Circulation

ACC/AHA/SCAI CLINICAL PRACTICE GUIDELINE

2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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AIM: The guideline for coronary artery revascularization replaces the 2011 coronary artery bypass graft surgery and the 2011 and 2015 percutaneous coronary intervention guidelines, providing a patient-centric approach to guide clinicians in the treatment of patients with significant coronary artery disease undergoing coronary revascularization as well as the supporting documentation to encourage their use.

METHODS: A comprehensive literature search was conducted from May 2019 to September 2019, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from PubMed, EMBASE, the Cochrane Collaboration, CINHL Complete, and other relevant databases. Additional relevant studies, published through May 2021, were also considered.

STRUCTURE: Coronary artery disease remains a leading cause of morbidity and mortality globally. Coronary revascularization is an important therapeutic option when managing patients with coronary artery disease. The 2021 coronary artery revascularization guideline provides recommendations based on contemporary evidence for the treatment of these patients. The recommendations present an evidence-based approach to managing patients with coronary artery disease who are being considered for coronary revascularization, with the intent to improve quality of care and align with patients' interests.

Key Words: AHA Scientific Statements ■ percutaneous coronary intervention ■ angioplasty ■ coronary artery bypass graft surgery ■ myocardial infarction ■ cardiac surgery, stent(s) ■ angiogram ■ angiography ■ percutaneous transluminal coronary angioplasty ■ coronary atherosclerosis ■ saphenous vein graft ■ internal mammary artery graft ■ internal thoracic artery graft ■ arterial graft ■ post-bypass ■ non–ST-segment–elevated myocardial infarction ■ vein graft lesions ■ myocardial revascularization ■ multivessel PCI ■ left ventricular dysfunction

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ACC/AHA Joint Committee on Clinical Practice Guidelines Members, see page e80.

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TOP 10 TAKE-HOME MESSAGES

1. Treatment decisions regarding coronary revascularization in patients with coronary artery disease should be based on clinical indications, regardless of sex, race, or ethnicity, because there is no evidence that some patients benefit less than others, and efforts to reduce disparities of care are warranted.
2. In patients being considered for coronary revascularization for whom the optimal treatment strategy is unclear, a multidisciplinary Heart Team approach is recommended. Treatment decisions should be patient centered, incorporate patient preferences and goals, and include shared decision-making.
3. For patients with significant left main disease, surgical revascularization is indicated to improve survival relative to that likely to be achieved with medical therapy. Percutaneous revascularization is a reasonable option to improve survival, compared with medical therapy, in selected patients with low to medium anatomic complexity of coronary artery disease and left main disease that is equally suitable for surgical or percutaneous revascularization.
4. Updated evidence from contemporary trials supplement older evidence with regard to mortality benefit of revascularization in patients with stable ischemic heart disease, normal left ventricular ejection fraction, and triple-vessel coronary artery disease. Surgical revascularization may be reasonable to improve survival. A survival benefit with percutaneous revascularization is uncertain. Revascularization decisions are based on consideration of disease complexity, technical feasibility of treatment, and a Heart Team discussion.
5. The use of a radial artery as a surgical revascularization conduit is preferred versus the use of a saphenous vein conduit to bypass the second most important target vessel with significant stenosis after the left anterior descending coronary

artery. Benefits include superior patency, reduced adverse cardiac events, and improved survival.

6. Radial artery access is recommended in patients undergoing percutaneous intervention who have acute coronary syndromes or stable ischemic heart disease, to reduce bleeding and vascular complications compared with a femoral approach. Patients with acute coronary syndromes also benefit from a reduction in mortality rate with this approach.
7. A short duration of dual antiplatelet therapy after percutaneous revascularization in patients with stable ischemic heart disease is reasonable to reduce the risk of bleeding events. After consideration of recurrent ischemia and bleeding risks, select patients may safely transition to P2Y12 inhibitor monotherapy and stop aspirin after 1 to 3 months of dual antiplatelet therapy.
8. Staged percutaneous intervention (while in hospital or after discharge) of a significantly stenosed nonculprit artery in patients presenting with an ST-segment–elevation myocardial infarction is recommended in select patients to improve outcomes. Percutaneous intervention of the nonculprit artery at the time of primary percutaneous coronary intervention is less clear and may be considered in stable patients with uncomplicated revascularization of the culprit artery, low-complexity nonculprit artery disease, and normal renal function. In contrast, percutaneous intervention of the non-culprit artery can be harmful in patients in cardiogenic shock.
9. Revascularization decisions in patients with diabetes and multivessel coronary artery disease are optimized by the use of a Heart Team approach. Patients with diabetes who have triple-vessel disease should undergo surgical revascularization; percutaneous coronary intervention may be considered if they are poor candidates for surgery.
10. Treatment decisions for patients undergoing surgical revascularization of coronary artery disease should include the calculation of a patient's surgical risk with the Society of Thoracic Surgeons score. The usefulness of the SYNTAX score calculation in treatment decisions is less clear because of the interobserver variability in its calculation and its absence of clinical variables.

PREAMBLE

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a foundation for the delivery of quality cardiovascular care. The ACC and AHA sponsor the development and publication of clinical practice guidelines without commercial support, and members volunteer their time to the writing and review efforts. Guidelines are official policy of the ACC and AHA. For some guidelines, the ACC and AHA partner with other organizations.

Intended Use

Clinical practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease (CVD). The focus is on medical practice in the United States, but these guidelines are relevant to patients throughout the world. Although guidelines may be used to inform regulatory or payer decisions, the intent is to improve quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances and should not replace clinical judgment.

Clinical Implementation

Management, in accordance with guideline recommendations, is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.

Methodology and Modernization

The ACC/AHA Joint Committee on Clinical Practice Guidelines (Joint Committee) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations, including the Institute of Medicine,[1,2] and on the basis of internal reevaluation. Similarly, presentation and delivery of guidelines are reevaluated and modified in response to evolving technologies and other factors to optimally facilitate dissemination of information to health care professionals at the point of care.

Numerous modifications to the guidelines have been implemented to make them shorter and enhance "user-friendliness." Guidelines are written and presented in a modular, "knowledge chunk" format, in which each chunk includes a table of recommendations, a brief synopsis, recommendation-specific supportive text and, when appropriate, flow diagrams or additional tables. Hyperlinked references are provided for each modular knowledge chunk to facilitate quick access and review.

In recognition of the importance of cost–value considerations, in certain guidelines, when appropriate and feasible, an analysis of value for a drug, device, or

intervention may be performed in accordance with the ACC/AHA methodology.[3]

To ensure that guideline recommendations remain current, new data will be reviewed on an ongoing basis by the writing committee and staff. Going forward, targeted sections or knowledge chunks will be revised dynamically after publication and timely peer review of potentially practice-changing science. The previous designations of "full revision" and "focused update" will be phased out. For additional information and policies on guideline development, readers may consult the ACC/AHA guideline methodology manual[4] and other methodology articles.[5-7]

Selection of Writing Committee Members

The Joint Committee strives to ensure that the guideline writing committee contains requisite content expertise and is representative of the broader cardiovascular community by selection of experts across a spectrum of backgrounds, representing different geographic regions, sexes, races, ethnicities, intellectual perspectives/biases, and clinical practice settings. Organizations and professional societies with related interests and expertise are invited to participate as partners or collaborators.

Relationships With Industry and Other Entities

The ACC and AHA have rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found online. Appendix 1 of the guideline lists writing committee members' relevant RWI; for the purposes of full transparency, their comprehensive disclosure information is available in a Supplemental Appendix. Comprehensive disclosure information for the Joint Committee is also available online.

Evidence Review and Evidence Review Committees

In developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data.[4,5] 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 key references are cited.

An independent evidence review committee is commissioned when there are ≥1 questions deemed of utmost clinical importance and merit formal systematic review to determine which patients are most likely to benefit from a drug, device, or treatment strategy, and to what degree. Criteria for commissioning an evidence review committee and formal systematic review include absence of a current authoritative systematic review, feasibility of defining the benefit and risk in a time frame consistent with the writing of a guideline, relevance to a substantial number of patients, and likelihood that the findings can be translated into actionable recommendations. Evidence review committee members may include methodologists, epidemiologists, clinicians, and biostatisticians. Recommendations developed by the writing committee on the basis of the systematic review are marked "SR".

Guideline-Directed Management and Therapy

The term guideline-directed medical therapy (GDMT) encompasses clinical evaluation, diagnostic testing, and both pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm dosage with product insert material and evaluate for contraindications and interactions. Recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.

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Chair, ACC/AHA Joint Committee on Clinical Practice Guidelines

1. INTRODUCTION

1.1. Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence based. An initial extensive evidence review, which included literature derived from research involving human subjects, published in English, and indexed in the US National Library of Medicine and the National Center for Biotechnology information (through PubMed), EMBASE, the Cochrane Collaboration, CINHL Complete, and other selected databases relevant to this guideline, was conducted from May 2019 to September 2019. Key search words included but were not limited to the following: *percutaneous coronary intervention, angioplasty, coronary artery bypass graft (CABG) surgery, myocardial infarction, cardiac surgery, stent(s), angiogram, angiography, percutaneous transluminal coronary angioplasty, coronary atherosclerosis, saphenous vein graft, internal mammary artery (IMA) graft, internal thoracic artery graft, arterial graft, post-bypass, non-ST elevated myocardial infarction, vein graft lesions, myocardial revascularization, multivessel PCI*, and *left ventricular dysfunction*. Additional relevant studies, published through May 2021 during the guideline writing process, were also considered by the writing committee and added to the evidence tables when appropriate. The final evidence tables are included in the Online Data Supplement and summarize the evidence used by the writing committee to formulate recommendations. References selected and published in the present document are representative and not all-inclusive.

Table 1. Associated Guidelines and Statements

Title	Organization	Publication Year (Reference)
Guidelines		
2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death	AHA/ACC/HRS	2017[7]
2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease	ACC/AHA	2020[8]
2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease	ACC/AHA	2019[9]
2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery	ACC/AHA	2016[10]
2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol	AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA	2019[11]
2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease	AHA/ACC	2019[12]
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation	AHA/ACC/HRS	2014[13]
Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation	AHA/ACC/HRS	2019[14]
ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 Multimodality Appropriate Use Criteria for the Detection and Risk Assessment of Stable Ischemic Heart Disease	ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS	2014[15]
ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction *Levine et al., 2016 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction, is now replaced and retired by the present 2021 guideline.*	ACC/AHA	2016[3]
2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes	AHA/ACC	2014[6]
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	ACCF/AHA	2013[5]
2013 ACCF/AHA Guideline for the Management of Heart Failure	ACCF/AHA	2013[16]
2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure	ACC/AHA/HFSA	2017[17]
2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery *Hillis et al., 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, is now replaced and retired by the present 2021 guideline.*	ACCF/AHA	2011[1]
2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention *Levine et al., 2013 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, is now replaced and retired by the present 2021 guideline.*	ACCF/AHA/SCAI	2013[2]
2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death	AHA/ACC/HRS	2018[7]
2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults	ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA	2018[18]
2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients with Stable Ischemic Heart Disease	ACCF/AHA/ACP/AATS/PCNA/SCAI/STS	2012[4]
Statements		
2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment	ACC	2018[19]
Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff: A Clinical Practice Guideline for Treating Tobacco Use and Dependence: 2008 Update: A US Public Health Service Report	US Public Health Service report	2008[20]
AATS Expert Consensus Review on Prevention and Management of Sternal Wound Infections	AATS	2016[21]

(*Continued*)

Table 1. Continued

Title	Organization	Publication Year (Reference)
2018 ACC/AHA Clinical Performance and Quality Measures for Cardiac Rehabilitation	ACC/AHA	2018[22]
Spontaneous Coronary Artery Dissection: Current State of the Science	AHA	2018[23]
Contemporary Management of Cardiogenic Shock	AHA	2017[24]
Secondary Prevention After Coronary Artery Bypass Graft Surgery: A Scientific Statement From the American Heart Association	AHA	2015[25]
Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes–2018	ADA	2018[26]

AACVPR indicates American Association of Cardiovascular and Pulmonary Rehabilitation; AAPA, American Association of Physician Assistants; AATS, American Association for Thoracic Surgery; ABC, Association of Black Cardiologists; ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; ACP, American College of Physicians; ACPM, American College of Preventive Medicine; ADA, American Diabetes Association; AGS, American Geriatrics Society; AHA, American Heart Association; APhA, American Public Health Association; ASE, American Society of Echocardiography; ASH, American Society of Hypertension; ASNC, American Society of Nuclear Cardiology; ASPC, American Society for Preventive Cardiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; NLA, National Lipid Association; NMA, National Medical Association; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; SCCT, Society of Cardiovascular Computed Tomography; SCMR, Society for Cardiovascular Magnetic Resonance; and STS, Society of Thoracic Surgeons.

1.2. Organization of the Writing Committee

The writing committee consisted of clinicians, general cardiologists, interventional cardiologists, cardiac surgeons, a cardiac anesthesiologist, an advanced nurse practitioner, and 2 lay/patient representatives. The writing committee included representatives from the ACC, AHA, Society for Cardiovascular Angiography and Interventions (SCAI), American Association for Thoracic Surgery, and Society of Thoracic Surgeons (STS). Appendix 1 of the present document lists writing committee members' relevant RWI. For the purposes of full transparency, the writing committee members' comprehensive disclosure information is available in a Supplemental Appendix.

1.3. Document Review and Approval

This document was reviewed by 2 official reviewers each nominated by the ACC and AHA; 1 reviewer each from the ACC, AHA, STS, American Association for Thoracic Surgery, and SCAI; and 31 individual content reviewers. Reviewers' RWI information was distributed to the writing committee and is published in Appendix 2.

The present document was approved for publication by the governing bodies of the ACC, AHA, and SCAI.

1.4. Scope of the Guideline

The scope of the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization" is to provide an update to and to consolidate the 2011 coronary artery bypass graft (CABG) surgery[1] and the 2011 and 2015 percutaneous coronary intervention (PCI) guidelines,[2,3] with the added consideration of using a patient-centric disease approach. The applicable sections on revascularization from the 2012 stable ischemic heart disease (SIHD) guideline,[4] as well as the 2013 ST-segment–elevation myocardial infarction (STEMI)[5] and 2014 non–ST-segment–elevation myocardial infarction (NSTEMI) guidelines,[6] will also be updated. This present guideline will affect the following documents:

1. Replace/retire the 2011 PCI guideline.[2]
2. Replace/retire the 2011 CABG guideline.[1]
3. Replace/retire the 2015 update in PCI in STEMI guideline.[3]
4. Replace/retire the 2013 STEMI guideline, Sections 4.1, 4.2, 4.3, 4.4, 5.3 (deals with transfer after lytic with intent to do PCI), 6.2, 6.4, 7.1, and 7.2.[5]
5. Replace/retire 2014 non–ST-segment–elevation acute coronary syndrome (NSTE-ACS) guideline, Sections 4.4.4, 5.1.1, 5.1.2.1, 5.1.2.2, 5.1.2.3, and 5.2.[6]
6. Replace/retire the 2012 SIHD guideline, Section 5.[4]

The intended primary target audience consists of cardiovascular clinicians who are involved in the care of patients for whom revascularization is considered or indicated. Coronary artery disease (CAD) is to be approached with the most current treatment options and treated as a "condition." Recommendations are stated in reference to the patients and their condition. The focus is to provide the most up-to-date evidence to inform the clinician during shared decision-making with the patient. Although the document is not intended to be a procedural-based manual of recommendations that outlines the best practice for coronary revascularization, there are certain techniques that surgeons or interventional cardiologists might use that are associated with improved clinical outcomes.

In developing the 2021 coronary artery revascularization guideline, the writing committee reviewed previously published guidelines and related statements. Table 1 contains a list of these

Table 2. Applying American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE‡
CLASS 1 (STRONG) — **Benefit >>> Risk** **Suggested phrases for writing recommendations:** • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	**LEVEL A** • High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
CLASS 2a (MODERATE) — **Benefit >> Risk** **Suggested phrases for writing recommendations:** • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	**LEVEL B-R (Randomized)** • Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
CLASS 2b (WEAK) — **Benefit ≥ Risk** **Suggested phrases for writing recommendations:** • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	**LEVEL B-NR (Nonrandomized)** • Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
CLASS 3: No Benefit (MODERATE) (Generally, LOE A or B use only) — **Benefit = Risk** **Suggested phrases for writing recommendations:** • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	**LEVEL C-LD (Limited Data)** • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
Class 3: Harm (STRONG) — **Risk > Benefit** **Suggested phrases for writing recommendations:** • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	**LEVEL C-EO (Expert Opinion)** • Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

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

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

publications and statements deemed pertinent to this writing effort and is intended for use as a resource, thus obviating the need to repeat existing guideline recommendations.

1.5. Class of Recommendation and Level of Evidence

The Class of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 2).[1]

1.6. Abbreviations

Abbreviation	Meaning/Phrase
ACS	acute coronary syndrome
AKI	acute kidney injury
AMI	acute myocardial infarction
AVR	aortic valve replacement
BIMA	bilateral internal mammary artery
BMS	bare-metal stent
CABG	coronary artery bypass graft
CAD	coronary artery disease
CKD	chronic kidney disease

(*Continued*)

1.6. Abbreviations Continued

Abbreviation	Meaning/Phrase
COR	Class of Recommendation
CTO	chronic total occlusion
CVD	cardiovascular disease
DAPT	dual antiplatelet therapy
DES	drug-eluting stent
ECG	electrocardiogram
FFR	fractional flow reserve
GDMT	guideline-directed medical therapy
iFR	instantaneous wave-free ratio
IMA	internal mammary artery
ISR	in-stent restenosis
IVUS	intravascular ultrasound
LAD	left anterior descending
LIMA	left internal mammary artery
LOE	Level of Evidence
MACE	major adverse cardiovascular events
MI	myocardial infarction
NSTE-ACS	non–ST-segment–elevation acute coronary syndrome
NSTEMI	non–ST-segment–elevation myocardial infarction
OCT	optical coherence tomography
PCI	percutaneous coronary intervention
RCT	randomized controlled trial
SCAD	spontaneous coronary artery dissection
SIHD	stable ischemic heart disease
STEMI	ST-segment–elevation myocardial infarction
SVG	saphenous vein graft
SYNTAX	Synergy Between PCI With TAXUS and Cardiac Surgery
TAVR	transcatheter aortic valve replacement
UFH	unfractionated heparin
VT	ventricular tachycardia

2. IMPROVING EQUITY OF CARE IN REVASCULARIZATION AND SHARED DECISION-MAKING

2.1. Improving Equity of Care in Revascularization

Recommendation to Improve Equity of Care in Revascularization Referenced studies that support the recommendation are summarized in Online Data Supplement 1.

COR	LOE	Recommendation
1	B-NR	1. In patients who require coronary revascularization, treatment decisions should be based on clinical indication, regardless of sex[1-7] or race or ethnicity,[8-10] and efforts to reduce disparities of care are warranted.[11,12]

Synopsis

Health disparities by sex and race are evident across the spectrum of CVD in the United States,[7,9,13-15] and mounting evidence demonstrates that social factors are strongly associated with cardiovascular health outcomes.[16, 17] Differences in access to care, cardiovascular treatment, mortality rate, and readmission outcomes persist by important sociodemographic characteristics that include but are not limited to socioeconomic status, race, and ethnicity.[18-22] African Americans,[23-25] Hispanics,[24] and South Asians[26] (with substantial heterogeneity within Asian subgroups) have a higher prevalence of cardiovascular risk factors and crude mortality.[16] Although access to health care remains a problem, even after entering into the health care system, women and non-White patients are less likely to receive reperfusion therapy, an invasive strategy, or revascularization[9,13,27-37] and more likely to have worse outcomes.[37-40] As compared with White male patients, women and Black patients with acute coronary syndrome (ACS) receive less guideline-based therapy in hospital and at discharge.[27,32,41,42] Differences in comorbidities, health education, presentation, socioeconomic status, regional hospital capability and quality, and insurance and health care access[15,28,29,35,37,43-48] contribute to the problem, but disparities can persist despite adjustment for these factors.[7,30-32,49,50] In a study of patients with cardiac symptoms, clinicians were less likely to recommend cardiac catheterization to women and non-White patients than to White male patients, despite being given the exact same clinical vignette for White male patients.[51] Continued vigilance against conscious and unconscious gender, racial, and ethnic discrimination and purposeful efforts to increase the implementation of guideline-based therapy for all patients, regardless of sex, race, or ethnicity, are needed.

Recommendation-Specific Supportive Text

After controlling for greater baseline comorbidities among patients undergoing revascularization, several observational studies have demonstrated that Black,[28,52-54] Hispanic,[24,50] and Asian[55,56] patients have outcomes similar to those of White patients. Similarly, after controlling for baseline comorbidities and treatment strategy, most studies demonstrate similar outcomes in women and men.[1-6] Post hoc analyses of randomized trials evaluating revascularization provide compelling evidence, inasmuch as enrolled patients are more similar and the decision to revascularize is protocol driven. In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial, revascularization rates were lowest and mortality rates highest for Hispanics and

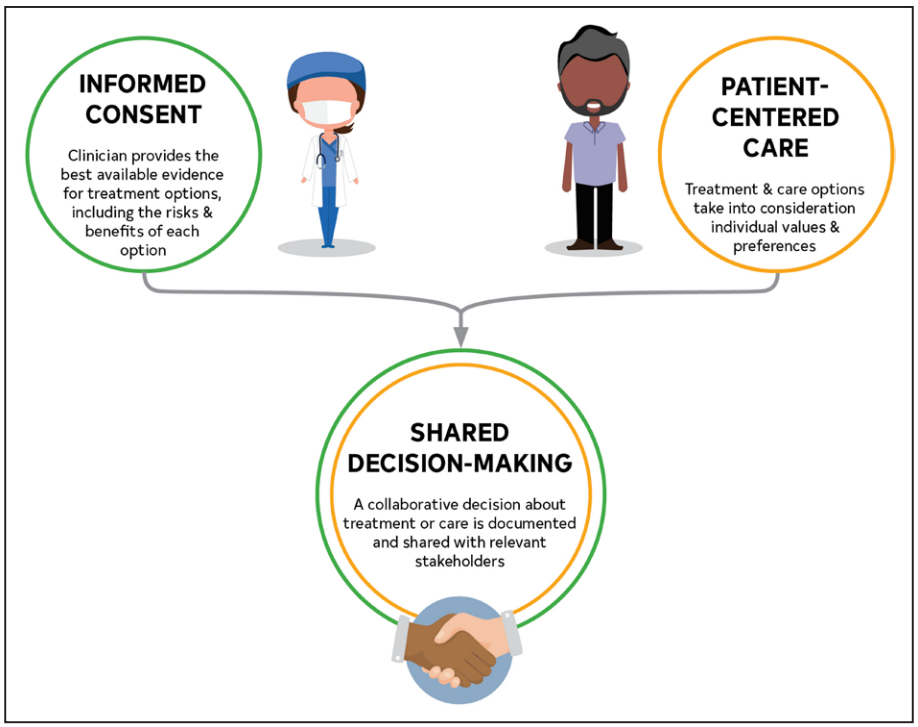

Figure 1. Shared Decision-Making Algorithm.

African Americans, but there was no interaction between race and the mortality benefit of revascularization.[9] Similar results have been reported for women with shock in the CULPRIT-SHOCK (Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock trial.[57] In the TACTICS-TIMI 18 (Treat Angina With Aggrastat and Determine Cost of Therapy With Invasive or Conservative Strategy—Thrombolysis In Myocardial Infarction 18) trial, evaluating patients with NSTE-ACS, non-White patients and female patients had more comorbidity and more major adverse cardiovascular event (MACE) outcomes than White and male patients but were revascularized at the same rate. After adjustment for baseline characteristics, the invasive strategy was equally beneficial for all patients, without evidence of racial differences.[10] A meta-analysis of RCT of invasive vs conservative strategies in women and men with NSTE-ACS reported a similar proportional benefit of an invasive strategy in women and men, (although low risk women with biomarker negative ACS did not derive a benefit to an early invasive strategy).[1] Additionally, studies have shown similar relative benefits of primary PCI[3] and revascularization in SIHD.[5,6] for women and men. In view of these findings, the decision to offer revascularization should be made on the basis of a patient's clinical characteristics, and preferences and should be the same for all patients, regardless of sex, race, or ethnicity.

2.2. Shared Decision-Making and Informed Consent

Recommendations for Shared Decision-Making and Informed Consent		
COR	**LOE**	**Recommendations**
1	C-LD	1. In patients undergoing revascularization, decisions should be patient centered—that is, considerate of the patient's preferences and goals, cultural beliefs, health literacy, and social determinants of health—and made in collaboration with the patient's support system.[1,2]
1	C-LD	2. In patients undergoing coronary angiography or revascularization, adequate information about benefits, risks, therapeutic consequences, and potential alternatives in the performance of percutaneous and surgical myocardial revascularization should be given, when feasible, with sufficient time for informed decision-making to improve clinical outcomes.[3-5]

Synopsis

Shared decision-making (Figure 1) is a collaborative approach that provides patients with unbiased, evidence-based information on treatment choices and encourages a dialogue between patients and providers, with the aim of making decisions that use scientific evidence and align with the patient's values and preferences.[3,4,6] It is essential that the clinician use terminology that the patient understands to allow effective processing of health information and to foster the patient's

Table 3. Ideal Components of the Shared Decision-Making and Informed Consent Process

Patient-Centered Care
Assess a patient's ability to understand complex health information
Seek support of family/others
Elicit and respect cultural, racial, ethnic, or religious preferences and values
Evaluate social determinants of health (education, income, access to health care)
Improve telephone/telemedicine access
Discuss treatment alternatives and how each affects the patient's quality of life
Shared Decision-Making
Encourage questions and explain the patient's role in the decision-making partnership
Clearly and accurately communicate the potential risks and benefits of a particular procedure and alternative treatments
Ensure that patients have a key role in deciding what revascularization approach is appropriate
Use shared decision aids: Alphabetical List of Decision Aids by Health Topic, Ottawa Hospital Research Institute (https://decisionaid.ohri.ca/implement.html)[27] SHARE Approach Curriculum Tools, Agency for Health care Research and Quality (https://www.ahrq.gov/health-literacy/curriculum-tools/shareddecisionmaking/tools/tool-1/index.html)[28]
Spend sufficient time to engage in shared decision-making; allow for a second opinion
Work with a chaplain, social worker, or other team members to facilitate shared decision-making
Encourage patients to share their fears, stress, or other emotions, and address appropriately
Negotiate decision in partnership with the patient and family members
Respect patient's autonomy to decline recommended treatment
Consent Procedures
Use plain language, avoiding jargon, and adopt the patient's words; integrate pictures to teach
Document teach-back of patient's knowledge and understanding
Conduct conversations with a trained interpreter, as needed
Provide patient-specific short- and long-term risks, benefits, and alternative treatments
Provide unbiased, evidence-based, reliable, accessible, and relevant information to patient
Discuss specific risks and benefits with regard to survival, relief of angina, quality of life, and potential additional intervention, as well as uncertainties associated with different treatment strategies
Provide patient time to reflect on the trade-offs imposed by the outcome estimates
Provide information on the level of operator expertise, volume of the facility, and local results in the performance of coronary revascularization options
Clearly inform of the need for continued medical therapy and lifestyle modifications

participation in treatment decisions.[7] The use of online modules, decision aids, or videos about treatment options can help patients better understand the risks and benefits of various therapies. Patients are interested in how a recommended treatment might impact their prognosis and quality of life.[8] In the treatment decision-making process, the patient's best interest should be placed first, and the active participation of the patient and significant others should be engaged. The contributions of social determinants of health to CVD are poorly understood.[9,10] but may impact a patient's decision with regard to treatments. In high-income countries, 4 socioeconomic status metrics have been associated with CVD: income level, educational attainment, employment status, and environmental factors.[11-13]

Recommendation-Specific Supportive Text

1. Shared decision-making is vital to patient-centered care. Shared decision-making improves patients' understanding of treatment options, increases realistic expectations of benefits and harms, stimulates engagement in decision-making, and improves concordance between patients' values and treatment choices.[14-17] Factors complicating effective shared decision-making include low health literacy, adverse social determinants of health, cultural beliefs, language barriers, advanced age, and complex comorbidities. Health literacy is associated with socioeconomic position, English proficiency, and the development of general literacy.[18] Incorporating a patient's preferences into the decision-making process improves the patient's well-being through better treatment adherence and higher satisfaction with health outcomes.[5,19,20] A patient's right to decline recommended treatments must be respected and should be acknowledged in a written document after the patient has received sufficient information from the Heart Team.[8]
2. Patients cannot engage in shared decision-making until they know the potential benefits and risks of all treatment options. Clinicians must provide evidence-based estimates of risks, benefits, and costs of therapeutic options.[8,21,22] Procedure-related and long-term risks and benefits, such as survival, quality of life, and the need for late reintervention, should be included in such discussions (Table 3).[8] Patients should also be educated about the need for continued medical therapy with or without revascularization, as well as lifestyle modification and other secondary prevention strategies.[21,23] In some situations, in which the optimal treatment strategy is uncertain, it may be appropriate to defer revascularization to allow time for consultation and discussion. The clinician must act in the patient's best interest and convey the risks and benefits of all revascularization treatment options, consult with additional specialists when appropriate, and allow the patient to consult family.[24,25] Challenges exist

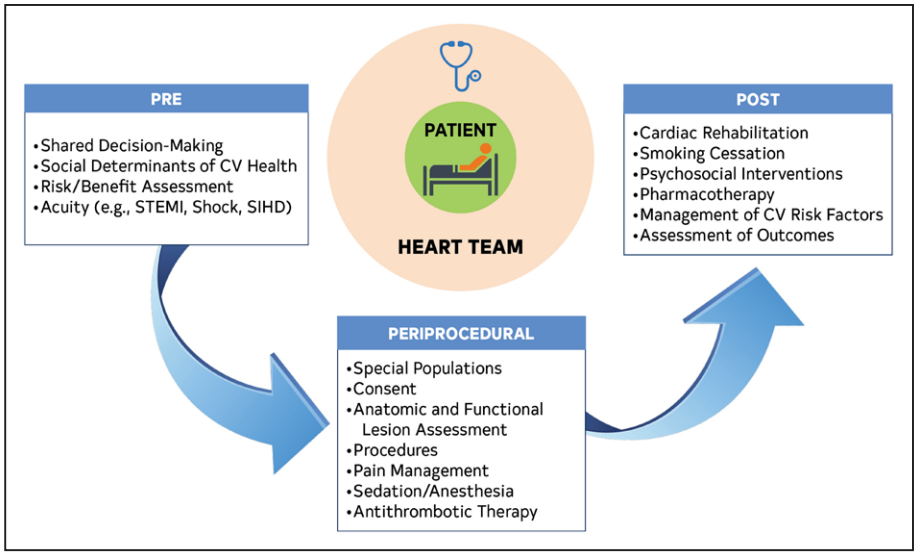

Figure 2. Phases of Patient-Centric Care in the Treatment of Coronary Artery Disease.
CV indicates cardiovascular; SIHD, stable ischemic heart disease; and STEMI, ST-segment–elevation myocardial infarction.

when scientific data support a treatment, but the patient prefers an alternative treatment; in 1 study, patients preferred PCI over CABG, even when the risk of death with PCI was double the risk with CABG.[26]

3. PREPROCEDURAL ASSESSMENT AND THE HEART TEAM

3.1. The Heart Team

Recommendation for the Heart Team
Referenced studies that support the recommendation are summarized in Online Data Supplement 2.

