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

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

## 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. MD. FACC, FAHA¶¶; Richard Kovacs, MD, FACC, FAHA: Hochman. J. 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

\*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.

J Nucl Cardiol 2015;22:162-215.

1071-3581/\$34.00

Copyright  $\circledast$  2014 by the American College of Cardiology Foundation and the American Heart Association, Inc.

¶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. 0000000000000105/-/DC1.

The online-only Data Supplement files are available with this article at http://circ.ahajournals.org/ lookup/suppl/doi:10.1161/CIR.000000000000105/-/DC2.

The American Society of Nuclear Cardiology 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: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Nucl Cardiol. DOI 10.1007/ s12350-014-0025-z. Online date [xxx].

This article has been copublished in the Journal of the American College of Cardiology, Circulation and Journal of Nuclear 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.

Permissions: Multiple copies, modification, alteration, enhancement, and/or distribution of this document are not permitted without the express permission of the American Heart Association. Instructions for obtaining permission are located at http://www.heart.org/HEARTORG/ General/Copyright-Permission-Guidelines\_UCM\_300404\_ Article.jsp. A link to the "Copyright Permissions Request Form" appears on the right side of the page.

 $\ensuremath{\mathbb{C}}$  2014 by the American College of Cardiology Foundation and the American Heart Association, Inc.

#### 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<sup>1,2</sup> 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<sup>3</sup> and 2014 perspective article.<sup>4</sup> The latter recounts the history of the collaboration, changes over time, current policies, and planned initiatives to meet the needs of an evolving health-care environment. Recommendations on value in proportion to resource utilization will be incorporated as highquality comparative-effectiveness data become available.<sup>5</sup> The relationships between CPGs and data standards, appropriate use criteria, and performance measures are addressed elsewhere.<sup>4</sup>

**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.<sup>6</sup> 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.<sup>1</sup>

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.<sup>3,4</sup> 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" (i.e., <sup>SR</sup>) 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; i.e., 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).<sup>4</sup>

**Relationships With Industry and Other Entities**—The ACC and AHA exclusively sponsor the work of GWCs, 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/Guide lines-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.<sup>7</sup> 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 (e.g., 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. The reader is encouraged to consult the full-text CPG<sup>8</sup> for additional guidance and details about perioperative cardiovascular evaluation and noncardiac surgery, because the executive summary contains mainly the recommendations.

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

#### **INTRODUCTION**

#### **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

#### Table 1. Applying Classification of Recommendations and Level of Evidence

		SIZE OF TREA	TMENT EFFECT	
	CLASS I Banalii >>> Risk Procedure/Treatment SHOULD be performed/ administered	CLASS IIa Benefit >> Risk Additional studies with focased objectives needed IT IS REASONABLE to per- form procedure/administer treatment.	CLASS IIb Benefit ≥ Risk Additional stadles with broad objectives needed; additional registry data would be balaful Procedure/Treatment MAY BE CONSIDERED	CLASS III No Benefit or GLASS III Norm Precedent/ Test Treatment OBR III: Not No Preven No benefit Helpful OBR III: Excess Cost Harmful Harm No Benefit to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Sufficient evidence from multiple randomized trials or meta-analyses</li> </ul>	<ul> <li>Recommendation in tavor of treatment or procedure being useful/effective</li> <li>Some conflicting evidence from multiple randomized trials or meta-analyses</li> </ul>	Recommendation's usefulness/efficacy less well established     Greater conflicting evidence from multiple randomized trials or meta-analyses	Recommendation that precedure or treatment is not useful/effective and may be barmful     Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Evidence from single randomized trial or nonrandomized studies</li> </ul>	Recommendation in taxor 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 aschuleffective and may be harmfal     Evidence from single randomized trial or nonrandomized staties
LEVEL C Very limited populations evaluated" Only consensus opinion of experts, case statles, or standard of care	<ul> <li>Recommendation that procedure or treatment is useful/effective</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>	<ul> <li>Recommendation in tavor of treatment or procedure being useful/effective</li> <li>Only diverging export opinion, case studies, or standard of care</li> </ul>	Recommendation's uselulness/efficacy less well established     Only diverging expert opinion, case studies, or standard of care	<ul> <li>Recommendation that procedure or treatment is not useful/effective and may be hanntal</li> <li>Only expert opinion, case studies, or standard of care</li> </ul>
Suggested phrases for writing recommendations	should is recommended is indicated is useful/inflective/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 er not well established	COR II: COR II: No Benefit Harm is not potentially recommended harmful is not indicated causes harm should not be associated with
Comparative effectiveness phrases?	beatment/strategy A is recommended/indicated in preference to treatment B beatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is neasonable to choose treatment A over treatment B		should not be performed/ administered/ other is not useful/ penficial/ administered/ penficial/ administered/ administered/ effective

#### SIZE OF TREATMENT EFFECT

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.

included a literature review through July 2013. Other selected references published through May 2014 were also incorporated by the GWC. Literature included was conducted in human subjects, published in English, and indexed in MEDLINE (through Pub-Med), 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 critical question, the results of which were incorporated into this CPG. See the systematic review report published in conjunction with this  $CPG^9$  and its respective data supplements.

#### **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, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society for Vascular Medicine.

#### **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.

#### 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 (e.g., 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 (i.e., 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.<sup>10</sup> The GWC reviewed 2 reports from Erasmus University published on the Internet,<sup>10,11</sup> as well as other relevant articles on this body of scientific investigation.<sup>12</sup>–<sup>14</sup> 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.<sup>10</sup> 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 (i.e., 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 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.

## **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.<sup>35,36</sup> Procedures with a risk of MACE of  $\geq 1\%$ are considered elevated risk. Many previous risk-stratification schema have included intermediate- and highrisk 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.<sup>37</sup> Approaches to establishing low and elevated risk are developed more fully in Section 3 in the full-text CPG.

## CLINICAL RISK FACTORS: RECOMMENDATIONS

## Valvular Heart Disease

See the 2014 valvular heart disease CPG for the complete set of recommendations and specific definitions of disease severity.<sup>16</sup>

#### Table 2. Associated CPGs and Statements

Title	Organization	Publication Year (Reference)
CPGs		
Management of patients with atrial fibrillation	AHA/ACC/HRS	2014 <sup>15</sup>
Management of valvular heart disease	AHA/ACC	2014 <sup>16</sup>
Management of heart failure	ACC/AHA	2013 <sup>17</sup>
Performing a comprehensive transesophageal echocardiographic examination	ASE/SCA	2013 <sup>18</sup>
Management of ST-elevation myocardial infarction	ACC/AHA	2013 <sup>19</sup>
Diagnosis and management of patients with	ACC/AHA/AATS/PCNA/	2012 <sup>19a</sup>
stable ischemic heart disease	SCAI/STS	2014 <sup>20</sup>
Focused update incorporated into the 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction*	ACC/AHA	2012 <sup>21</sup>
Red blood cell transfusion	AABB	2012 <sup>22</sup>
Management of patients with peripheral artery	ACC/AHA	2011 <sup>23</sup>
disease: focused update and guideline		2006 <sup>24</sup>
Diagnosis and treatment of hypertrophic cardiomyopathy	ACC/AHA	2011 <sup>25</sup>
Coronary artery bypass graft surgery	ACC/AHA	2011 <sup>26</sup>
Percutaneous coronary intervention	ACC/AHA/SCAI	2011 <sup>27</sup>
Perioperative transesophageal echocardiography	American Society of Anesthesiologists/SCA	2010 <sup>28</sup>
Management of adults with congenital heart disease Statements	ACC/AHA	2008 <sup>29</sup>
Perioperative beta blockade in noncardiac surgery: a systematic review	ACC/AHA	2014 <sup>9</sup>
Basic perioperative transesophageal echocardiography examination	ASE/SCA	2013 <sup>30</sup>
Practice advisory for preanesthesia evaluation	American Society of Anesthesiologists	2012 <sup>31</sup>
Cardiac disease evaluation and management among kidney and liver transplantation candidates	AHA/ACC	2012 <sup>32</sup>
Inclusion of stroke in cardiovascular risk prediction instruments	AHA/American Stroke Association	2012 <sup>33</sup>
Perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management	HRS/American Society of Anesthesiologists	2011 <sup>34</sup>

