued until 30 min following surgery	Placebo infusion	Myocardial ischemia as detected by Holter monitor	N/A	N/A	No difference in ischemia between pts receiving IV NTG or placebo, p=0.93; 7/23 controls, 7/22 NTG pts	Only 1 dosage of NTG; anesthesiologists were unblinded
Fusciardi J, et al., 1986 (195) 3085552	To determine if NTG infusion during airway instrumentation decreased the incidence of myocardial ischemia in pts with chronic	Randomized	46	20	26	Angina	LBBB, MI within prior 6 mo	NTG 0.9 mcg/kg/min	Fentanyl infusion alone	Myocardial ischemia as detected by 1mm ST depression on ECG lead V;	N/A	N/A	Reduced ischemia in pts receiving NTG (p<0.05)	Unblinded, no placebo control; small study; rudimentary analysis

	stable angina									PCWP>18				
Thomson IR, et al., 1984 (196) [6435481](6435481)	To determine the effect of prophylactic NTG on the incidence of intraoperative myocardial ischemia in pts with CAD undergoing CABG	Randomized, placebo controlled	20	9	11	Elective CABG	Abnormal leads II and V5 at baseline	NTG 0.5 mcg/kg/min	Placebo	Myocardial ischemia as detected by 1mm ST segment depression	N/A	N/A	No significant difference in incidence of ischemia between the two groups	Randomized study population was not balanced with regard to treatment arms: Nitroglycerin group received significantly more bypass grafts, suggesting a higher burden of CAD which may increase the incidence of ischemia; beta blocker withheld the night before surgery in both groups

BP indicates blood pressure; CABG, coronary artery bypass graft; CAD, coronary artery disease; ECG, electrocardiogram; HR, hazard ratio; hx, history; IV, intravenous; LBBB, left bundle-branch block; MI, myocardial infarction; N/A, not applicable; NTG, nitroglycerin; PCWP, pulmonary capillary wedge pressure; pts, patients; ST, stent thrombosis; and WPW, Wolff–Parkinson–White.

Data Supplement 30. Maintenance of Body Temperature (Section 7.5)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints				Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***	**P Values, OR: HR: RR & 95% CI:**	
Sumer BD, et al., 2009 (197) [19620590](19620590)	To determine if intraoperative hypothermia correlates with periop complications	Retrospective medical record chart review	136	None	None	Any pt undergoing head and neck surgery for tumors that required a free flap	None	None	Pts with temp ≤35 degrees Celsius vs. pts with temp >35 Celsius as measured by urinary catheter	Correlation of intraoperative hypothermia with postop complications (within 3 wk of surgery): Pneumonia, wound infections, other infections; flap loss, hematoma, fistula, wound breakdown, CSF leak, cardiac	N/A	Correlation of other study variables with postop complications	OR: 5.12; 95% CI: 1.317–19.917; p=0.002. Examining only local wound complications and infectious complications yielded same results (OR: 5.075; CI: 1.363–18.896).	Retrospective review from single institution; no documentation of periop antibiotic administration, smoking Hx, vasopressor use or preop radiation to the head and neck

										complications, donor site breakdown, DVT, death; This study showed that hypothermia was independently associated with a significant increase in postop complications in pts undergoing head and neck cancer surgery				
Kurz A, et al., 1996 (198) 8606715	To determine if intraoperative hypothermia increases the susceptibility to surgical wound infection and increases hospitalization	Randomized, double-blind	400	96	104	18–80 y of age undergoing elective colorectal resection for cancer or inflammatory bowel disease	Corticosteroid or immunosuppressive therapy within 4 wk of surgery; recent fever or infection; bowel obstruction; malnutrition (albumin <3.3 g/dL, wbc<2500 cell/mL; >20% weight loss)	Fluid warmer activation; forced-air cover at 40 degrees Celsius to maintain core temp near 36.5 degrees Celsius (tympanic membrane temp)	No fluid warming; forced air warmer at ambient temperature to 34.5 degrees Celsius	Postop wound infections increased in hypothermia group (6/104 in normothermia group vs. 18/96 in hypothermia group); d of hospitalization increased in hypothermia group (12 d in normothermia group vs. 14.7 in hypothermia group	N/A	Collagen deposition increased, d to first solid food decreased, d to suture removal decreased in normothermia group	p value for infection =0.009; OR: 4.9 (1.7–14.5)	Pts with hypothermia required more blood transfusion which may have confounded the results; smokers had a very high rate of complications, but were evenly distributed between the 2 groups
Frank SM, et al.,1997 (199) 9087467	To assess he relationship between body temperature and cardiac morbidity during the periop period	Randomized; cardiac outcomes double-blind	300	142	158	≥60 y of age undergoing peripheral vascular, abdominal, or thoracic surgery AND admitted to the ICU and had CAD or high risk of CAD	LBBB, LVH with strain, digitalis effect paced, preop hyper/ hypothermia, Raynaud, thyroid disorders	Upper or lower body forced air warmer full body warmer first 2 h postop adjusted to maintain temp at or near 37 degrees Celsius	No forced air warmer	Cardiac events (MI, UA, ischemia, arrest within 24 h postop); Significant increase in ECG event and morbid cardiac event (ischemia/UA, arrest, infarction) in hypothermic group	N/A	No difference in intraoperative cardiac events	Major cardiac event p=0.02;ECG event p=0.02; no significant difference in postop ischemia	Low overall incidence in postop ischemia (7%)

Nguyen HP, et al., 2010 (200) 20571361	To determine if periop hypothermia increased SAH-related cardiac abnormalities	Randomized; cardiac outcomes double-blind	1,000	499	501	Pts with subarachnoid hemorrhage who undergo cerebral aneurysm surgery	Intubated at the time of enrollment	Hypothermia (esophageal temp 33 degrees Celsius)	Normothermia 36.5 degrees Celsius	No increased incidence of any single or composite cardiovascular event as defined intraoperatively and postoperatively: hypo/HTN unintended, vasopressor use, ischemia or infarction, cardiogenic shock, CHEF, pulmonary edema, VF, VT, CPR, pacemaker placement, angioplasty and stenting. Hypothermia does not increase the incidence of cardiovascular events, at least in pts with a low preop risk of CAD	N/A	N/A	Any cardiovascular event p=0.11, OR: 1.24 (CI: 0.96–1.61)	Post hoc study; low incidence of many of the cardiovascular events