COR	LOE	Recommendation
1	B-NR	1. In patients for whom the optimal treatment strategy is unclear, a Heart Team approach that includes representatives from interventional cardiology, cardiac surgery, and clinical cardiology is recommended to improve patient outcomes.[1-7]

Synopsis

The multidisciplinary Heart Team, which involves the cardiologist, cardiac surgeon, and other specialists, has become a critical component of the revascularization decision. Initially, the Heart Team approach to decision-making for coronary disease arose within the context of randomized trials comparing PCI with CABG to ensure selected patients were equally suited for either strategy before randomization.[8] Subsequently, the Heart Team has become an important paradigm in clinical practice, emphasizing the importance of team consensus on the optimal approach to revascularization. Ideal situations for Heart Team consideration include patients with complex coronary disease, comorbid conditions that could impact the success of the revascularization strategy, and other clinical or social situations that may impact outcomes (Figure 2 and Table 4). The Heart Team process should rest on the principles of collegiality, mutual respect, and commitment to excellence. The logistics of convening the Heart Team should depend on local resources and workflows. Models include daily to weekly scheduled meetings and ad hoc activation.[1,2,4,6,9] Remote conferences have also been advocated.[9] Additionally, there should be a process for rapid activation of the Heart Team for urgent or emergency clinical situations.

Recommendation-Specific Supporting Text

1. Observational studies using the Heart Team have included interventional cardiology, cardiac surgery, and noninvasive cardiologists[1-4,6] Additional professionals who offer input may include the patient's primary physician, as well as palliative care, critical care, anesthesiology, and imaging specialists. Observational studies have demonstrated favorable outcomes when the Heart Team was used in cases of unprotected left main disease, triple-vessel disease, double-vessel disease involving the proximal left anterior descending (LAD) artery, or single-vessel disease involving the proximal LAD artery in the context of diabetes, or in cases in which the referring physician requested such evaluation.[5-7,10,11] Heart Team decisions are generally reproducible[4] and associated with good outcomes.[2,6]

Table 4. Factors for Consideration by the Heart Team

Coronary Anatomy
Left main disease
Multivessel disease
High anatomic complexity (ie, bifurcation disease, high SYNTAX score)
Comorbidities
Diabetes
Systolic dysfunction
Coagulopathy
Valvular heart disease
Frailty
Malignant neoplasm
End-stage renal disease
Chronic obstructive pulmonary disease
Immunosuppression
Debilitating neurological disorders
Liver disease/cirrhosis
Prior CVA
Calcified/porcelain aorta
Aortic aneurysm
Procedural Factors
Local and regional outcomes
Access site for PCI
Surgical risk
PCI risk
Patient Factors
Unstable presentation or shock
Patient preferences
Inability or unwillingness to adhere to DAPT
Patient social support
Religious beliefs
Patient education, knowledge, and understanding

CVA indicates cerebrovascular accident; DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention; and SYNTAX, Synergy Between PCI With TAXUS and Cardiac Surgery.

3.2. Predicting Patient Risk of Death With CABG

Recommendation for Predicting Patient Risk of Death With CABG Referenced studies that support the recommendation are summarized in Online Data Supplements 3.

COR	LOE	Recommendation
1	B-NR	1. In patients who are being considered for CABG, calculation of the STS risk score is recommended to help stratify patient risk.[1,2]

Synopsis

The STS risk score is designed to predict adverse outcomes in patients undergoing CABG, including the risk of death, renal failure, permanent stroke, prolonged ventilation, deep sternal wound infection, reoperation, and prolonged length of stay. The STS risk score is derived from data on patients undergoing CABG in the United States. The STS score is periodically updated to reflect new risk models for CABG, with the most recent update in 2018 based on the Adult Cardiac Surgery Database from 2011–2014.[3,4] Similar to the STS score, the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II, developed in 2011, is designed to predict adverse outcomes in patients undergoing isolated CABG.[5]

Table 5. Assessment of Risk Factors Not Quantified in the STS Score

Risk Factor	Assessment Tool
Cirrhosis	Model for End-Stage Liver Disease (MELD) score[1-6]
Frailty	Gait speed[8,10-14,16]
Malnutrition	Malnutrition Universal Screening Tool (MUST)[7,9,15,16]

STS indicates Society of Thoracic Surgeons.

Recommendation-Specific Supporting Text

1. The STS risk score has been validated in several studies and demonstrates excellent predictive value for estimating risk of adverse events.[2-4] The STS risk score serves as a useful tool when a choice is being made among various treatment strategies because it allows the clinician, the patient, and the patient's family to have a reasonable estimate of operative risk. The STS risk score performs better than the EuroSCORE II for the patient population with CABG, particularly at higher (>5%) predicted mortality rates.[1,2] Commonly used cardiac surgery risk models, such as the STS and EuroSCORE II, are limited in assessing the influence of risk factors, including cirrhosis, frailty, and malnutrition, on outcome. Patients with liver cirrhosis, frailty, and malnutrition have increased risk of perioperative morbidity and mortality after cardiac surgery[6-17] and may be assessed by other tools (Table 5).

4. DEFINING LESION SEVERITY

4.1. Angiography to Define Anatomy and Assess Lesion Severity

Coronary angiography remains the default method to define coronary anatomy and characterize the severity of coronary arterial stenoses. A visually estimated diameter stenosis severity of ≥70% for non–left main disease and ≥50% for left main disease has been used to define significant stenosis and to guide revascularization strategy. Although the length of a lesion may contribute to physiological lesion severity (ie, a longer moderate lesion may result in more ischemia than a focal severe lesion), there are no standard cutoffs for lesion length used to classify a

severe stenosis. An angiographically intermediate coronary stenosis is defined as a diameter stenosis severity of 40% to 69%, and generally warrants additional investigation to assess physiological significance. There is controversy over whether visually estimated diameter stenosis or quantitative coronary angiography better predicts the functional significance of a coronary stenosis.[1,2] The difference in mean diameter stenosis between quantitative coronary angiography and visual estimation varies from 10% to 20% and is dependent on stenosis severity.[3-5] The use of optimal angiographic projections, multiple angiographic views, and adjunct imaging or physiology may aid in the assessment of coronary anatomy when coronary angiography is used.

4.2. Defining Coronary Artery Lesion Complexity: Calculation of the SYNTAX (Synergy Between PCI With TAXUS and Cardiac Surgery) Score

Recommendation for Defining Coronary Artery Lesion Complexity: Calculation of the SYNTAX Score
Referenced studies that support the recommendation are summarized in Online Data Supplement 4.

COR	LOE	Recommendation
2b	B-NR	1. In patients with multivessel CAD, an assessment of CAD complexity, such as the SYNTAX score, may be useful to guide revascularization.[1-4]

Synopsis

The anatomic complexity of lesions, expected completeness of revascularization, predicted risk of death, and other adverse outcomes are important factors to consider for determining the type of revascularization for patients with CAD. Many factors contribute to the estimation of the complexity of CAD (Table 6). The SYNTAX score was prospectively derived from the SYNTAX trial to aid in this decision-making process by providing an objective measure to grade the anatomic complexity of CAD in patients with multivessel disease.[1] Its value as an independent predictor of long-term major adverse cardiac and cerebrovascular events and death was established in the SYNTAX trial cohort and subsequently validated in external studies of patients treated with PCI but not CABG.[2-4] The SYNTAX II score and the revised SYNTAX Score II 2020 was retrospectively developed from the SYNTAX trial cohort.[5,6] to incorporate clinical variables in addition to the anatomic variables. These scores demonstrate modest discrimination in predicting adverse clinical events after revascularization.[6]

Table 6. Angiographic Features Contributing to Increasing Complexity of CAD

Multivessel disease
Left main or proximal LAD artery lesion
Chronic total occlusion
Trifurcation lesion
Complex bifurcation lesion
Heavy calcification
Severe tortuosity
Aorto-ostial stenosis
Diffusely diseased and narrowed segments distal to the lesion
Thrombotic lesion
Lesion length >20 mm

CAD indicates coronary artery disease; and LAD, left anterior descending.

Recommendation-Specific Supporting Text

1. The SYNTAX score remains the most widely used and validated risk score to guide the choice of revascularization in patients with multivessel disease. Important limitations of this score include the cumbersome scoring system required for each lesion and the interobserver variability in its calculation.[7,8] Additionally, the absence of clinical variables limits its use in estimating the risk of clinical events after CABG. When estimating a patient's complexity of disease, it is important to consider variables that contribute to disease complexity which might impact the success and outcomes of revascularization (Table 6).

4.3. Use of Coronary Physiology to Guide Revascularization With PCI

Recommendations for the Use of Coronary Physiology to Guide Revascularization With PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 5.

COR	LOE	Recommendations
1	A	1. In patients with angina or an anginal equivalent, undocumented ischemia, and angiographically intermediate stenoses, the use of fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) is recommended to guide the decision to proceed with PCI.[1-6]
3: No benefit	B-R	2. In stable patients with angiographically intermediate stenoses and FFR >0.80 or iFR >0.89, PCI should not be performed.[7-10]

Synopsis

FFR and iFR are 2 of the most commonly used physiological methods of assessing lesion significance. FFR is defined as the ratio of maximal blood flow in a region distal to a lesion compared with the normal maximal blood flow of an artery. iFR, an index of lesion severity, is the instantaneous wave-free ratio (in diastole) of coronary pressure distal to the coronary lesion (Pd) to the aortic pressure (Pa) The potential advantage of iFR, which is a resting physiological index, is that it obviates the use of adenosine because it does not require a state of maximal hyperemia. These 2 measures—FFR and iFR—have

been studied in randomized trials with clinical endpoints of death, myocardial infarction (MI), or repeat revascularization.[1-5] There are other resting indices that have been compared with iFR or FFR in observational studies.[9,10] These resting indices have varying degrees of accuracy relative to FFR and iFR but have not been studied in randomized trials with clinical endpoints. The FAME 2 (Fractional Flow-Reserve-Guided PCI versus Medical Therapy in Stable Coronary Disease) trial[2] tested a strategy of PCI for all lesions with abnormal FFR compared with optimal medical therapy alone. Recruitment into the trial was stopped early because of a significant benefit of PCI over medical therapy in patients with an abnormal FFR with respect to death, MI, or urgent revascularization, with the benefit derived largely from a reduction in ischemia-driven revascularization.

The role of FFR in guiding surgical revascularization is uncertain. Multiple small observational studies, as well as RCTs and meta-analyses of these trials, suggest that fewer distal anastomoses are performed, and off-pump CABG is more often chosen in patients undergoing CABG with FFR-guided revascularization than in those undergoing CABG with angiogram-guided revascularization.[11-14] However, in these studies, no differences were found in clinical outcomes in patients undergoing CABG with FFR guidance compared with patients undergoing CABG with angiogram guidance.[11-14] Additionally, not all studies included an angiogram-guided comparison group. Large, randomized trials that are appropriately powered are warranted to guide the use of FFR in patients undergoing surgical revascularization.

Recommendation-Specific Supportive Text

1. In the FAME trial, PCI for a stenosis ≥50% with an abnormal FFR reduced the risk of the composite endpoint at 1 year as compared with PCI guided by angiography only,[1] a benefit that was maintained at 2 years[9] but not at 5 years. The DEFINE-FLAIR (Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation and the Instantaneous Wave-free Ratio versus Fractional Flow Reserve in Patients with Stable Angina Pectoris or Acute Coronary Syndrome)[4] and the iFR-SWEDEHEART (Instantaneous Wave-free Ratio versus Fractional Flow Reserve in Patients with Stable Angina Pectoris or Acute Coronary Syndrome) trials[6] compared outcomes with the use of iFR- or FFR-guided PCI. In these trials, iFR-guided PCI was found to be noninferior to FFR-guided PCI. As compared with FFR, the use of iFR was associated with lower rates of procedure-related chest pain and shorter procedural time. In randomized trials, the rates of short- and long-term MACE were lower among patients who had PCI guided by physiology with either FFR or iFR.[4,6]
2. Deferral of PCI when the FFR is >0.80 or the iFR is >0.89 is associated with low rates of long-term MACE.[8-10] The DEFER (Deferral of Percutaneous Intervention) trial demonstrated similar rates of MACE in follow-up when PCI for angiographic intermediate lesions and FFR >0.75 was deferred, rather than performed, at 2 and 5 years of follow-up.[8] Additionally, there were lower rates of MI in the deferred group at long-term follow-up.[7] In patients enrolled in the FAME trial who had an FFR >0.80, 2-year rates of MI and revascularization were low, at 0.2% and 3.2%, respectively.[9] Finally, in the DEFINE-FLAIR and the iFR-SWEDEHEART trials, rates of MACE in patients who had PCI deferred on the basis of an FFR >0.80 or an iFR >0.89 were 4.05% and 4.12%, respectively,[10] with unplanned revascularization being the most frequent cause of MACE. The cutoffs of FFR and iFR provided were those used in the clinical trials. On occasion, borderline values may warrant further ischemia testing or additional investigations.

4.4. Intravascular Ultrasound to Assess Lesion Severity

Recommendation for Intravascular Ultrasound to Assess Lesion Severity
Referenced studies that support the recommendation are summarized in Online Data Supplement 6.

COR	LOE	Recommendation
2a	B-NR	1. In patients with intermediate stenosis of the left main artery, intravascular ultrasound (IVUS) is reasonable to help define lesion severity.[1-5]

Synopsis

IVUS can offer important anatomic information beyond what is seen on coronary angiography. IVUS is particularly useful in lesions involving the left main artery where there may be limitations in coronary angiography due to overlapping vessels or foreshortening. IVUS offers significantly greater spatial resolution than angiography alone (IVUS axial resolution is 100 to 150 μm, and coronary angiography axial resolution is 300 μm). Detailed cross-sectional images provide accurate evaluation of lesion characteristics, including lumen dimensions, lesion length, plaque morphology and location, thrombus, dissection, and stent apposition and expansion. Additionally, minimal lumen area on IVUS has been shown to correlate with physiological indices.[6]

Recommendation-Specific Supportive Text

1. In the case of indeterminate left main disease, studies have shown that IVUS evaluation with deferral of intervention for a minimum lumen area of ≥6 to 7.5 mm^2 is safe,[1,2] although a smaller cutoff (4.5–4.8 mm^2) may be more appropriate in patients of Asian descent.[3] Moderate correlations

between FFR values and IVUS minimal lumen area cutoffs have been demonstrated in left main disease.[4,5] Compared with the left main artery, smaller cutoffs have been suggested for IVUS of the LAD artery.[7] Developed more recently, optical coherence tomography (OCT) has been shown to correlate well with IVUS measurements.[8] However, because OCT requires blood clearance, its effectiveness for imaging ostial left main disease is limited.

5. REVASCULARIZATION IN STEMI

5.1. Revascularization of the Infarct Artery in Patients With STEMI

Recommendations for Revascularization of the Infarct Artery in Patients With STEMI
Referenced studies that support the recommendations are summarized in Online Data Supplement 7.

COR	LOE	Recommendations
1	A	1. In patients with STEMI and ischemic symptoms for <12 hours, PCI should be performed to improve survival.[1-5]
1	B-R	2. In patients with STEMI and cardiogenic shock or hemodynamic instability, PCI or CABG (when PCI is not feasible) is indicated to improve survival, irrespective of the time delay from MI onset.[6,7]
1	B-NR	3. In patients with STEMI who have mechanical complications (eg, ventricular septal rupture, mitral valve insufficiency because of papillary muscle infarction or rupture, or free wall rupture), CABG is recommended at the time of surgery, with the goal of improving survival.[8,9]
1	C- LD	4. In patients with STEMI and evidence of failed reperfusion after fibrinolytic therapy, rescue PCI of the infarct artery should be performed to improve clinical outcomes.[10-13]
2a	B-R	5. In patients with STEMI who are treated with fibrinolytic therapy, angiography within 3 to 24 hours with the intent to perform PCI is reasonable to improve clinical outcomes.[14-20]
2a	B-NR	6. In patients with STEMI who are stable and presenting 12 to 24 hours after symptom onset, PCI is reasonable to improve clinical outcomes.[21,22]
2a	B-NR	7. In patients with STEMI in whom PCI is not feasible or successful, with a large area of myocardium at risk, emergency or urgent CABG can be effective as a reperfusion modality to improve clinical outcomes.[23,24]
2a	C-EO	8. In patients with STEMI complicated by ongoing ischemia, acute severe heart failure, or life-threatening arrhythmia, PCI can be beneficial to improve clinical outcomes, irrespective of time delay from MI onset.
3: No Benefit	B-R	9. In asymptomatic stable patients with STEMI who have a totally occluded infarct artery >24 hours after symptom onset and are without evidence of severe ischemia, PCI should not be performed.[25,26]

Recommendations for Revascularization of the Infarct Artery in Patients With STEMI (Continued)

COR	LOE	Recommendations
3: Harm	C-EO	10. In patients with STEMI, emergency CABG should not be performed after failed primary PCI: • In the absence of ischemia or a large area of myocardium at risk, or • If surgical revascularization is not feasible because of a no-reflow state or poor distal targets.

Synopsis

Immediate reperfusion therapy for patients with STEMI improves mortality rate, and primary PCI has been shown to be superior to fibrinolytic therapy[1] (Figure 3).[6,23,27-29] Fibrinolytic therapy is recommended only in cases in which primary PCI is not immediately available and the delay from hospital presentation to PCI is anticipated to be >120 minutes.[30] Because approximately 35% of patients treated with fibrinolysis do not achieve reperfusion,[31] and an additional 10% have ineffective reperfusion (TIMI [Thrombolysis In Myocardial Infarction] flow grade <3),[1] early transfer of patients to centers capable of performing PCI will facilitate early catheterization and/or PCI.[15-17,19] CABG has a limited role in the acute phase of STEMI, and its use in this setting continues to decrease.[23] Older case series have highlighted a potential excess mortality risk when CABG is performed early after STEMI.[32] However, contemporary modifications to the standard operative approach, improved anesthesia and monitoring, improved technical methods, and adjunctive temporary mechanical circulatory support devices may lead to improved rates of survival after CABG (Figure 3).

Recommendation-Specific Supportive Text

1. Multiple RCTs and meta-analyses have shown that primary PCI reduces death, MI, stroke, and major bleeding as compared with fibrinolysis, especially when treatment delays are minimized.[1-5] This benefit is seen even among patients transferred from non-PCI hospitals if transfer times are reasonable and total ischemic time after presentation is <120 minutes.[4,30]
2. In patients with STEMI complicated by cardiogenic shock, an early revascularization strategy is associated with a significant survival benefit.[6] In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial, although the primary endpoint of 30-day survival for patients with STEMI and cardiogenic shock was not improved with early revascularization, compared with initial medical stabilization,[6] the secondary outcome of mortality rate at 6 months was significantly lower in the group of patients randomized to early revascularization and treated with either PCI or CABG.

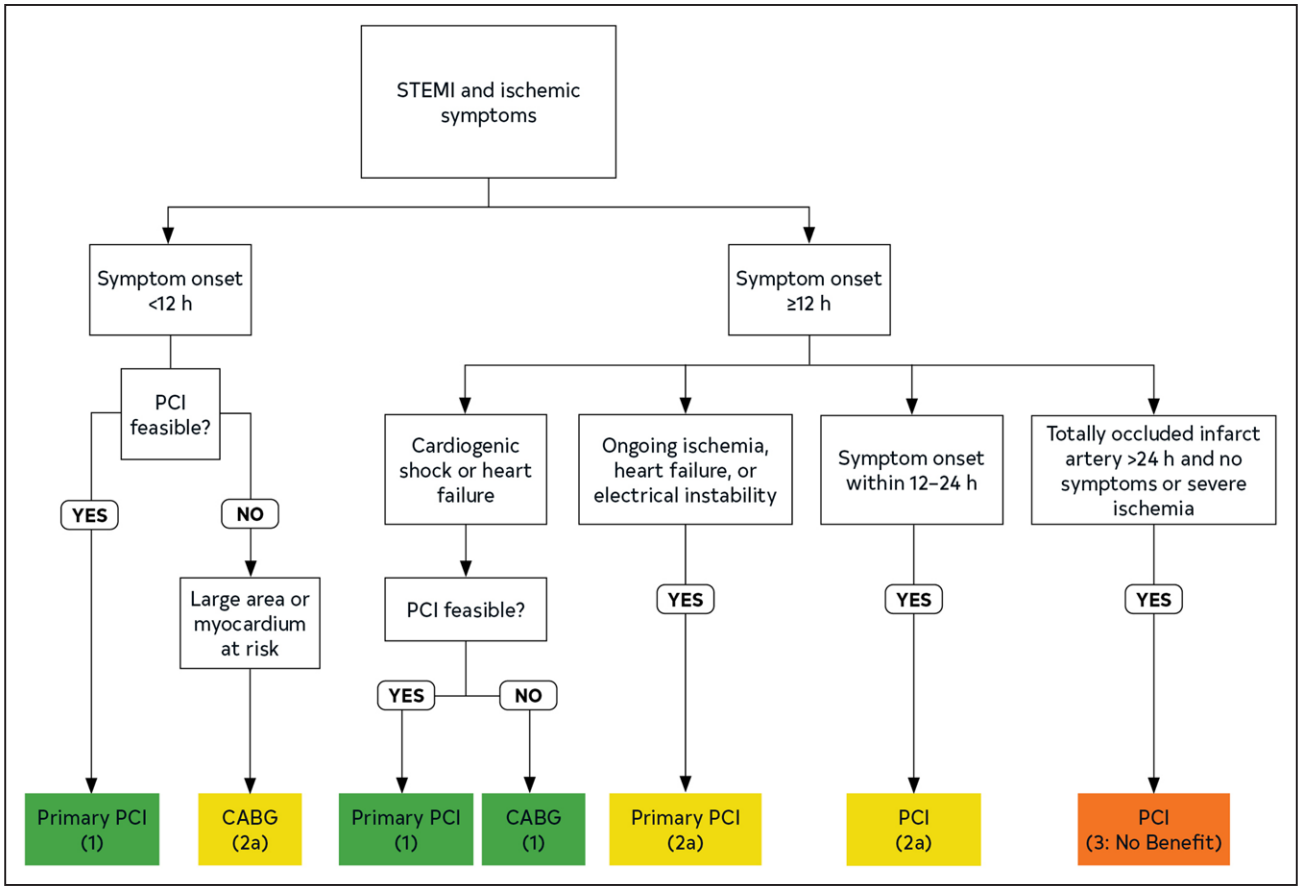

Figure 3. Indications for Revascularization in STEMI (Patients Without Fibrinolytics).
Colors correspond to Table 2.
CABG indicates coronary artery bypass graft; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction. This algorithm summarizes the recommendations in this guideline for revascularization of the infarct artery in STEMI. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Additionally, in situations that lack sufficient data to make formal recommendations for care, please see Section 17, "Unanswered Questions and Future Directions."

3. The mortality rate associated with emergency CABG and surgical management of a mechanical complication of STEMI remains high.[33] However, there are currently few medical or percutaneous treatment methods to effectively treat ventricular rupture, papillary muscle rupture leading to severe mitral regurgitation, or ischemic ventricular septal defect. CABG and these associated procedures may be necessary to treat the mechanical complications of STEMI or cardiogenic shock in the emergency setting.[34-38] Placement of a mechanical support device may be useful in temporizing a patient with a mechanical complication of STEMI, and urgent or emergency surgery remains the best treatment.[39,40] No RCT has examined the benefit of adding CABG at the time of emergent cardiac surgery for treatment of a mechanical complication of STEMI versus emergent surgery for the treatment of a mechanical complication alone. In addition, no RCT has examined the benefit of emergent cardiac surgery for the treatment of a mechanical complication of STEMI versus initial medical stabilization and delayed surgery.
4. Rescue PCI performed in patients with evidence of failed reperfusion after fibrinolytic therapy has been associated with a reduction in cardiovascular events,[10-13] when compared with conservative care or repeat fibrinolysis. In these studies, patients randomized to rescue PCI had higher rates of bleeding and cerebrovascular accident.[10-12] All these studies were performed in the era of femoral artery access, with limited options for antiplatelet and anticoagulant therapy. Previous concerns about increased bleeding or increased stroke risk in patients undergoing rescue PCI could be mitigated by using half-dose tenecteplase in patients >75 years of age,[31] by substituting radial access in place of femoral access,[41] or by eliminating the routine use of platelet glycoprotein IIb/IIIa inhibitors. With these techniques, the reduced complications associated with PCI would provide a more favorable balance of risk

to benefit with rescue PCI than with conservative care.