\*The 2012 UA/NSTEMI  $CPG^{21}$  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

#### Class I

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.<sup>39</sup> (Level of Evidence: C)

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.<sup>16</sup> (Level of Evidence: C)

#### Class IIa

Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable to perform in patients with asymptomatic severe aortic stenosis.<sup>40–50</sup> (Level of Evidence: B)

Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable in adults with asymptomatic severe MR. (*Level of Evidence: C*)

Elevated-risk elective noncardiac surgery with appropriate intraoperative and postoperative hemodynamic monitoring is reasonable in adults with asymptomatic severe aortic regurgitation and a normal left ventricular ejection fraction. (*Level of Evidence: C*)

#### Class IIb

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)

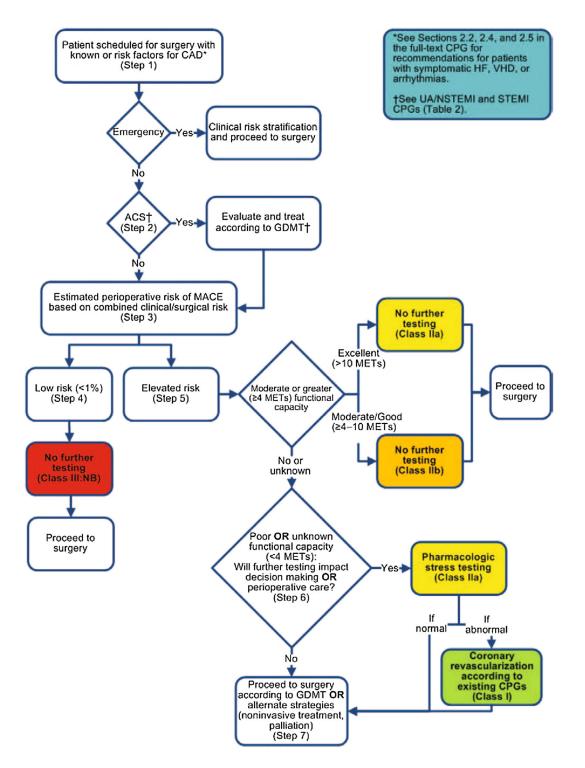
#### **Other Clinical Risk Factors**

See Section 5.8 for intraoperative/postoperative cardiovascular implantable electronic device (CIED) management.

#### Class I

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*) Chronic pulmonary vascular targeted therapy (i.e., phosphodiesterase type 5 inhibitors, soluble guanylate

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 2.5 in the full-text CPG for more information on CAD). (For patients with symptomatic HF, VHD, or arrhythmias, see Sections. 2.2, 2.4, and 2.5 in the full-text CPG 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.<sup>19,21</sup> 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 62 with an estimation of surgical risk. For example, a patient undergoing very low-risk surgery (e.g., 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 (see Section 3 in the full-text CPG). 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 in the full-text CPG). 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.<sup>63</sup> If the patient has moderate, good, or excellent functional capacity  $(\geq 4 \text{ METs})$ , then proceed to surgery without further evaluation (Section 4.1 in the full-text CPG). 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 (e.g., 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 (e.g., radiation therapy for cancer) or palliation. If the test is normal, proceed to surgery according to GDMT (Section 4.3). 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 (e.g., 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, guidelinedirected 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 3. Summary of Recommendations for Supplemental Preoperative Evaluation

Province defense	007	LOD	D - É
Recommendations	COR	LOE	References
The 12-lead ECG			_
Preoperative resting 12-lead ECG is reasonable for patients with known coronary	IIa	В	64–66
heart disease or other significant structural heart disease, except for low-risk			
surgery			
Preoperative resting 12-lead ECG may be considered for asymptomatic patients,	Пр	В	59, 65–67
except for low-risk surgery			
Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients	III: No Benefit	в	36, 68
undergoing low-risk surgical procedures			
Assessment of LV function			
It is reasonable for patients with dyspnea of unknown origin to undergo preoperative	IIa	С	N/A
evaluation of LV function		-	
It is reasonable for patients with HF with worsening dyspnea or other change in	Па	С	N/A
clinical status to undergo preoperative evaluation of LV function	11a	C	IV/A
Reassessment of LV function in clinically stable patients may be considered	Пр	С	N/A
			_
Routine preoperative evaluation of LV function is not recommended	III: No Benefit	В	69-71
Exercise stress testing			
For patients with elevated risk and excellent functional capacity, it is reasonable to	IIa	В	72–76
forgo further exercise			
testing and proceed to surgery			
For patients with elevated risk and unknown functional capacity it may be	IIb	В	75–77
reasonable to perform exercise			
testing to assess for functional capacity if it will change management			
Cardiopulmonary exercise testing may be considered for patients undergoing	IIb	В	78-86
elevated risk procedures			
For patients with elevated risk and moderate to good functional capacity, it may be	IIb	В	72-74
reasonable to forgo			
further exercise testing and proceed to surgery			
For patients with elevated risk and poor or unknown functional capacity it may be	Пр	с	N/A
reasonable to perform			
exercise testing with cardiac imaging to assess for myocardial ischemia			
Routine screening with noninvasive stress testing is not useful for low-risk	III: No Benefit	В	87, 88
noncardiac surgery			
Noninvasive pharmacological stress testing before noncardiac surgery			
It is reasonable for patients at elevated risk for noncardiac surgery with poor	IIa	В	89-93
functional capacity to undergo			
either DSE or MPI if it will change management			
Routine screening with noninvasive stress testing is not useful for low-risk	III: No Benefit	В	88, 87
noncardiac surgery			
Preoperative coronary angiography			
Routine preoperative coronary angiography is not recommended	III: No Benefit	С	N/A
	ECG_electrocardiog		

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.

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

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.<sup>51</sup>\* (Level of Evidence: C)

### APPROACH TO PERIOPERATIVE CARDIAC TESTING

## Multivariate Risk Indices: Recommendations

#### Class IIa

A validated risk-prediction tool can be useful in predicting the risk of perioperative MACE in patients undergoing noncardiac surgery.<sup>59</sup>–<sup>61</sup> (Level of Evidence: B)

#### **Class III: No Benefit**

For patients with a low risk of perioperative MACE, further testing is not recommended before the planned operation.<sup>35,36</sup> (*Level of Evidence: B*)

## Stepwise Approach to Perioperative Cardiac Assessment: Treatment Algorithm

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

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.

## SUPPLEMENTAL PREOPERATIVE EVALUATION: RECOMMENDATIONS

See Table 3 for a summary of recommendations for supplemental preoperative evaluation.

# The 12-Lead Electrocardiogram

#### **Class IIa**

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.<sup>64</sup>–<sup>66</sup> (Level of Evidence: B)

#### Class IIb

Preoperative resting 12-lead ECG may be considered for asymptomatic patients without known coronary heart disease, except for those undergoing low-risk surgery.<sup>59,65</sup>\_67 (Level of Evidence: B)

### **Class III: No Benefit**

Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures.<sup>36,68</sup> (*Level of Evidence: B*)

# Assessment of Left Ventricular Function

## Class IIa

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

## Class IIb

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.<sup>69\_71</sup> (Level of Evidence: B)