CAD, coronary artery disease; CPR, cardio-pulmonary resuscitation; CHEF, contour-clamped homogeneous electric field gel; CI, confidence interval; CSF, cerebrospinal fluid; DVT, deep vein thrombosis; ECG, electrocardiogram; hx, history; HTN, hypertension; ICU, intensive care unit; LBBB, left bundle-branch block; LVH, left ventricular hypertrophy; MI, myocardial infarction; periop, perioperative; postop, postoperative; preop, preoperative; pt, patient; pts, patients; UA, unstable angina; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Data Supplement 31. Perioperative Use of Pulmonary Artery Catheters (Section 7.7)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	***Exclusion Criteria***			***Primary Endpoint (efficacy) and Results***	***Safety Endpoint and Results***	***Secondary Endpoint and Results***		
Sandham JD, et al., 2003 (201) 12510037	RCT of PAC use in high-risk surgical pts	Prospective	1,994	997	997	ASA Class III/IV risk, ≥60 y old, scheduled for urgent or elective abdominal, thoracic, vascular or hip fracture surgery	N/A	PAC use	No PAC use, although a central venous catheter was permitted	In-hospital mortality	N/A	6 mo mortality, 12 mo mortality, and in-hospital morbidity	In-hospital mortality (p=0.93)	Increased incidence of pulmonary embolism in the PA catheter arm, 8 vs. 0, p=0.004
Valentine RJ, et al., 1998 (202) 9510275	RCT of PAC in aortic surgery	Prospective	120	120	60	Pts undergoing elective abdominal aortic reconstruction	MI w/in 3 mo, CABG within 6 wk, severe aortic/mitral valve disease, overt CHF	PAC use and presurgery hemodynamic optimization	No PAC and hydration	MI, arrhythmias, CHF, acute renal failure, CVA, graft thrombosis, pulmonary insufficiency, death	N/A	Duration of ventilation, ICU stay length, hospital stay length	All p=NS for MI, pulmonary insufficiency, CVA, death	Underpowered
Bender JS, et al., 1997 (203) 9339929	RCT of PAC in major elective vascular surgery (infra-renal aortic reconstruction or lower limb revasc)	Prospective	104	51	53	Major elective vascular surgery	Suprarenal cross-clamp, MI w/in 3 mo or UA, overt CHF, CABG within 6 wk, symptomatic aortic or mitral valve disease	PAC use	Radial artery catheter	Not defined (a lot of morbidity outcomes)	N/A	N/A	Postop complications no different between groups	Underpowered

ASA indicates American Society of Anesthesiologists; CABG, coronary artery bypass graft; CHF, congestive heart failure; CVA, cerebrovascular accident; ICU, intensive care unit; MI, myocardial infarction; N/A, not applicable; NS, nonsignificant; PAC, pulmonary-artery catheter; pts, patients; postop, postoperative; RCT, randomized controlled trial; revasc, revascularization; and UA, unstable angina.

Data Supplement 32. Surveillance and Management for Perioperative MI (Section 8.1)

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR & 95% CI:	Study Limitations & Adverse Events
						Inclusion Criteria	*Exclusion Criteria*			*Primary Endpoint (efficacy) and Results*	*Safety Endpoint and Results*	*Secondary Endpoint and Results*		
Garcia S, et al., 2013 (204) 22975335	ECG and TnI postop prognosis	Retrospective	337	N/A	N/A	Pts undergoing vascular surgery	Incomplete data, amputations, low-risk procedures	N/A	ECG & TnI	HR for mortality with abnormal ECG/TnI	N/A	N/A	ECG & TnI NS for 30-d mortality	Retrospective
Van Waes JA, et al., 2013 (205) 23667270	TnT and postop prognosis	Prospective	2,232	TnT drawn on POD 1,2,3	N/A	Intermediate= and high-risk surgery pts (hospital stay >24 h)	Lost to follow up within 30 d	N/A	TnT	HR for mortality with TnI elevation	N/A	Mortality 3% MI (universal definition) 0.6%	HR: 2.4 TnI: 0.07 -0.59 ug/L, p<0.01 and 4.2 for TnI ≥0.6; p<0.01	N/A
Shroff GR, et al., 2012 (206) 22286592	TnI and postop prognosis	Retrospective	376	TnI drawn q8 h × 3 after arriving from OR	N/A	Renal and renal/pancreas transplant pts	None	N/A	TnI	HR for mortality with TnI elevation	N/A	25% abnormal TnI, 8 in-hospital cardiac events	HR: 4.6 TnI >1 ng/mL (95% CI: 2.04–14.6)	Retrospective
Devereaux PJ, et al., 2012 (207) 22706835	TnT and postop prognosis	Prospective	15,133	TnT 6–12 h postop and POD 1,2,3	N/A	Noncardiac surgery >44 y old, and had an overnight stay	Outpt surgery or declined consent	N/A	TnT	In-hospital mortality	N/A	Mortality 1.9% MI	N/A	N/A
Beattie WS, et al., 2012 (208) 22961610	Compare TnI ordered on a clinical basis vs. regularly scheduled post-op	Retrospective	51,791	TnI	N/A	Moderate to high-risk noncardiac surgery pts	Same day surgery, cardiac surgery, transplantation, eye surgery, and duplicate procedures	N/A	N/A	In-hospital mortality	N/A	2.1% 30-d mortality, 11.1% TnI elevated >0.7 mc/L	HR: 6.5 (5.4 7.9) for mortality with TnI >0.7	N/A
Redfern G, et	Troponin	Meta-	2,195	TnI drawn	N/A	Pts	N/A	N/A	N/A	30-d mortality	N/A	N/A	OR: 5.0;	N/A

al., 2011 (209) 21564046	and 30-d and 180-d outcomes in pts undergoing vascular surgery	analysis				undergoing vascular surgery							95% CI: 2.9–8.8. 30 d mortality with elevated TnI	
Nagele P, et al., 2011 (210) 20886662	TnI and Postop MI and death	Retrospective	378	TnI elevated	N/A	Head and neck cancer surgery and had TnI measured	No TnI measured	N/A	N/A	30-d mortality	N/A	57 pts (15%) had elevated TnI, 10 pts (2.6%) had MI	OR: 5.8 (0.8 42) 30-d mortality	N/A
Levy M, et al., 2011 (211) 21336095	TnI and postop death	Meta-analysis	3,318	Troponin elevated	N/A	Troponin measured	Poor studies	N/A	N/A	OR: 3.4 (95% CI: 2.2–5.2) 30-d mortality	N/A	5% had periop MI. 30-d mortality 11.6% with periop MI and 2.2% without MI	N/A	Significant heterogeneity in group (I2=56%)
Devereaux PJ, et al., 2011 (212) 21502650	TnI and postop events	Prospective	8,351	Troponin elevated	N/A	Noncardiac surgery >44 y old, and had an overnight stay and at-risk for cardiovascular disease	N/A	N/A	N/A	1.7% had symptomatic MI, 3.3% had asymptomatic MI, and 8.3% had isolated troponin rise	N/A	HR: for death 4.76 with symptomatic MI and 4.0 for asymptomatic MI	N/A	N/A
McFalls EO, et al., 2008 (213) 18245121	TnI and events	Prospective	377	TNI ≥0.1 ug/L	N/A	CARP Trial and samples stored	N/A	N/A	N/A	30-d mortality 9 (p=NS), 1 y mortality significantly higher 20% vs. 4.7%)	N/A	N/A	N/A	N/A

CARP indicates Coronary Artery Revascularization Prophylaxis; CI, confidence interval; DVT, deep vein thrombosis; ECG, electrocardiogram; HR, hazard ratio; MI; myocardial infarction; N/A, not applicable; NS, nonsignificant; POD, postoperative day; pts, patients; TnI, troponin I; TnT, troponin T I.