5. Studies have shown a reduction in MACE when routine early angiography with the intent to perform PCI is performed after fibrinolytic therapy.[15,16,18-20,42] This was further supported by several meta-analyses of these trials, which showed a reduction in death or infarction with an early invasive approach after fibrinolytic therapy.[14,17] In these early-transfer studies, more than 80% of patients who were transferred underwent PCI to treat a significant residual stenosis or suboptimal flow of the infarct artery. The benefit of immediate angiography was most notable in patients undergoing angiography early after symptom onset or after administration of fibrinolytic therapy.[14]
6. The benefit of PCI for asymptomatic patients presenting 12 to 24 hours after symptom onset is not well studied. The BRAVE-2 (Beyond 12 Hours Reperfusion Alternative Evaluation-2) trial examined the benefits of PCI in reducing infarct size in asymptomatic patients with STEMI and symptom onset >12 hours but <48 hours before presentation.[21] In this small study, an invasive strategy of coronary stenting was associated with a reduction in left ventricular infarct size (primary endpoint) compared with a conservative strategy.[21] Moreover, an invasive strategy was associated with a reduction in adjusted 4-year mortality rate compared with the conservative strategy.[43] Observational data from the Prospective National Observational study also supported a lower adjusted 1-year mortality rate in patients with STEMI and symptom onset 12 to 24 hours before presentation.[22] This information should be balanced by the potential for "harm" when PCI of a totally occluded artery is performed more than 24 hours after symptom onset. Therefore, delayed PCI of an infarct artery beyond 24 hours should be considered only in patients with a patent artery.
7. In patients with STEMI, there may be situations in which PCI is not possible for anatomic reasons or because of the presence of severe left main or multivessel CAD. Additionally, in unusual circumstances, PCI may not be successful. In such cases, CABG can be an effective primary reperfusion strategy, particularly if there is a large area of myocardium at risk.[23,24]
8. There are no RCTs examining the benefit of PCI in patients with STEMI presenting >12 hours after symptom onset who have clinical evidence of ongoing ischemia, acute severe heart failure, or life-threatening arrhythmias. Intuitively, a strategy of delayed reperfusion in these unstable patient subsets would be expected to improve symptoms and outcomes, and for this reason PCI should be considered.
9. In OAT (Occluded Artery Trial), PCI of a totally occluded vessel did not reduce cardiovascular events at 4 years of follow-up,[25] and there was a trend toward a higher rate of recurrent infarction in the group of patients randomized to PCI. Patients who had severe ischemia on noninvasive stress testing were not enrolled in this trial. Similar findings were noted in the DECOPI (Desobstruction Coronaire en Post-Infarctus) trial, which enrolled patients with an occluded artery presenting 2 to 15 days after symptom onset.[26]
10. Emergency CABG to restore flow to the infarct artery after failed PCI should be considered only in patients with ongoing ischemia and a large area of myocardium at risk. In some cases, after primary PCI, the vessel remains occluded or with slow flow caused by distal embolization (no reflow). The no-reflow phenomenon refers to unsuccessful microvascular reperfusion even in the presence of a widely patent epicardial coronary artery. This usually occurs with reperfusion in the setting of PCI for the treatment of STEMI, after prolonged myocardial ischemia, or with a large thrombus burden. Because CABG is unlikely to improve perfusion to the subtended myocardium in the setting of no-reflow, emergency CABG may be harmful in this setting and may subject the patient to unnecessary risk.

5.2. Revascularization of the Non-Infarct Artery in Patients With STEMI

Recommendations for Revascularization of the Non-Infarct Artery in Patients With STEMI
Referenced studies that support the recommendations are summarized in Online Data Supplement 8.

COR	LOE	Recommendations
1	A	1. In selected hemodynamically stable patients with STEMI and multivessel disease, after successful primary PCI, staged PCI of a significant non-infarct artery stenosis is recommended to reduce the risk of death or MI.[1-4]
2a	C-EO	2. In selected patients with STEMI with complex multivessel non-infarct artery disease, after successful primary PCI, elective CABG is reasonable to reduce the risk of cardiac events.
2b	B-R	3. In selected hemodynamically stable patients with STEMI and low-complexity multivessel disease, PCI of a non-infarct artery stenosis may be considered at the time of primary PCI to reduce cardiac event rates.[1,2,5-7]
3: Harm	B-R	4. In patients with STEMI complicated by cardiogenic shock, routine PCI of a non-infarct artery at the time of primary PCI should not be performed because of the higher risk of death or renal failure.[8-10]

Synopsis

A Heart Team approach is utilized to determine optimal revascularization strategy in patients with STEMI and multivessel CAD. Revascularization strategies (Figure 4) for patients with STEMI and multivessel disease include multivessel PCI at the time of primary PCI, PCI of the infarct artery only followed by staged PCI of a non-infarct artery, PCI of the infarct artery only with an ischemia-guided approach to treatment of a non-infarct artery, or PCI of the infarct artery only with elective CABG. Observational studies and meta-analyses have reported conflicting results for the superiority of one approach over another.[11] Recent randomized trials of PCI in STEMI support the safety and efficacy of multivessel PCI in selected patients with STEMI.[2-4,6,7] The data are strongest for patients undergoing staged PCI.[4] It should be noted that only one-third of enrolled patients in these trials had triple-vessel disease, and most of these trials excluded patients with left main disease, chronic total occlusion (CTO) of the non-infarct artery, or complex non-infarct artery disease. For this reason, CABG remains a reasonable option in patients with residual complex non-infarct artery disease. Ideal patients who may benefit from revascularization of non-infarct arteries include those with a large area of myocardium at risk and those without significant comorbidities that would increase the risk of revascularization.

Recommendation-Specific Supportive Text

1. RCTs have demonstrated a reduction in MACE with staged PCI (either in hospital or after discharge) compared with culprit vessel–only PCI.[1-4] This benefit is driven largely by a reduction in the risk of repeat revascularization or re-infarction. Most recently, the COMPLETE (Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI) trial enrolled 4041 patients and demonstrated a 3-year reduction in the combined endpoint of death or MI with staged PCI of the non-infarct artery (performed within 45 days of STEMI), compared with conservative care.[4] These benefits were consistent, irrespective of the timing of the non-infarct artery PCI.[12] Most of these trials included patients with low-complexity disease. No trial has shown a difference in the outcome of mortality rate alone between the strategies. In the COMPLETE trial, <1% of enrolled patients had non-infarct artery disease involving the left main artery, and the baseline SYNTAX score of the enrolled patients was low. Additionally, these trials enrolled patients with lesions that had a >70% diameter stenosis. For intermediate lesions, physiological testing with iFR or FFR may be useful to guide PCI.[4]
2. In patients with STEMI and complex multivessel CAD, elective CABG remains an appropriate revascularization option after successful PCI of an infarct artery in patients who meet criteria for CABG (Table 7). Although the COMPLETE trial demonstrated that staged PCI of the non-infarct artery is associated with a reduction in the risk of death or recurrent infarction in follow-up, patients intended for a planned surgical revascularization procedure were not included in this study. In patients with complex non-infarct artery disease, the decision to proceed with PCI versus CABG of the non-infarct artery should include a Heart Team discussion.
3. Randomized trials have shown a reduction in MACE with a multivessel PCI strategy performed at the time of primary PCI as compared with culprit artery–only PCI.[1,2,5-7] The benefits reported in these trials were driven largely by a reduction in repeat revascularization with multivessel PCI. PCI of a non-infarct artery stenosis may be considered at the time of successful primary PCI, but patients should be carefully selected. Patients who are most appropriate for complete revascularization at the time of primary PCI include those with uncomplicated PCI of the infarct artery and with low-complexity non-infarct artery disease who have normal left ventricular filling pressures and normal renal function. Clinicians should integrate clinical data, lesion severity and complexity, patient stability, risk of volume overload, and risk of contrast nephropathy before embarking on an immediate multivessel primary PCI strategy.
4. Culprit vessel–only primary PCI is recommended as the primary PCI strategy in most patients with STEMI complicated by cardiogenic shock who have multivessel disease. This is based on consistent findings from observational data and 1 randomized trial that showed no advantage for immediate multivessel PCI.[8-10] In the CULPRIT-SHOCK (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) trial of patients with acute MI (AMI) complicated by cardiogenic shock, multivessel PCI at the time of primary PCI resulted in a higher risk of the primary endpoint of death or need for renal replacement therapy.[8,9] Of note, in this trial, investigators were permitted to proceed with PCI of all non-infarct vessels with >70% diameter stenosis that were ≥2 mm in diameter, including those that were chronically occluded. The risks associated with immediate multivessel PCI include volume overload, contrast nephropathy, and ischemic complications in the non-infarct artery that could cause further hemodynamic deterioration.

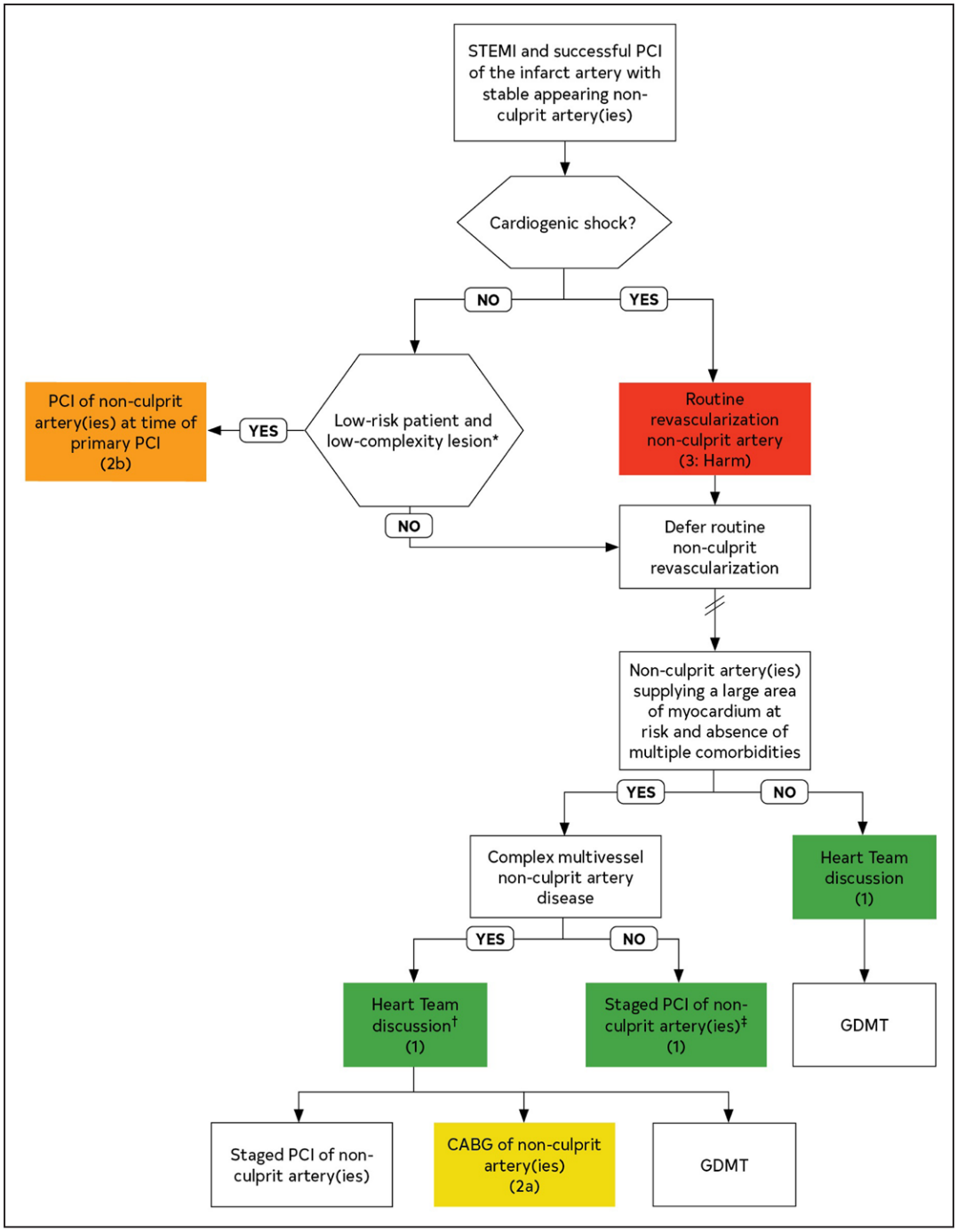

Figure 4. Revascularization of Noninfarct-Related Coronary Artery Lesions in Patients With STEMI.
Colors correspond to Table 2.
CABG indicates coronary artery bypass graft; GDMT, guideline-directed medical therapy; PCI, percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.
*Normal blood pressure and heart rate left ventricular end-diastolic pressure <20 mm Hg, no chronic renal insufficiency or acute kidney injury, and expected total contrast volume <3× glomerular filtration rate, simple lesion anatomy. †In making the decision about the need for and mode of revascularization the Heart Team should consider the suitability of the non-culprit artery for PCI, the coronary complexity and the risk of revascularization, the extent of myocardium at risk, and patient comorbidities, including life expectancy or other significant patient comorbidities, such as chronic renal insufficiency or acute kidney injury. ‡Staged PCI can be performed in hospital or after discharge, up to 45 days post MI.
Symbol denotes time elapsed before proceeding to the next procedure. This algorithm summarizes the recommendations in this guideline for the care of patients with STEMI and noninfarct artery disease. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Additionally, in situations that lack sufficient data to make formal recommendations for care, please see Section 17, "Unanswered Questions and Future Directions."

6. REVASCULARIZATION IN NSTE-ACS

6.1. Coronary Angiography and Revascularization in Patients With NSTE-ACS

Recommendations for Coronary Angiography and Revascularization in Patients With NSTE-ACS
Referenced studies that support the recommendations are summarized in Online Data Supplement 9.

COR	LOE	Recommendations
1	A	1. In patients with NSTE-ACS who are at elevated risk of recurrent ischemic events and are appropriate candidates for revascularization, an invasive strategy with the intent to proceed with revascularization is indicated to reduce cardiovascular events.[1-4]
1	B-R	2. In patients with NSTE-ACS and cardiogenic shock who are appropriate candidates for revascularization, emergency revascularization is recommended to reduce risk of death.[5-9]
1	C-LD	3. In appropriate patients with NSTE-ACS who have refractory angina or hemodynamic or electrical instability, an immediate invasive strategy with intent to perform revascularization is indicated to improve outcomes.[10]
2a	B-R	4. In patients with NSTE-ACS who are initially stabilized and are at high risk of clinical events, it is reasonable to choose an early invasive strategy (within 24 hours) over a delayed invasive strategy to improve outcomes.[11-16]
2a	B-R	5. In patients with NSTE-ACS who are initially stabilized and are at intermediate or low risk of clinical events, an invasive strategy with intent to perform revascularization is reasonable before hospital discharge to improve outcomes.[11-16]
2a	B-NR	6. In patients with NSTE-ACS who have failed PCI and have ongoing ischemia, hemodynamic compromise, or threatened occlusion of an artery with substantial myocardium at risk, who are appropriate candidates for CABG, emergency CABG is reasonable.[5-7,17]
3: Harm	B-R	7. In patients with NSTE-ACS who present in cardiogenic shock, routine multivessel PCI of non-culprit lesions in the same setting should not be performed.[18,19]

Synopsis

A routine invasive approach for patients with NSTE-ACS is associated with improved outcomes.[1-4,20,21] Risk stratification with a validated score (ie, GRACE or TIMI) has been recommended to guide the timing of coronary angiography.[22,23] The GRACE score has been used in most clinical trials to identify patients who were at high risk of death or MI. It enables a direct estimation of the mortality risk during hospitalization and at longer term followup.[24] Traditionally, a GRACE score of >140 had been used to denote a patient at higher risk of in-hospital clinical events. Other factors associated with higher risk include older age (≥75 years), elevated TIMI risk score (https://timi.org/calculators/timi-risk-score-calculator-for-ua-nstemi/),[25] and elevated cardiac markers.[11,26] Factors indicating a need for an urgent revascularization (Table 7) with either PCI or CABG include threatening anatomy, ongoing ischemia, or hemodynamic compromise. In such patients and in those with complex CAD, treatment should be individualized and involve a Heart Team discussion.

Table 7. Patient Clinical Status Definitions to Guide Revascularization[13-15]

Elective	The patient's cardiac function has been stable in the days or weeks before intervention (whether surgical or procedural). The intervention could be deferred without increased risk of compromise to cardiac outcome.
Urgent	Intervention is required during the same hospitalization to minimize chance of further clinical deterioration. Examples include, but are not limited to, worsening sudden chest pain, heart failure, acute myocardial infarction, anatomy, intra-aortic balloon pump, unstable angina, with intravenous nitroglycerin, or rest angina.
Emergency	Patients requiring emergency intervention will have ongoing, refractory (difficult, complicated, and/or unmanageable), unrelenting cardiac compromise, with or without hemodynamic instability, and not responsive to any form of therapy except cardiac intervention. An emergency intervention is one in which there should be no delay in providing operative intervention.
Emergency/ salvage	Patients requiring emergency/salvage intervention are those who require cardiopulmonary resuscitation en route to the operating room, or procedure room, before induction of anesthesia or who require extracorporeal membrane oxygenation to maintain life.

Recommendation-Specific Supportive Text

1. In patients with NSTE-ACS, an initial invasive approach is associated with a lower rate of the combined endpoint of death, MI, or refractory angina at 4 to 6 months' follow-up[1-4] (Figure 5). Pooled trial data have demonstrated lower rates of recurrent infarction and recurrent ischemia with an invasive strategy.[4] The benefits of an invasive approach are most pronounced among patients with elevated biomarkers or other higher-risk findings.[1] The invasive approach also provides important prognostic information, such as extent and severity of CAD, hemodynamics, and left ventricular function, allowing for precise determination of risk, antithrombotic treatment guidance, and suitability for revascularization with PCI or CABG. Roughly 20% to 25% of patients enrolled in the early trials examining the benefits of a routine invasive approach underwent CABG. In patients with multivessel disease, the mode of revascularization should be based on the acuity of the patient's condition, the angiographic characteristics of the culprit lesion, and the complexity of the

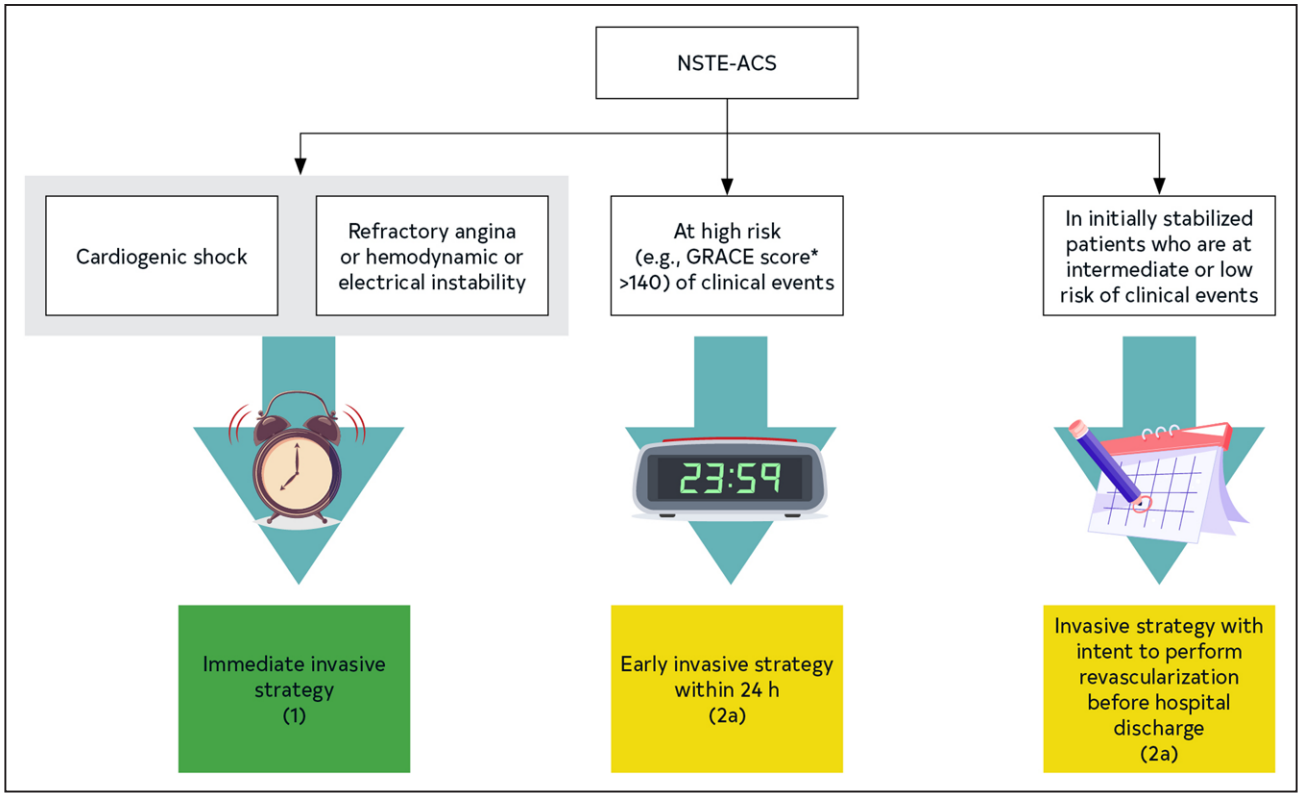

Figure 5. Recommendations for the Timing of Invasive Strategy in Patients With NSTE-ACS.
Colors correspond to Table 2.
GRACE indicates Global Registry of Acute Coronary Events; and NSTE-ACS, non–ST-segment–elevation acute coronary syndrome.
*https://www.mdcalc.com/grace-acs-risk-mortality-calculator.[31] This algorithm summarizes the recommendations in this guideline for coronary artery angiography with the intent to perform revascularization in NSTE-ACS. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Additionally, in situations that lack sufficient data to make formal recommendations for care, please see Section 17, "Unanswered Questions and Future Directions."

patient's anatomy and, when appropriate, should include a Heart Team discussion.

2. In the SHOCK trial, patients were randomized to medical therapy or emergency revascularization. Among the patients randomized to revascularization, two-thirds of patients were referred for PCI and one-third for CABG, and the decision to proceed with PCI or CABG was made by the treating physician.[9] Median time from randomization to revascularization was 0.9 hours for PCI and 2.7 hours for CABG. The SHOCK trial supported a strategy of emergency angiography with immediate revascularization in patients with AMI complicated by cardiogenic shock. At 6 months, the mortality rate was significantly lower in patients randomized to revascularization than in those randomized to medical therapy.[9] In the SHOCK trial, there was no difference in mortality rate with PCI or CABG for those patients randomized to early revascularization, with a similar survival regardless of the mode of revascularization at 30 days and 1 year. Additionally, observational studies[5-7,17] of patients with cardiogenic shock referred for CABG have reported acceptable outcomes with emergency revascularization. Patients with shock may benefit from mechanical circulatory support devices before revascularization, especially if CABG is planned.[27]
3. Patients with NSTE-ACS who are clinically unstable because of refractory angina, intractable arrhythmias, or hemodynamic instability have been consistently excluded from clinical trials evaluating the optimal timing of coronary angiography.[11,28] Although evidence from clinical trial data is lacking, intuitively, immediate angiography (within 2 hours) with plans for appropriate revascularization would be expected to improve outcomes if revascularization stabilizes the clinical condition.
4. An early invasive strategy performed within 24 hours in high-risk (GRACE score >140) patients is associated with a lower incidence of recurrent ischemia or need for urgent revascularization and a shorter hospital stay.[11,12,14-16] Although clinical trials have not demonstrated a clear advantage with an early invasive strategy (within 24 hours) as opposed to a delayed invasive strategy in the overall population of patients with NSTE-ACS,[12,16] prespecified subgroup analyses of these trials

support the use of an early invasive strategy for high-risk patients.[11,12,16] The TIMACS (Timing of Intervention in Acute Coronary Syndromes) trial, in which patients were enrolled within 24 hours of symptoms and randomized to angiography at ≤ 24 hours versus ≥ 36 hours from time of randomization, and the VERDICT (Very Early vs Deferred Invasive Evaluation Using Computerized Tomography) trial, in which patients were randomized to angiography at <12 hours versus 48 to 72 hours from time of diagnosis, both evaluated the value of early invasive management of symptoms for patients with NSTE-ACS and demonstrated a lower rate of cardiovascular events in follow-up in the high-risk subgroup of patients randomized to early angiography.

5. In intermediate- or low-risk patients, timing is not critical, and a delayed invasive strategy within 48 to 72 hours has been demonstrated to be acceptable[11-16,28] Randomized trial data have not demonstrated differences in rates of death and MI between an early invasive strategy (coronary angiography <24 hours after admission) and a delayed invasive approach (48–72 hours) in a nonselected population of patients with NSTEMI.[11-16,29,30] However, low-risk patients benefit from a routine invasive strategy before hospital discharge, with a significant reduction in the risk of cardiovascular death or MI, compared with a selective invasive strategy.[21]
6. Although there are no randomized trials specifically evaluating emergency CABG versus medical therapy or delayed revascularization in patients with NSTE-ACS and failed PCI who have ongoing ischemia or hemodynamic compromise, multiple retrospective reviews have noted a reduced mortality rate in patients with an emergency approach.[6,9,17] The appropriate safe timing of CABG is carefully determined with a Heart Team approach in patients with NSTE-ACS who are on dual antiplatelet therapy (DAPT).
7. In the CULPRIT-SHOCK trial, almost 40% of enrolled patients had an NSTEMI. As mentioned in section 5.2, patients were included in the trial if they had 2 or more vessels with >70% diameter stenosis that were ≥2 mm in diameter. Those with chronic total occlusions were eligible for inclusion in the study. Patients in the CULPRIT-SHOCK trial who were randomized to culprit-only PCI with the option of staged revascularization of non-culprit lesions had a lower rate of the composite endpoint of death and dialysis at 30 days and 1 year. Culprit-vessel PCI was associated with a significant all-cause mortality rate reduction at 30 days but not at 1 year.[18,19] As was noted in patients with STEMI, the results of the CULPRIT-SHOCK trial showed no benefit to immediate multivessel PCI in NSTEMI.

7. REVASCULARIZATION IN SIHD

7.1. Revascularization to Improve Survival in SIHD Compared With Medical Therapy

Recommendations for Revascularization to Improve Survival in SIHD Compared With Medical Therapy
Referenced studies that support the recommendations are summarized in Online Data Supplement 10.