# Table 4. Summary of Recommendations for Perioperative Therapy

Recommendations	COR	LOE	References
Coronary revascularization before noncardiac surgery			L
Revascularization before noncardiac surgery is recommended when indicated by	I	С	26, 27
existing CPGs			
Coronary revascularization is not recommended before noncardiac surgery	III: No Benefit	в	97
exclusively to reduce			
perioperative cardiac events			
Timing of elective noncardiac surgery in patients with previous PCI			
Noncardiac surgery should be delayed after PCI		C: 14 d after	N/A
		balloon	
	I	angioplasty	
		B: 30 d	99–101
		after BMS implantation	
Noncardiac surgery should optimally be delayed 365 d after DES implantation	I	В	102-105
A consensus decision as to the relative risks of discontinuation or continuation of	IIa	С	N/A
antiplatelet therapy can be useful			-
Elective noncardiac surgery after DES implantation may be considered after 180 d	IIb*	В	102, 106
Elective noncardiac surgery should not be performed in patients in whom DAPT will			99–105, 107
need to be discontinued perioperatively within 30 d after BMS implantation or within	III: Harm	В	
12 mo after DES implantation			
Elective noncardiac surgery should not be performed within 14 d of balloon	III: Harm	С	N/A
angioplasty in patients in whom aspirin will need to be discontinued perioperatively			
Perioperative beta-blocker therapy			
Continue beta blockers in patients who are on beta blockers chronically	Ι	B <sup>SR</sup> †	111–117
Guide management of beta blockers after surgery by clinical circumstances	Па	B <sup>SR</sup>	110,117,118
In patients with intermediate- or high-risk preoperative tests, it may be reasonable to	IIb	C SR	119
begin beta blockers			
In patients with $\geq$ 3 RCRI factors, it may be reasonable to begin beta blockers before	IIb	B SR	117
surgery			
Initiating beta blockers in the perioperative setting as an approach to reducing			111, 117,
perioperative risk is of uncertain benefit in those with a long-term indication but no	IIb	B <sup>SR</sup>	120
other RCRI risk factors			
It may be reasonable to begin perioperative beta blockers long enough in advance to	IIb	B sr	110, 121–
assess safety and tolerability, preferably >1 d before surgery			123
Beta-blocker therapy should not be started on the d of surgery	III: Harm	B SR	110
Perioperative statin therapy			J
Continue statins in patients currently taking statins	I	В	131–134
Perioperative initiation of statin use is reasonable in patients undergoing vascular	IIa	В	135
surgery			
Perioperative initiation of statins may be considered in patients with a clinical risk	IIb	с	N/A
factor who are undergoing elevated-risk procedures			
			J

#### Table 4. continued

	60 <b>P</b>	LOP	D (
Recommendations	COR	LOE	References
Alpha-2 agonists			
Alpha-2 agonists are not recommended for prevention of cardiac events	III: No Benefit	В	136–140
ACE inhibitors		•	
Continuation of ACE inhibitors or ARBs is reasonable perioperatively	IIa	В	141, 142
If ACE inhibitors or ARBs are held before surgery, it is reasonable to restart as soon	IIa	С	N/A
as clinically feasible postoperatively			
Antiplatelet agents		1	
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	Ι	С	N/A
benefit of stent thrombosis prevention			
In patients with stents undergoing surgery that requires discontinuation of $\ensuremath{\text{P2Y}_{12}}$	I	с	N/A
inhibitors, continue aspirin and restart the $P2Y_{12}$ platelet receptor–inhibitor as soon			
as possible after surgery			
Management of perioperative antiplatelet therapy should be determined by consensus	I	С	N/A
of treating			
clinicians and the patient			
In patients undergoing nonemergency/nonurgent noncardiac surgery without prior			
coronary stenting, it may be reasonable to continue aspirin when the risk of increased	IIb	В	143, 144
cardiac events outweighs the risk of increased bleeding			
Initiation or continuation of aspirin is not beneficial in patients undergoing elective		в	143
noncardiac noncarotid surgery who have not had previous coronary stenting		C: If risk of	
		ischemic	
	III: No Benefit	events	
		outweighs	N/A
		risk of surgical	
		bleeding	
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.	Ι	С	145
Ensure that ICDs are reprogrammed to active therapy			

\*Because of new evidence, this is a new recommendation since the publication of the 2011 PCI  $\text{CPG}^{27}$ 

†These recommendations have been designated with a <sup>SR</sup> 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 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 <sup>SR</sup>, systematic review

#### Class IIa

For patients with elevated risk and excellent (>10 metabolic equivalents [METs]) functional capacity, it is reasonable to forgo further exercise testing with cardiac imaging and proceed to surgery.<sup>72</sup>–<sup>76</sup> (*Level of Evidence: B*)

## Class IIb

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.<sup>75</sup>–<sup>77</sup> (*Level of Evidence: B*)

Cardiopulmonary exercise testing may be considered for patients undergoing elevated risk procedures in whom functional capacity is unknown.<sup>78</sup>–<sup>86</sup> (Level of Evidence: B)

For patients with elevated risk and moderate to good ( $\geq$ 4METs to 10 METs) functional capacity, it may be reasonable to forgo further exercise testing with cardiac imaging and proceed to surgery.<sup>72–74</sup> (*Level of Evidence: B*)

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

Routine screening with noninvasive stress testing is not useful for patients at low risk for noncardiac surgery.<sup>87,88</sup> (Level of Evidence: B)

# Noninvasive Pharmacological Stress Testing Before Noncardiac Surgery

#### **Class IIa**

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 or pharmacological stress myocardial perfusion imaging) if it will change management.<sup>89\_93</sup> (Level of Evidence: B)

## **Class III: No Benefit**

Routine screening with noninvasive stress testing is not useful for patients undergoing low-risk noncardiac surgery.<sup>87,88</sup> (Level of Evidence: B)

# **Preoperative Coronary Angiography**

## **Class III: No Benefit**

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

## PERIOPERATIVE THERAPY: RECOMMENDATIONS

See Table 4 for a summary of recommendations for perioperative therapy.

# Coronary Revascularization Before Noncardiac Surgery

#### Class I

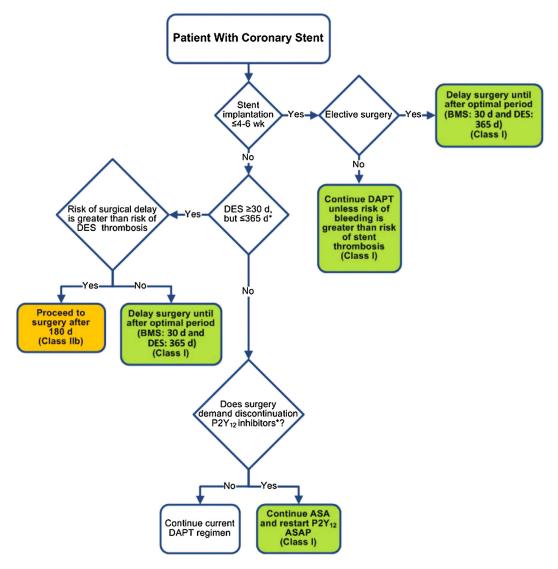
Revascularization before noncardiac surgery is recommended in circumstances in which revascularization is indicated according to existing CPGs.<sup>26,27</sup> (*Level of Evidence: C*) (See Table A in Appendix 3 for related recommendations.)

### Class III: No Benefit

It is not recommended that routine coronary revascularization be performed before noncardiac surgery exclusively to reduce perioperative cardiac events.<sup>97</sup> (*Level of Evidence: B*)

Patients undergoing risk stratification surgery before elective noncardiac procedures and whose evaluation recommends coronary artery bypass graft surgery should undergo coronary revascularization before an elevated-risk surgical procedure.<sup>98</sup> 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 coronary artery bypass graft surgery CPG and the 2011 percutaneous coronary intervention (PCI) CPG and the accumulated data on which those conclusions were based.<sup>26,27</sup> (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



**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.

coronary artery disease who would be appropriate candidates for emergency or urgent revascularization.<sup>26,27</sup> Patients with ST-elevation MI or non–STelevation acute coronary syndrome benefit from early invasive management.<sup>27</sup> 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.

# Timing of Elective Noncardiac Surgery in Patients With Previous PCI

Elective noncardiac surgery should be delayed 14 days after balloon angioplasty (*Level of Evidence: C*) and 30 days after BMS implantation.<sup>99–101</sup> (*Level of Evidence B*)

Elective noncardiac surgery should optimally be delayed 365 days after drug-eluting stent (DES) implantation.<sup>102</sup> $^{-105}$  (Level of Evidence: B)

## Class IIa

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 I

#### Class IIb\*

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.<sup>102,106</sup> (Level of Evidence: B)

## Class III: Harm

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 will need to be discontinued perioperatively.<sup>99</sup>–<sup>105,107</sup> (Level of Evidence: B)

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*)

## **Perioperative Beta-Blocker Therapy**

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 betablocker therapy.<sup>9</sup> These recommendations have been designated with a 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 5.3 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<sup>9</sup> 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 betablocker administration and adverse outcomes, such as bradycardia and stroke.
- These findings were quite consistent even when the DECREASE studies<sup>108,109</sup> in question or POISE (Perioperative Ischemic Evaluation Study)<sup>110</sup> were excluded. Stated alternatively, exclusion of these studies did not substantially affect estimates of risk or benefit.