References

1. Wijeysundera DN, Wijeysundera HC, Yun L, et al. Risk of elective major noncardiac surgery after coronary stent insertion: a population-based study. Circulation. 2012;126:1355-62.
2. Mashour GA, Shanks AM, Kheterpal S. Perioperative stroke and associated mortality after noncardiac, nonneurologic surgery. Anesthesiology. 2011;114:1289-96.
3. Healy KO, Waksmonski CA, Altman RK, et al. Perioperative outcome and long-term mortality for heart failure patients undergoing intermediate- and high-risk noncardiac surgery: impact of left ventricular ejection fraction. Congest Heart Fail. 2010;16:45-9.
4. Ferket BS, Genders TS, Colkesen EB, et al. Systematic review of guidelines on imaging of asymptomatic coronary artery disease. J Am Coll Cardiol. 2011;57:1591-600.
5. Wijeysundera DN, Beattie WS, Austin PC, et al. Non-invasive cardiac stress testing before elective major non-cardiac surgery: population based cohort study. BMJ. 2010;340:b5526.
6. Bateman BT, Schumacher HC, Wang S, et al. Perioperative acute ischemic stroke in noncardiac and nonvascular surgery: incidence, risk factors, and outcomes. Anesthesiology. 2009;110:231-8.
7. Rogers SO, Jr., Kilaru RK, Hosokawa P, et al. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. J Am Coll Surg. 2007;204:1211-21.
8. Dasgupta M, Rolfson DB, Stolee P, et al. Frailty is associated with postoperative complications in older adults with medical problems. Arch Gerontol Geriatr. 2009;48:78-83.
9. Hammill BG, Curtis LH, Bennett-Guerrero E, et al. Impact of heart failure on patients undergoing major noncardiac surgery. Anesthesiology. 2008;108:559-67.
10. Hernandez AF, Whellan DJ, Stroud S, et al. Outcomes in heart failure patients after major noncardiac surgery. J Am Coll Cardiol. 2004;44:1446-53.
11. van DS, Bakal JA, McAlister FA, et al. Mortality and readmission of patients with heart failure, atrial fibrillation, or coronary artery disease undergoing noncardiac surgery: an analysis of 38 047 patients. Circulation. 2011;124:289-96.
12. Xu-Cai YO, Brotman DJ, Phillips CO, et al. Outcomes of patients with stable heart failure undergoing elective noncardiac surgery. Mayo Clin Proc. 2008;83:280-8.
13. The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. Eur Heart J. 2012;33:1750-7.
14. Kazmers A, Cerqueira MD, Zierler RE. Perioperative and late outcome in patients with left ventricular ejection fraction of 35% or less who require major vascular surgery. J Vasc Surg. 1988;8:307-15.
15. Kazmers A, Cerqueira MD, Zierler RE. The role of preoperative radionuclide left ventricular ejection fraction for risk assessment in carotid surgery. Arch Surg. 1988;123:416-9.
16. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med. 1977;297:845-50.
17. Detsky AS, Abrams HB, McLaughlin JR, et al. Predicting cardiac complications in patients undergoing non-cardiac surgery. J Gen Intern Med. 1986;1:211-9.
18. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100:1043-9.
19. Agarwal S, Rajamanickam A, Bajaj NS, et al. Impact of aortic stenosis on postoperative outcomes after noncardiac surgeries. Circ Cardiovasc Qual Outcomes. 2013;6:193-200.
20. Calleja AM, Dommaraju S, Gaddam R, et al. Cardiac risk in patients aged >75 years with asymptomatic, severe aortic stenosis undergoing noncardiac surgery. Am J Cardiol. 2010;105:1159-63.
21. Leibowitz D, Rivkin G, Schiffman J, et al. Effect of severe aortic stenosis on the outcome in elderly patients undergoing repair of hip fracture. Gerontology. 2009;55:303-6.
22. Zahid M, Sonel AF, Saba S, et al. Perioperative risk of noncardiac surgery associated with aortic stenosis. Am J Cardiol. 2005;96:436-8.
23. Torsher LC, Shub C, Rettke SR, et al. Risk of patients with severe aortic stenosis undergoing noncardiac surgery. Am J Cardiol. 1998;81:448-52.
24. Lai H-C, Lai H-C, Lee W-L, et al. Impact of chronic advanced aortic regurgitation on the perioperative outcome of noncardiac surgery. Acta Anaesthesiol Scand. 2010;54:580-8.
25. Bajaj NS, Agarwal S, Rajamanickam A, et al. Impact of severe mitral regurgitation on postoperative outcomes after noncardiac surgery. Am J Med. 2013;126:529-35.
26. Lai H-C, Lai H-C, Wang K-Y, et al. Severe pulmonary hypertension complicates postoperative outcome of non-cardiac surgery. Br J Anaesth. 2007;99:184-90.
27. Biteker M, Duman D, Tekkesin AI. Predictive value of preoperative electrocardiography for perioperative cardiovascular outcomes in patients undergoing noncardiac, nonvascular surgery. Clin Cardiol. 2012;35:494-9.
28. Mahla E, Rotman B, Rehak P, et al. Perioperative ventricular dysrhythmias in patients with structural heart disease undergoing noncardiac surgery. Anesth Analg. 1998;86:16-21.
29. Mangano DT, Browner WS, Hollenberg M, et al. Long-term cardiac prognosis following noncardiac surgery. The Study of Perioperative Ischemia Research Group. JAMA. 1992;268:233-9.
30. O'Kelly B, Browner WS, Massie B, et al. Ventricular arrhythmias in patients undergoing noncardiac surgery. The Study of Perioperative Ischemia Research Group. JAMA. 1992;268:217-21.
31. Ramakrishna G, Sprung J, Ravi BS, et al. Impact of pulmonary hypertension on the outcomes of noncardiac surgery: predictors of perioperative morbidity and mortality. J Am Coll Cardiol. 2005;45:1691-9.
32. Minai OA, Venkateshiah SB, Arroliga AC. Surgical intervention in patients with moderate to severe pulmonary arterial hypertension. Conn Med. 2006;70:239-43.
33. Kaw R, Pasupuleti V, Deshpande A, et al. Pulmonary hypertension: an important predictor of outcomes in patients undergoing non-cardiac surgery. Respir Med. 2011;105:619-24.
34. Price LC, Montani D, Jaïs X, et al. Noncardiothoracic nonobstetric surgery in mild-to-moderate pulmonary hypertension. Eur Respir J. 2010;35:1294-302.
35. Meyer S, McLaughlin VV, Seyfarth H-J, et al. Outcomes of noncardiac, nonobstetric surgery in patients with PAH: an international prospective survey. Eur Respir J. 2013;41:1302-7.
36. McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med. 2004;351:2795-804.
37. Davenport DL, O'Keeffe SD, Minion DJ, et al. Thirty-day NSQIP database outcomes of open versus endoluminal repair of ruptured abdominal aortic aneurysms. J Vasc Surg. 2010;51:305-9.e1.