COR	LOE	Recommendations
Left ventricular dysfunction and multivessel CAD		
1	B-R	1. In patients with SIHD and multivessel CAD appropriate for CABG with severe left ventricular systolic dysfunction (left ventricular ejection fraction <35%), CABG is recommended to improve survival.[1,2]
2a	B-NR	2. In selected patients with SIHD and multivessel CAD appropriate for CABG and mild-to-moderate left ventricular systolic dysfunction (ejection fraction 35%–50%), CABG (to include a left internal mammary artery [LIMA] graft to the LAD) is reasonable to improve survival.[3-8]
Left main CAD		
1	B-R	3. In patients with SIHD and significant left main stenosis, CABG is recommended to improve survival.[9-12]
2a	B-NR	4. In selected patients with SIHD and significant left main stenosis for whom PCI can provide equivalent revascularization to that possible with CABG, PCI is reasonable to improve survival.[9]
Multivessel CAD		
2b	B-R	5. In patients with SIHD, normal ejection fraction, significant stenosis in 3 major coronary arteries (with or without proximal LAD), and anatomy suitable for CABG, CABG may be reasonable to improve survival.[10,13-15]
2b	B-R	6. In patients with SIHD, normal ejection fraction, significant stenosis in 3 major coronary arteries (with or without proximal LAD), and anatomy suitable for PCI, the usefulness of PCI to improve survival is uncertain.[14-24]
Stenosis in the proximal LAD artery		
2b	B-R	7. In patients with SIHD, normal left ventricular ejection fraction, and significant stenosis in the proximal LAD, the usefulness of coronary revascularization to improve survival is uncertain.[10,14,17,24-27]
Single- or double-vessel disease not involving the proximal LAD		
3: No Benefit	B-R	8. In patients with SIHD, normal left ventricular ejection fraction, and 1- or 2-vessel CAD not involving the proximal LAD, coronary revascularization is not recommended to improve survival.[10,14,16,26,28,29]
3: Harm	B-NR	9. In patients with SIHD who have ≥1 coronary arteries that are not anatomically or functionally significant (<70% diameter of non–left main coronary artery stenosis, FFR >0.80), coronary revascularization should not be performed with the primary or sole intent to improve survival.[26,30]

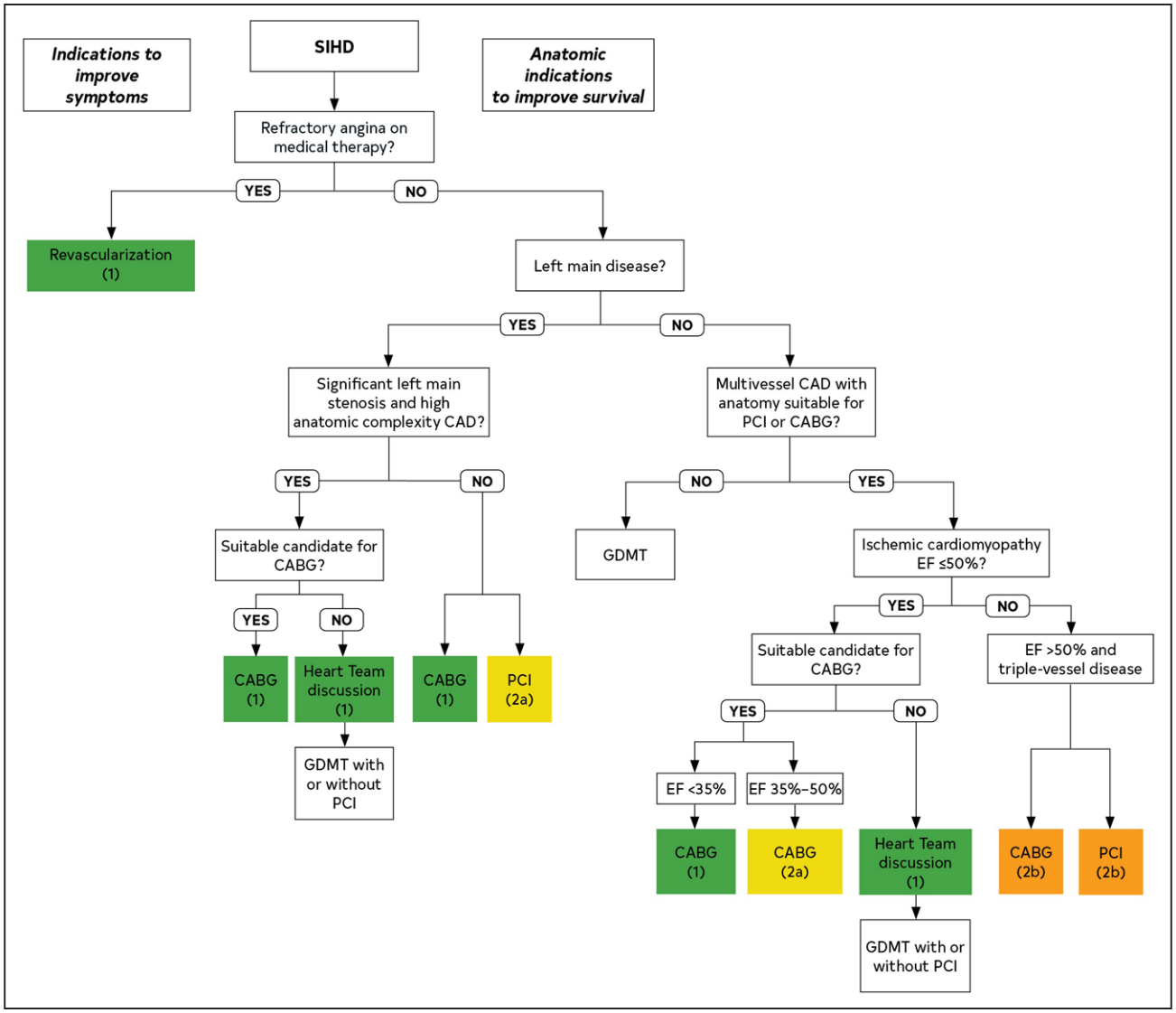

Figure 6. Revascularization in Patients With SIHD.

Colors correspond to Table 2.

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; EF, ejection fraction; GDMT, guideline-directed medical therapy; PCI, percutaneous coronary intervention; and SIHD, stable ischemic heart disease. This algorithm summarizes the recommendations in this guideline for the care of patients with stable CAD. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Additionally, in situations that lack sufficient data to make formal recommendations for care, please see Section 17, "Unanswered Questions and Future Directions."

Synopsis

Studies have shown that CABG confers a survival benefit over medical therapy in multiple subsets of patients, including those with left main CAD (Figure 6),[9-12] triple-vessel CAD,[13] and ischemic cardiomyopathy.[1,3-7,31-33] Many of these studies were conducted before the widespread use of antiplatelet and statin therapies and before the broad recognition of benefit from beta-blockers and ACE inhibitors/ARBs. There are no RCTs that have demonstrated a survival advantage of PCI over medical therapy in patients with SIHD.[14,17,34-38] There may be an advantage of PCI over medical therapy in patients who have a clinical indication for CABG but are deemed prohibitive surgical risk. For this reason, the Heart Team must weigh the risks and benefits of PCI as compared to medical therapy in such patients. The ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial randomized patients with SIHD and moderate-to-severe ischemia on stress testing to an initial invasive strategy versus an initial conservative strategy. Patients with left main disease or an ejection fraction <35% were excluded from enrollment. As compared with a strategy of medical therapy alone, an invasive strategy including revascularization with PCI or CABG was not associated with improved outcomes.[14]

Recommendation-Specific Supporting Text

Left Ventricular Dysfunction and Multivessel CAD

1. The strongest evidence in the past decade to support revascularization with CABG in patients with left ventricular dysfunction and CAD appropriate for CABG has been the STICH (Surgical Treatment for Ischemic Heart Failure) trial,[1,39,40] which randomized patients with left ventricular dysfunction (ejection fraction ≤35%) to either CABG with medical therapy or medical therapy alone. This study initially did not demonstrate a survival benefit for CABG over a median follow-up of 5 years,[39] but a subsequent report from this trial evaluating long-term follow-up at 10 years reported a survival benefit of CABG compared with medical therapy alone.[1,40] The use of myocardial viability studies in this study population demonstrated no relevance to study outcomes; however, this testing was not standardized.[41] There are insufficient data to make recommendations for using PCI in this patient population.
2. Evidence for a survival advantage with CABG in patients with SIHD and moderate left ventricular dysfunction comes from subgroup analyses of patients enrolled in the Coronary Artery Surgery Study[3] and the Veterans Administration Coronary Artery Bypass Cooperative Study with LV dysfunction,[42] as well as a meta-analysis[10] of the RCTs of CABG versus medical therapy. In these studies, patients with left ventricular dysfunction had a significant survival benefit with CABG, particularly patients with accompanying triple-vessel disease. Several registry studies have supported these findings.[4-7,31-33] The use of PCI in this patient population requires more study.

Left Main CAD

3. The Veterans Administration Coronary Artery Bypass Surgery Cooperative Study randomized patients with SIHD to a strategy of CABG versus medical therapy.[43] In this study, close to 15% of enrolled patients had significant left main disease.[43] At 42 months' follow-up, CABG was associated with a significant survival benefit in the subgroup of patients with left main disease.[11] Additionally, a meta-analysis of the RCTs comparing CABG with medical therapy supported these findings, with a 70% reduction in 5-year mortality rate with CABG versus medical therapy for the group of patients with left main disease.[10] Subsequent studies have supported these findings.[9,44-46] Although the evidence to support revascularization with CABG is derived mainly from older RCTs, there are no new data to refute this evidence, as all of the contemporary clinical trials comparing revascularization with medical therapy have excluded patients with significant stenoses of the left main artery.[14,24]
4. The evidence for a survival advantage for PCI over medical therapy in patients with left main CAD is inferential but plausible. Several registry studies have suggested a survival benefit of PCI over medical therapy in patients with left main CAD.,[47,48] A network meta-analysis of 19 studies found that the survival advantage for PCI over medical therapy in patients with left main CAD was identical to the survival advantage for CABG over medical therapy.[9] Additionally, RCTs and meta-analyses of these trials evaluating outcomes of PCI versus CABG in patients with low-to-medium anatomic complexity of CAD and with left main disease that is equally suitable for surgical or percutaneous revascularization have reported similar survival with PCI and CABG.[49-55]

Multivessel CAD

5. The new Class 2b recommendation, which represents a downgrade from a Class 1 recommendation in the 2011 CABG guideline,[56] reflects new evidence showing no advantage of CABG over medical therapy alone to improve survival in patients with 3-vessel CAD with preserved LV function and no LM disease. The older recommendation was based on evidence from registry studies,[26,29,48,57] a meta-analysis,[10] and a single RCT,[13] all of which were completed >20 to 40 years ago before the development of newer surgical techniques or advances in medical therapy associated with improved prognosis.[58,59] Newer evidence from the ISCHEMIA trial[14] and from meta-analyses, which incorporated[15,60-62] or did not incorporate[37] the ISCHEMIA results, as well as a more detailed review of earlier studies[63] supported this downgrade. After several hours of deliberation, the writing committee concluded that using CABG as a revascularization strategy versus medical therapy alone "may be reasonable" to improve survival in stable patients with 3-vessel CAD. The writing committee recognized that an adequately powered trial to test this hypothesis is unfeasible in the current era but proposed that revascularization confers other benefits to patients with multivessel CAD and SIHD. Accordingly, Section 7.3. highlights the advantages of revascularization over medical therapy for the prevention of cardiovascular events.
6. The writing committee reviewed newer evidence and concluded that the ability of PCI to improve survival, compared with medical therapy alone in patients with multivessel CAD, remains uncertain. The recommendation, which reflects a weaker endorsement for PCI than for CABG in patients with multivessel CAD, is supported by evidence from an older registry study[48] and a subgroup analysis of patients receiving everolimus-eluting stents in a network meta-analysis[37] that did not incorporate the results of the ISCHEMIA trial.[14]

The preponderance of newer evidence against a survival advantage of PCI comes from the ISCHEMIA trial itself,[14] which is consistent with the results of multiple earlier RCTs[17-23] and multiple contemporary meta-analyses[15,60-62] incorporating the ISCHEMIA trial results,[14] all of which have not shown a survival advantage for PCI over medical therapy for patients with multivessel CAD.

Stenosis in the Proximal LAD Artery

7. An earlier meta-analysis[10] and several earlier registry studies[26,29] suggested a survival advantage of CABG over medical therapy in patients with disease in the proximal LAD. Additionally, a network meta-analysis found a survival advantage for PCI.[37] However, a dedicated RCT found no survival advantage for either CABG or PCI over medical therapy in this setting,[64,65] and the ISCHEMIA trial[14] showed no difference in event rates with either CABG or PCI over medical therapy when patients had multivessel CAD involving the proximal LAD. In the ISCHEMIA trial, close to half of enrolled patients had >50% stenosis of the proximal LAD; in this study, there was no heterogeneity of treatment effect on outcomes with the presence of LAD disease.

Single- or Double-Vessel Disease Not Involving the Proximal LAD

8. A clinical principle from several studies is that the more myocardium is at risk, the greater is the survival advantage of revascularization over medical therapy, and in patients with little myocardium at risk (1- or 2-vessel CAD without LAD involvement), there is likely no survival benefit of revascularization in patients with SIHD.[10,17,26,29,37]
9. In patients without clinical or physiological evidence of significant disease, bypass surgery of nonobstructive disease has been reported to stimulate progression of CAD,[66] and PCI may precipitate periprocedural MIs[23] and is not associated with improved outcomes.[30,67-69]

7.2. Revascularization to Reduce Cardiovascular Events in SIHD Compared With Medical Therapy

Recommendation for Revascularization to Reduce Cardiovascular Events in SIHD Compared With Medical Therapy
Referenced studies that support the recommendation are summarized in Online Data Supplement 11.

COR	LOE	Recommendation
2a	B-R	1. In patients with SIHD and multivessel CAD appropriate for either CABG or PCI, revascularization is reasonable to lower the risk of cardiovascular events such as spontaneous MI, unplanned urgent revascularizations, or cardiac death.[1-8]

Synopsis

Clinical practice guidelines have traditionally included recommendations for revascularization in patients with SIHD based on the ability of CABG or PCI to improve overall survival (Section 7.1.) or to reduce ischemic symptoms (Section 7.3.), as compared with medical therapy alone. However, there are other clinical events that can affect a patient's overall prognosis, and that remain important considerations for patients. Several studies suggest that revascularization with CABG or PCI lowers the risk of adverse events such as cardiac death, MI, or urgent revascularization compared with medical therapy alone.[2,5,6,9,10]

Recommendation-Specific Supporting Text

1. In MASS (Medicine, Angioplasty or Surgery Study) II, the 10-year rates of cardiac death were lower after CABG or PCI than after medical therapy alone.[2] Lower rates of cardiac death were seen after revascularization than with medical therapy alone in a meta-analysis of 25 studies enrolling 19806 patients.[3] However, a statistically nonsignificant reduction was seen in a concurrent meta-analysis of 12103 patients enrolled in 7 RCTs.[8] Several other studies found no difference in cardiac death after revascularization than with medical therapy alone.[10,11]

   Cardiac death may be related to the occurrence of MI after revascularization.[12] The relative prognostic importance of procedural MIs versus that of late spontaneous MIs remains uncertain.[13] In the ISCHEMIA trial,[1] the incidence of procedural type 4a or type 5 MIs was increased with revascularization, but the incidence of late MI (spontaneous MI [type 1], demand-induced MI [type 2], or MIs associated with stent thrombosis [type 4b] or with restenosis [type 4c]) was reduced. A preplanned analysis of the MI patterns in the ISCHEMIA trial[4] found that all-cause death was increased with spontaneous MIs but not with procedural MIs. A large network meta-analysis found that spontaneous MI was reduced by revascularization compared with medical therapy alone.[3] However, a concurrent analysis found an increased rate of procedural MI, a reduced rate of nonprocedural MI, and no difference in overall MI.[11] On the contrary, another meta-analysis of stable patients, did not show a reduction in MI with revascularization,[10] and 1 other study reported reduction in MI with CABG but not with PCI.[9] Revascularization with CABG or PCI may reduce the need for subsequent urgent revascularization or hospitalization for acute coronary events.[5-8]

7.3. Revascularization to Improve Symptoms

Recommendations for Revascularization to Improve Symptoms Referenced studies that support the recommendations are summarized in Online Data Supplement 12.		
COR	LOE	Recommendations
1	A	1. In patients with refractory angina despite medical therapy and with significant coronary artery stenoses amenable to revascularization, revascularization is recommended to improve symptoms.[1-6]
3: Harm	C-LD	2. In patients with angina but no anatomic or physiological criteria for revascularization, neither CABG nor PCI should be performed.[7,8]

Synopsis

One of the main goals of coronary revascularization with either PCI or CABG surgery is to improve symptoms (Figure 6). In the treatment of patients with SIHD, medical therapy can often be an effective option. However, studies have shown that revascularization results in a greater improvement in angina or quality of life than does medical therapy alone.[1-6] Additionally, some patients may be intolerant of or unwilling to take anti-anginal medications. For these reasons, revascularization is frequently used to provide symptom relief.

Recommendation-Specific Supportive Text

1. Multiple RCTs have confirmed that revascularization improves anginal symptoms to a greater degree than optimal medical therapy.[1-4,6,9,10] The results of the small ORBITA (Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) trial,[11] which randomized patients to PCI or a "sham" procedure, did not support an improvement in symptoms with PCI and raised questions about the placebo effect of PCI. However, the larger ISCHEMIA trial reported a clinically relevant improvement in symptoms at 3 years after PCI or CABG,[1] long after a placebo effect should have dissipated. This difference was most pronounced among the patients with more frequent angina at baseline. In the FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) trial,[4] both revascularization options were associated with significant improvement in angina and quality of life as compared with baseline. A greater improvement in health status was noted with CABG compared with PCI at intermediate-term follow-up, but this difference was no longer significant in longer-term follow-up.
2. Inappropriate revascularization of nonobstructive plaques with CABG can lead to progression of underlying CAD,[7] and inappropriate use of PCI can cause periprocedural MIs[8] and would not be expected to improve quality of life or anginal symptoms.

8. SITUATIONS IN WHICH PCI OR CABG WOULD BE PREFERRED

8.1. Patients With Complex Disease

Recommendations for Patients With Complex Disease Referenced studies that support the recommendations are summarized in Online Data Supplement 13.		
COR	LOE	Recommendations
1	B-R	1. In patients who require revascularization for significant left main CAD with high-complexity CAD, it is recommended to choose CABG over PCI to improve survival.[1,2]
2a	B-R	2. In patients who require revascularization for multivessel CAD with complex or diffuse CAD (eg, SYNTAX score >33), it is reasonable to choose CABG over PCI to confer a survival advantage.[2-5]

Synopsis

Revascularization with either CABG or PCI is indicated to treat symptoms or improve outcomes in specific subsets of patients. However, CABG and PCI are inherently different in the mechanisms by which they improve blood flow to the jeopardized myocardium. PCI will directly relieve a discrete obstruction and increase the arterial lumen in the stented area but will have no effect on preventing plaque progression or rupture in other diseased segments within the artery. In contrast, bypass of a coronary artery will improve blood flow to the jeopardized myocardium supplied by the diseased artery and will also protect the distal myocardial beds from future ischemic insult caused by proximal plaque progression or rupture. Although most studies comparing CABG and PCI have reported similar survival,[1,3,5-17] certain subgroups of patients have been shown to derive a survival benefit from CABG compared with PCI.[1,2,4,18] Additionally, compared with PCI, CABG may be more effective at reducing the risk of late spontaneous MI.[11,19]

Recommendation-Specific Supporting Text

1. The SYNTAX trial, which included 705 patients with left main stenoses and a range of complexity of disease, showed a significantly higher MACE and cardiac mortality rate at 5 years for the subgroup of patients with left main and high-complexity disease (defined as a SYNTAX score >33) who were treated with PCI.[1] With the exception of the SYNTAX trial, the other RCTs comparing PCI with CABG in patients with left main disease excluded patients with complex disease.[6,8,20] Individual factors that contribute to anatomic complexity (severe

tortuosity, heavy calcification, complex bifurcation or trifurcation lesion, aorto-ostial stenosis, thrombotic lesion, etc) are listed in Table 6. In choosing between CABG and PCI, it is important to use the Heart Team to determine the optimal revascularization strategy, with specific considerations of anatomic complexity, medication compliance, and patient preference.

2. In the SYNTAX trial, which randomized patients with multivessel disease to a strategy of CABG or PCI with DES, the SYNTAX score was used a priori to define the complexity of disease in enrolled patients. Although the SYNTAX trial reported similar mortality rates with CABG and PCI in the overall group of patients, extended follow-up of the SYNTAX trial found a 40% higher mortality rate with PCI in the group of patients with triple-vessel disease.[4] Several analyses found that the extent and diffuseness of CAD on angiography, as evaluated qualitatively by visual assessment or quantitatively with the SYNTAX score,[3] predicted a survival advantage of CABG over PCI.[5] Specifically, the all-cause mortality rate observed after CABG was lower than that observed after PCI in patients with a diffuse CAD–associated high SYNTAX score of ≥33.[2,4,5] In patients with SYNTAX scores <33, there was no difference in mortality rate.[2-5] Of note, the SYNTAX trial included patients with first-generation DES, and significant progress has been made in stent design since this trial.

8.2. Patients With Diabetes

Recommendations for Patients With Diabetes Referenced studies that support the recommendations are summarized in Online Data Supplement 14.		
COR	**LOE**	**Recommendations**
1	A	1. In patients with diabetes and multivessel CAD with the involvement of the LAD, who are appropriate candidates for CABG, CABG (with a LIMA to the LAD) is recommended in preference to PCI to reduce mortality and repeat revascularizations.[1-8]
2a	B-NR	2. In patients with diabetes who have multivessel CAD amenable to PCI and an indication for revascularization and are poor candidates for surgery, PCI can be useful to reduce long-term ischemic outcomes.[9,10]
2b	B-R	3. In patients with diabetes who have left main stenosis and low- or intermediate-complexity CAD in the rest of the coronary anatomy, PCI may be considered an alternative to CABG to reduce major adverse cardiovascular outcomes.[5,11]

Synopsis

Revascularization decisions in patients with diabetes and multivessel CAD are complex and are optimized via a Heart Team approach, with consideration of left ventricular function, patient preferences, symptoms, clinical presentation, comorbidities, and expected survival.[1,12-14] Diabetes is associated with 2- to 4-fold increased mortality risk from heart disease, and patients with diabetes have more aggressive atherosclerosis, more diffuse coronary lesions, smaller coronary vessels, and more extensive disease. After coronary revascularization, patients with diabetes experience a higher mortality rate and greater need for repeat revascularization procedures.[15] Clinical trials of patients with diabetes and multivessel CAD have demonstrated that PCI is associated with a higher mortality rate at 5 years than that associated with CABG. The survival advantage of CABG becomes evident after 2 years and attenuates after 8 years, as patients treated with CABG experience a late mortality catch-up.[2,16] Of note, CABG is associated with an increased risk of stroke that persists up to 5 years.[17] The need for repeat revascularization is higher after PCI, regardless of the use of latest-generation DES.[1,4-8]

Recommendation-Specific Supportive Text

1. Multiple RCTs comparing PCI with CABG in patients with multivessel CAD have included patients with diabetes[1-3] or have prespecified patients with diabetes as a subgroup of interest.[4,5,7] The FREEDOM trial was the largest study, comparing CABG with PCI exclusively in 1900 patients with diabetes.[4,5,7] Inclusion criteria for the FREEDOM trial were multivessel disease with stenosis of 70% in ≥2 major epicardial vessels involving at least 2 separate territories and without left main stenosis. After enrollment, 82% of patients in the PCI group and 85% of patients in the CABG group had 3-vessel disease, and 91% of patients had involvement of the LAD artery. At 5-year follow-up, the all-cause mortality rate was higher in patients treated with PCI than in those treated with CABG; however, the cardiovascular mortality rate was not statistically different between the groups. There was no statistical interaction between SYNTAX score, revascularization strategy, or mortality rate, which suggests that a benefit was noted irrespective of the complexity of disease.[1] In the FREEDOM follow-up study, the all-cause mortality rate up to 8 years was also significantly higher with PCI. A meta-analysis including individual patient data from 11 RCTs demonstrated consistent results, with a nearly 50% higher increased 5-year mortality risk among patients treated with PCI than among those treated with CABG.[4,5,7] A Heart Team discussion may be useful for determining the optimal approach to care for patients with less extensive disease, including those with double-vessel disease without involvement of the left main or LAD artery.

2. Patients with diabetes who are at high surgical risk and require coronary revascularization are more likely to be treated with PCI in current practice.[9] In an observational registry that included high-risk patients with refractory ischemia, 5-year survival rates were similar among those treated with CABG and PCI.[10]
3. There are no RCTs specifically comparing PCI with CABG in patients with diabetes and left main CAD. However, a large RCT exclusively enrolled patients with left main CAD, and the subgroup analysis of patients with diabetes informs this recommendation.[13] In the EXCEL trial, which included patients with left main CAD and low- or intermediate-complexity CAD, approximately 30% of patients had diabetes. At 3 years, the composite of death, stroke, or MI was not significantly different between PCI and CABG among patients with diabetes. However, the all-cause mortality rate was almost 2 times higher in the PCI group. There was no interaction between diabetes status and revascularization modality.

8.3. Patients With Previous CABG

Recommendations for Patients With Previous CABG
Referenced studies that support the recommendations are summarized in Online Data Supplement 15.

COR	LOE	Recommendations
2a	B-NR	1. In patients with previous CABG with a patent LIMA to the LAD who need repeat revascularization, if PCI is feasible, it is reasonable to choose PCI over CABG.[1,2]
2a	C-LD	2. In patients with previous CABG and refractory angina on GDMT that is attributable to LAD disease, it is reasonable to choose CABG over PCI when an internal mammary artery (IMA) can be used as a conduit to the LAD.[3,4]
2b	B-NR	3. In patients with previous CABG and complex CAD, it may be reasonable to choose CABG over PCI when an IMA can be used as a conduit to the LAD.[3,4]

Synopsis

A Heart Team approach and shared decision-making are important in patients who require repeat revascularization after CABG. There are no randomized trials comparing medical therapy with revascularization in patients with previous CABG. PCI and repeat CABG in patients with previous CABG are associated with higher rates of procedural failure and complications[5,6] and worse outcomes than those of patients without previous CABG.[6-8] The need for any repeat revascularization after PCI or CABG is itself an independent predictor of higher mortality risk.[9] Factors that influence the choice of revascularization modality include the availability of the IMA for grafting, a patent graft to the LAD, comorbid conditions, patient factors and preferences, the quality of the target vessels, anatomic complexity of the native and graft disease, and the feasibility and risks of the revascularization method.

Recommendation-Specific Supportive Text

1. In patients with previous CABG, percutaneous intervention of a native vessel or a saphenous vein graft (SVG) is probably indicated in preference to redo CABG, particularly if a LIMA-LAD is not planned or if the patient already has a patent LIMA-LAD, which increases the risk of a redo sternotomy. Randomized and retrospective comparisons of PCI versus repeat CABG show lower in-hospital stroke and mortality rates associated with PCI,[2,3] although long-term mortality rates appeared similar. In circumstances of acute graft closure, PCI of the native vessel is often performed in preference to redo CABG[10] or treating an acutely thrombosed graft with fresh suture lines.[11]
2. A patient with previous CABG faces increased risk during revascularization via CABG,[9] including higher rates of in-hospital death and stroke, compared with patients who undergo revascularization via PCI.[2,3] Observational data suggest that the use of CABG over PCI may result in improved long-term outcomes; however, results are inconsistent and not supported by high-quality RCTs.[3,12,13] If PCI is not an option, if a patent IMA to LAD is not present, or if an IMA is available to be used as a conduit for the LAD, CABG is often chosen as the revascularization strategy in patients with previous CABG and refractory angina who are at an acceptable risk for reoperation.[3,4]
3. Two large observational studies with propensity matching in patients with previous CABG and complex CAD inform decisions about revascularization. The first noted that current clinical practice favored redo CABG over PCI for patients at higher risk and with fewer functional grafts, more CTOs, and lower systolic function, whereas PCI was favored in patients with a patent LIMA and amenable anatomy.[3] The second noted that LIMA grafting to the LAD confers a long-term survival advantage.[4] Thus, decisions about revascularization should involve consideration of factors that may favor repeat CABG, such as the availability of an IMA for LAD grafting, ability to provide left main revascularization, recurrent restenosis of stents, or high-complexity PCI, in such patients.

8.4. DAPT Adherence

Recommendation for DAPT Adherence Referenced studies that support the recommendation are summarized in Online Data Supplement 16.		
COR	LOE	Recommendation
2a	B-NR	1. In patients with multivessel CAD amenable to treatment with either PCI or CABG who are unable to access, tolerate, or adhere to DAPT for the appropriate duration of treatment, CABG is reasonable in preference to PCI.[1-10]

Synopsis

In patients undergoing coronary revascularization, careful consideration should be given to factors that may affect adherence to medications, including patient preferences and comorbidities, socioeconomic status, and lifestyle factors. Premature cessation of DAPT after PCI is associated with stent thrombosis and poor outcomes, including death.[1-10] Therefore, PCI is not favored as the mode of revascularization among patients manifesting risk factors for poor adherence.

Recommendation-Specific Supporting Tex

1. Stent thrombosis after PCI is associated with large-territory MI and poor outcomes, with death rates as high as 50% for early thrombosis cases.[1,5,9] Risk factors for stent thrombosis are many and include patient-, lesion-, and treatment-specific factors.[2] Early DAPT interruption—for bleeding, procedures, or nonadherence—is a reversible risk factor that is strongly associated with stent thrombosis, particularly early after PCI, with the relative increase in stent thrombosis rates between 2-fold and >20-fold.[2,4,8,10] Given the morbidity and mortality associated with stent thrombosis and the strong association of nonuse of DAPT with stent thrombosis, CABG is a safe revascularization option in patients who are not likely to be adherent to DAPT.