#### Class I

Beta blockers should be continued in patients undergoing surgery who have been on beta blockers chronically.<sup>111</sup>–<sup>117</sup> (*Level of Evidence: B*)<sup>SR</sup>

#### Class IIa

It is reasonable for the management of beta blockers after surgery to be guided by clinical circumstances, independent of when the agent was started.<sup>110,117,118</sup> (*Level of Evidence: B*)<sup>SR</sup>

#### Class IIb

In patients with intermediate- or high-risk myocardial ischemia noted in preoperative risk stratification tests, it may be reasonable to begin perioperative beta blockers.<sup>119</sup> (*Level of Evidence: C*)<sup>SR</sup>

In patients with 3 or more RCRI risk factors (e.g., diabetes mellitus, HF, coronary artery disease, renal insufficiency, cerebrovascular accident), it may be reasonable to begin beta blockers before surgery.<sup>117</sup> (*Level of Evidence: B*)<sup>SR</sup>

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.<sup>111,117,120</sup> (*Level of Evidence: B*)<sup>SR</sup>

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.<sup>110,121–123</sup> (Level of Evidence: B)<sup>SR</sup>

#### Class III: Harm

Beta-blocker therapy should not be started on the day of surgery.<sup>110</sup> (Level of Evidence: B)<sup>SR</sup>

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).<sup>124</sup> This recommendation is consistent with the Surgical Care Improvement Project National Measures (CARD-2) as of November 2013.<sup>125</sup> Particular attention should be paid to the need to modify or temporarily discontinue beta blockers as clinical circumstances (e.g., hypotension, bradycardia,<sup>126</sup> bleeding).<sup>118</sup> dictate.

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.<sup>119,120</sup> The decision to begin beta blockers should be influenced by whether a

Table 5.	Summary	y of Recommendations for	Anesthetic	Consideration and	Intraoperative Management
----------	---------	--------------------------	------------	-------------------	---------------------------

Recommendations	COR	LOE	References
Choice of anesthetic technique and agent			
Use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients	IIa	А	146, 147
undergoing noncardiac surgery			
Neuraxial anesthesia for postoperative pain relief can be effective to reduce MI in patients undergoing	IIa	В	148
abdominal aortic surgery			
Preoperative epidural analgesia may be considered to decrease the incidence of preoperative cardiac	IIb	В	149
events in patients with hip fracture			
Intraoperative management			
Emergency use of perioperative TEE in patients with hemodynamic instability is reasonable in	IIa	С	N/A
patients			
undergoing noncardiac surgery if expertise is readily available			
Maintenance of normothermia may be reasonable to reduce perioperative cardiac events	IIb	В	150, 151
Use of hemodynamic assist devices may be considered when urgent or emergency noncardiac	IIb	С	N/A
surgery is required in the setting of acute severe cardiac dysfunction			
Use of pulmonary artery catheterization may be considered when underlying medical conditions	IIb	С	N/A
that significantly affect hemodynamics cannot be corrected before surgery			
Routine use of pulmonary artery catheterization is not recommended	III: No Benefit	А	152–154
Prophylactic intravenous nitroglycerin is not effective in reducing myocardial ischemia in patients	III: No Benefit	В	137, 155, 156
undergoing noncardiac surgery			
Routine use of intraoperative TEE during noncardiac surgery is not recommended	III: No Benefit	С	N/A

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

patient is at risk for stroke  ${}^{128}{}_{-}{}^{130}$  and whether the patient has other relative contraindications (such as uncompensated HF). Observational data suggest that patients appear to benefit from use of beta blockers in the perioperative setting if they have  $\geq 3$  RCRI risk factors. It may be reasonable to begin beta blockers long enough in advance of the operative date that clinical effectiveness and tolerability can be assessed.  ${}^{110,121}{}_{-}{}^{123}$  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.  ${}^{121}{}_{-}{}^{123}$ 

#### Perioperative Statin Therapy

#### Class I

Statins should be continued in patients currently taking statins and scheduled for noncardiac surgery.<sup>131</sup>–<sup>134</sup> (*Level of Evidence: B*)

#### Class IIa

Perioperative initiation of statin use is reasonable in patients undergoing vascular surgery.<sup>135</sup> (Level of Evidence: B)

## **Class IIb**

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*)

# Alpha-2 Agonists

#### **Class III: No Benefit**

Alpha-2 agonists for prevention of cardiac events are not recommended in patients who are undergoing noncardiac surgery.<sup>136</sup>–<sup>140</sup> (*Level of Evidence: B*)

## **Angiotensin-Converting Enzyme Inhibitors**

#### Class IIa

Continuation of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers perioperatively is reasonable.<sup>141,142</sup> (Level of Evidence: B)

If angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers are held before surgery, it is reasonable to restart as soon as clinically feasible postoperatively. (*Level of Evidence: C*)

## **Antiplatelet Agents**

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

## Class I

In patients undergoing urgent noncardiac surgery during the first 4 to 6 weeks after BMS or DES implantation, dual antiplatelet therapy should be continued unless the relative risk of bleeding outweighs the benefit of the prevention of stent thrombosis. (Level of Evidence: C)

In patients who have received coronary stents and must undergo surgical procedures that mandate the discontinuation of P2Y<sub>12</sub> platelet receptor-inhibitor therapy, it is recommended that aspirin be continued if possible and the P2Y<sub>12</sub> platelet receptor-inhibitor be restarted as soon as possible after surgery. (Level of Evidence: C)

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

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.<sup>143,144</sup> (*Level of Evidence: B*)

### Class III: No Benefit

Initiation or continuation of aspirin is not beneficial in patients undergoing elective noncardiac noncarotid surgery who have not had previous coronary stenting <sup>143</sup> (Level of Evidence: B), unless the risk of ischemic events outweighs the risk of surgical bleeding. (Level of Evidence: C)

## Perioperative Management of Patients With CIEDs

#### Class I

Patients with implantable cardioverter-defibrillators 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 implantable cardioverter-defibrillators are reprogrammed to active therapy before discontinuation of cardiac monitoring and discharge from the facility.<sup>145</sup> (*Level of Evidence: C*)

#### ANESTHETIC CONSIDERATION AND INTRAOPERATIVE MANAGEMENT: RECOMMENDATIONS

See Table 5 for a summary of recommendations for anesthetic consideration and intraoperative management.

# Choice of Anesthetic Technique and Agent

## **Class IIa**

Use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients undergoing noncardiac surgery, and the choice is determined by factors other than the prevention of myocardial ischemia and MI.<sup>146,147</sup> (*Level of Evidence: A*) Neuraxial anesthesia for postoperative pain relief can be effective in patients undergoing abdominal aortic surgery to decrease the incidence of perioperative MI.<sup>148</sup> (*Level of Evidence: B*)

#### Class IIb

Perioperative epidural analgesia may be considered to decrease the incidence of preoperative cardiac events in patients with a hip fracture.<sup>149</sup> (*Level of Evidence: B*)

#### **Intraoperative Management**

#### Class IIa

The emergency use of perioperative transesophageal echocardiogram 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 IIb

Maintenance of normothermia may be reasonable to reduce perioperative cardiac events in patients undergoing noncardiac surgery.<sup>150,151</sup> (Level of Evidence: B) Use of hemodynamic assist devices may be considered when urgent or emergency noncardiac surgery is required in the setting of acute severe cardiac dysfunction (i.e., acute MI, cardiogenic shock) that cannot be corrected before surgery. (Level of Evidence: C)

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

#### Class III: No Benefit

Routine use of pulmonary artery catheterization in patients, even those with elevated risk, is not recommended.  $^{152}-^{154}$  (*Level of Evidence: A*)

Prophylactic intravenous nitroglycerin is not effective in reducing myocardial ischemia in patients undergoing noncardiac surgery.<sup>137,155,156</sup> (*Level of Evidence: B*) The routine use of intraoperative transesophageal echocardiogram 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*)

# SURVEILLANCE AND MANAGEMENT FOR PERIOPERATIVE MI: RECOMMENDATIONS

#### Class I

Measurement of troponin levels is recommended in the setting of signs or symptoms suggestive of myocardial ischemia or MI.<sup>157,158</sup> (*Level of Evidence: A*)

Obtaining an ECG is recommended in the setting of signs or symptoms suggestive of myocardial ischemia, MI, or arrhythmia.<sup>158,159</sup> (*Level of Evidence: B*)

#### Class IIb

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.<sup>160</sup>–<sup>166</sup> (Level of Evidence: B)

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.<sup>158,159,167</sup>–<sup>169</sup> (Level of Evidence: B)

#### Class III: No Benefit

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.<sup>157,158</sup> (Level of Evidence: B)

#### **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.

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 betablocker-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. RCTs are needed to demonstrate when to start beta-blocker therapy before noncardiac surgery, the optimal type and dose, and titration protocol.