38. Jordan SW, Mioton LM, Smetona J, et al. Resident involvement and plastic surgery outcomes: an analysis of 10,356 patients from the American College of Surgeons National Surgical Quality Improvement Program database. Plast Reconstr Surg. 2013;131:763-73.
39. Leung JM, Dzankic S. Relative importance of preoperative health status versus intraoperative factors in predicting postoperative adverse outcomes in geriatric surgical patients. J Am Geriatr Soc. 2001;49:1080-5.
40. Reilly DF, McNeely MJ, Doerner D, et al. Self-reported exercise tolerance and the risk of serious perioperative complications. Arch Intern Med. 1999;159:2185-92.
41. Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. Chest. 1999;116:355-62.
42. Wiklund RA, Stein HD, Rosenbaum SH. Activities of daily living and cardiovascular complications following elective, noncardiac surgery. Yale J Biol Med. 2001;74:75-87.
43. Crawford RS, Cambria RP, Abularrage CJ, et al. Preoperative functional status predicts perioperative outcomes after infrainguinal bypass surgery. J Vasc Surg. 2010;51:351-8.
44. Goswami S, Brady JE, Jordan DA, et al. Intraoperative cardiac arrests in adults undergoing noncardiac surgery: incidence, risk factors, and survival outcome. Anesthesiology. 2012;117:1018-26.
45. Tsiouris A, Horst HM, Paone G, et al. Preoperative risk stratification for thoracic surgery using the American College of Surgeons National Surgical Quality Improvement Program data set: functional status predicts morbidity and mortality. J Surg Res. 2012;177:1-6.
46. Carliner NH, Fisher ML, Plotnick GD, et al. The preoperative electrocardiogram as an indicator of risk in major noncardiac surgery. Can J Cardiol. 1986;2:134-7.
47. Gold BS, Young ML, Kinman JL, et al. The utility of preoperative electrocardiograms in the ambulatory surgical patient. Arch Intern Med. 1992;152:301-5.
48. Jeger RV, Probst C, Arsenic R, et al. Long-term prognostic value of the preoperative 12-lead electrocardiogram before major noncardiac surgery in coronary artery disease. Am Heart J. 2006;151:508-13.
49. Landesberg G, Einav S, Christopherson R, et al. Perioperative ischemia and cardiac complications in major vascular surgery: importance of the preoperative twelve-lead electrocardiogram. J Vasc Surg. 1997;26:570-8.
50. Liu LL, Dzankic S, Leung JM. Preoperative electrocardiogram abnormalities do not predict postoperative cardiac complications in geriatric surgical patients. J Am Geriatr Soc. 2002;50:1186-91.
51. Payne CJ, Payne AR, Gibson SC, et al. Is there still a role for preoperative 12-lead electrocardiography? World J Surg. 2011;35:2611-6.
52. Schein OD, Katz J, Bass EB, et al. The value of routine preoperative medical testing before cataract surgery. Study of Medical Testing for Cataract Surgery. N Engl J Med. 2000;342:168-75.
53. Seymour DG, Pringle R, MacLennan WJ. The role of the routine pre-operative electrocardiogram in the elderly surgical patient. Age Ageing. 1983;12:97-104.
54. Turnbull JM, Buck C. The value of preoperative screening investigations in otherwise healthy individuals. Arch Intern Med. 1987;147:1101-5.
55. van Klei WA, Bryson GL, Yang H, et al. The value of routine preoperative electrocardiography in predicting myocardial infarction after noncardiac surgery. Ann Surg. 2007;246:165-70.
56. Baron JF, Mundler O, Bertrand M, et al. Dipyridamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. N Engl J Med. 1994;330:663-9.
57. Kontos MC, Brath LK, Akosah KO, et al. Cardiac complications in noncardiac surgery: relative value of resting two-dimensional echocardiography and dipyridamole thallium imaging. Am Heart J. 1996;132:559-66.
58. Halm EA, Browner WS, Tubau JF, et al. Echocardiography for assessing cardiac risk in patients having noncardiac surgery. Study of Perioperative Ischemia Research Group. Ann Intern Med. 1996;125:433-41.
59. Rohde LE, Polanczyk CA, Goldman L, et al. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. Am J Cardiol. 2001;87:505-9.
60. Cutler BS, Wheeler HB, Paraskos JA, et al. Applicability and interpretation of electrocardiographic stress testing in patients with peripheral vascular disease. Am J Surg. 1981;141:501-6.
61. Gerson MC, Hurst JM, Hertzberg VS, et al. Cardiac prognosis in noncardiac geriatric surgery. Ann Intern Med. 1985;103:832-7.
62. Arous EJ, Baum PL, Cutler BS. The ischemic exercise test in patients with peripheral vascular disease. Implications for management. Arch Surg. 1984;119:780-3.
63. Carliner NH, Fisher ML, Plotnick GD, et al. Routine preoperative exercise testing in patients undergoing major noncardiac surgery. Am J Cardiol. 1985;56:51-8.
64. Leppo J, Plaja J, Gionet M, et al. Noninvasive evaluation of cardiac risk before elective vascular surgery. J Am Coll Cardiol. 1987;9:269-76.
65. McPhail N, Calvin JE, Shariatmadar A, et al. The use of preoperative exercise testing to predict cardiac complications after arterial reconstruction. J Vasc Surg. 1988;7:60-8.
66. Sgura FA, Kopecky SL, Grill JP, et al. Supine exercise capacity identifies patients at low risk for perioperative cardiovascular events and predicts long-term survival. Am J Med. 2000;108:334-6.
67. Hartley RA, Pichel AC, Grant SW, et al. Preoperative cardiopulmonary exercise testing and risk of early mortality following abdominal aortic aneurysm repair. Br J Surg. 2012;99:1539-46.
68. Thompson AR, Peters N, Lovegrove RE, et al. Cardiopulmonary exercise testing provides a predictive tool for early and late outcomes in abdominal aortic aneurysm patients. Ann R Coll Surg Engl. 2011;93:474-81.
69. Prentis JM, Trenell MI, Jones DJ, et al. Submaximal exercise testing predicts perioperative hospitalization after aortic aneurysm repair. J Vasc Surg. 2012;56:1564-70.
70. Carlisle J, Swart M. Mid-term survival after abdominal aortic aneurysm surgery predicted by cardiopulmonary exercise testing. Br J Surg. 2007;94:966-9.
71. Older P, Smith R, Courtney P, et al. Preoperative evaluation of cardiac failure and ischemia in elderly patients by cardiopulmonary exercise testing. Chest. 1993;104:701-4.
72. Snowden CP, Prentis JM, Anderson HL, et al. Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery. Ann Surg. 2010;251:535-41.
73. Snowden CP, Prentis J, Jacques B, et al. Cardiorespiratory fitness predicts mortality and hospital length of stay after major elective surgery in older people. Ann Surg. 2013;257:999-1004.
74. Wilson RJT, Davies S, Yates D, et al. Impaired functional capacity is associated with all-cause mortality after major elective intra-abdominal surgery. Br J Anaesth. 2010;105:297-303.
75. Junejo MA, Mason JM, Sheen AJ, et al. Cardiopulmonary exercise testing for preoperative risk assessment before hepatic resection. Br J Surg. 2012;99:1097-104.