9. SPECIAL POPULATIONS AND SITUATIONS

9.1. Revascularization in Pregnant Patients

Recommendations for Revascularization in Pregnant Patients Referenced studies that support the recommendations are summarized in Online Data Supplement 17.		
COR	LOE	Recommendations
2a	C-LD	1. In pregnant patients with STEMI not caused by spontaneous coronary artery dissection (SCAD), it is reasonable to perform primary PCI as the preferred revascularization strategy.[1,2]
2a	C-LD	2. In pregnant patients with NSTE-ACS, an invasive strategy is reasonable if medical therapy is ineffective for the management of life-threatening complications.[1,2]

Synopsis

In pregnant patients, an expanded, multidisciplinary Heart Team approach is often used to determine the appropriate coronary revascularization treatment, with consideration of patient preferences, comorbidities, and clinical status. Decisions in pregnant patients are often difficult and must include consideration of the risk to the unborn fetus, as well as the risks and benefits to the mother. Pregnant women are generally excluded from clinical trials, and therefore there is limited evidence regarding the safety of antiplatelet agents during pregnancy, especially during the third trimester. Low-dose aspirin is generally felt to be safe throughout pregnancy. If clopidogrel is needed, it should be used for the shortest duration possible[3,4] with close monitoring. In a recent systematic review of 39 publications with 42 live births, the outcomes for both mothers and neonates when exposed to clopidogrel at varying durations throughout gestation, did not suggest higher than acceptable risk, with a congenital anomaly rate comparable to background risk. The evidence regarding the use of other antiplatelet agents remains limited.[4]

Recommendation-Specific Supportive Text

1. The coronary revascularization treatment in the pregnant patient with STEMI is typically via PCI,[5] and CABG is usually performed when medical therapy or PCI fails and the mother's life is threatened.[1,2] In a large, retrospective review of pregnant patients with AMI, STEMI was noted in 42% of these patients. Approximately 25% to 40% of pregnant patients with AMI were referred for invasive evaluation, and roughly 25% of pregnant patients received coronary revascularization (with most patients receiving PCI). Compared with a conservative approach, an invasive approach for the treatment of the AMI was associated with a significantly lower adjusted in-hospital mortality rate.
2. In a large database of pregnant patients with AMI,[2] a larger proportion of patients with NSTE-ACS were conservatively treated. If medical therapy is ineffective for the management of these patients because of ongoing ischemia, hemodynamic comprise, or electrical instability, an invasive approach was noted to be reasonable.[2,5,6]

9.2. Revascularization in Older Patients

Recommendation for Revascularization in Older Patients Referenced studies that support the recommendation are summarized in Online Data Supplement 18.		
COR	LOE	Recommendation
1	B-NR	1. In older adults, as in all patients, the treatment strategy for CAD should be based on an individual patient's preferences, cognitive function, and life expectancy.[1,2]

Synopsis

Although the terms "elderly" or "older" have been used to describe various patient-age subgroups in the literature, most clinical trials have defined older patients as those ≥75 years of age.[3] Older patients form a vulnerable subset of patients undergoing coronary revascularization because of their more complex presentations and higher prevalence of comorbidities.[4,5] In addition, they have an increased risk of bleeding complications and stroke after PCI.[3,6-8] However, the optimal treatment for older patients with an indication for revascularization remains poorly defined because most studies have excluded older patients and included only low-risk populations.[9]

Recommendation-Specific Supportive Text

1. Older patients constitute a growing, high-risk population with increased rates of adverse events.[10-12] These patients pose additional challenges because of adverse interactions caused by polypharmacy and age-related changes in cardiovascular function and coronary anatomy.[5,13-15] Although older patients benefit from revascularization to the same, if not greater, extent as younger patients,[16] the optimal strategy should be chosen according to patient-centered goals of care.[17] Subgroup analyses from recent randomized trials have demonstrated that relative outcomes after PCI and CABG are comparable in older patients, with CABG being better at achieving complete revascularization, whereas PCI is preferred for frail patients at higher risk of periprocedural events.[18-21] Careful consideration of risks and benefits using a Heart Team, and in accordance with the patient's preferences, while accounting for frailty and cognitive status, is vital in decisions about the appropriate revascularization plan for older patients.

9.3. Revascularization in Patients With Chronic Kidney Disease (CKD)

Recommendations for Revascularization in Patients With CKD
Referenced studies that support the recommendations are summarized in Online Data Supplement 19.

COR	LOE	Recommendations
1	C-LD	1. In patients with CKD undergoing contrast media injection for coronary angiography, measures should be taken to minimize the risk of contrast-induced acute kidney injury (AKI).[1-3]
1	C-EO	2. In patients with STEMI and CKD, coronary angiography and revascularization are recommended, with adequate measures to reduce the risk of AKI.
2a	B-NR	3. In high-risk patients with NSTE-ACS and CKD, it is reasonable to perform coronary angiography and revascularization, with adequate measures to reduce the risk of AKI.[4,5]
2a	C-EO	4. In low-risk patients with NSTE-ACS and CKD, it is reasonable to weigh the risk of coronary angiography and revascularization against the potential benefit.
3: No benefit	B-R	5. In asymptomatic patients with stable CAD and CKD, routine angiography and revascularization are not recommended if there is no compelling indication.[6]

Synopsis

Patients with CKD constitute a growing subset of the population[7,8] and have been found to have worse outcomes after AMI or PCI.[9,10] Risk of cardiovascular death has been shown to be inversely proportional to estimated glomerular filtration rate, with impaired renal function being an independent predictor of cardiovascular risk.[11,12] Although about 30% to 40% of all patients undergoing PCI have concomitant CKD,[13,14] data on optimal treatment strategies in this population remain scarce because most RCTs have traditionally excluded patients with severe CKD. Patients with CKD who present with ACS are less likely to receive GDMT or invasive angiography than are patients with normal renal function, and the likelihood of undergoing cardiovascular interventions decreases with increasing severity of CKD.[9,15-17] Before coronary angiography is performed, the risks of AKI and the benefits of obtaining diagnostic information should be carefully considered. Preexisting CKD is the strongest independent risk factor for the development of AKI, with a higher stage of CKD associated with incrementally higher risk.[6,7]

Recommendation-Specific Supportive Text

1. Adequate hydration[18-20] and minimization of the volume of contrast media[21-23] remain the principal strategies for contrast-induced nephropathy prevention (Table 8). High-dose statins before diagnostic catheterization have been demonstrated to reduce the occurrence of contrast-induced AKI[21,24,25] because of their pleotropic effects that decrease systemic inflammation, possibly by decreasing the synthesis of endothelin-1 and inhibiting tissue-factor expression by macrophages.[26-29] Atheroembolism may have a role in AKI after PCI,[30] and a transfemoral approach may increase this risk because of the proximity to renal arteries.[31] Consistent with this, the use of radial access has been shown to significantly reduce the risk of AKI compared with femoral access.[31-33] All other measures believed to reduce the risk of contrast-induced AKI have not demonstrated significant clinical benefit.[12,31]

Table 8. Best Practices in the Catheterization Laboratory for Patients With CKD Undergoing Angiography

Assess the risk of contrast-induced AKI before the procedure[1-3]
Administer adequate preprocedural hydration[19,20]
Record the volume of contrast media administered, and minimize contrast use[18,22,23]
Pretreat with high-intensity statins[21,24,25]
Use radial artery if feasible[31-33]
Do not administer N-acetyl-L-cysteine to prevent contrast-induced AKI[38-40]
Do not give prophylactic renal replacement therapy[41,42]
Delay CABG in stable patients after angiography beyond 24 hours when clinically feasible[43-45]

AKI indicates acute kidney injury; CABG, coronary artery bypass graft; and CKD, chronic kidney disease.

2. On the basis of multiple randomized trials, prompt coronary angiography and revascularization have been recommended for patients presenting with STEMI.[34] However, patients with severe CKD were often excluded from these studies because of their higher risk of adverse ischemic and bleeding events, as well as their higher risk of contrast-induced AKI. Nonetheless, the mortality benefit of revascularization in patients with STEMI and CKD outweighs the risk of adverse outcomes when adequate measures to reduce the risk of AKI are taken before, during, and after the procedure.
3. Several observational studies have reported worse in-hospital outcomes and long-term mortality rate for patients with NSTE-ACS and CKD than for those without CKD.[35-37] Despite this, an early invasive strategy in high-risk patients with NSTE-ACS was shown to be associated with significant risk reduction versus a noninvasive approach.[9] Although the use of PCI for NSTE-ACS has been found to decrease with increasing CKD severity, revascularization in these patients is associated with a lower in-hospital mortality rate than that seen with medical management.[5]
4. Although a routine invasive approach has been shown to improve outcomes in patients presenting with NSTE-ACS, this risk reduction was evident mostly in the high-risk subgroups.[9] The risk–benefit ratio of revascularization in patients with low-risk NSTE-ACS remains uncertain because of limited evidence. Therefore, in low-risk patients with NSTE-ACS with CKD, astute clinical judgment weighing the trade-off between risks and benefits is required to determine the optimal approach in this patient subgroup.
5. ISCHEMIA-CKD was the first randomized trial to test the benefit of adding cardiac catheterization and, if feasible, revascularization to GDMT in stable patients with moderate CKD and at least moderate ischemia.[6] With patients randomized to either an invasive or conservative strategy, an initial invasive strategy did not demonstrate a reduced risk of clinical outcomes or improved quality-of-life measures compared with an initially conservative strategy.

9.4. Revascularization in Patients Before Noncardiac Surgery

Recommendation for Revascularization in Patients Before Noncardiac Surgery Referenced studies that support the recommendation are summarized in Online Data Supplement 20.		
COR	**LOE**	**Recommendation**
3: No benefit	**B-R**	1. In patients with non–left main or noncomplex CAD who are undergoing noncardiac surgery, routine coronary revascularization is not recommended solely to reduce perioperative cardiovascular events.[1]

Synopsis

Patients with significant CAD who are undergoing high-risk surgery, such as solid organ transplantation[2] or vascular surgery,[3] have an increased incidence of perioperative cardiovascular events. Routine prophylactic revascularization does not reduce the risk of death or cardiovascular events.[1] Clinical studies have excluded or randomized few patients with high-risk coronary anatomy such as unprotected left main and multivessel CAD. Additionally, these studies did not include patients referred for solid organ transplantation. In such patients, a Heart Team approach would be used to determine the risks and benefits of revascularization. In symptomatic patients or patients with other clinical indications for revascularization, coronary revascularization should be considered in accordance with the recommendations otherwise provided for such situations, but revascularization should not be done for the sole purpose of reducing perioperative complications.

Recommendation-Specific Supportive Text

1. One clinical trial has shown a lack of benefit for routine revascularization in patients before vascular surgery.[1] The CARP (Coronary Artery Revascularization Prophylaxis) study randomized 510 asymptomatic patients with ≥1 significant coronary lesion to revascularization with PCI or CABG or to medical therapy and found no difference in 30-day and 1-year rates of death or MI. Most patients in this study had only single- or 2-vessel CAD, and patients with left main CAD, left ventricular ejection fraction <20%, or severe aortic stenosis were excluded.[1] Nonrandomized patients with unprotected left main CAD who were excluded from the CARP study did derive benefit from revascularization.[3]

9.5. Revascularization in Patients to Reduce Ventricular Arrhythmias

Recommendations for Revascularization in Patients to Reduce Ventricular Arrhythmias Referenced studies that support the recommendations are summarized in Online Data Supplement 21.		
COR	**LOE**	**Recommendations**
1	B-NR	1. In patients with ventricular fibrillation, polymorphic ventricular tachycardia (VT), or cardiac arrest, revascularization of significant CAD is recommended to improve survival.[1-4]
3: No Benefit	C-LD	2. In patients with CAD and suspected scar-mediated sustained monomorphic VT, revascularization is not recommended for the sole purpose of preventing recurrent VT.[5-9]

Synopsis

In patients with ventricular arrhythmias, the evaluation for potential ischemic CAD will guide appropriate treatment, including coronary revascularization.[10,11] The "2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death" describes situations in which CABG or PCI may benefit patients with ischemic CAD.[12] Observational studies have shown that revascularization in patients with life-threatening ventricular arrhythmias[2,13] and in survivors of cardiac arrest[14] is associated with arrhythmia reduction and improved survival. Monomorphic VT may be seen in patients with large AMIs; however, it is often attributable to reentrant rhythms from scar and not acute ischemia. Therefore, revascularization alone has not been shown to improve patient outcomes.[15]

Recommendation-Specific Supportive Text

1. In patients who survive cardiac arrest or have ventricular fibrillation or polymorphic VT, revascularization with CABG[3] or PCI[2] is associated with a lower likelihood of death.[1,16] In patients with decreased left ventricular ejection fraction and ischemic heart disease amenable to CABG, the risk of sudden cardiac death is lower with CABG than with medical therapy.[17,18] Although definitive conclusions may not be drawn from these studies because of the selection and survival biases inherent to these observational studies, revascularization may reduce the burden of polymorphic VT and ventricular fibrillation, resulting in improved survival.
2. In contrast to ventricular fibrillation and polymorphic VT, monomorphic VT in the nonacute setting is typically attributable to scar-related reentry or increased automaticity, rather than coronary artery ischemia.[19] There are limited reports of AMIs presenting with monomorphic VT,[20] isolated coronary artery ischemia causing isolated bundle-branch VT that is successfully treated with PCI,[21] and exercise-induced VT associated with ischemia that resolves after CABG.[19,22] Retrospective studies show an association of incomplete or unsuccessful revascularization of CAD with a higher VT burden and worse outcomes, but the association is most likely because of patient-level factors rather than the success of the intervention.[1,9,23] In numerous large cohort studies, elective coronary artery revascularization alone has not been shown to reduce ventricular arrhythmias in stable patients.[5-8]

9.6. Revascularization in Patients With SCAD

Recommendations for Revascularization in Patients With SCAD Referenced studies that support the recommendations are summarized in Online Data Supplement 22.		
COR	**LOE**	**Recommendations**
2b	C-LD	1. In patients with SCAD who have hemodynamic instability or ongoing ischemia despite conservative therapy, revascularization may be considered if feasible.[1-5]
3: Harm	C-LD	2. Routine revascularization for SCAD should not be performed.[1-5]

Synopsis

SCAD is characterized by the interruption of the coronary artery intimal layer and intramural hematoma, causing vessel compression, and typically presenting as an ACS. Although most dissections will heal without intervention, a notable subset is associated with ongoing symptomatic ischemia, which can progress to complete occlusion. Treatment of patients with SCAD is challenging, and guidance from randomized trials is lacking. Observational studies indicate that most conservatively managed patients recover without further intervention. In patients with ongoing ischemia, vessel occlusion, or patient instability, selective revascularization may be necessary. However, unlike other forms of ACS, routine revascularization for patients with SCAD may not confer the same benefit. PCI wires may propagate the dissection, and balloons and stents can extend the hematoma and lead to vessel occlusion. CABG onto a dissected vessel or one with a propensity to dissect is challenging, and as many as 30% of patients have acute graft closure.[5] The current state of the science and best practices for treating SCAD are described in the AHA scientific statement, which is based on an evaluation of retrospective studies and expert opinion.[6]

Recommendation-Specific Supportive Text

1. Although SCAD will often heal with conservative management, patients with ongoing ischemia, vessel occlusion, or instability may require urgent revascularization. In a retrospective study of 53 patients with SCAD and presenting with STEMI,

62% underwent revascularization with PCI and 7.5% with CABG. Although rates of revascularization and PCI success were lower in patients with SCAD than in age-matched patients with STEMI attributable to atherosclerosis, overall survival was higher in patients with SCAD.[3] A single-center, retrospective study of 189 patients with SCAD reported similar mortality rates at 5 years with a strategy of revascularization and with conservative care. In this cohort of patients, there was a higher rate of emergency or urgent CABG in patients with a patent vessel when they were treated with PCI versus conservative care.[5] Although there are no RCTs comparing revascularization with conservative care in patients who have failed medical therapy, it is reasonable to consider revascularization in the presence of ongoing ischemia and hemodynamic instability.

2. Three large, single-center retrospective studies of patients undergoing PCI for SCAD described a failure rate of 35% to 53% and a need for urgent CABG of 9% to 13%. In these studies, conservatively treated patients experienced recurrent symptoms leading to revascularization only 2% to 10% of the time.[1,2,5,7] Two meta-analyses evaluated the outcomes of patients who were treated conservatively compared with those who were acutely revascularized.[1,4] There were no differences in short- or long-term mortality rate, MI, heart failure, or SCAD recurrence between the groups. However, in the 3 largest retrospective studies, there was a strong indication that there were more cardiovascular events in patients who had a first-line revascularization strategy. These studies are limited by selection and treatment biases, as revascularization was typically performed on higher-risk patients who were more likely to have an occluded artery.[2,5,7] Nevertheless, despite these limitations, the data support a conservative management approach in clinically stable patients.

9.7. Revascularization in Patients With Cardiac Allografts

Recommendation for Revascularization in Patients With Cardiac Allografts		
COR	LOE	Recommendation
2a	C-LD	1. In patients with cardiac allograft vasculopathy and severe, proximal, discrete coronary lesions, revascularization with PCI is reasonable.[1,2]

Synopsis

In patients after orthotopic heart transplantation, the onset of allograft vasculopathy presents a challenging treatment dilemma. Cardiac allograft vasculopathy is a major cause of death after the first year following orthotopic heart transplantation.[3-5] Cardiac allograft vasculopathy is often diffuse and characterized by concentric and rapidly progressive intimal hyperplasia.[6,7] Multiple immunologic and nonimmunologic risk factors have been linked to the accelerated progression of disease.[8,9] Treatment options are limited, with retransplantation being the only definitive therapy for cardiac allograft vasculopathy.[10] However, the scarcity of donor organs and worse outcomes, compared with initial transplantation, remain important limitations.[11,12] Revascularization with PCI serves as a palliative treatment option in patients with focal disease.[2,13] Studies have demonstrated lower periprocedural and intermediate-term mortality rates with stent implantation than with balloon angioplasty.[9]

Recommendation-Specific Supportive Text

1. Because the pathogenesis of cardiac allograft vasculopathy involves more diffuse intimal hyperplasia than focal atherosclerotic plaques, rates of death and MI remain higher in these patients.[13,14] Use of PCI can be beneficial in patients with cardiac allograft vasculopathy who present with severe, proximal, discrete lesions.[1,2] Although DES have demonstrated a clear benefit over bare-metal stents (BMS) for native CAD, patients with cardiac allograft vasculopathy were not included in these trials. However, there is a signal toward better outcomes with DES, especially with regard to the occurrence of restenosis.[4,15,16]

9.8. Revascularization in Patients Before Transcatheter Aortic Valve Replacement (TAVR)

9.8.1. Special Considerations Before Transcatheter Valve Therapy

Recommendations for revascularization in patients before TAVR should be accessed in the 2020 valvular heart disease guideline.[1]

9.9. Revascularization in Patients With Anomalous Coronary Artery

Coronary artery anomalies are among the most common congenital cardiovascular abnormalities. These include the anomalous aortic origin of a coronary artery, coronary fistula, and myocardial bridge. Natural history and presentation can be extremely variable, and much of the historical data from autopsy and surgical studies are now being more fully informed by increasing diagnostic capability.[1,2] Sudden cardiac death and myocardial ischemia remain the major clinical concerns. The presentation and most appropriate management of these patients was reviewed extensively in the "2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Dis-

ease," which has provided guidance that reflects the current state of the evolving evidence.[3]

10. GENERAL PROCEDURAL ISSUES FOR PCI

10.1. Radial and Femoral Approaches for PCI

Recommendations for Radial and Femoral Approaches for PCI Referenced studies that support the recommendations are summarized in Online Data Supplement 23.		
COR	**LOE**	**Recommendations**
1	A	1. In patients with ACS undergoing PCI, a radial approach is indicated in preference to a femoral approach to reduce the risk of death, vascular complications, or bleeding.[1-4]
1	A	2. In patients with SIHD undergoing PCI, the radial approach is recommended to reduce access site bleeding and vascular complications.[4-7]

Synopsis

Over the past decade, the proportion of patients undergoing radial artery catheterization and PCI has increased exponentially.[8] Patients prefer the transradial approach,[9] and this approach offers the advantage of earlier time to ambulation, lower rate of vascular and bleeding complications, and improved cardiovascular outcomes in patients with ACS.[4] An important caveat to radial access trials[1,2,9] is that the treating physicians were required to have experience in radial artery access, and therefore, it is not surprising that femoral crossover rates were notably low among patients assigned to radial access.[1-4] For this reason, it is encouraged that all operators gain experience in radial artery access so that they may ultimately acquire the skills needed to have expertise with this approach. The decision to use the transradial approach should be tempered with the possibility that the radial artery may be needed for bypass grafting in the future. In patients for whom there is a high likelihood of future CABG, the choice of vascular access may require discussion with the patient and the cardiac surgeon. In centers where expertise in the transradial approach is unavailable, or in those patients who are unable to get radial artery catheterization because of anatomic or clinical limitations, femoral artery access remains the default strategy.

Recommendation-Specific Supportive Text

1. The MATRIX (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX Access) trial[2] demonstrated a significantly lower rate of the coprimary endpoint of net adverse clinical events (30-day death, nonfatal infarction and stroke, and non-CABG major bleeding) among patients with ACS randomized to the transradial approach than among those randomized to the transfemoral approach. This difference was driven by a lower rate of bleeding events and a lower 30-day mortality rate. A prespecified subgroup analysis of patients with STEMI enrolled in RIVAL (Trial of Trans-radial versus Trans-femoral Percutaneous Coronary Intervention Access Site Approach in Patients with Unstable Angina or Myocardial Infarction Managed with an Invasive Strategy) demonstrated a lower mortality rate at 30 days with transradial access. A meta-analysis of the RCT supported these findings and reported lower rates of mortality and bleeding with radial access in patients with ACS.[3,4] Although the SAFARI-STEMI (Safety and Efficacy of Femoral Access versus Radial for Primary Percutaneous Intervention in ST-Elevation Myocardial Infarction) trial showed no difference in 30-day mortality rate between radial and femoral access, this trial was stopped early for futility and enrolled less than half its planned sample size.[10] Of note, in patients with a high likelihood of needing future CABG, radial access of the dominant artery will allow preservation of the nondominant radial artery for use as a bypass graft.
2. In patients undergoing coronary angiography or PCI without ACS, the transradial approach significantly reduces bleeding and vascular access site complications but has not been shown to significantly reduce rates of MACE or mortality.[4]

10.2. Choice of Stent Type

Recommendation for Choice of Stent Type Referenced studies that support the recommendation are summarized in Online Data Supplement 24.		
COR	**LOE**	**Recommendation**
1	A	1. In patients undergoing PCI, DES should be used in preference to BMS to prevent restenosis, MI, or acute stent thrombosis.[1-4]

Synopsis

Earlier studies comparing outcomes with first-generation DES and BMS reported an increase in late stent thrombosis and increased mortality rate with DES.[5-8] Over the past 2 decades, there has been a significant evolution in DES technology, including the optimization of drug, polymer, and stent design, which has supported the safety as well as the efficacy of newer DES. To make sense of the small absolute differences between stent types, several large meta-analyses have been completed[1-4] and have suggested that the currently available DES have higher efficacy and safety and lower restenosis rates than both first-generation DES and BMS.[1-4]

Recommendation-Specific Supportive Text

1. In the evaluation of early or late stent thrombosis, several meta-analyses suggest that stents can be ranked from more safe to less safe as follows: durable-polymer DES ≥ biodegradable-polymer DES > BMS.[1-4] A meta-analysis of individual-level data of 20 RCTs (N=26 616), in which 29% of patients had SIHD, 14% had unstable angina, 25% had NSTEMI, and 28% had STEMI,[1] confirmed a significantly reduced risk of MI and stent thrombosis, as well as a trend toward a lower cardiac mortality rate, with a newer-generation DES compared with a BMS. Newer-generation DES were defined as any DES released after the original sirolimus-eluting or paclitaxel-eluting DES. For this reason, there are limited roles for the use of BMS except for unusual circumstances, such as a lack of DES availability or unique patient circumstances that warrant extremely short-duration DAPT (ie, <1 month).

10.3. Use of Intravascular Imaging

Recommendations for Use of Intravascular Imaging Referenced studies that support the recommendations are summarized in Online Data Supplement 25.

COR	LOE	Recommendations
2a	B-R	1. In patients undergoing coronary stent implantation, IVUS can be useful for procedural guidance, particularly in cases of left main or complex coronary artery stenting, to reduce ischemic events.[1-10]
2a	B-R	2. In patients undergoing coronary stent implantation, OCT is a reasonable alternative to IVUS for procedural guidance, except in ostial left main disease.[11-13]
2a	C-LD	3. In patients with stent failure, IVUS or OCT is reasonable to determine the mechanism of stent failure.[14-17]

Synopsis

Because of limitations in angiography, intracoronary imaging can be a useful tool to guide coronary stent implantation, particularly in cases involving the left main artery or complex lesions. IVUS enables full-thickness visibility of the vessel wall, enabling pre-PCI assessment of plaque burden, extent of calcification, lesion length, and external elastic lamina diameter for stent sizing and post-PCI assessment of minimum stent area, malapposition, underexpansion, tissue protrusion, edge disease, and edge dissection.[18,19] OCT uses infrared light to generate high-resolution images of the vessel wall, with particular advantages in assessing calcium thickness, lipid, thrombus, fibroatheroma, and plaque rupture, as well as stent strut neointimal thickness and apposition, and edge dissections.[20] However, OCT has more limited depth of imaging. It also requires blood clearance through the use of contrast injection, which diminishes its use in ostial left main disease. IVUS and OCT can assist with assessing the need for lesion preparation, stent sizing, minimizing geographic miss, verifying stent expansion, evaluating complications, and identifying causes of stent failure.[20]

Recommendation-Specific Supportive Text

1. In patients undergoing PCI, multiple meta-analyses[2,3,21-23] have shown a reduction in MACE with IVUS-guided versus angiographic-guided PCI. The ULTIMATE (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-Comers" Coronary Lesions) trial, which was the largest trial of routine IVUS-guided PCI, demonstrated a lower rate of target-vessel failure (cardiac death, target-vessel infarction, and clinically driven target-vessel revascularization) with IVUS-guided PCI than with angiographic-guided PCI at 12 months.[6] Additionally, at 3 years, there was a significantly lower rate of stent thrombosis and target-vessel revascularization with IVUS-guided PCI.[10] Most of the RCTs focusing on the use of IVUS in complex lesions (left main, CTOs, and long lesions) were small and not powered to evaluate clinical endpoints. Some of these trials have reported lower MACE with IVUS-guided PCI in long lesions,[4] CTOs,[8] or left main stenting.[5] A meta-analysis of RCTs of complex lesions also demonstrated lower rates of MACE, target-vessel revascularization, and target-lesion revascularization when IVUS guidance was used.[1]
2. The ILUMIEN (Optical Coherence Tomography Compared to Intravascular Ultrasound and Angiography to Guide Coronary Stent Implantation: a Multicenter Randomized Trial in Percutaneous Coronary Intervention) study showed noninferiority of OCT compared with IVUS with respect to the primary endpoint of post-PCI minimum stent area, with similarly low rates of procedural MACE.[11] The OPINION (Optical Frequency Domain Imaging Versus Intravascular Ultrasound in Percutaneous Coronary Intervention) study showed noninferiority of OCT- compared with IVUS-guided PCI for the combined endpoint of cardiac death, target-vessel MI, and ischemia-driven target-lesion revascularization at 1 year.[24] The DOCTORS (Does Optical Coherence Tomography Optimize Results of Stenting) trial demonstrated that, compared with angiography-guided PCI, OCT-guided PCI resulted in improved post-PCI FFR.[12] Randomized and registry data have shown that an OCT minimum stent area of <4.5 to 5.0 mm^2 is an independent predictor of MACE.[25,26] The ILUMIEN IV (Optical Coherence Tomography [OCT] Guided Coronary Stent Implantation Compared to Angiography: a Multicenter Randomized Trial in PCI) trial is an ongoing trial designed to evaluate clinical

outcomes in patients with OCT-guided PCI versus angiography-guided PCI.[11]

3. A combination of stent-, procedure-, and patient-related factors are involved in the pathophysiology of stent thrombosis or restenosis.[14,27] Early stent thrombosis is more commonly a result of residual target-lesion thrombus, stent failure, or nonadherence to DAPT, whereas late stent thrombosis is associated with inadequate neointimal coverage or incomplete healing. Assessment of the cause of stent thrombosis with intracoronary imaging is important to guide subsequent treatment. Similarly, advanced imaging techniques have an important role in detecting underlying mechanical and pathophysiological factors that contribute to in-stent restenosis (ISR), such as neointimal hyperplasia, stent underexpansion, and fractures.[14,15] Detailed intrastent visualization allows new possibilities for tissue characterization and may help better identify patients at risk of ISR.[28] Registry and case series data have demonstrated that IVUS and OCT can be useful for evaluating the mechanisms of stent restenosis and stent thrombosis.[16,17,29,30] OCT is better at differentiating between stent-related mechanisms, whereas IVUS is preferred for in-depth vessel wall characterization.[30,31]

10.4. Thrombectomy

Recommendation for Thrombectomy
Referenced studies that support the recommendation are summarized in Online Data Supplement 26.