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. 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, FACC, 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

Elliot 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

**Keywords** AHA Scientific Statements, adrenergic betaantaquerygonists, anesthesia and analgesia, diagnostic techniques, cardiovascular, monitoring, intraoperative, perioperative care, troponin, platelet aggregation inhibitors, referral and consultation

ES
2
Z
2

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

Committee Member	Emoloyment	Consul	Speakers	Ownership/ Partnership/ Princinal	Personal Recearch	Institutional, Organizational, or Other Financial Renefit	Expert Wit	Voting Recusals by Section *
Lee A. Fleisher	University of	None	None	None	None	None	None	None
(Chair)	Pennsylvania							
	Health System							
	Department of							
	Anesthesiology							
	and Critical							
	Care-Chair							
Kirsten E.	UCSF School of	None	None	None	None	None	None	None
Fleischmann	Medicine,							
(Vice Chair)	Division of							
	Cardiology-							
	Professor of							
	<b>Clinical Medicine</b>							
Andrew D.	UCSF Division of	None	None	None	None	None	None	None
Auerbach	Hospital							
	Medicine-							
	Professor of							
	Medicine in							
	Residence							

ed
inu
ont
Ŭ.
x 1
ipu
per
Ģ

Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Wit -ness	Voting Recusals by Section*
Susan A. Barnason	University of Nebraska Medical Center, College of Nursing– Professor and Director of the Doctor of Nursing Practice	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	<ul> <li>AstraZeneca</li> <li>Bristol-</li> <li>Myers</li> <li>Squibb†</li> <li>Novartis†</li> <li>Merck</li> </ul>	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

Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ Speakers Partnership/ Bureau Principal	<b>Personal</b> <b>Research</b>	Institutional, Organizational, or Other Financial Benefit	Expert Wit ness	Voting Recusals by Section*
Biykem Bozkurt	Winters Center for None Heart Failure Research, Baylor College of Medicine– The Mary and Gordon Cain Gordon Cain Gordon Cain Gordon Cain Gordon Cain Chair, Professor of Medicine, and Director; Michael E. DeBakey VA Medical Center Cardiology	None	None	None	• Forest Pharmaceu -ticals (PI)†	• Novartis	None	6.2.1, 6.2.2, and 6.2.5
Victor G. Davila- Roman	Secuon-Curer Washington University School of Medicine Anesthesiology and Radiology and Radiology Cardiovascular Division- Professor of Medicine	<ul> <li>ValveXchange† None</li> <li>Boston</li> <li>Boston</li> <li>Scientific†</li> <li>St. Jude</li> <li>Medical†</li> </ul>	+ 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

Fleisher et al 2014 ACC/AHA Perioperative Guideline

184

	רטוווומכת							
Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Wit -ness	Voting Recusals by Section*
Marie D. Gerhard- Herman	Harvard Medical None School– Associate	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

continued	
<b>-</b>	
Appendix	

Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Wit -ness	Voting Recusals by Section*
Garvan C. Kane	Mayo Clinic, Division None of Cardiovascular Diseases- Codirector and Echocar-diography Laboratory Consultant; Associate Professor of Medicine	None	None	None	None	None	None	None
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	Лоне	None	None

	Ownership/ Consul Speakers Partnership/ -tant Bureau Principal
	onsul Speakers -tant Bureau
	Consul -tant
continued	Employment
Appendix 1. continued	Committee Member

Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Wit -ness	Voting Recusals by Section*
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

σ
ā
Ē
2
Ë.
H
0
Ū
•
-
-
ix 1
ix 1
l xibu
ndix 1
l xibu
pendix 1
ndix 1
pendix 1

Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ nsul Speakers Partnership/ ant Bureau Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Wit -ness	Voting Recusals by Section*
Henry H. Ting	Mayo Clinic–Professor of None Medicine; Mayo Clinic Quality Academy– Director; Mayo School for Continuous Professional Development–	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	None

σ
Ū
ž
Ē
÷Ξ
5
ō
- ŭ
•
•
_
×
÷
τ
2
e
2
2
_

Committee Member	Employment	Consul -tant	Speakers Bureau	Ownership/ Consul Speakers Partnership/ -tant Bureau Principal	Personal Research	Organizational, or Other Financial Benefit	Expert Wit -ness	Recusals by Section *
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

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  $\geq$ 5% of the voting stock or share of the business entity, or ownership of  $\geq$ \$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 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 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 the *document*; or c) the *person or a member of the person's household* has a reasonable potential for financial, professional, 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. Section numbers pertain to those in the full-text CPG

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; CPG, clinical practice guideline; ERC, Evidence Review Committee; PI, principal inves-

igator; UCSF, University of California, San Francisco; and VA, Veterans Affairs

Expert Witness	None	None
Institutional, Organizational, or Other Financial Benefit	None	None
Personal Research	• GORE • Medtronic	None
Ownership/ Partnership/ Principal	None	None
Speak ,ers Bureau	None	None
Consul -tant	None	None
Employment	University of Michigan Health System– Albion Walter Hewlett Professor of Internal Medicine	Hoag Memorial Hospital Presbyterian– Robert and Georgia Roth Chair for Excellence in Cardiac Care; Director of Disease Management
Repre -sentation	Official Reviewer- AHA	Official Reviewer- ACC Board of Trustees
Reviewer	Kim Eagle	Dipti Itchha -poria

Reviewer	Repre -sentation	Employment	Consul -tant	Speak , ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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 Professor of Medicine	<ul><li>Merck</li><li>Pfizer</li><li>Servier</li></ul>	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 Cardio thoracic	None	None	None	None	<ul> <li>CSL Behring</li> <li>The Medicines</li> <li>Company</li> </ul>	None
Michael Baker	Organizational Reviewer— ASE	Vanderbilt University– Assistant Professor of Medicine	None	None	None	None	• Medtronic†	None

continued
2
Appendix

Reviewer	Repre -sentation	Employment	Consul -tant	Speak ~ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Michael England	Organizational Reviewer— ASA	Tufts University School of Medicine– Division Chief, Cardiac Anesthesiology; Assistant Professor	None	• Hospira	None	None	None	None
Feldman	Organizational Reviewer– SHM	Johns Hopkins School of Medicine- Director, Medicine- Pediatrics Urban Health Residency Program; Assistant Professor of Pediatrics; Assistant Professor of Medicine Medicine	None	None	None	None	None	<ul> <li>Defendant, pulmonary embolism, 2013</li> <li>Defendant, aortic dissection, 2013</li> <li>Defendant, stroke, 2013</li> <li>Defendant, stroke, 2013</li> </ul>
Jason Kovacic	Organi -zational Reviewer— SCAI	Mount Sinai School • AstraZeneca* • AstraZeneca None of Medicine- Assistant Professor of Medicine	<ul> <li>AstraZeneca</li> </ul>	<ul> <li>AstraZeneca</li> </ul>	None	None	None	None