76. Beattie WS, Abdelnaem E, Wijeysundera DN, et al. A meta-analytic comparison of preoperative stress echocardiography and nuclear scintigraphy imaging. Anesth Analg. 2006;102:8-16.
77. Eagle KA, Brundage BH, Chaitman BR, et al. Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Committee on Perioperative Cardiovascular Evaluation for Noncardiac Surgery. Circulation. 1996;93:1278-317.
78. Younis LT, Aguirre F, Byers S, et al. Perioperative and long-term prognostic value of intravenous dipyridamole thallium scintigraphy in patients with peripheral vascular disease. Am Heart J. 1990;119:1287-92.
79. Hendel RC, Whitfield SS, Villegas BJ, et al. Prediction of late cardiac events by dipyridamole thallium imaging in patients undergoing elective vascular surgery. Am J Cardiol. 1992;70:1243-9.
80. Lette J, Waters D, Cerino M, et al. Preoperative coronary artery disease risk stratification based on dipyridamole imaging and a simple three-step, three-segment model for patients undergoing noncardiac vascular surgery or major general surgery. Am J Cardiol. 1992;69:1553-8.
81. Brown KA, Rowen M. Extent of jeopardized viable myocardium determined by myocardial perfusion imaging best predicts perioperative cardiac events in patients undergoing noncardiac surgery. J Am Coll Cardiol. 1993;21:325-30.
82. Bry JD, Belkin M, O'Donnell TF, et al. An assessment of the positive predictive value and cost-effectiveness of dipyridamole myocardial scintigraphy in patients undergoing vascular surgery. J Vasc Surg. 1994;19:112-21.
83. Marshall ES, Raichlen JS, Forman S, et al. Adenosine radionuclide perfusion imaging in the preoperative evaluation of patients undergoing peripheral vascular surgery. Am J Cardiol. 1995;76:817-21.
84. Stratmann HG, Younis LT, Wittry MD, et al. Dipyridamole technetium-99m sestamibi myocardial tomography in patients evaluated for elective vascular surgery: prognostic value for perioperative and late cardiac events. Am Heart J. 1996;131:923-9.
85. Cohen MC, Siewers AE, Dickens JD, et al. Perioperative and long-term prognostic value of dipyridamole Tc-99m sestamibi myocardial tomography in patients evaluated for elective vascular surgery. J Nucl Cardiol. 2003;10:464-72.
86. Harafuji K, Chikamori T, Kawaguchi S, et al. Value of pharmacologic stress myocardial perfusion imaging for preoperative risk stratification for aortic surgery. Circ J. 2005;69:558-63.
87. Lane RT, Sawada SG, Segar DS, et al. Dobutamine stress echocardiography for assessment of cardiac risk before noncardiac surgery. Am J Cardiol. 1991;68:976-7.
88. Lalka SG, Sawada SG, Dalsing MC, et al. Dobutamine stress echocardiography as a predictor of cardiac events associated with aortic surgery. J Vasc Surg. 1992;15:831-40.
89. Eichelberger JP, Schwarz KQ, Black ER, et al. Predictive value of dobutamine echocardiography just before noncardiac vascular surgery. Am J Cardiol. 1993;72:602-7.
90. Langan EM, Youkey JR, Franklin DP, et al. Dobutamine stress echocardiography for cardiac risk assessment before aortic surgery. J Vasc Surg. 1993;18:905-11.
91. Davila-Roman VG, Waggoner AD, Sicard GA, et al. Dobutamine stress echocardiography predicts surgical outcome in patients with an aortic aneurysm and peripheral vascular disease. J Am Coll Cardiol. 1993;21:957-63.
92. Shafritz R, Ciocca RG, Gosin JS, et al. The utility of dobutamine echocardiography in preoperative evaluation for elective aortic surgery. Am J Surg. 1997;174:121-5.
93. Bossone E, Martinez FJ, Whyte RI, et al. Dobutamine stress echocardiography for the preoperative evaluation of patients undergoing lung volume reduction surgery. J Thorac Cardiovasc Surg. 1999;118:542-6.
94. Ballal RS, Kapadia S, Secknus MA, et al. Prognosis of patients with vascular disease after clinical evaluation and dobutamine stress echocardiography. Am Heart J. 1999;137:469-75.
95. Das MK, Pellikka PA, Mahoney DW, et al. Assessment of cardiac risk before nonvascular surgery: dobutamine stress echocardiography in 530 patients. J Am Coll Cardiol. 2000;35:1647-53.
96. Morgan PB, Panomitros GE, Nelson AC, et al. Low utility of dobutamine stress echocardiograms in the preoperative evaluation of patients scheduled for noncardiac surgery. Anesth Analg. 2002;95:512-6.
97. Torres MR, Short L, Baglin T, et al. Usefulness of clinical risk markers and ischemic threshold to stratify risk in patients undergoing major noncardiac surgery. Am J Cardiol. 2002;90:238-42.
98. Labib SB, Goldstein M, Kinnunen PM, et al. Cardiac events in patients with negative maximal versus negative submaximal dobutamine echocardiograms undergoing noncardiac surgery: importance of resting wall motion abnormalities. J Am Coll Cardiol. 2004;44:82-7.
99. Raux M, Godet G, Isnard R, et al. Low negative predictive value of dobutamine stress echocardiography before abdominal aortic surgery. Br J Anaesth. 2006;97:770-6.
100. Umphrey LG, Hurst RT, Eleid MF, et al. Preoperative dobutamine stress echocardiographic findings and subsequent short-term adverse cardiac events after orthotopic liver transplantation. Liver Transpl. 2008;14:886-92.
101. Lerakis S, Kalogeropoulos AP, El-Chami MF, et al. Transthoracic dobutamine stress echocardiography in patients undergoing bariatric surgery. Obes Surg. 2007;17:1475-81.
102. Monaco M, Stassano P, Di TL, et al. Systematic strategy of prophylactic coronary angiography improves long-term outcome after major vascular surgery in medium- to high-risk patients: a prospective, randomized study. J Am Coll Cardiol. 2009;54:989-96.
103. Kaluza GL, Joseph J, Lee JR, et al. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol. 2000;35:1288-94.
104. Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. J Am Coll Cardiol. 2003;42:234-40.
105. Sharma AK, Ajani AE, Hamwi SM, et al. Major noncardiac surgery following coronary stenting: when is it safe to operate? Catheter Cardiovasc Interv. 2004;63:141-5.
106. Reddy PR, Vaitkus PT. Risks of noncardiac surgery after coronary stenting. Am J Cardiol. 2005;95:755-7.
107. Brichon PY, Boitet P, Dujon A, et al. Perioperative in-stent thrombosis after lung resection performed within 3 months of coronary stenting. Eur J Cardiothorac Surg. 2006;30:793-6.
108. Nuttall GA, Brown MJ, Stombaugh JW, et al. Time and cardiac risk of surgery after bare-metal stent percutaneous coronary intervention. Anesthesiology. 2008;109:588-95.
109. Compton PA, Zankar AA, Adesanya AO, et al. Risk of noncardiac surgery after coronary drug-eluting stent implantation. Am J Cardiol. 2006;98:1212-3.
110. Brotman DJ, Bakhru M, Saber W, et al. Discontinuation of antiplatelet therapy prior to low-risk noncardiac surgery in patients with drug-eluting stents: a retrospective cohort study. J Hosp Med. 2007;2:378-84.
111. Conroy M, Bolsin SN, Black SA, et al. Perioperative complications in patients with drug-eluting stents: a three-year audit at Geelong Hospital. Anaesth Intensive Care. 2007;35:939-44.
112. Rhee SJ, Yun KH, Lee SR, et al. Drug-eluting stent thrombosis during perioperative period. Int Heart J. 2008;49:135-42.
113. Godet G, Le MY, Lesache F, et al. Drug-eluting stent thrombosis in patients undergoing non-cardiac surgery: is it always a problem? Br J Anaesth. 2008;100:472-7.