COR	LOE	Recommendation
3: No Benefit	A	1. In patients with STEMI, routine aspiration thrombectomy before primary PCI is not useful.[1-5]

Synopsis

Many patients with STEMI will have thrombotic occlusion of the infarct artery on the initial angiogram. Therefore, it is natural to consider the use of a device that would decrease thrombus burden to decrease the risk of distal embolization and the no-reflow phenomenon. However, patients in trials with STEMI undergoing primary PCI did not derive any clinical benefit from routine rheolytic thrombectomy.[6,7] Additionally, although the initial studies of aspiration thrombectomy in STEMI demonstrated an improvement in myocardial blush grades and rates of ST-segment–elevation resolution,[8-10] larger studies have not demonstrated improved cardiovascular outcomes with thrombus aspiration.[1-5]

Recommendation-Specific Supporting Text

1. Patients enrolled in contemporary trials did not derive a benefit of reduction in infarct size[5] or improvement in death, reinfarction, stent thrombosis, or target-lesion revascularization at 30 days or 1 year[1,4] or cardiovascular death, recurrent MI, cardiogenic shock, or NYHA Class IV heart failure at 3 months or 1 year[2,3] with aspiration thrombectomy compared with routine stenting. In the TOTAL (Thrombectomy with PCI vs. PCI Alone in patients with STEMI) trial, patients who were assigned to aspiration thrombectomy were found to have a small but statistically significant increased risk of stroke.[2,3] A patient-level meta-analysis found no significant reduction in cardiovascular death at 30 days with routine aspiration thrombectomy but did find a trend toward a higher rate of stroke.[11] Moreover, in the subgroup of patients with high thrombus burden, thrombus aspiration was associated with a small but statistically significant reduced rate of cardiovascular death and a small but statistically significant increased rate of stroke. For this reason, additional dedicated studies focusing on the selective use of thrombus aspiration in patients with high thrombus burden are needed.

10.5. Treatment of Calcified Lesions

Recommendations for the Treatment of Calcified Lesions
Referenced studies that support the recommendations are summarized in Online Data Supplement 27.

COR	LOE	Recommendations
2a	B-R	1. In patients with fibrotic or heavily calcified lesions, plaque modification with rotational atherectomy can be useful to improve procedural success.[1-3]
2b	B-NR	2. In patients with fibrotic or heavily calcified lesions, plaque modification with orbital atherectomy, balloon atherotomy, laser angioplasty, or intracoronary lithotripsy may be considered to improve procedural success.[4-8]

Synopsis

Fibrotic or heavily calcified lesions can hinder stent expansion. The presence of calcium deposits thicker than 500 μm or calcium involving an arc of the vessel >270° on intravascular imaging predicts the need for lesion modification to facilitate stent delivery.[9] Lesions can be modified by using rotational atherectomy, orbital atherectomy, cutting balloon atherotomy, intracoronary lithotripsy, or excimer laser angioplasty. Despite promising results from hundreds of small mechanistic studies, dozens of large, randomized trials have shown that the routine use of atheroablative devices does not improve clinical or angiographic outcomes.[1-3,10] However, the use of atheroablative devices may enhance procedural success in specific circumstances.

Recommendation-Specific Supportive Text

1. Rotational atherectomy excavates inelastic atherosclerotic tissue through the use of a diamond-tipped

burr that rotates at high speeds. Although older studies have shown that the use of rotational atherectomy is associated with increased rates of restenosis[3] and increased late lumen loss,[1] RCTs have demonstrated enhanced stent delivery and expansion in heavily calcified vessels with rotational atherectomy as compared with the use of conventional balloons[1] or cutting or sculpting balloons.[2] For this reason, despite the lack of data to support improved long-term outcomes with rotational atherectomy, rotational atherectomy remains an important tool in certain situations to properly "prepare" a lesion for stenting.

2. Orbital atherectomy has many features in common with rotational atherectomy and has similar clinical indications for use.[4,5] Cutting balloons[6] and scoring balloons[7] section atheromatous plaque through a technique called balloon atherotomy, but their value may be limited to the technical advantage of slipping less often than conventional balloons in ostial lesions or lesions associated with ISR. Excimer laser coronary angioplasty uses a photo-acoustic mechanism[11] that may facilitate the treatment of calcified lesions or nonexpandable stents.[12,13] In certain lesion subsets, such as stent underexpansion that cannot be dilated with high-pressure balloon inflations, high-energy laser angioplasty can disrupt the calcific lesion beneath the stent struts and facilitate stent expansion.[14] The evidence base for additional techniques to modify calcified or fibrotic lesions, including atherectomy, cutting balloons, or laser, are limited to registry studies and case series.[10] Other potentially emerging modalities include intracoronary lithotripsy.[8,15]

10.6. Treatment of Saphenous Vein Graft (SVG) Disease (Previous CABG)

Recommendations for Treatment of SVG Disease (Previous CABG) Referenced studies that support the recommendations are summarized in Online Data Supplement 28.

COR	LOE	Recommendations
2a	B-R	1. In select patients with previous CABG undergoing PCI of a SVG, the use of an embolic protection device, when technically feasible, is reasonable to decrease the risk of distal embolization.[1-3]
2a	B-NR	2. In patients with previous CABG, if PCI of a diseased native coronary artery is feasible, then it is reasonable to choose PCI of the native coronary artery over PCI of the severely diseased SVG.[4-6]
3: No Benefit	C-LD	3. In patients with a chronic occlusion of a SVG, percutaneous revascularization of the SVG should not be performed.[7,8]

Synopsis

In patients with previous CABG undergoing PCI of an SVG, the incidence of MACE is significantly higher than those with native coronary artery PCI because of the higher risk of procedural complications, including the no-reflow phenomenon and periprocedural MI.[6] Compared with native coronary arteries, atherosclerotic plaques in SVGs are more diffuse, with thinner, more friable fibrous caps that increase the risk of distal debris embolization during PCI.[9] In several large prospective registries, patients who underwent SVG PCI were more likely to have no-reflow,[5] stent thrombosis, ischemia-driven target-vessel revascularization, increased overall adjusted MACE, and increased risk of death[4,5,10] in long-term follow-up than were those who underwent non-SVG PCI.

Recommendation-Specific Supportive Text

1. The term "embolic protection devices" refers to the group of devices designed to prevent distal embolization. The SAFER (Saphenous vein graft Angioplasty Free of Emboli Randomized) trial comparing the outcomes of SVG PCI with the use of an embolic protection device (Medtronic Guardwire, Minneapolis, MN) with conventional stenting of the SVG demonstrated a significant reduction in the primary endpoint of death, MI, emergency bypass, or target-lesion revascularization at 30 days with the GuardWire distal protection device.[1] A subsequent study comparing different embolic protection devices reported noninferiority of the FilterWire EX device (Boston Scientific, Marlborough, MA) to the GuardWire.[2] In contemporary PCI, embolic protection devices are used in only 14% to 21% of patients,[11,12] and only the filter-based devices are currently in use. Observational studies exploring the "real-world" benefits of embolic protection devices provide conflicting findings, with 1 study showing no benefit of embolic protection devices and another showing significant harm when embolic protection devices are not used.[11,12] A meta-analysis of 2 randomized studies and 6 observational reports showed no benefit with the use of embolic protection devices, although selection biases and unmeasured confounders are important limitations of these observational studies.[13]
2. In patients with previous CABG who require PCI, two-thirds of these procedures are performed on the native artery instead of the bypass graft.[4,5] Although there are no randomized studies comparing PCI of a diseased native artery with PCI of an SVG, observational studies have shown that intervening in a native coronary artery instead of an SVG is associated with improved outcomes. In a large prospective registry, patients with prior CABG who underwent SVG PCI had higher rates of cardiac death, stent thrombosis, ischemia-driven target-vessel revascularization, and overall MACE at 2 years than did those who underwent PCI of the native vessel.[10] The risk of MACE remained elevated

even after adjustment for baseline variables and propensity matching.[10] Another observational study, examining patients with prior CABG undergoing PCI, reported higher rates of in-hospital death, no-reflow, periprocedural MI, and cardiogenic shock in patients who underwent SVG PCI than in patients who underwent PCI of the native vessel. At 3 years, SVG PCI was associated with higher rates of post discharge death, MI, and repeat revascularization than those seen with native coronary PCI.[5]

3. In patients with chronic occlusion of an SVG, PCI of the SVG has been associated with low success rates and excessive risk of needing repeat intervention.[7,8] However, experienced operators have used occluded SVGs as conduits for retrograde recanalization of CTOs in native coronary arteries.[13]

10.7. Treatment of CTO

Recommendation for Treatment of CTO Referenced studies that support the recommendation are summarized in Online Data Supplement 29.		
COR	**LOE**	**Recommendation**
2b	**B-R**	1. In patients with suitable anatomy who have refractory angina on medical therapy, after treatment of non-CTO lesions, the benefit of PCI of a CTO to improve symptoms is uncertain.[1-4]

Synopsis

A CTO is found in approximately one-quarter of patients undergoing coronary angiography.[5,6] Considerable progress in the technical aspects of interventional revascularization has yielded success rates in excess of 80% in the hands of skilled operators.[7] However, the 30-day mortality rate after CTO PCI is 1.3%, and perforations occur in 4.8% of cases.[8] Enthusiasm for treating these lesions was fueled by retrospective data suggesting improved clinical outcomes for those patients who underwent successful recanalization compared with those who had failed.[9] However, RCTs have not demonstrated improved function[4,10] and have been equivocal with regard to symptoms.[1,2] For this reason, shared decision-making should inform the treatment of patients with refractory angina despite GDMT with remaining CTO coronary lesion, with careful discussions of the limitations of treating these lesions, as well as the potential benefits.

Recommendation-Specific Supportive Text

1. Despite considerable retrospective and registry data suggesting a clinical benefit of PCI of a CTO, a clear demonstration of benefit from prospective randomized trials has not been forthcoming.[11,12] The EXPLORE (Evaluating Xience and left ventricular function in PCI on occlusions after STEMI) and the REVASC (Randomized Trial to Assess Regional Left Ventricular Function After Stent Implantation in Chronic Total Occlusion) trials did not demonstrate any improvement in ventricular function with CTO PCI versus optimal medical therapy.[4,10] Although the EURO CTO (Randomized Multicentre Trial to Compare Revascularization With Optimal Medical Therapy for the Treatment of Chronic Total Occlusions) trial demonstrated a greater reduction in angina frequency and improved quality of life with PCI of a CTO than with optimal medical therapy,[2] a much larger trial, the DECISION-CTO (Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients With Chronic Total Occlusion) trial, did not demonstrate any difference in symptoms or clinical outcomes with CTO PCI.[1] Future trials with more definitive endpoints may change the current landscape.[3,13,14]

10.8. Treatment of Patients With Stent Restenosis

Recommendations for Treatment of Patients With Stent Restenosis Referenced studies that support the recommendations are summarized in Online Data Supplement 30.		
COR	**LOE**	**Recommendations**
1	**A**	1. In patients who develop clinical in-stent restenosis (ISR) for whom repeat PCI is planned, a DES should be used to improve outcomes if anatomic factors are appropriate and the patient is able to comply with DAPT.[1-4]
2a	**C-EO**	2. In patients with symptomatic recurrent diffuse ISR with an indication for revascularization, CABG can be useful over repeat PCI to reduce recurrent events.
2b	**B-NR**	3. In patients who develop recurrent ISR, brachytherapy may be considered to improve symptoms.[5]

Synopsis

The increasing use of newer-generation DES has led to a significant reduction in the risk of ISR and subsequent target-lesion revascularization compared with BMS and first-generation DES.[6-8] Nevertheless, ISR is still reported in 5% to 10% of patients undergoing PCI.[9,10] The primary mechanism of ISR after stent implantation is neointimal hyperplasia, with angiographic and histopathological studies demonstrating considerable differences in tissue characteristics based on the type of stent.[11-14] The risk of restenosis is also linked to clinical presentation, patient profile, lesion location, and procedural characteristics.[15,16] Numerous approaches to the treatment of restenosis have been explored and include balloon angioplasty, DES, drug-coated balloons, scoring or cutting balloons, vascular brachytherapy, atheroablative therapies, and CABG. Compared with other therapies, DES appears to provide the most benefit. However, the type of ISR (ie, focal versus diffuse) may also affect the decision to treat with one modality over another and, therefore, treatment

of ISR should be individualized. Importantly, intensive medical therapy is also vital in these patients.

Recommendation-Specific Supportive Text

1. In patients with ISR, studies have shown that treatment with a DES resulted in lower rates of target-vessel restenosis in follow-up than those seen with BMS or balloon angioplasty.[3,4,17] Network meta-analyses comparing various treatment options (DES, BMS, vascular brachytherapy, drug-coated balloons, conventional balloons, or rotational atherectomy) have shown that PCI with a DES was associated with the lowest rates of restenosis and target-vessel revascularization. Of the different DES stent types, everolimus-eluting stents appeared to have the best efficacy.[1,2] In these studies, there were no significant differences in other clinical outcomes, including death or MI, among the therapies examined.
2. In patients with recurrent episodes of restenosis despite repeat PCI with DES, or in patients who have diffuse ISR in large vessels or a complex presentation such as CTO with multivessel disease, CABG maybe the preferred approach if the anatomy is suitable.
3. In patients who already have multiple stent layers or have recurrent ISR with an artery that is unfavorable to receive another DES, who are not good candidates for bypass surgery, vascular brachytherapy provides an additional tool to aid revascularization.[5] Vascular brachytherapy circumvents the need to implant another stent, and in these challenging situations it remains a reasonable option.

10.9. Hemodynamic Support for Complex PCI

Recommendation for Hemodynamic Support in Complex PCI
Referenced studies that support the recommendation are summarized in Online Data Supplement 31.

COR	LOE	Recommendation
2b	B-R	1. In selected high-risk patients, elective insertion of an appropriate hemodynamic support device as an adjunct to PCI may be reasonable to prevent hemodynamic compromise during PCI.[1,2]

Synopsis

Patients undergoing complex PCI are at risk of hypotension, decompensated heart failure, shock, or arrhythmias that may lead to rapid hemodynamic deterioration or death. Intra-aortic balloon pump counterpulsation provides minimal hemodynamic support for PCI but improves coronary and cerebral perfusion. Its use is limited in patients with severe peripheral artery or aortic disease. Its advantages are ease of use and smaller catheter diameter, leading to lower rates of vascular access site complications. The Impella percutaneous left ventricular–assist devices (Abiomed, Danvers, MA) provide greater left ventricular support. The use of the Impella support devices is limited in patients with left ventricular thrombus, aortic stenosis, peripheral artery disease, or aortic disease. Extracorporeal membrane oxygenation and the TandemHeart (CardiacAssist, Inc, Pittsburgh, PA) devices are rarely used to support complex PCI. New hemodynamic support devices are undergoing evaluation in clinical trials.

Recommendation-Specific Supporting Text

1. The routine use of hemodynamic support devices for complex PCI has not been shown to reduce cardiovascular events.[1,2] In the BCIS-1 (Balloon Pump–Assisted Coronary Intervention) study, there was no difference in the primary composite outcome (death, MI, cerebrovascular event, or repeat revascularization) with intra-aortic balloon counterpulsation.[1] Major procedural complications (mostly hypotension) were lower with intra-aortic balloon counterpulsation. The PROTECT II (Prospective, Multi-center, Randomized Controlled Trial of the Impella Recover LP 2.5 System Versus Intra Aortic Balloon Pump [IABP] in Patients Undergoing Non Emergent High Risk PCI II) trial, comparing the Impella System with intra-aortic balloon counterpulsation for high-risk PCI, was halted for futility after an interim analysis showed no benefit in the primary endpoint of MACE.[2] Compared with balloon counterpulsation, Impella provided better hemodynamic support. Observational studies have further challenged the efficacy, safety, and cost of hemodynamic support devices.[3,4] Despite these findings, these devices can provide hemodynamic support in select patients during complex PCI with multivessel disease, left main disease, or disease of the last patent conduit and severe left ventricular dysfunction or cardiogenic shock.[5-9]

11. PHARMACOTHERAPY IN PATIENTS UNDERGOING PCI

11.1. Aspirin and Oral P2Y12 Inhibitors in Patients Undergoing PCI

Recommendations for Aspirin and Oral P2Y12 Inhibitors in Patients Undergoing PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 32.

COR	LOE	Recommendations
1	B-R	1. In patients undergoing PCI, a loading dose of aspirin, followed by daily dosing, is recommended to reduce ischemic events.[1-4*]

*Contraindications to ticagrelor: previous intracranial hemorrhage or ongoing bleeding. Contraindications to prasugrel: previous intracranial hemorrhage, previous ischemic stroke or transient ischemic attack, or ongoing bleeding. Prasugrel should be used with caution at a lower dose in patients ≥75 years of age or with a body weight <60 kg.

Recommendations for Aspirin and Oral P2Y12 Inhibitors in Patients Undergoing PCI (Continued)		
COR	LOE	Recommendations
1	B-R	2. In patients with ACS undergoing PCI, a loading dose of P2Y12 inhibitor, followed by daily dosing, is recommended to reduce ischemic events.[5-15]
1	C-LD	3. In patients with SIHD undergoing PCI, a loading dose of clopidogrel, followed by daily dosing, is recommended to reduce ischemic events.[8,12,15-19]
1	C-LD	4. In patients undergoing PCI within 24 hours after fibrinolytic therapy, a loading dose of 300 mg of clopidogrel, followed by daily dosing, is recommended to reduce ischemic events.[5]
2a	B-R	5. In patients with ACS undergoing PCI, it is reasonable to use ticagrelor or prasugrel in preference to clopidogrel to reduce ischemic events, including stent thrombosis.[6,14,20]
2b	B-R	6. In patients <75 years of age undergoing PCI within 24 hours after fibrinolytic therapy, ticagrelor may be a reasonable alternative to clopidogrel to reduce ischemic events.[21]
3: Harm	B-R	7. In patients undergoing PCI who have a history of stroke or transient ischemic attack, prasugrel should not be administered.[6]

Synopsis

DAPT with aspirin and oral P2Y12 inhibitors remains the cornerstone of therapy for the prevention of thrombotic complications with PCI. In the early days of PCI, aspirin was found to be effective at decreasing coronary thrombosis with balloon angioplasty,[1] and since that time, aspirin has remained a key agent for patients with chronic vascular disease.[2-4] The contemporary oral P2Y12 inhibitors used in PCI include clopidogrel, ticagrelor, and prasugrel. Patients should be treated with a loading dose of these agents, either before PCI or otherwise at the time of PCI (Table 9). Clopidogrel is the least potent agent, requiring longer time to platelet inhibition after a loading dose. In patients with stable angina, there is no compelling evidence to support routine pretreatment with a P2Y12 inhibitor before coronary angiography when the coronary anatomy is not known.[22] This is especially important because the need for CABG still occurs in a nonnegligible proportion of patients referred for angiography, and pretreatment can result in postponement of surgery.[18] The duration of treatment with DAPT is discussed in Section 14.

Recommendation-Specific Supportive Text

1. Aspirin is protective in most types of patients with an increased risk of occlusive vascular events, including those with an AMI or ischemic stroke, unstable or stable angina, and previous MI.[2,3] Aspirin reduces the frequency of ischemic complications after PCI and should be given in the periprocedural period.[1,23] Although the minimum effective dose of aspirin in the setting of PCI has not been established, non–enteric-coated aspirin (325 mg) is commonly administered before PCI in those patients who were not previously on aspirin.[1,24]

Table 9. Oral and Parenteral Antiplatelet Agents for Patients Undergoing PCI

Drug	Loading Dose	Maintenance Dose
Oral antiplatelet agents		
Aspirin	Loading dose of 162-325 mg orally[11] Aspirin may be chewed to achieve faster action	Maintenance dose of 75-100 mg orally daily[24,25]
Clopidogrel	Loading dose of 600 mg orally[19] A lower loading dose of 300 mg should be considered in patients after fibrinolytic therapy[5]	Maintenance dose of 75 mg orally daily[34]
Prasugrel	Loading dose of 60 mg orally[20]	Maintenance dose of 10 mg orally daily[20] In patients with body weight <60 kg, a maintenance dose of 5 mg orally daily is recommended[35] In patients ≥75 years of age, a dose of 5 mg orally daily can be used if deemed necessary[35]
Ticagrelor	Loading dose of 180 mg orally[14] Ticagrelor may be chewed to achieve faster action	Maintenance dose of 90 mg orally twice a day[14]
Intravenous antiplatelet agents		
Abciximab (GPI)*	Bolus of 0.25 mg/kg[36]	Maintenance of 0.125 μg/kg/min infusion (maximum 10 g/min) for 12 h.[36]
Eptifibatide (GPI)	Double bolus of 180 μg/kg (given at a 10-min interval)[37]	Maintenance infusion of 2.0 μg/kg/min for up to 18 h[37]
Tirofiban (GPI)	Bolus of 25 μg/kg over 3 min[38]	Maintenance infusion of 0.15 μg/kg/min for up to 18 h[38]
Cangrelor	Bolus of 30 μg/kg[39]	Maintenance infusion 4 μg/kg/min for at least 2 h or duration of the procedure, whichever is longer[39]

GPI indicates glycoprotein IIb/IIIa inhibitor; and PCI, percutaneous coronary intervention.
*Abciximab may not be readily available to clinicians in the United States.

Observational data and retrospective analyses of RCTs have demonstrated that a lower dose of chronic daily aspirin (<100 mg) after PCI results in the best combination of safety and efficacy.[24-26] On the basis of an analysis of aspirin dosing and outcomes in the PLATO (Trial to Assess The Study of Platelet Inhibition and Patient Outcomes) study, a low dose of aspirin (<100 mg) should be used in patients treated with ticagrelor. There are data to suggest that in the treatment of ACS, a chewable aspirin formulation may be preferable to solid tablet aspirin.[27]

2. P2Y12 inhibitors are essential for treating patients undergoing PCI. Their use was first evaluated in studies exploring the optimal antithrombotic regimens after coronary stent implantation. In these earlier studies, ticlopidine was found to be superior to aspirin alone or the combination of aspirin and anticoagulant therapy[10,11,13] in reducing ischemic events after coronary stent implantation. Because of unacceptable side effects of ticlopidine, clopidogrel was later used in place of ticlopidine, with clinical trials demonstrating similar efficacy but lower rates of drug discontinuation attributable to noncardiac events.[16] With clopidogrel, the introduction of prasugrel and ticagrelor supported the use of a more potent P2Y12 inhibitor agent for PCI in ACS.[6,14] A loading dose of a P2Y12 agent should be given to minimize the time to platelet inhibition. There are conflicting data on the benefits of pretreatment with a P2Y12 inhibitor before the anatomy is known, particularly in patients with NSTE-ACS.[7,17,28-31] In contemporary times, with most patients with ACS undergoing early angiography, a strategy of loading with a P2Y12 inhibitor after the anatomy is known appears to offer similar benefit to preloading.[31]
3. The CREDO (Clopidogrel for the Reduction of Events During Observation) trial[18] demonstrated a reduction in ischemic events, including the risk of death, MI, or stroke, with a loading dose of clopidogrel and treatment up to 9 months after elective PCI. There was a trend toward a lower event rate when preloading with a 300-mg clopidogrel dose was given >3 hours before PCI. A 600-mg loading dose of clopidogrel is associated with a shorter time to platelet inhibition and therefore is the preferred dose. Ticagrelor and prasugrel have not been studied for long-term clinical outcomes in patients with SIHD undergoing PCI.
4. Patients with STEMI who were treated with fibrinolytic therapy and referred for PCI are at increased bleeding and ischemic risk. Clopidogrel is the only P2Y12 inhibitor agent studied in patients immediately after the administration of fibrinolytic therapy. In the CLARITY (Clopidogrel as Adjunctive Reperfusion Therapy) trial, clopidogrel pretreatment in conjunction with fibrinolytic therapy resulted in a 46% reduction in the rate of cardiovascular death or recurrent MI or stroke at 30 days among patients referred for PCI.[5] Major and minor bleeding was similar between the groups. In this study, patients randomized to clopidogrel were administered a 300-mg load during or immediately after fibrinolytic therapy, followed by 75 mg daily.[5] In contemporary times, the loading dose of clopidogrel for patients undergoing PCI after fibrinolytic therapy should be individualized. A larger loading dose of 600 mg may be used for most patients, whereas the lower 300-mg loading dose is generally reserved for older patients or those at higher risk of bleeding.
5. TRITON-TIMI-38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction)[6] and PLATO[14] demonstrated that treatment with prasugrel (TRITON-TIMI-38) and ticagrelor (PLATO), compared with clopidogrel, reduced the rate of the composite endpoint of death from vascular causes, MI, or stroke. These agents were also associated with a lower rate of stent thrombosis. In the TRITON-TIMI 38 trial, non-CABG major bleeding was significantly higher with prasugrel.[6] In PLATO, although there were no significant differences in the rates of study-defined bleeding events with ticagrelor, non-CABG major bleeding was significantly higher among patients treated with ticagrelor[14] than among patients treated with clopidogrel.[14] Because of the increased bleeding risk, these more potent agents should be used with caution in older patients. One study suggested that clopidogrel may be a reasonable alternative for older patients with ACS undergoing PCI, with similar rates of ischemic events and less bleeding.[32] The open-labeled design of this trial and the high rate of crossover limit the generalization of the study results. Further studies are needed to determine the ideal P2Y12 inhibitor for use in older patients with ACS undergoing PCI.
6. In patients with fibrinolytic-treated STEMI, ticagrelor is associated with a greater inhibition of platelet reactivity than that seen with clopidogrel.[33] In PLATO, patients were excluded from enrollment if they were treated with fibrinolytic therapy within 24 hours of enrollment. Therefore, although PLATO supported the use of ticagrelor over clopidogrel in patients with STEMI treated with fibrinolytic therapy, there were limited data on the safety of ticagrelor when given early after fibrinolytic therapy. The TREAT (Ticagrelor in Patients With ST Elevation Myocardial Infarction Treated With Pharmacological Thrombolysis) trial was designed

to examine the safety of ticagrelor in patients treated with fibrinolytic therapy for STEMI.[21] In this study, ticagrelor was found to be noninferior to clopidogrel in rates of TIMI major bleeding, fatal bleeding, and intracranial bleeding.[21]

7. A more detailed analysis of the TRITON study that was designed to evaluate net clinical benefit (MACE events plus bleeding) with prasugrel demonstrated no net benefit of prasugrel compared with clopidogrel for patients with low body weight (<60 kg) or those ≥75 years of age and found net harm with prasugrel for patients with previous transient ischemic attack or cerebrovascular accident.[6] For this reason, prasugrel is contraindicated in patients with a history of transient ischemic attack or stroke. Caution is advised in the use of prasugrel in patients weighing <60 kg or in patients ≥75 years of age.

11.2. Intravenous P2Y12 Inhibitors in Patients Undergoing PCI

Recommendation for Intravenous P2Y12 Inhibitors in Patients Undergoing PCI Referenced studies that support the recommendation are summarized in Online Data Supplement 33.		
COR	**LOE**	**Recommendation**
2b	**B-R**	1. In patients undergoing PCI who are P2Y12 inhibitor naïve, intravenous cangrelor may be reasonable to reduce periprocedural ischemic events.[1-3]

Synopsis

Cangrelor is a potent, direct, reversible, short-acting intravenous P2Y12 inhibitor with rapid onset of platelet inhibition and restoration of platelet function within 1 hour of discontinuation. Cangrelor thus provides rapid, predictable, and profound inhibition of platelets. It can be efficacious in preventing stent thrombosis and may be considered in patients who have not been pretreated with a P2Y12 inhibitor, in patients whose absorption of oral medications may be inhibited, or in patients who are unable to take oral medications. Cangrelor has been investigated within the CHAMPION (Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition) program and compared with a loading dose of clopidogrel given at the time of PCI in 3 large-scale clinical trials.[1,2,4] There are no studies comparing cangrelor with a loading dose of ticagrelor or prasugrel given at the time of PCI.