Expert Witness	None	None
Institutional, Organizational, or Other Financial Benefit	None	None
Personal Research	None	None
Ownership/ Partnership/ Principal	None	None
Speak ~ers Bureau	None	• Astellas
Consul -tant	None	• Astellas
Employment	University of California, San Francisco Medical Center – Professor of Clinical	University of Chicago Medicine- Director, Cardiac Rehabilitation; Assistant Professor of Medicine
Repre -sentation	Organizational Reviewer– SCA	Organi -zational Reviewer— ASNC
Reviewer	Martin London	Rupa Mehta Sanghani

Journal of Nuclear Cardiology® Volume 22, Number 1;162–215

Appendix 2. continued

continued
2
Appendix

Expert Witness	None	None	None
Institutional, Organizational, or Other Financial Benefit	None	<ul> <li>Boston Scientific</li> <li>Medtronic</li> </ul>	None
Personal Research	None	None	None
Ownership/ Partnership/ Principal	None	None	None
Speak ~ers Bureau	None	None	None
Consul -tant	None	<ul> <li>Biotronik</li> <li>Boston Scientific*</li> <li>Medtronic</li> <li>St. Jude Medical</li> </ul>	None
Employment	Brigham and Women's Hospital, Prevention Brigham and Women's Hospital– Associate Physician; Harvard Medical School, Professor	University of Washington– Professor of Medicine, Division of Cardiology	University of Oklahoma Health Sciences Center–John A. Schilling Professor and Chairman, Department of Surgery
Repre -sentation	Organizational Reviewer— SVM	Organizational Reviewer— HRS	Organizational Reviewer ACS
Reviewer	Reena Pande	Jeanne Poole	Russell Postier

Reviewer	Repre -sentation	Employment	Consul ,tant	Speak -ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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 Cuidelines	Intermountain Medical Center– Associate Chief of Cardiology	<ul> <li>Sanofi-aventis</li> <li>The Medicines Company</li> </ul>	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

Journal of Nuclear Cardiology® Volume 22, Number 1;162–215

Reviewer	Repre -sentation	Employment	Consul -tant	Speak ~ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Steven Cohn Content Reviev	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	<ul> <li>AstraZeneca*</li> <li>Bristol-Myers</li> <li>Squibb*</li> <li>Glaxo-</li> <li>SmithKline*</li> <li>Merck*</li> <li>Pfizer*</li> </ul>	None	None	<ul> <li>Defendant, venous thromboemboli pulmonary embolism, 2013</li> <li>Defendant, preoperative evaluation, 2013</li> </ul>
George Crossley	Content Reviewer– ACC Electro- physiology Section Leadership Council	St. Thomas Heart– Medical Director, Cardiac Services	<ul> <li>Boston</li> <li>Scientific</li> <li>Med- tronic*</li> </ul>	• Medtronic* None • Sanofi- -aventis	None	None	None	<ul> <li>Defendant, pacemaker complication, 2012</li> <li>Defendant, EP procedure complication, 2013</li> </ul>

Repre -sentation		Consul -tant	Speak , ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
	McMaster University – Associate Professor, Departments of Clinical Epidemiology and Biostatistics; Juravinski Hospital and Cancer Centre-Head of Cardiology and the Perioperative Cardiovas -cular Service	None	None	None	<ul> <li>Abbott</li> <li>Diagnostics*</li> <li>Bayer*</li> <li>Boehringer</li> <li>Ingelheim*</li> <li>Roche</li> <li>Diagnostics*</li> <li>Stryker*</li> </ul>	Canadian Perioperative Guideline Chair	None
	University of Texas Health Science Center at San Antonio– Professor of Medicine	None	None	None	None	None	None

continued
2
Appendix

Reviewer	Repre -sentation	Employment	Consul -tant	Speak ~ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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 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; Division of Cardiovascular Medicine; Cardiovascular Institute Medical– Medical–	<ul> <li>Actelion</li> <li>Bayer</li> <li>Gilead</li> <li>Lung</li> <li>Biotech-</li> <li>nology</li> </ul>	• Actelion	None	<ul> <li>Cardioki -netics</li> <li>CVRx</li> <li>CVRx</li> <li>Gilead</li> <li>Ikaria</li> <li>Medtronic</li> <li>St. Jude</li> <li>Medical</li> </ul>	None	None

Reviewer	Repre -sentation	Employment	Consul - tant	Speak ~ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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	<ul> <li>Abiomed*</li> <li>AstraZeneca</li> <li>Daiichi-Sankyo*</li> <li>Gilead Sciences</li> <li>Janssen Pharmaceuticals*</li> <li>Janssen Pharmaceuticals</li> <li>Sanofi-aventis*</li> <li>The Medicines Company</li> </ul>	None	None	<ul> <li>Eli Lilly*</li> <li>Gilead</li> <li>Sciences*</li> </ul>	None	None
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

Appendix 2. continued

Reviewer	Repre -sentation	Employment	Consul -tant	Speak -ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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

Fleisher et al 2014 ACC/AHA Perioperative Guideline

200

Appendix 2. continued

Reviewer	Repre -sentation	Employment	Consul -tant	Speak -ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
John Erwin	Content Reviewer	Scott and White None Hospital and Clinic—Senior Staff Cardiologist, Associate Professor of Medicine	None	None	None	• Eli Lilly (Pl)*	None	None
Samuel Gidding	Content Reviewer– ACC/AHA Task Force on Practice Guidelines	Ž	None	None	None	• GlaxoSmithKline* None	None	None
Robert Hendel	Content Reviewer	University of Miami School of Medicine- Director Cardiac Imaging and Outpatient Services	<ul> <li>Adenosine Therapeutics</li> <li>Astellas</li> <li>Bayer</li> </ul>	None	None	None	None	None

Journal of Nuclear Cardiology® Volume 22, Number 1;162–215

Appendix 2. continued

continued	
2	
Appendix	

Expert Witness	None	None	None
Institutional, Organizational, or Other Financial Benefit	None	None	None
Personal Research	None	None	None
Ownership/ Partnership/ Principal	None	None	None
Speak -ers Bureau	None	None	None
Consul -tant	None	None	None
Employment	Baylor College of Medicine– Associate Professor of Medicine	Mayo Clinic Minnesota – Associate Professor of Medicine	Mayo Clinic Arizona— Professor of Medicine
Repre -sentation	Content Reviewer	Content Reviewer	Content Reviewer– ACC/AHA Task Force on Practice Guidelines
Reviewer	Glenn Levine	Karen Mauck	Win-Kuang Shen

Reviewer	Repre -sentation	Employment	Consul -tant	Speak ~ers 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 Electrophys -iology Fellowship	<ul> <li>Biotronik</li> <li>Medtronic</li> <li>St. Jude</li> <li>Medical *</li> </ul>	None	None	None	• LifeWatch*	None
L. Samuel Wann	Content Reviewer	Program Columbia St. Mary's Cardiovascular Physicians– Clinical Cardiologist	None	None	None	None	None	None

Appendix 2. continued

Ð
Ē
חכ
H
드
0
ō
-
. :
N
vibu
<u>۲</u>
5
ູ
2

σ

Reviewer	Repre -sentation	Employment	Consul ,tant	Speak ,ers Bureau	Ownership/ Partnership/ Principal	Personal Research	Organizational, or Other Financial Benefit	Expert Witness
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

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  $\geq$ 5% of the voting stock or share of the business entity, or ownership of  $\geq$ \$10 000 of the fair market value of the business entity; or if funds received 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 and determined to 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 peer review þ were disclosed at the time unless otherwise noted. Names are listed in alphabetical order within each category of review entities that and other represents the relationships of reviewers with industry This table

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 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, other personal gain or loss as a result of the issues/content addressed in the document

\*Significant relationship

\*No financial benefit

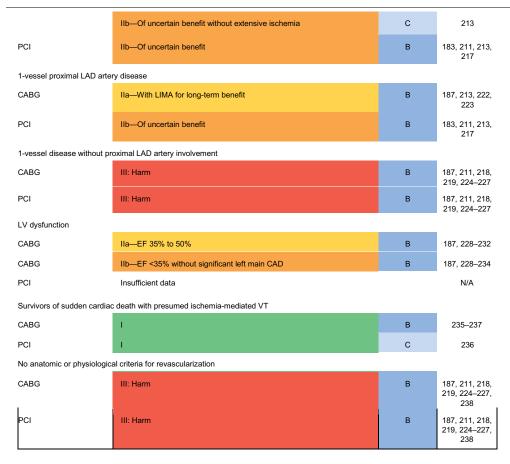
ACC indicates American College of Cardiology: ACS, American College of Surgeons: AHA, American Heart Association; ASA, American Society of Anesthesiologists; ASE, American Society of Echocardiography: ASNC, American Society of Nuclear Cardiology; DSMB, data safety monitoring board; EP, electrophysiology; 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**