114. Rabbitts JA, Nuttall GA, Brown MJ, et al. Cardiac risk of noncardiac surgery after percutaneous coronary intervention with drug-eluting stents. Anesthesiology. 2008;109:596-604.
115. Chia KK, Park JJ, Postle J, et al. Frequency of late drug-eluting stent thrombosis with non-cardiac surgery. Am J Cardiol. 2010;106:1-3.
116. Anwaruddin S, Askari AT, Saudye H, et al. Characterization of post-operative risk associated with prior drug-eluting stent use. JACC Cardiovasc Interv. 2009;2:542-9.
117. Assali A, Vaknin-Assa H, Lev E, et al. The risk of cardiac complications following noncardiac surgery in patients with drug eluting stents implanted at least six months before surgery. Catheter Cardiovasc Interv. 2009;74:837-43.
118. Berger PB, Kleiman NS, Pencina MJ, et al. Frequency of major noncardiac surgery and subsequent adverse events in the year after drug-eluting stent placement results from the EVENT (Evaluation of Drug-Eluting Stents and Ischemic Events) Registry. JACC Cardiovasc Interv. 2010;3:920-7.
119. Gandhi NK, Abdel-Karim ARR, Banerjee S, et al. Frequency and risk of noncardiac surgery after drug-eluting stent implantation. Catheter Cardiovasc Interv. 2011;77:972-6.
120. Brilakis ES, Cohen DJ, Kleiman NS, et al. Incidence and clinical outcome of minor surgery in the year after drug-eluting stent implantation: results from the Evaluation of Drug-Eluting Stents and Ischemic Events Registry. Am Heart J. 2011;161:360-6.
121. Kim HL, Park KW, Kwak JJ, et al. Stent-related cardiac events after non-cardiac surgery: drug-eluting stent vs. bare metal stent. Int J Cardiol. 2008;123:353-4.
122. Schouten O, van Domburg RT, Bax JJ, et al. Noncardiac surgery after coronary stenting: early surgery and interruption of antiplatelet therapy are associated with an increase in major adverse cardiac events. J Am Coll Cardiol. 2007;49:122-4.
123. van Kuijk J-P, Flu W-J, Schouten O, et al. Timing of noncardiac surgery after coronary artery stenting with bare metal or drug-eluting stents. Am J Cardiol. 2009;104:1229-34.
124. Cruden NLM, Harding SA, Flapan AD, et al. Previous coronary stent implantation and cardiac events in patients undergoing noncardiac surgery. Circ Cardiovasc Interv. 2010;3:236-42.
125. Albaladejo P, Marret E, Samama CM, et al. Non-cardiac surgery in patients with coronary stents: the RECO study. Heart. 2011;97:1566-72.
126. Brancati MF, Giammarinaro M, Burzotta F, et al. Outcome of non-cardiac surgery after stent implantation in the DES era: results of the Surgery After Stent (SAS) registry. J Invasive Cardiol. 2011;23:44-9.
127. Tokushige A, Shiomi H, Morimoto T, et al. Incidence and outcome of surgical procedures after coronary bare-metal and drug-eluting stent implantation: a report from the CREDO-Kyoto PCI/CABG registry cohort-2. Circ Cardiovasc Interv. 2012;5:237-46.
128. Wijeysundera DN, Duncan D, Nkonde-Price C, et al. Perioperative Beta Blockade in Noncardiac Surgery: A Systematic Review for the 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. In Press. Journal of the American College of Cardiology. 2014;
129. Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. N Engl J Med. 1996;335:1713-20.
130. Jakobsen CJ, Bille S, Ahlburg P, et al. Perioperative metoprolol reduces the frequency of atrial fibrillation after thoracotomy for lung resection. J Cardiothorac Vasc Anesth. 1997;11:746-51.
131. Bayliff CD, Massel DR, Inculet RI, et al. Propranolol for the prevention of postoperative arrhythmias in general thoracic surgery. Ann Thorac Surg. 1999;67:182-6.
132. Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. N Engl J Med. 1999;341:1789-94.
133. Raby KE, Brull SJ, Timimi F, et al. The effect of heart rate control on myocardial ischemia among high-risk patients after vascular surgery. Anesth Analg. 1999;88:477-82.
134. Zaugg M, Tagliente T, Lucchinetti E, et al. Beneficial effects from beta-adrenergic blockade in elderly patients undergoing noncardiac surgery. Anesthesiology. 1999;91:1674-86.
135. Urban MK, Markowitz SM, Gordon MA, et al. Postoperative prophylactic administration of beta-adrenergic blockers in patients at risk for myocardial ischemia. Anesth Analg. 2000;90:1257-61.
136. Brady AR, Gibbs JSR, Greenhalgh RM, et al. Perioperative beta-blockade (POBBLE) for patients undergoing infrarenal vascular surgery: results of a randomized double-blind controlled trial. J Vasc Surg. 2005;41:602-9.
137. Juul AB, Wetterslev J, Gluud C, et al. Effect of perioperative beta-blockade in patients with diabetes undergoing major non-cardiac surgery: randomised placebo controlled, blinded multicentre trial. BMJ. 2006;332:1482.
138. Lai R-C, Xu M-X, Huang WQ, et al. [Beneficial effects of metoprolol on perioperative cardiac function of elderly esophageal cancer patients]. Ai Zheng. 2006;25:609-13.
139. Yang H, Raymer K, Butler R, et al. The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 2006;152:983-90.
140. Neary WD, McCrirrick A, Foy C, et al. Lessons learned from a randomised controlled study of perioperative beta blockade in high risk patients undergoing emergency surgery. Surgeon. 2006;4:139-43.
141. Zaugg M, Bestmann L, Wacker J, et al. Adrenergic receptor genotype but not perioperative bisoprolol therapy may determine cardiovascular outcome in at-risk patients undergoing surgery with spinal block: the Swiss Beta Blocker in Spinal Anesthesia (BBSA) study: a double-blinded, placebo-controlled, multicenter trial with 1-year follow-up. Anesthesiology. 2007;107:33-44.
142. Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomized controlled trial. Lancet. 2008;371:1839-47.
143. Yang X, Wu X, Wang S, et al. [Effects of metoprolol on perioperative cardiovascular events in patients with risk or at high risk for coronary artery disease undergoing non-cardiac surgery]. Zhonghua Yi Xue Za Zhi. 2008;88:1476-80.
144. Dunkelgrun M, Boersma E, Schouten O, et al. Bisoprolol and fluvastatin for the reduction of perioperative cardiac mortality and myocardial infarction in intermediate-risk patients undergoing noncardiovascular surgery: a randomized controlled trial (DECREASE-IV). Ann Surg. 2009;249:921-6.
145. Matyal R, Mahmood F, Panzica P, et al. Sex-related differences in outcome after high-risk vascular surgery after the administration of beta-adrenergic-blocking drugs. J Cardiothorac Vasc Anesth. 2008;22:354-60.
146. Sanders RD, Nicholson A, Lewis SR, et al. Perioperative statin therapy for improving outcomes during and after noncardiac vascular surgery. Cochrane Database Syst Rev. 2013;7:CD009971.
147. Raju MG, Pachika A, Punnam SR, et al. Statin therapy in the reduction of cardiovascular events in patients undergoing intermediate-risk noncardiac, nonvascular surgery. Clin Cardiol. 2013;36:456-61.
148. Lau WC, Froehlich JB, Jewell ES, et al. Impact of adding aspirin to beta-blocker and statin in high-risk patients undergoing major vascular surgery. Ann Vasc Surg. 2013;27:537-45.