Recommendation-Specific Supporting Text

1. The CHAMPION PLATFORM and the CHAMPION PCI trials did not show a reduction in the primary outcome (ie, death, MI, or ischemia-driven revascularization at 48 hours) with cangrelor. However, in CHAMPION PLATFORM, cangrelor resulted in lower rates of the prespecified secondary outcomes of stent thrombosis and death.[1] In the CHAMPION PHOENIX trial, the primary endpoint, which included death, MI, ischemia-driven revascularization, or stent thrombosis, was significantly reduced with cangrelor.[2] This was driven mainly by a reduction in periprocedural MI and intraprocedural stent thrombosis. A pooled patient-level meta-analysis of the CHAMPION trials supported these findings, demonstrating a lower rate of the composite endpoint of death, MI, ischemia-driven revascularization, or stent thrombosis at 48 hours with cangrelor than with clopidogrel.[3] Additionally, cangrelor was associated with a 41% reduction in stent thrombosis. Although major bleeding was similar between the groups, minor bleeding was more frequent in the cangrelor group.[3]

11.3. Intravenous Glycoprotein IIb/IIIa Inhibitors in Patients Undergoing PCI

Recommendations for Intravenous Glycoprotein IIb/IIIa Inhibitors in Patients Undergoing PCI Referenced studies that support the recommendations are summarized in Online Data Supplement 34.		
COR	**LOE**	**Recommendations**
2a	**C-LD**	1. In patients with ACS undergoing PCI with large thrombus burden, no-reflow, or slow flow, intravenous glycoprotein IIb/IIIa inhibitor agents are reasonable to improve procedural success.[1,2]
3: No Benefit	**B-R**	2. In patients with SIHD undergoing PCI, the routine use of an intravenous glycoprotein IIb/IIIa inhibitor agent is not recommended.[3-5]

Synopsis

Glycoprotein IIb/IIIa receptor inhibitors are direct-acting antiplatelet agents targeting the glycoprotein IIb/IIIa platelet receptor. Many of the trials of glycoprotein IIb/IIIa inhibitors in the setting of ACS were conducted in an era before the use of potent P2Y12 inhibitors or before routine stenting.[2,6] Additionally, in the earlier trials, the time from presentation to coronary angiography was often prolonged. In the contemporary era of shorter revascularization times and use of potent DAPT, the benefit of glycoprotein IIb/IIIa receptor inhibitor agents is diminished.[2,7]

Recommendation-Specific Supporting Text

1. In trials of patients with ACS, glycoprotein IIb/IIIa receptor inhibitors have not been associated with improved clinical outcomes and may increase bleeding complications.[7,8] Because the addition of glycoprotein IIb/IIIa receptor inhibitors can decrease thrombus burden by further inhibiting

platelet aggregation,[9] the use of glycoprotein IIb/IIIa receptor inhibitors in the era of more potent antiplatelet agents is generally reserved for patients with a large thrombus burden or no-reflow or slow flow that is believed to be attributable to distal embolization of thrombus.

2. In patients with SIHD who are undergoing PCI, the use of glycoprotein IIb/IIIa receptor inhibitors in addition to a clopidogrel load does not reduce ischemic events.[3,4] Patients enrolled in the ISAR-REACT (iNtracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment) trial who were randomized to pretreatment with abciximab and a 600-mg loading dose of clopidogrel had outcomes similar to those of patients receiving clopidogrel alone.[3] Major bleeding was not significantly different between the 2 groups, although the rate of severe thrombocytopenia was significantly higher in the abciximab group.[3] A subgroup analysis of the ESPRIT (Enhance Suppression of the Platelet IIB/IIIA receptor with Integrilin Therapy) trial showed no benefit in the primary endpoint of death, MI, urgent target-vessel revascularization, and thrombotic bailout with glycoprotein IIb/IIIa inhibitor therapy with eptifibatide at 48 hours in the group of patients undergoing PCI for stable angina.[5] Six-month rates of death or MI were also not significantly different in this subgroup of patients.[4]

11.4. Heparin, Low-Molecular-Weight Heparin, and Bivalirudin in Patients Undergoing PCI

Recommendations for Heparin, Low-Molecular-Weight Heparin, and Bivalirudin in Patients Undergoing PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 35.

COR	LOE	Recommendations
1	C-EO	1. In patients undergoing PCI, administration of intravenous unfractionated heparin (UFH) is useful to reduce ischemic events.
1	C-LD	2. In patients with heparin-induced thrombocytopenia undergoing PCI, bivalirudin or argatroban should be used to replace UFH to avoid thrombotic complications.[1,2]
2b	A	3. In patients undergoing PCI, bivalirudin may be a reasonable alternative to UFH to reduce bleeding.[3-12]
2b	B-R	4. In patients treated with upstream subcutaneous enoxaparin for unstable angina or NSTE-ACS, the use of intravenous enoxaparin may be considered at the time of PCI to reduce ischemic events.[13-17]
3: Harm	B-R	5. In patients on therapeutic subcutaneous enoxaparin, in whom the last dose was administered within 12 hours of PCI, UFH should not be used for PCI and may increase bleeding.[14,18,19]

Synopsis

Antithrombotic therapy is a mainstay of treatment in patients undergoing PCI. Currently, there are 3 antithrombotic agents that have been studied in PCI. These are UFH, bivalirudin, and enoxaparin. Fondaparinux is no longer recommended as the only anticoagulant in PCI because of a higher incidence of guiding-catheter thrombosis.[20,21] Consideration of the patient's clinical presentation (eg, stable disease, NSTE-ACS, or STEMI) and bleeding risk profile[22] may influence selection of the optimal anticoagulant type. Suggested dosing regimens of parenteral agents are shown in Table 10.

Recommendation-Specific Supportive Text

1. As the only anticoagulant available for many years, UFH has been the standard of care by default and the primary comparator for novel agents in RCTs.[23] Dosing recommendations were established from early studies that demonstrated a relationship between activated clotting times and ischemic complications,[23-26] but it is unclear that these analyses translate to the modern coronary stent era.[27-31] Thus, the exact use of dosing based on activated clotting times in current practice is uncertain. The routine use of full-dose anticoagulation therapy after PCI is no longer indicated.
2. Heparin-induced thrombocytopenia occurs when the heparin molecule binds to platelet factor 4. Argatroban and bivalirudin are direct thrombin inhibitors and do not bind to platelet factor 4. Because of their different mechanism of action, argatroban[1] and bivalirudin[2] are acceptable alternative anticoagulants for use in patients with heparin-induced thrombocytopenia.
3. RCTs comparing bivalirudin and heparin have reported no difference in ischemic endpoints; however, less bleeding was reported with bivalirudin.[3-7,9,29,32-37] Although the reduction in bleeding complications with the use of bivalirudin was seen in most trials, in real-world practice, this benefit may be less pronounced with routine use of radial artery intervention and low rates of glycoprotein IIb/IIIa inhibitor use. Meta-analyses of clinical trial data support these findings, highlighting that the magnitude of the lower bleeding risk with bivalirudin in various trials depended on variable inclusion of a glycoprotein IIb/IIIa inhibitor.[10,11] The VALIDATE-SWEDEHEART (Bivalirudin vs Heparin in NSTEMI and STEMI in Patients on Modern Antiplatelet Therapy in SWEDEHEART) study[38] examined a prolonged bivalirudin infusion versus UFH. Patients were treated with the more potent P2Y12 inhibitors, 90% had radial artery access, and there was a low rate of glycoprotein IIb/IIIa

Table 10. Anticoagulant Dosing During PCI*

Dosing of Parenteral Anticoagulants During PCI		
Drug	**Patient Has Received Previous Anticoagulant Therapy**	**Patient Has Not Received Previous Anticoagulant Therapy**
UFH	Additional UFH as needed (eg, 2000–5000 U) to achieve an ACT of 250-300 s*	70–100 U/kg initial bolus to achieve target ACT of 250–300 s*
Enoxaparin	For previous treatment with enoxaparin, if the last SC dose was administered 8–12 h earlier or if only 1 SC dose of enoxaparin has been administered, an IV dose of 0.3 mg/kg of enoxaparin should be given[43-45] If the last SC dose was administered within the previous 8 h, no additional enoxaparin should be given	0.5–0.75 mg/kg IV bolus
Bivalirudin	For patients who have received UFH, repeat ACT If ACT is not in therapeutic range, then give 0.75 mg/kg IV bolus, then 1.75 mg/kg/h IV infusion	0.75 mg/kg bolus, 1.75 mg/kg/h IV infusion
Argatroban	200 μg/kg IV bolus, then 15 μg/kg/min IV infusion	350 μg/kg, then 15 μg/kg/min IV infusion

ACS indicates acute coronary syndrome; ACT, activated clotting time; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; and UFH, unfractionated heparin.

*Target ACTs for UFH dosing shown for HemoTec (GmbH, Switzerland) or I-Stat (Abbott) device. For Hemochron ACT (Werfen) devices, ACT goals are 50 s higher. In the case of CTO or ACS, consider higher target ACT. If IV glycoprotein IIb/IIIa receptor inhibitor is planned, target ACT 200–250 s.[26,27,31,40-42]

inhibitor use. Compared with UFH, bivalirudin was not associated with improved rates of MACE, major bleeding, or stent thrombosis at 6 months.

4. Enoxaparin is considered a safe alternative to UFH.[15,16] In the SYNERGY (Superior Yield of the New Strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa Inhibitors)[14] and AtoZ (Aggrastat to Zocor)[13] trials of patients with NSTE-ACS, enoxaparin was shown to be noninferior to UFH, with no difference in rates of death, MI, or major bleeding. In primary PCI, the ATOLL (Acute STEMI Treated With Primary Angioplasty and Intravenous Lovenox or UFH to Lower Ischemic and Bleeding Events)[15] trial compared intravenous enoxaparin and UFH and showed a reduction in the main secondary endpoint (composite of death, recurrent ACS, and urgent revascularization) in the enoxaparin arm, without more bleeding. These findings have been supported by a subsequent large meta-analysis that included patients undergoing PCI for STEMI and NSTE-ACS, which showed a reduction in rates of all-cause death and bleeding.[16] Almost all patients undergoing elective PCI who are administered enoxaparin (0.5 mg/kg IV) will have a peak anti-Xa level >0.5 IU/mL.[31,39]
5. In clinical trials, patients who were given upstream enoxaparin and then switched to UFH had more complications, which are attributed at least in part to stacking both medications at the time of PCI, even when heparin is administered as long as 10 hours after the last dose of enoxaparin.[18,19] While these trials were performed prior to the widespread use of radial artery access, it is preferable to avoid the administration of UFH in patients that have received enoxaparin in the previous 12 hours to reduce risk of bleeding.

12. GENERAL PROCEDURAL ISSUES FOR CABG

12.1. Perioperative Considerations in Patients Undergoing CABG

Recommendation for Perioperative Considerations in Patients Undergoing CABG Referenced studies that support the recommendation are summarized in Online Data Supplement 36.		
COR	**LOE**	**Recommendation**
1	B-NR	1. For patients undergoing CABG, establishment of multidisciplinary, evidence-based perioperative management programs is recommended to optimize analgesia, minimize opioid exposure, prevent complications and to reduce time to extubation, length of stay, and health care costs.[1-3]

Synopsis

Previous recommendations with regard to perioperative management assessed the role of certain monitoring modalities to guide intraoperative and postoperative decision-making and also emphasized the use of fast-track cardiac anesthesia, which uses short-acting anesthetic agents to improve outcomes after CABG.[4] More recently, cardiac surgical service lines have been encouraged to expand the scope of these efforts to develop multidisciplinary perioperative programs that incorporate bundled evidence-based surgical, anesthetic, and nursing interventions, including the targeted use of appropriate monitoring modalities, to optimize care and improve patient recovery.

Recommendation-Specific Supporting Text

1. Fast-track cardiac anesthesia was extensively studied in the early 2000s and was found to reduce

Table 11. Perioperative Anesthetic and Monitoring Considerations for CABG

Anesthetic considerations	
Perioperative analgesia	Nonopioid medications (eg, acetaminophen, ketamine, dexmedetomidine) and/or regional techniques (eg, truncal nerve blocks), particularly as part of a multimodal analgesic approach, have been shown to reduce perioperative opioid use in cardiac surgery.[1-16]
Maintenance anesthesia	Although volatile (versus intravenous) anesthesia may facilitate earlier extubation,[2,6-8,12,14] recent evidence suggests that the choice of maintenance anesthetic likely does not impact mortality rate after cardiac surgery.[17-21]
Mechanical ventilation	An intraoperative lung-protective ventilation strategy (ie, tidal volume of 6–8 mL/kg predicted body weight + positive end-expiratory pressure) has been shown to improve pulmonary mechanics and reduce postoperative pulmonary complications.[21-25]
Goal-directed therapy	Goal-directed therapy, which creates protocols for the use of fluids and vasopressors to target specific hemodynamic goals, has yielded inconsistent results and requires additional investigation to determine its use in cardiac surgery.[26,27]
TEE	
CABG + valve procedures	Intraoperative TEE aids in the real-time assessment of heart valve function and pathology in those undergoing combination CABG and valve surgery.[28-30]
Isolated CABG procedures	The use of intraoperative TEE in isolated CABG is less established but has been shown to aid in surgical and anesthetic decision-making as a tool for real-time assessment of hemodynamic status, regional wall motion, ventricular function, valve anatomy, and diastolic function.[28-35]
Pulmonary artery catheters	
High-risk surgery	Highly selective use of pulmonary artery catheters for high-risk patients (ie, older, with congestive heart failure, pulmonary hypertension, or previous multiple valve procedures) may be safe and may potentially aid in the surveillance and treatment of hemodynamic instability.[36-38]
Low-risk surgery	The use of pulmonary artery catheters in low-risk or clinically stable patients is discouraged because the practice is associated with increased interventions that incur greater health care expense without associated improvement in morbidity or mortality rates.[38-40]
CNS monitoring	
Cerebral oxygen saturation	Intraoperative monitoring of cerebral oxygen saturation (ie, near-infrared spectroscopy) to detect cerebral hypoperfusion has been shown to guide anesthetic decision-making and may prevent postoperative neurocognitive dysfunction.[41-47]
Processed electroencephalogram	Routine use of intraoperative monitoring of processed electroencephalogram (ie, bispectral index) has yielded inconsistent results with respect to the prevention of recall, determination of depth of anesthesia, or improvement in rate of recovery after cardiac surgery.[48-51]

CABG indicates coronary artery bypass graft; CNS, central nervous system; and TEE, transesophageal echocardiography.

opioid use and hasten extubation[5,6]; however, it did not uniformly reduce complications or length of stay in patients after CABG.[7,8] More recently, cardiac surgical service lines have expanded on fast-track anesthetic agents and implemented enhanced recovery programs, which use more extensive phase-specific perioperative interventions. Such programs have been shown to prevent early postoperative complications, minimize exposure to opioid-based analgesia, and reduce time to extubation, time in the intensive care unit, and hospital length of stay after CABG.[1-3] Components of such programs may include liberation of "nothing by mouth" status, bundled surgical site infection prevention, multimodal nonopioid analgesics, protocolized short-acting anesthetics, targeted-organ perfusion strategies, and early postoperative ambulation. Assessment of enhanced recovery programs has been generally limited to moderate-sized observational studies, and additional research is required to determine the necessary features and implementation strategies. Providers may consider the use of specific anesthetic and monitoring modalities outlined in Table 11.

12.2. Bypass Conduits in Patients Undergoing CABG

Recommendations for Bypass Conduits in Patients Undergoing CABG Referenced studies that support the recommendations are summarized in Online Data Supplement 37.

COR	LOE	Recommendations
1	B-R	1. In patients undergoing isolated CABG, the use of a radial artery is recommended in preference to a saphenous vein conduit to graft the second most important, significantly stenosed, non–LAD vessel to improve long-term cardiac outcomes.[1-3]
1	B-NR	2. In patients undergoing CABG, an IMA, preferably the left, should be used to bypass the LAD when bypass of the LAD is indicated to improve survival and reduce recurrent ischemic events.[4-9]
2a	B-NR	3. In patients undergoing CABG, bilateral IMA (BIMA) grafting by experienced operators can be beneficial in appropriate patients to improve long-term cardiac outcomes.[3,10-12]

Synopsis

In the choice of conduits for CABG, both clinical and technical factors (eg, life expectancy, presence of diabetes, presence of CKD, degree of target stenosis) are considered (Table 12). Decades of data have supported the use of the LIMA to graft the LAD to prolong survival. These data are from observational studies and, for the most part, were derived before the introduction of current optimal medical therapy. The LIMA is preferable unless specific contraindications are present. The right IMA

Table 12. Best Practices for the Use of Bypass Conduits in CABG

Objectively assess palmar arch completeness and ulnar compensation before harvesting the radial artery. Use the arm with the best ulnar compensation for radial artery harvesting.
Use radial artery grafts to target vessels with subocclusive stenoses.
Avoid the use of the radial artery after transradial catheterization.
Avoid the use of the radial artery in patients with chronic kidney disease and a high likelihood of rapid progression to hemodialysis.
Use oral calcium channel blockers for the first postoperative year after radial artery grafting.
Avoid bilateral percutaneous or surgical radial artery procedures in patients with coronary artery disease to preserve the artery for future use.
Harvest the internal mammary artery using the skeletonization technique to reduce the risk of sternal wound complications.
Use an endoscopic saphenous vein harvest technique in patients at risk of wound complications.
Use a no-touch saphenous vein harvest technique in patients at low risk of wound complications.
Use the skeletonized right gastroepiploic artery to graft right coronary artery target vessels with subocclusive stenosis if the operator is experienced with the use of the artery.

CABG indicates coronary artery bypass graft.

can be used to graft the LAD if the LIMA is unusable, or the right IMA can be used in conjunction with the LIMA (BIMA grafting). Several randomized trials and meta-analyses have demonstrated better mid- and long-term patency rates for the radial artery than for the saphenous vein. A pooled analysis of 6 randomized trials has shown improved clinical outcomes at 10 years' follow-up.[13]

The right IMA is biologically equivalent to the LIMA, and BIMA grafting has shown a survival advantage compared with CABG with a single IMA in observational studies. The extensive use of arterial conduits (>2) instead of SVGs for multivessel CABG may provide an additional late mortality benefit compared with CABG with 2 arterial grafts.

Recommendation-Specific Supportive Text

1. Several randomized trials and meta-analyses have reported better mid- and long-term patency rates for the radial artery than for the saphenous vein,[2,14] while observational studies and meta-analyses have suggested a survival benefit when the radial artery is used instead of the saphenous vein for CABG.[3] A pooled analysis of 6 randomized trials showed improved clinical outcome with regard to adverse cardiac events at 5 and 10 years after surgery when the radial artery was used instead of the saphenous vein to revascularize the most important non-LAD artery coronary target.[1,13] Patients <75 years of age, women, and patients with preserved renal function seem to benefit the most from the use of the radial artery. The evidence is based largely on the use of the radial artery constructed as an aortocoronary graft. In observational studies, composite radial artery grafts have been found to be more vulnerable to the effect of chronic native competitive flow, but the evidence is limited.[15]
2. Data supporting the LIMA versus an SVG for grafting of the LAD are derived almost exclusively from observational studies reported 25 to 35 years ago.[5-7] In the CASS (Coronary Artery Surgery Study) registry, survival was improved in patients who received the LIMA-LAD compared with the SVG group after multivariable adjustment.[7] In another series of nearly 6000 patients undergoing CABG, LIMA grafting reduced deaths, recurrent infarction, rehospitalization for cardiac events, and repeat revascularization.[6] In this study, postoperative angiography revealed substantially higher LIMA patency. A single small RCT also found improved cardiac event–free survival at 10 years in the LIMA arm.[4,5]
3. The benefit of BIMA in CABG is supported by observational studies and in several meta-analyses.[3,10,11,16] A meta-analysis of 38 studies, including 174 205 patients, noted a decreased mortality rate at 7.25 years with BIMA use.[16] However, a single large RCT compared BIMA with single IMA in 3102 patients and reported no difference in 10-year all-cause mortality rate or in the composite of death, MI, or stroke.[12] However, a high rate of crossover was noted (14% from BIMA to single IMA, and 22% of the patients with a single IMA received a radial artery). An as-treated analysis reported improved survival in patients who received multiple arterial grafts.[12] Increasing BIMA volume was associated with protocol adherence, which suggests the importance of surgical expertise.[12] Low institutional BIMA volume has also been associated with a higher operative mortality rate with BIMA grafting.[17] Observational studies and 2 meta-analyses support the use of ≥3 arterial grafts, including total arterial revascularization.[18,19] The increased risk of sternal infection with BIMA grafting should be considered during preoperative planning.[17]

12.3. CABG in Patients Undergoing Other Cardiac Surgery

Recommendations for CABG in Patients Undergoing Other Cardiac Surgery
Referenced studies that support the recommendations are summarized in Online Data Supplement 38.

COR	LOE	Recommendations
1	C-LD	1. In patients undergoing valve surgery, aortic surgery, or other cardiac operations who have significant CAD, CABG is recommended with a goal of reducing ischemic events.[1-11]
2b	C-LD	2. In patients undergoing valve surgery, aortic surgery, or other cardiac operations who have intermediate CAD, CABG may be reasonable with a goal of reducing ischemic events.[5,7,10,12]

Synopsis

The decision to add CABG to another planned cardiac surgery in patients with significant CAD is multifactorial. Considerations include but are not limited to comorbidities, technical feasibility of CABG, extent of the jeopardized myocardium, availability of conduit, left ventricular ejection fraction, and the additional time needed to construct the coronary bypass while on cardiopulmonary bypass. A multidisciplinary discussion with a Heart Team can help weigh the risks and benefits of adding CABG to the index cardiac operation. Age does not appear to be a prohibitive risk factor for the addition of CABG to other cardiac surgery in patients between the ages of 75 and 84 years,[1,2,4] but risk increases in patients ≥85 years of age.[12] The available evidence supporting CABG at the time of cardiac surgery performed for another primary indication (ie, valve, aortic, or other cardiac surgery) is limited and complicated because many studies include patients with CAD defined as at least 1 vessel with stenosis ≥50%, thus including both intermediate and significant CAD. The knowledge that incomplete revascularization is associated with reduced long-term survival rates after surgery compared with patients who receive complete revascularization may inform decisions about adding CABG to other cardiac surgery.[5,10] Additionally, it has become standard practice to bypass significant coronary artery stenoses in patients undergoing other cardiac surgery.

Recommendation-Specific Supporting Text

1. Several observational studies and meta-analyses compared clinical outcomes in patients undergoing aortic valve replacement (AVR) with and without significant CAD (≥70% stenosis of any major epicardial coronary vessel, including side branches, or ≥50% stenosis of the left main).[6-9,12] Patients who underwent AVR with concomitant CABG demonstrated long-term survival and health-related quality of life similar to that of patients without CAD. Concomitant CABG may increase the risk of perioperative morbidity and mortality compared with isolated AVR.[2-4] In patients with significant CAD who underwent isolated AVR or AVR plus CABG, concomitant CABG was associated with a reduced late all-cause mortality rate (hazard ratio, 0.62; 95% CI, 0.49–0.79; $P<0.001$).[10] A large study of 6151 patients found that patients with extensive CAD (>50% left main stenosis or ≥3 diseased vessels) undergoing AVR with CABG had more comorbidities and had more perioperative morbidity, but not mortality, than did patients with less extensive CAD undergoing AVR with CABG.[12] A large study that propensity-matched patients undergoing AVR to patients undergoing AVR with CABG demonstrated no differences in morbidity or mortality between groups, which suggests that survival is dominated largely by patient comorbidities.[7] Studies focusing on CABG as a secondary procedure during other cardiac operations, including mitral valve, tricuspid valve, aortic, and pericardial surgery, are limited.
2. Limited data are available comparing CABG for intermediate CAD (stenosis, 40%–69%) in patients undergoing other cardiac surgery. Observational studies comparing patients undergoing AVR with and without CABG for intermediate CAD suggest that the addition of CABG may reduce ischemic events.[5,7,10,12] Patients with intermediate CAD may benefit from physiological testing with iFR or FFR to guide decision-making.

12.4. Use of Epiaortic Ultrasound in Patients Undergoing CABG

Recommendation for Use of Epiaortic Ultrasound in Patients Undergoing CABG
Referenced studies that support the recommendation are summarized in Online Data Supplement 39.

COR	LOE	Recommendation
2a	B-NR	1. In patients undergoing CABG, the routine use of epiaortic ultrasound scanning can be useful to evaluate the presence, location, and severity of plaque in the ascending aorta to reduce the incidence of atheroembolic complications.[1-10]

Synopsis

Atherosclerotic disease of the aorta is common in patients who undergo CABG surgery, with a reported prevalence that varies between 19% and 90%, depending on the patient population and modality of examination.[2,11-16] There has been a clear association between aortic atherosclerosis and stroke,[17] especially in patients undergoing CABG.[11,12,18-21] Epiaortic ultrasound has been demonstrated to be far superior to either surgical digital palpation or transesophageal echocardiography for defining the presence and extent of disease and has come to be recognized as the "gold standard" for the detection of aortic atherosclerosis.[13-15,22-24] There has been considerable variability in the extent to which epiaortic ultrasound has changed operative strategy, varying from 4% to 22%.[1,2,6,9,16]

Recommendation-Specific Supporting Text

1. The ability of routine epiaortic ultrasound to decrease stroke risk in patients undergoing CABG is unclear. One small prospective trial failed to meet a prespecified 50% difference in neurocognitive testing.[4] Although it is not uniformly reported,[3]

several large retrospective and registry studies,[1,2,6,7,9,10] as well as most single-center prospective studies, found an association with reduced risk of stroke.[3-5,8] Procedural risk, extra time required, and cost are minimal. The use of epiaortic ultrasound to evaluate the presence, location, and severity of atherosclerotic plaque in the ascending aorta allows for the intraoperative adjustment of operative technique to avoid atheroembolic complications.

12.5. Use of Cardiopulmonary Bypass in Patients Undergoing CABG

Recommendations for Use of Cardiopulmonary Bypass in Patients Undergoing CABG
Referenced studies that support the recommendations are summarized in Online Data Supplement 40.

COR	LOE	Recommendations
2a	B-R	1. In patients with significant calcification of the aorta, the use of techniques to avoid aortic manipulation (off-pump techniques or beating heart) is reasonable to decrease the incidence of perioperative stroke when performed by experienced surgeons.[1,2]
2b	B-R	2. In patients with significant pulmonary disease, off-pump surgery may be reasonable to reduce perioperative risk when performed by experienced surgeons.[2-6]

Synopsis

When the operative strategy for CABG for a patient is being planned, it may be determined that the risks of aortic manipulation preclude the safe use of a cross-clamp or cannulation of the ascending aorta, and significant pulmonary disease may increase risk of cardiopulmonary bypass. In such cases, the risks and benefits of alternative operative strategies (off-pump or beating heart) are considered, along with surgeon experience with such strategies. Excellent surgical results can be achieved by surgeons experienced in off-pump techniques with either on-pump or off-pump CABG.[2,4-15] The major concerns with the off-pump approach relate to the technical difficulty of bypassing coronary arteries in the circumflex distribution, as well as the small and intramyocardial segments. These issues have resulted in a tendency toward fewer grafts per patient,[2,16,17] a potential for incomplete revascularization,[2,15] and a concern about long-term graft patency.[17-20]

Recommendation-Specific Supportive Text

1. Off-pump CABG was developed to reduce the risks associated with cardiopulmonary bypass and aortic manipulation and the associated potential for neurological, renal, and myocardial injury. There are discrepant findings between observational and retrospective studies and prospective RCTs.[6,12,15,16,20,21] The use of an off-pump approach with minimized aortic manipulation may result in a decreased incidence of perioperative stroke in the presence of a calcified ascending aorta.[1,2] Reported short-term benefits of decreased blood product use and length of stay may be operator driven rather than procedure driven and may be achievable with either approach.[22] Reduced perioperative renal injury may not be sustained on longer follow-up.[23] To the extent that the off-pump technique permits less manipulation of the aorta, there appears to be a decreased incidence of perioperative stroke that is difficult to discern from individual studies.[1,2]
2. Off-pump CABG has been shown to be associated with earlier extubation, reduced blood transfusion, and reduced duration of mechanical ventilation compared with on-pump CABG and may improve outcomes for patients with increased pulmonary risk, which is perhaps related to avoidance of the systemic inflammatory response attributable to cardiopulmonary bypass and its impact on pulmonary function.[2-6]

13. PHARMACOTHERAPY IN PATIENTS UNDERGOING CABG

13.1. Insulin Infusion and Other Measures to Reduce Sternal Wound Infection in Patients Undergoing CABG

Recommendations for Insulin Infusion and Other Measures to Reduce Sternal Wound Infection in Patients Undergoing CABG
Referenced studies that support the recommendations are summarized in Online Data Supplement 41.