# **Table A.** Related Recommendations From Other CPGs. 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	с	170–172
CABG and PCI	IIa—Calculation of the STS and SYNTAX scores	В	170, 173–180
UPLM*			
CABG	1	В	181–187
PCI	<ul> <li>IIa—For SIHD when both of the following are present:</li> <li>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)</li> <li>Clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (eg, STS-predicted risk of operative mortality ≥5%)</li> </ul>	В	173, 176, 180, 188–206
	IIa—For UA/NSTEMI if not a CABG candidate	В	173, 194–197, 202, 203, 205– 207
	IIa—For STEMI when distal coronary flow is TIMI flow grade <3 and PCI can be performed more rapidly and safely than CABG	С	191, 208, 209
	<ul> <li>IIb—For SIHD when <i>both</i> of the following are present:</li> <li>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 &lt;33, bifurcation left main CAD)</li> <li>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 &gt;2%)</li> </ul>	В	173, 176, 180, 188–206, 210
	III: Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG	В	173, 176, 180– 187, 189, 190
3-vessel disease with or wi	thout proximal LAD artery disease*		
CABG	1	В	183, 187, 211– 214
	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	В	190, 205, 213, 215, 216
PCI	IIb—Of uncertain benefit	В	183, 204, 211,
2-vessel disease with proxi	mal LAD artery disease*		213, 217
CABG	1	В	183, 187, 211– 214
PCI	IIb—Of uncertain benefit	В	183, 211, 213, 217
2-vessel disease without p	roximal LAD artery disease⁺		-
CABG	IIa—With extensive ischemia	В	218–221
	IIb—Of uncertain benefit without extensive ischemia	с	213
PCI	IIb—Of uncertain benefit	В	183, 211, 213, 217
1-vessel proximal LAD arte	ry disease		•
CABG	IIa-With LIMA for long-term benefit	В	187, 213, 222, 223

## Table A. continued



\*In patients with multivessel disease who also have diabetes mellitus, it is reasonable to choose CABG (with LIMA) over  $PCI^{220,239}_{-246}$  (*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.<sup>27</sup> and Hillis et al.<sup>26</sup>

### 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 $\leq$ 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.) <sup>247</sup> <sup>249</sup> (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. <sup>250</sup> <sup>252</sup> ( <i>Level of Evidence: B</i> )
	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. <sup>250</sup> <sup>252</sup> ( <i>Level of Evidence: B</i> )
	2. It is reasonable to give beta-blocker therapy in patients with LV systolic dysfunction (EF $\leq$ 40%) without HF or prior MI. ( <i>Level of Evidence: C</i> )
ACS indicates	acute coronary syndrome; CPG, clinical practice guideline; EF, ejection fraction; GDMT, guideline-directed medical

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.<sup>124</sup>

\*Because of new evidence, this is a new recommendation since the publication of the 2011 PCI CPG<sup>27</sup>

\*Features of increased perioperative risk in patients with pulmonary hypertension include: 1) diagnosis of Group 1 pulmonary hypertension (i.e., 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 right ventricular 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<sup>52</sup>,<sup>58</sup>

### References

- 1. Institute of Medicine (U.S.). Clinical Practice Guidelines We Can Trust. Washington, DC: National Academies Press; 2011.
- Institute of Medicine (U.S.). Finding What Works in Health Care: Standards for Systematic Reviews. Washington, DC: National Academies Press; 2011.
- 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.
- Jacobs AK, Anderson JL, Halperin JL (2014) The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey [published online ahead of print August 4, 2014]. Circulation. doi:10.1161/CIR.00000000000090.
- 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.
- ACC/AHA Task Force on Practice Guidelines (2014) 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.cardio source.com/Methodology\_Manual\_for\_ACC\_AHA\_Writing\_Com mittees.pdf and http://my.americanheart.org/idc/groups/ahamahpublic/@wcm/@sop/documents/downloadable/ucm\_319826.pdf. Accessed May 9, 2014.
- Arnett DK, Goodman R, Halperin JL, et al (2014) AHA/ACC/ HHS integrating comorbidities into cardiovascular practice guidelines: a call for comprehensive clinical relevance. [published online ahead of print September 11, 2014]. Circulation. doi:10.1161/CIR.00000000000128.
- Fleisher LA, Fleischmann KE, Auerbach AD, et al. (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 [published online ahead of print August 1, 2014]. Circulation. doi: 10.1161/CIR.000000000000106.

- 9. Wijeysundera DN, Duncan D, Nkonde-Price C, et al (2014) 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 [published online ahead of print August 1, 2014]. Circulation. doi:10.1161/CIR.000000000000104.
- Erasmus MC (2012) Follow-up Investigation Committee. Report on the 2012 Follow-Up Investigation of Possible Breaches of Academic Integrity. September 30, 2012.
- Erasmus MC Follow-up Investigation Committee (2011) Investigation Into Possible Violation of Scientific Integrity—Report Summary. November 16, 2011.
- 12. Luscher TF. The codex of science: honesty, precision, and truth—and its violations. Eur Heart J. 2013;34:1018–23.
- Chopra V, Eagle KA. Perioperative mischief: the price of academic misconduct. Am J Med. 2012;125:953–5.
- 14. Chopra V, Eagle KA. The reply. Am J Med. 2013;126:e7.
- 15. 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. Published online before print March 28, 2014. doi:10.1161/CIR.0000000000000041.
- 16. 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.
- 17. 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.

- 18. 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.
- 19. 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.
- 19a. 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 Cardiovas-cular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2012;126:e354– 471.
- 20. 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. Published online before print July 28, 2014. doi:10.1161/CIR.000000000000095.
- 21. 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.
- 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.
- 23. 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.
- 24. 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.
- 25. 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.

- 26. 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.
- 27. 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.
- 28. 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.
- 29. 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.
- 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.
- 31. 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.
- 32. 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.
- 33. 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.
- 34. 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.
- 35. 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.
- 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.
- 37. 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(833–842):e1–3.

- 38. Deleted in press.
- 39. 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.
- 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.
- 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.
- 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.
- 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.
- 44. 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.
- Feldman T. Balloon aortic valvuloplasty: still under-developed after two decades of use. Catheter Cardiovasc Interv. 2013;81:374–5.
- 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.
- 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.
- 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.
- 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.
- 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.
- 51. 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.
- 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.
- Minai OA, Venkateshiah SB, Arroliga AC. Surgical intervention in patients with moderate to severe pulmonary arterial hypertension. Conn Med. 2006;70:239–43.
- 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.

- 55. 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.
- Price LC, Montani D, Jaïs X, et al. Noncardiothoracic nonobstetric surgery in mild-to-moderate pulmonary hypertension. Eur Respir J. 2010;35:1294–302.
- 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.
- Minai OA, Yared J-P, Kaw R, et al. Perioperative risk and management in patients with pulmonary hypertension. Chest. 2013;144:329–40.
- 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.
- 60. 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(336–346):e1.
- 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.
- 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.
- Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief selfadministered questionnaire to determine functional capacity (the Duke Activity Status Index). Am J Cardiol. 1989;64:651–4.
- 64. 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.
- 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.
- 66. 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- 72. 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.
- 73. 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.

- 74. 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- Carlisle J, Swart M. Mid-term survival after abdominal aortic aneurysm surgery predicted by cardiopulmonary exercise testing. Br J Surg. 2007;94:966–9.
- 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.
- 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.
- 84. 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.
- 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.
- 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.
- 87. 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.
- 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.
- 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.
- Cutler BS, Leppo JA. Dipyridamole thallium 201 scintigraphy to detect coronary artery disease before abdominal aortic surgery. J Vasc Surg. 1987;5:91–100.
- 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.