149. Durazzo AES, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. J Vasc Surg. 2004;39:967-75.
150. Oliver MF, Goldman L, Julian DG, et al. Effect of mivazerol on perioperative cardiac complications during non-cardiac surgery in patients with coronary heart disease: the European Mivazerol Trial (EMIT). Anesthesiology. 1999;91:951-61.
151. Stuhmeier KD, Mainzer B, Cierpka J, et al. Small, oral dose of clonidine reduces the incidence of intraoperative myocardial ischemia in patients having vascular surgery. Anesthesiology. 1996;85:706-12.
152. Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. Anesthesiology. 2004;101:284-93.
153. Wijeysundera DN, Beattie WS. Calcium channel blockers for reducing cardiac morbidity after noncardiac surgery: a meta-analysis. Anesth Analg. 2003;97:634-41.
154. Kashimoto S, Seki M, Ishiguro T, et al. Nicorandil decreases cardiac events during and after noncardiac surgery. J Clin Anesth. 2007;19:44-8.
155. Turan A, You J, Shiba A, et al. Angiotensin converting enzyme inhibitors are not associated with respiratory complications or mortality after noncardiac surgery. Anesth Analg. 2012;114:552-60.
156. Hawn MT, Graham LA, Richman JS, et al. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. JAMA. 2013;310:1462-72.
157. Polanczyk CA, Goldman L, Marcantonio ER, et al. Supraventricular arrhythmia in patients having noncardiac surgery: clinical correlates and effect on length of stay. Ann Intern Med. 1998;129:279-85.
158. Amar D, Zhang H, Roistacher N. The incidence and outcome of ventricular arrhythmias after noncardiac thoracic surgery. Anesth Analg. 2002;95:537-43, table.
159. Roselli EE, Murthy SC, Rice TW, et al. Atrial fibrillation complicating lung cancer resection. J Thorac Cardiovasc Surg. 2005;130:438-44.
160. Amar D, Zhang H, Leung DHY, et al. Older age is the strongest predictor of postoperative atrial fibrillation. Anesthesiology. 2002;96:352-6.
161. Amar D, Zhang H, Heerdt PM, et al. Statin use is associated with a reduction in atrial fibrillation after noncardiac thoracic surgery independent of C-reactive protein. Chest. 2005;128:3421-7.
162. Amar D, Zhang H, Shi W, et al. Brain natriuretic peptide and risk of atrial fibrillation after thoracic surgery. J Thorac Cardiovasc Surg. 2012;144:1249-53.
163. Balser JR, Martinez EA, Winters BD, et al. Beta-adrenergic blockade accelerates conversion of postoperative supraventricular tachyarrhythmias. Anesthesiology. 1998;89:1052-9.
164. Bhave PD, Goldman LE, Vittinghoff E, et al. Incidence, predictors, and outcomes associated with postoperative atrial fibrillation after major noncardiac surgery. Am Heart J. 2012;164:918-24.
165. Bhave PD, Goldman LE, Vittinghoff E, et al. Statin use and postoperative atrial fibrillation after major noncardiac surgery. Heart Rhythm. 2012;9:163-9.
166. Borgeat A, Petropoulos P, Cavin R, et al. Prevention of arrhythmias after noncardiac thoracic operations: flecainide versus digoxin. Ann Thorac Surg. 1991;51:964-7.
167. Brathwaite D, Weissman C. The new onset of atrial arrhythmias following major noncardiothoracic surgery is associated with increased mortality. Chest. 1998;114:462-8.
168. Cardinale D, Martinoni A, Cipolla CM, et al. Atrial fibrillation after operation for lung cancer: clinical and prognostic significance. Ann Thorac Surg. 1999;68:1827-31.
169. Christians KK, Wu B, Quebbeman EJ, et al. Postoperative atrial fibrillation in noncardiothoracic surgical patients. Am J Surg. 2001;182:713-5.
170. Ojima T, Iwahashi M, Nakamori M, et al. Atrial fibrillation after esophageal cancer surgery: an analysis of 207 consecutive patients. Surg Today. 2013.
171. Onaitis M, D'Amico T, Zhao Y, et al. Risk factors for atrial fibrillation after lung cancer surgery: analysis of the Society of Thoracic Surgeons general thoracic surgery database. Ann Thorac Surg. 2010;90:368-74.
172. Riber LP, Christensen TD, Jensen HK, et al. Amiodarone significantly decreases atrial fibrillation in patients undergoing surgery for lung cancer. Ann Thorac Surg. 2012;94:339-44.
173. Tisdale JE, Wroblewski HA, Wall DS, et al. A randomized trial evaluating amiodarone for prevention of atrial fibrillation after pulmonary resection. Ann Thorac Surg. 2009;88:886-93.
174. Tisdale JE, Wroblewski HA, Wall DS, et al. A randomized, controlled study of amiodarone for prevention of atrial fibrillation after transthoracic esophagectomy. J Thorac Cardiovasc Surg. 2010;140:45-51.
175. Vaporciyan AA, Correa AM, Rice DC, et al. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. J Thorac Cardiovasc Surg. 2004;127:779-86.
176. Cheng A, Nazarian S, Spragg DD, et al. Effects of surgical and endoscopic electrocautery on modern-day permanent pacemaker and implantable cardioverter-defibrillator systems. Pacing Clin Electrophysiol. 2008;31:344-50.
177. Fiek M, Dorwarth U, Durchlaub I, et al. Application of radiofrequency energy in surgical and interventional procedures: are there interactions with ICDs? Pacing Clin Electrophysiol. 2004;27:293-8.
178. Hauser RG, Kallinen L. Deaths associated with implantable cardioverter defibrillator failure and deactivation reported in the United States Food and Drug Administration Manufacturer and User Facility Device Experience Database. Heart Rhythm. 2004;1:399-405.
179. Mahlow WJ, Craft RM, Misulia NL, et al. A perioperative management algorithm for cardiac rhythm management devices: the PACED-OP protocol. Pacing Clin Electrophysiol. 2013;36:238-48.
180. Matzke TJ, Christenson LJ, Christenson SD, et al. Pacemakers and implantable cardiac defibrillators in dermatologic surgery. Dermatol Surg. 2006;32:1155-62.
181. Pili-Floury S, Farah E, Samain E, et al. Perioperative outcome of pacemaker patients undergoing non-cardiac surgery. Eur J Anaesthesiol. 2008;25:514-6.
182. Barbosa FT, Jucá MJ, astro AA, et al. Neuraxial anaesthesia for lower-limb revascularization. Cochrane Database Syst Rev. 2013;7:CD007083.
183. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: a randomized, controlled Veterans Affairs cooperative study. Ann Surg. 2001;234:560-9.
184. Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. Anesthesiology. 2001;95:1054-67.
185. Guarracino F, Landoni G, Tritapepe L, et al. Myocardial damage prevented by volatile anesthetics: a multicenter randomized controlled study. J Cardiothorac Vasc Anesth. 2006;20:477-83.
186. Zangrillo A, Testa V, Aldrovandi V, et al. Volatile agents for cardiac protection in noncardiac surgery: a randomized controlled study. J Cardiothorac Vasc Anesth. 2011;25:902-7.
187. Landoni G, Fochi O, Bignami E, et al. Cardiac protection by volatile anesthetics in non-cardiac surgery? A meta-analysis of randomized controlled studies on clinically relevant endpoints. HSR Proc Intensive Care Cardiovasc Anesth. 2009;1:34-43.

188. Conzen PF, Fischer S, Detter C, et al. Sevoflurane provides greater protection of the myocardium than propofol in patients undergoing off-pump coronary artery bypass surgery. Anesthesiology. 2003;99:826-33.
189. Landoni G, Biondi-Zoccai GG, Zangrillo A, et al. Desflurane and sevoflurane in cardiac surgery: a meta-analysis of randomized clinical trials. J Cardiothorac Vasc Anesth. 2007;21:502-11.
190. Bignami E, Greco T, Barile L, et al. The effect of isoflurane on survival and myocardial infarction: a meta-analysis of randomized controlled studies. J Cardiothorac Vasc Anesth. 2013;27:50-8.
191. Nishimori M, Low JH, Zheng H, et al. Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery. Cochrane Database Syst Rev. 2012;7:CD005059.
192. Wu CL, Anderson GF, Herbert R, et al. Effect of postoperative epidural analgesia on morbidity and mortality after total hip replacement surgery in medicare patients. Reg Anesth Pain Med. 2003;28:271-8.
193. Matot I, Oppenheim-Eden A, Ratrot R, et al. Preoperative cardiac events in elderly patients with hip fracture randomized to epidural or conventional analgesia. Anesthesiology. 2003;98:156-63.
194. Dodds TM, Stone JG, Coromilas J, et al. Prophylactic nitroglycerin infusion during noncardiac surgery does not reduce perioperative ischemia. Anesth Analg. 1993;76:705-13.
195. Fusciardi J, Godet G, Bernard JM, et al. Roles of fentanyl and nitroglycerin in prevention of myocardial ischemia associated with laryngoscopy and tracheal intubation in patients undergoing operations of short duration. Anesth Analg. 1986;65:617-24.
196. Thomson IR, Mutch WA, Culligan JD. Failure of intravenous nitroglycerin to prevent intraoperative myocardial ischemia during fentanyl-pancuronium anesthesia. Anesthesiology. 1984;61:385-93.
197. Sumer BD, Myers LL, Leach J, et al. Correlation between intraoperative hypothermia and perioperative morbidity in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg. 2009;135:682-6.
198. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med. 1996;334:1209-15.
199. Frank SM, Fleisher LA, Breslow MJ, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. JAMA. 1997;277:1127-34.
200. Nguyen HP, Zaroff JG, Bayman EO, et al. Perioperative hypothermia (33 degrees C) does not increase the occurrence of cardiovascular events in patients undergoing cerebral aneurysm surgery: findings from the Intraoperative Hypothermia for Aneurysm Surgery Trial. Anesthesiology. 2010;113:327-42.
201. Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med. 2003;348:5-14.
202. Valentine RJ, Duke ML, Inman MH, et al. Effectiveness of pulmonary artery catheters in aortic surgery: a randomized trial. J Vasc Surg. 1998;27:203-11.
203. Bender JS, Smith-Meek MA, Jones CE. Routine pulmonary artery catheterization does not reduce morbidity and mortality of elective vascular surgery: results of a prospective, randomized trial. Ann Surg. 1997;226:229-36.
204. Garcia S, Marston N, Sandoval Y, et al. Prognostic value of 12-lead electrocardiogram and peak troponin I level after vascular surgery. J Vasc Surg. 2013;57:166-72.
205. van Waes JAR, Nathoe HM, de Graaff JC, et al. Myocardial injury after noncardiac surgery and its association with short-term mortality. Circulation. 2013;127:2264-71.
206. Shroff GR, Akkina SK, Miedema MD, et al. Troponin I levels and postoperative myocardial infarction following renal transplantation. Am J Nephrol. 2012;35:175-80.
207. Devereaux PJ, Chan MT, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. JAMA. 2012;307:2295-304.
208. Beattie WS, Karkouti K, Tait G, et al. Use of clinically based troponin underestimates the cardiac injury in non-cardiac surgery: a single-centre cohort study in 51,701 consecutive patients. Can J Anaesth. 2012;59:1013-22.
209. Redfern G, Rodseth RN, Biccard BM. Outcomes in vascular surgical patients with isolated postoperative troponin leak: a meta-analysis. Anaesthesia. 2011;66:604-10.
210. Nagele P, Rao LK, Penta M, et al. Postoperative myocardial injury after major head and neck cancer surgery. Head Neck. 2011;33:1085-91.
211. Levy M, Heels-Ansdell D, Hiralal R, et al. Prognostic value of troponin and creatine kinase muscle and brain isoenzyme measurement after noncardiac surgery: a systematic review and meta-analysis. Anesthesiology. 2011;114:796-806.
212. Devereaux PJ, Xavier D, Pogue J, et al. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. Ann Intern Med. 2011;154:523-8.
213. McFalls EO, Ward HB, Moritz TE, et al. Predictors and outcomes of a perioperative myocardial infarction following elective vascular surgery in patients with documented coronary artery disease: results of the CARP trial. Eur Heart J. 2008;29:394-401.