- 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.
- 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.
- 94. Deleted in press.
- 95. Deleted in press.
- 96. Deleted in press.
- McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med. 2004;351:2795–804.
- 98. Guidelines, 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.
- 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.
- 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.
- 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.
- 102. 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.
- 103. 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.
- Van Kuijk J-P, Flu W-J, Schouten O, et al. Timing of noncardiac surgery after coronary artery stenting with bare metal or drugeluting stents. Am J Cardiol. 2009;104:1229–34.
- 105. 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.
- 106. 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.
- 107. Grines CL, Bonow RO, Casey DE Jr, 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.
- 108. 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.
- 109. 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.

- 110. Devereaux PJ, Yang H, Guyatt GH, et al. Rationale, design, and organization of the PeriOperative ISchemic Evaluation (POISE) trial: a randomized controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. Am Heart J. 2006;152:223–30.
- 111. Lindenauer PK, Pekow P, Wang K, et al. Perioperative betablocker therapy and mortality after major noncardiac surgery. N Engl J Med. 2005;353:349–61.
- 112. Shammash JB, Trost JC, Gold JM, et al. Perioperative betablocker withdrawal and mortality in vascular surgical patients. Am Heart J. 2001;141:148–53.
- Wallace AW, Au S, Cason BA. Association of the pattern of use of perioperative beta-blockade and postoperative mortality. Anesthesiology. 2010;113:794–805.
- 114. Andersson C, Merie C, Jorgensen M, et al. Association of betablocker therapy with sisks 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.
- 115. 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.
- 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.
- 117. 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.
- 118. 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.
- 119. 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.
- 120. Brady AR, Gibbs JSR, Greenhalgh RM, et al. Perioperative betablockade (POBBLE) for patients undergoing infrarenal vascular surgery: results of a randomized double-blind controlled trial. J Vasc Surg. 2005;41:602–9.
- 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.
- 122. 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.
- 123. Flu W-J, van Kuijk J-P, Chonchol M, et al. Timing of preoperative Beta-blocker treatment in vascular surgery patients: influence on post-operative outcome. J Am Coll Cardiol. 2010;56:1922–9.
- 124. 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.
- 125. Surgical Care Improvement Project (2014) SCIP-Card-2: surgery patients on beta-blocker therapy prior to admission who received a beta-blocker during the perioperative period. Available at: http:// www.clinical-insights.com/resources-Aug09SCIP.html. Accessed July 24, 2014.

- 126. Devereaux PJ, Yang H, Yusuf S, et al. Effects of extendedrelease metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. Lancet. 2008;371:1839–47.
- 127. 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.
- 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.
- Ng JLW, Chan MTV, Gelb AW. Perioperative stroke in noncardiac, nonneurosurgical surgery. Anesthesiology. 2011;115: 879–90.
- 130. 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.
- Lindenauer PK, Pekow P, Wang K, et al. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. JAMA. 2004;291:2092–9.
- 132. 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.
- 133. 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.
- 134. 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.
- 135. 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.
- 136. 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.
- 137. Thomson IR, Mutch WA, Culligan JD. Failure of intravenous nitroglycerin to prevent intraoperative myocardial ischemia during fentanyl-pancuronium anesthesia. Anesthesiology. 1984;61:385–93.
- 138. 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.
- 139. 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.
- 140. 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.
- 141. 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.
- 142. Rosenman DJ, McDonald FS, Ebbert JO, et al. Clinical consequences of withholding versus administering renin-angiotensinaldosterone system antagonists in the preoperative period. J Hosp Med. 2008;3:319–25.
- Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370:1494– 503.

- 144. 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.
- 145. 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.
- 146. 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.
- 147. 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.
- 148. 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.
- 149. 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.
- 150. 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.
- 151. 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.
- 152. 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.
- 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.
- 154. 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.
- 155. 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.
- 156. 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.
- 157. 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.
- Devereaux PJ, Xavier D, Pogue J, et al. Characteristics and shortterm prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. Ann Intern Med. 2011;154:523–8.
- 159. Garcia S, Marston N, Sandoval Y, et al. Prognostic value of 12lead electrocardiogram and peak troponin I level after vascular surgery. J Vasc Surg. 2013;57:166–72.
- 160. 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.

- 161. 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.
- 162. 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.
- 163. 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.
- 164. 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.
- 165. 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.
- 166. 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.
- 167. 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.
- 168. 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.
- 169. 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.
- 170. Serruys PW, Morice M-C, 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.
- 171. 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.
- 172. 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.
- 173. Morice M-C, 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.
- 174. Perioperative sympatholysis: beneficial effects of the alpha 2adrenoceptor agonist mivazerol on hemodynamic stability and myocardial ischemia. McSPI-Europe Research Group. Anesthesiology. 1997;86:346–63.
- 175. 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.
- 176. 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.

- 177. 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.
- 178. 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.
- 179. 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.
- 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.
- 181. 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.
- 182. 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.
- 183. 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.
- 184. Takaro T, Hultgren HN, Lipton MJ, et al. The VA cooperative randomized study of surgery for coronary arterial occlusive disease. subgroup with significant left main lesions. Circulation. 1976;54:III107–17.
- 185. 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.
- 186. 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.
- 187. 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.
- 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.
- 189. 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.
- 190. 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.
- 191. 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.
- 192. 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.

- 193. 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.
- 194. 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.
- 195. 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.
- 196. 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.
- 197. 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.
- 198. Makikallio TH, Niemela 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.
- 199. 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.
- 200. 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.
- 201. 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.
- 202. Rodes-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.
- Sanmartin 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.
- 204. 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.
- 205. Seung KB, Park D-W, Kim Y-H, et al. Stents versus coronaryartery bypass grafting for left main coronary artery disease. N Engl J Med. 2008;358:1781–92.
- 206. 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.

- 207. 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.
- 208. 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.
- 209. 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.
- 210. 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.
- 211. 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.
- 212. 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.
- 213. 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.
- Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med. 1988;319:332–7.
- 215. 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.
- 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.
- 217. 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.
- 218. 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.
- 219. 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.
- 220. 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.
- 221. 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.
- 222. Cameron A, Davis KB, Green G, et al. Coronary bypass surgery with internal-thoracic-artery grafts–effects on survival over a 15year period. N Engl J Med. 1996;334:216–9.
- 223. 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.

- 224. 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.
- 225. Pijls NH, De BB, 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.
- 226. Tonino PA, De BB, Pijls NHJ, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009;360:213–24.
- 227. 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.
- 228. 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.
- 229. O'Connor CM, Velazquez EJ, Gardner LH, et al. Comparison of coronary artery bypass grafting versus medical therapy on longterm outcome in patients with ischemic cardiomyopathy (a 25year experience from the Duke Cardiovascular Disease Databank). Am J Cardiol. 2002;90:101–7.
- Phillips HR, O'Connor CM, Rogers J. Revascularization for heart failure. Am Heart J. 2007;153:65–73.
- 231. 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.
- Tsuyuki RT, Shrive FM, Galbraith PD, et al. Revascularization in patients with heart failure. CMAJ. 2006;175:361–5.
- 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.
- 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.
- 235. 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.
- 236. 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.
- 237. Kaiser GA, Ghahramani A, Bolooki H, et al. Role of coronary artery surgery in patients surviving unexpected cardiac arrest. Surgery. 1975;78:749–54.
- 238. 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.
- 239. 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.
- Investigators BARI. The final 10-year follow-up results from the BARI randomized trial. J Am Coll Cardiol. 2007;49:1600–6.
- 241. 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.
- 242. 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: oneto eight-year outcomes. J Am Coll Cardiol. 2003;41:1293–304.

- 243. 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.
- 244. 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.
- 245. 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.
- 246. 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.
- 247. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure.

U.S. Carvedilol Heart Failure Study Group. N Engl J Med. 1996;334:1349–55.

- 248. 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.
- 249. 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.
- 250. Freemantle N, Cleland J, Young P, et al. Beta-blockade after myocardial infarction: systematic review and meta regression analysis. BMJ. 1999;318:1730–7.
- 251. 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.
- 252. De Lima LG, Soares BGO, Saconato H, et al. Beta-blockers for preventing stroke recurrence. Cochrane Database Syst Rev. 2013;5:CD007890.