COR	LOE	Recommendations
1	B-R	1. In patients undergoing CABG, an intraoperative continuous insulin infusion should be initiated to maintain serum glucose level <180 mg/dL to reduce sternal wound infection.[1-3]
1	B-R	2. In patients undergoing CABG, the use of continuous intravenous insulin to achieve and maintain an early postoperative blood glucose concentration of <180 mg/dL while avoiding hypoglycemia is indicated to reduce the incidence of adverse events, including deep sternal wound infection.[3-6]
1	B-NR	3. In patients undergoing CABG, a comprehensive approach to reduce sternal wound infection is recommended.[7-14]
2b	B-R	4. In patients undergoing CABG, the usefulness of continuous intravenous insulin designed to achieve a target intraoperative blood glucose concentration <140 mg/dL is uncertain.[4,15]

Synopsis

Sternal wound infection has become less common in CABG surgery, with current rates reported to be <1%.[16] However, the associated risk of death may

Table 13. Best Practices to Reduce Sternal Wound Infection in Patients Undergoing CABG

Perform nasal swab testing for *Staphylococcus aureus*.[8]
Apply mupirocin 2% ointment to known nasal carriers of *S aureus*.[8]
Apply preoperative intranasal mupirocin 2% ointment to those patients whose nasal culture or PCR result is unknown.[8]
Redose prophylactic antimicrobials for long procedures (>2 half-lives of the antibiotic) or in cases of excessive blood loss during CABG.[10,11,27]
Measure perioperative HbA_{1c}.[31]
Treat all distant extrathoracic infections before nonemergency surgical coronary revascularization.[19]
Advise smoking cessation before elective CABG surgery.[7]
Apply topical antibiotics (vancomycin) to the cut edges of the sternum on opening and before closing in cardiac surgical procedures involving a median sternotomy.[4,32]
Use skeletonized harvest of IMA in BIMA grafting.[16]
Do not continue prophylactic antibiotics beyond 48 hours.[9,11]

BIMA indicates bilateral internal mammary artery; CABG, coronary artery bypass graft; HbA_{1c}, glycated hemoglobin A_{1c}; IMA, internal mammary artery; and PCR, polymerase chain reaction.

increase several-fold,[17] while the associated morbidity and expense can be considerable.[7] Management of hyperglycemia with perioperative insulin infusion to maintain a glucose level <180 mg/dL, both in patients with known diabetes and in patients with stress hyperglycemia, has emerged as an important strategy to prevent infection, as well as to improve survival and reduce recurrent ischemic events.[1-3,18,19] Continuous intravenous insulin infusion after CABG reduces postoperative complications, such as mediastinitis, cardiac arrhythmias, deep sternal would infections, renal failure, and length of stay.[3,5,6] In addition to standard antibiotic prophylaxis, several other strategies have emerged as best practices to reduce the risk of sternal infection (Table 13).

Recommendation-Specific Supportive Text

1. Continuous intravenous infusion of insulin is effective in maintaining blood glucose <180 mg/dL in patients undergoing CABG with the intent of reducing the risk of sternal wound infection. Perioperative glucose management has been found to be effective both in patients who are recognized to have diabetes and in those who experience stress hyperglycemia.[1-3,19]
2. The optimal level of glycemic control needed to improve outcomes in patients undergoing cardiac surgery remains controversial. One study evaluating intensive insulin therapy to target a glucose level of between 100 mg/dL and 140 mg/dL in the intensive care unit did not demonstrate reduced perioperative complications after CABG compared with a target glucose level of between 141 mg/dL and 180 mg/dL.[4] An RCT and multiple observational studies have demonstrated that continuous intravenous insulin infusion is associated with reduced variability in glucose concentration, reduced hospital length of stay, reduced ischemic events, reduced wound complications, and improved survival compared with subcutaneous insulin in patients with diabetes who undergo CABG.[3,5,6,20,21]
3. With an aggressive preventive approach, some centers report zero incidence of sternal infection.[14,22] However, there is no evidence-based preventive "bundle."[7,23-25] Strong evidence supports the perioperative administration of antibiotics,[9,26] with general agreement that continuation of prophylactic antibiotics for >48 hours lacks additional benefit. Mupirocin has been found to be effective in reducing *Staphylococcus aureus* infection in patients who are nasal carriers, and there is no evidence that it is beneficial for those who are not. Topical vancomycin paste may have benefit,[11,14,22] whereas the formerly ubiquitous use of bone wax is falling into increasing disfavor.[12,13,27] The use of BIMAs as bypass conduits has generally been associated with an increased risk of sternal wound infection,[28] although there is considerable center-specific evidence that this risk can be ameliorated by use of the "skeletonized" technique,[29] which may cause less disruption of sternal perfusion and lymphatic drainage.
4. An RCT of 400 patients compared intraoperative intensive treatment (glucose levels 80–100 mg/dL) or conventional treatment (insulin given only for a glucose concentration ≥200 mg/dL)[15] and found no difference between groups in a composite endpoint of death, deep sternal wound infection, prolonged ventilation, cardiac arrhythmias, stroke, or renal failure within 30 days. There was an increased incidence of death and stroke in the patients who received intensive treatment.[15] In another RCT, 381 patients without diabetes undergoing isolated CABG were given intraoperative infusions of insulin or placebo when their blood glucose concentrations exceeded 100 mg/dL. Insulin infusion during cardiopulmonary bypass had no significant effect on the combined incidence of neurological, neuro-ophthalmologic, or neurobehavioral deficits or neurological death and did not shorten the length of hospital stay.[30] Thus, these data highlight the evidence that extremely tight control of blood glucose after CABG is not associated with improved outcomes.

13.2. Antiplatelet Therapy in Patients Undergoing CABG

Recommendations for Antiplatelet Therapy in Patients Undergoing CABG
Referenced studies that support the recommendations are summarized in Online Data Supplement 42.

COR	LOE	Recommendations
1	B-R	1. In patients undergoing CABG who are already taking daily aspirin preoperatively, it is recommended that they continue taking aspirin until the time of surgery to reduce ischemic events.[1-7]
1	B-NR	2. In patients referred for urgent CABG, clopidogrel and ticagrelor should be discontinued for at least 24 hours before surgery to reduce major bleeding complications.[8-11]
1	B-NR	3. In patients undergoing CABG, discontinuation of short-acting glycoprotein IIb/IIIa inhibitors (eptifibatide and tirofiban) for 4 hours and abciximab for 12 hours before surgery is recommended to reduce the risk of bleeding and transfusion.[12-14]
2a	B-NR	4. In patients undergoing elective CABG who receive P2Y12 receptor inhibitors before surgery, it is reasonable to discontinue clopidogrel for 5 days, ticagrelor for 3 days, and prasugrel for 7 days before CABG to reduce risk of major bleeding and blood product transfusion.[8,9,11,15-23]
3: No benefit	B-R	5. In patients undergoing elective CABG who are not already taking aspirin, the initiation of aspirin (100–300 mg daily) in the immediate preoperative period (<24 hours before surgery) is not recommended.[24,25]

Synopsis

The use of aspirin and antiplatelet agents in patients undergoing CABG is discussed with the Heart Team to determine the optimal treatment for each patient, with careful consideration of the risk of myocardial ischemia, significant bleeding, reoperation, and transfusion. The present recommendations are based on the severity of the patient's condition and the associated surgical necessity. When the various therapies are considered, the urgency of the planned surgery should be determined, as outlined in Table 7 (Section 5.2).[26,27]

Recommendation-Specific Supporting Text

1. Most patients who undergo CABG are already taking aspirin for primary or secondary prevention of new cardiovascular events. Early observational data showed an association between preoperative aspirin administration and reduced in-hospital mortality rate.[1,2] Although more recent meta-analyses of randomized and nonrandomized trials have yielded somewhat conflicting results, continuation of existing preoperative aspirin is likely associated with a reduction in the risk of MI but not death.[3-5] Continuation of aspirin until the time of surgery is associated with an increased risk of perioperative bleeding and transfusion, although this does not appear to increase the likelihood of surgical reoperation.[3-7] Patients at risk of significant bleeding (eg, redo operations or underlying bleeding dyscrasias) may warrant individualized consideration but are underrepresented in the literature.
2. The coadministration of aspirin and a P2Y12 receptor inhibitor (ie, clopidogrel, ticagrelor, prasugrel) is common, particularly in the setting of ACS or recent stent placement. In such patients, the risk of ischemic events must be weighed against the risks of bleeding when decisions are made about the cessation of P2Y12 receptor inhibitors before CABG.[8-11]
3. Glycoprotein IIb/IIIa inhibitors (ie, eptifibatide, tirofiban, abciximab) are sometimes given to patients who are at high risk of acute ischemic events while they are awaiting CABG. The therapeutic half-life for each glycoprotein IIb/IIIa inhibitor, in addition to a patient's renal function, are considered in the determination of safe discontinuation before CABG, and data from observational studies have established optimal cessation periods before CABG for each agent with reasonable safety profiles.[12-14] Abciximab may not be readily available to clinicians in the United States.
4. CABG performed <5 days after the discontinuation of clopidogrel is associated with an increased risk of major bleeding complications, such as tamponade or reoperation, a finding that was suggested by early observational data.[9,15] and confirmed by more recent randomized and nonrandomized trials.[10,16-18] Early experience also suggested that preoperative ticagrelor should be withheld for a similar time frame (5 days) before surgery to reduce bleeding and blood product administration.[11,19] However, platelet inhibition assay results from 1 randomized study[20] and more recent data from 2 separate observational trials have revealed that delaying surgery for 72 hours is likely sufficient.[8,21] The timing for prasugrel is less established but results from the TRITON-TIMI-38 trial suggested that among patients who underwent CABG, prasugrel resulted in a higher rate of major bleeding than that seen with clopidogrel.[22] In a subset of patients in the ACCOAST (A Comparison of Prasugrel at PCI or Time of Diagnosis of Non–ST-Elevation Myocardial Infarction) study, early surgery (<3 days after discontinuation of prasugrel) led to an increased risk of bleeding and ischemic complications, whereas later surgery (>7 days) did not.[23]
5. Initiation of aspirin therapy in the immediate preoperative period (<24 hours) has been investigated in 2 randomized trials. In the first trial,[24] patients undergoing CABG who received 100 mg of aspirin

1 to 2 hours before surgery experienced a composite outcome of death and thrombotic complications at 30 days and an incidence of major bleeding and cardiac tamponade that were similar to those seen with placebo.[24] In the second trial,[25] patients randomized to receive 300 mg of aspirin the night before surgery had increased episodes of major bleeding (>750 mL in 24 hours, or 1000 mL overall) and increased transfusion rates, but no significant differences were found in major cardiovascular events at early (30 days) or long-term (36 months) time points[25] compared with placebo.

13.3. Beta Blockers and Amiodarone in Patients Undergoing CABG

Recommendations for Beta Blockers and Amiodarone in Patients Undergoing CABG
Referenced studies that support the recommendations are summarized in Online Data Supplement 43.

COR	LOE	Recommendations
2a	B-R	1. In patients undergoing CABG, who do not have a contraindication to beta blockers, the administration of beta blockers before surgery can be beneficial to reduce the incidence of postoperative atrial fibrillation.[1-8]
2a	B-R	2. In patients undergoing CABG, preoperative amiodarone is reasonable to reduce the incidence of postoperative atrial fibrillation.[9-11]
2b	B-NR	3. In patients undergoing CABG, who do not have a contraindication to beta blockers, preoperative use of beta blockers may be effective in reducing in-hospital and 30-day mortality rates.[12-18]
2b	B-NR	4. In patients undergoing CABG, the role of preoperative beta blockers for the prevention of acute postoperative myocardial ischemia, stroke, AKI, or ventricular arrhythmia is uncertain.[12-14,18]

Synopsis

In patients undergoing elective CABG, the risks and benefits of beta-blocker and amiodarone administration before surgery should be carefully considered. Although preoperative beta blockers are associated with reduced incidence of postoperative atrial fibrillation, recent data, including meta-analyses of RCTs and several large observational trials, have yielded conflicting results with regard to their impact on other outcomes, including death, MACE, and other arrhythmias.

Recommendation-Specific Supporting Text

1. Several small RCTs[1-5] and multiple meta-analyses of RCTs[6-8] have investigated preoperative beta blockers and found that their use is associated with a reduced incidence of atrial fibrillation after CABG. Although the recommendation stems from what is considered high-quality evidence, full interpretation of the data is limited because the trials tended to incorporate multiple intervention arms, had variable timing of initiation of therapy, and were unable to establish the relative impact of preoperative beta-blocker administration in the context of postoperative use. The overwhelming majority of trials investigating the use of preoperative beta blockers are confounded by concomitant postoperative administration. As a result, the optimal agent selection, schedule, and duration to prevent atrial fibrillation are unclear.
2. Studies have demonstrated that preoperative prophylactic oral amiodarone significantly decreased the incidence of postoperative atrial arrhythmias and stroke and reduced hospital length of stay compared with placebo without any adverse complications other than occasional bradycardia.[9,11,19] Amiodarone may cause toxicity or systemic hypotension, and thus its use is determined on an individualized basis, particularly in patients who are at high risk of developing atrial fibrillation.
3. Results from a large observational database suggested that preoperative beta-blocker administration was associated with a reduction in in-hospital and 30-day mortality rate after CABG.[16] These findings underpin the inclusion of preoperative beta blockers as a quality indicator for CABG surgery. Newer observational studies have yielded more conflicting results,[12-14] showing little or no mortality benefit, particularly when comparisons between propensity-matched participants are analyzed. Beta-blocker pharmacogenetic variation may have a role. One study found that, when compared with no preoperative beta blockers, noncytochrome P4502D6 metabolized agents (ie, atenolol and sotalol) were associated with a lower incidence of operative death; however, P4502D6 metabolized agents (ie, metoprolol, propranolol, carvedilol, and labetalol) were not.[17] The impact of preoperative beta-blocker administration in patients with reduced left ventricular ejection fraction requires additional investigation.[15,16]
4. Observational studies do not reveal a consistent association between preoperative beta-blocker use and other postoperative outcomes, including myocardial ischemia, stroke or transient ischemic attack, and AKI.[12-14] An area that likely requires further investigation is the efficacy of preoperative beta blockers in the prevention of ventricular arrhythmias. One meta-analysis of RCTs did suggest improved rates of ventricular arrhythmia, but most of the studies included the outcome as a secondary endpoint.[6,18] Patients undergoing CABG who receive beta blockers are closely monitored for bradycardia or hypotension, with subsequent dose adjustment to avoid these adverse effects .[4-7]

14. PHARMACOTHERAPY IN PATIENTS AFTER REVASCULARIZATION

14.1. Pharmacotherapy for Risk Factor Control in Patients After Revascularization

Patients undergoing coronary revascularization require aggressive secondary preventive measures, including lifestyle modifications and medications for control of cholesterol, blood sugar, and blood pressure, as well as antiplatelet therapies. A detailed discussion of the pharmacotherapies used for secondary prevention after revascularization and the lifestyle measures used to optimize heart health are beyond the scope of the present guideline and are discussed in more detail elsewhere.[1-4] This section will focus on the therapies that are especially relevant to patients undergoing revascularization.

14.2. Dual Antiplatelet Therapy in Patients After PCI

Recommendation for Dual Antiplatelet Therapy in Patients After PCI
Referenced studies that support the recommendation are summarized in Online Data Supplement 44.

COR	LOE	Recommendation
2a	A	1. In selected patients undergoing PCI, shorter-duration DAPT (1–3 months) is reasonable, with subsequent transition to P2Y12 inhibitor monotherapy to reduce the risk of bleeding events.[1-4]

Synopsis

After PCI, the use of DAPT prevents stent thrombosis and reduces ischemic events at the cost of increased bleeding.[5] Pooled data have demonstrated less bleeding with shorter-term DAPT (3–6 months) and fewer ischemic events (including stent thrombosis) with longer-term DAPT (>12 months)[5] (Figure 7). The 2016 guideline focused update on duration of DAPT[6] highlights the importance of balancing ischemic and bleeding risk when DAPT is considered and provides recommendations for short and prolonged DAPT followed by aspirin monotherapy after revascularization. Since the release of those guidelines, more recent trials have been published.[1-4,7] For this reason, additional recommendations for DAPT are provided. These recommendations should act as a supplement to the prior guideline focused update. Given the multiplicity of possible antiplatelet regimens available for use after revascularization, clinicians should weigh the risks of bleeding and recurrent ischemia when determining the choice of DAPT.

Recommendation-Specific Supporting text

1. Since the 2016 guideline focused update, 5 large trials have tested a strategy of shorter-duration DAPT followed by P2Y12 inhibitor monotherapy after PCI.[1-4,7] DAPT durations ranged from 1 month[3,7] to 3 months.[1,2,4] In aggregate, these data support a shorter course of DAPT followed by P2Y12 monotherapy, with a reduction in bleeding events (when compared with standard DAPT) and equivalent rates of ischemic events. Most supported clopidogrel and ticagrelor monotherapy, but prasugrel monotherapy was included in 1 trial.[2] A meta-analysis of the duration of DAPT incorporating these 5 trials reported a 40% reduction in the rate of major bleeding events with shorter-term DAPT followed by P2Y12 monotherapy and no significant difference in MACE. The trials evaluating the use of shorter-duration DAPT followed by P2Y12 monotherapy were not powered to assess differences in stent thrombosis. These trials included few patients with STEMI. No trial has compared short-term DAPT followed by P2Y12 monotherapy with short-term DAPT followed by aspirin alone.

14.3. Antiplatelet Therapy in Patients After CABG

Recommendations for Antiplatelet Therapy in Patients After CABG
Referenced studies that support the recommendations are summarized in Online Data Supplement 45.

COR	LOE	Recommendations
1	A	1. In patients undergoing CABG, aspirin (100–325 mg daily) should be initiated within 6 hours postoperatively and then continued indefinitely to reduce the occurrence of SVG closure and adverse cardiovascular events.[1-7]
2b	B-R	2. In selected patients undergoing CABG, DAPT with aspirin and ticagrelor or clopidogrel for 1 year may be reasonable to improve vein graft patency compared with aspirin alone.[8-10]

Synopsis

The mechanisms warranting DAPT therapy in patients who have undergone CABG are distinct from those in patients who have had ACS and have undergone PCI. The pathophysiology of vein graft occlusion involves a different mechanism from that of native vessel disease with atherosclerosis, plaque rupture, or stent thrombosis. Additionally, a larger percentage of the coronary tree is bypassed with CABG in contrast to the focal lesions treated with PCI. Finally, surgical bleeding is more of a concern in the perioperative and immediate postoperative period following CABG. Observational and small randomized trials and meta-analyses of these studies support that DAPT after CABG improves vein graft patency, primarily among patients undergoing off-pump surgery and those with higher SYNTAX scores. The role of DAPT in patients who undergo CABG after ACS is addressed in the DAPT guideline.[11] The role of prolonged DAPT for

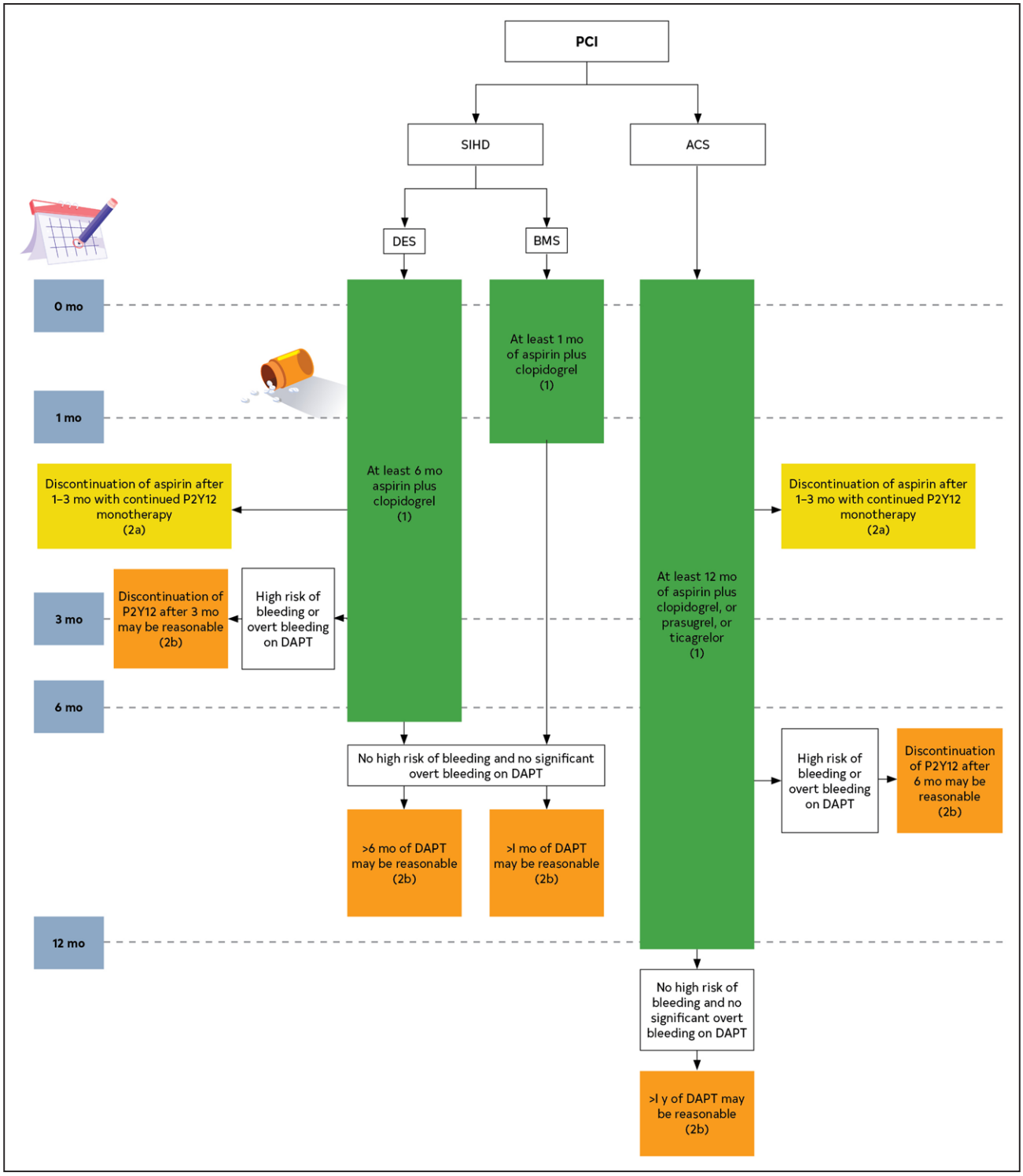

Figure 7. Use of DAPT for Patients After PCI.

Colors correspond to Table 2.

ACS indicates acute coronary syndrome; BMS, bare metal stent; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; P2Y12, platelet adenosine diphosphate P2Y12 receptor; PCI, percutaneous coronary intervention; and SIHD, stable ischemic heart disease. This algorithm is adapted from the 2016 DAPT guideline[6] and includes new recommendations from this guideline for the care of patients with CAD. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Additionally, in situations that lack sufficient data to make formal recommendations for care, please see Section 17, "Unanswered Questions and Future Directions."

general secondary prevention in patients with a distant history of CABG is not well established.

Recommendation-Specific Supporting Text

1. Surgical bleeding remains a concern in the perioperative and immediate postoperative periods, and therefore bleeding risk is an important consideration in the use of antiplatelet therapy. Older data have shown that aspirin improves vein graft patency.[1,2,5,6] Although 1 small study demonstrated higher rates of bleeding with aspirin after CABG,[12] the totality of evidence supports the early use[1-6] of aspirin to improve SVG patency and reduce ischemic complications.
2. Small RCTs, observational data, and meta-analyses have demonstrated that DAPT (mostly with aspirin and clopidogrel) after CABG improves vein graft patency, primarily among patients undergoing off-pump surgery. The DACAB (Different Antiplatelet Therapy Strategy After Coronary Artery Bypass Graft Surgery) trial[10] compared DAPT with a single antiplatelet regimen in 500 patients undergoing CABG. Off-pump procedures were performed in 75% of these patients. At 1-year follow-up, the DAPT group was found to have the highest vein graft patency, when assessed with coronary computed tomography angiogram, compared with aspirin alone.

14.4. Beta Blockers in Patients After Revascularization

Recommendation for Beta Blockers in Patients After Revascularization Referenced studies that support the recommendation are summarized in Online Data Supplement 46.		
COR	**LOE**	**Recommendation**
3: No benefit	**C-LD**	1. In patients with SIHD and normal left ventricular function, the routine use of chronic oral beta blockers is not beneficial to reduce cardiovascular events after complete revascularization.[1-6]

Synopsis

In patients who have undergone revascularization, the risks and benefits of beta blockers should be considered before the initiation of therapy. The benefit of beta blockers for secondary prevention after acute infarction or for those with left ventricular dysfunction has been clearly reported in clinical trials examining these subgroups, and recommendations based on this evidence are outlined in previous guidelines.[7,8] However, in patients without acute infarction or left ventricular dysfunction, there is a paucity of data to support a benefit of the routine use of beta blockers after revascularization, especially in patients without residual disease. Further risk reduction may not be useful in patients after MI with normal left ventricular ejection fraction in the presence of GDMT with antiplatelet treatment, statins, and angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. Thus, in the absence of new data to guide current therapy, clinicians will need to make decisions on an individualized basis.

Recommendation-Specific Supportive Text

1. A large meta-analysis of patients undergoing PCI for stable angina showed no differences in adjusted rates of death, MI, stroke, or revascularization but a higher rate of heart failure readmissions among patients who were prescribed a beta blocker at hospital discharge.[1] The REACH (Reduction of Atherothrombosis for Continued Health) Registry's investigators showed that, after a median of 44 months' follow-up, beta-blocker use was not associated with a reduction in the composite cardiovascular outcome in a large cohort of patients with SIHD.[2] Additional studies have also supported an increased incidence of heart failure in patients treated with beta blockers in the reperfusion era.[9] In a large cohort of patients with newly diagnosed CAD, a modest benefit of beta-blocker use was reported, although this benefit was noted only in patients with a previous MI.[4] Hence, the decision to continue beta blockers in the long term in patients after revascularization should be made on an individualized basis.

14.5. Beta Blockers for the Prevention of Atrial Fibrillation After CABG

Recommendation for Beta Blockers for the Prevention of Atrial Fibrillation After CABG Referenced studies that support the recommendation are summarized in Online Data Supplement 47.		
COR	**LOE**	**Recommendation**
1	**B-R**	1. In patients after CABG, beta blockers are recommended and should be started as soon as possible to reduce the incidence or clinical sequelae of postoperative atrial fibrillation.[1-7]

Synopsis

New-onset postoperative atrial fibrillation occurs in about 18% of patients after CABG and is associated with a 4-fold increased risk of stroke and a 3-fold increase in all-cause mortality rate.[8,9] Postoperative atrial fibrillation after CABG can be challenging to prevent and treat.

Recommendation-Specific Supportive Text

1. RCTs have yielded conflicting results with regard to the ability of beta blockers to influence perioperative cardiovascular morbidity and mortality. A large meta-analysis found that beta-blocker use may reduce the incidence of atrial fibrillation and

ventricular arrhythmias and hospital stay[10] but found no evidence of a difference in rates of early all-cause death, MI, cerebrovascular events, hypotension, or bradycardia.[10]

14.6. Antiplatelet Therapy in Patients With Atrial Fibrillation on Anticoagulation After PCI

Recommendations for Antiplatelet Therapy in Patients With Atrial Fibrillation on Anticoagulation After PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 48.

COR	LOE	Recommendations
1	B-R	1. In patients with atrial fibrillation who are undergoing PCI and are taking oral anticoagulant therapy, it is recommended to discontinue aspirin treatment after 1 to 4 weeks while maintaining P2Y12 inhibitors in addition to a non–vitamin K oral anticoagulant (rivaroxaban, dabigatran, apixaban, or edoxaban) or warfarin to reduce the risk of bleeding.[1-7]
2a	B-R	2. In patients with atrial fibrillation who are undergoing PCI, are taking oral anticoagulant therapy, and are treated with DAPT or a P2Y12 inhibitor monotherapy, it is reasonable to choose a non–vitamin K oral anticoagulant over warfarin to reduce the risk of bleeding.[1,3,4]

Synopsis

Patients undergoing PCI frequently have or develop concomitant indications for anticoagulant therapy, including atrial fibrillation, venous thromboembolism, and prosthetic heart valves. The most robust evidence for anticoagulant management in such patients comes from trials in patients with atrial fibrillation. The 2019 focused update of the atrial fibrillation guidelines[8] gave a Class 2a recommendation to a P2Y12 inhibitor with a non–vitamin K oral anticoagulant (rivaroxaban or dabigatran) or a vitamin K antagonist (warfarin) rather than triple therapy with an anticoagulant and DAPT. Since the publication of this guideline focused update, there have been 2 additional trials[1,4] examining the benefits of dual anticoagulant therapy after PCI in patients with atrial fibrillation. On the basis of analyses of these trials, the recommendations for antiplatelet and anticoagulant therapy after PCI in patients with atrial fibrillation have been updated.

Recommendation-Specific Supporting Text

1. Two recent trials—the AUGUSTUS (Safety and Efficacy of Apixaban Versus Vitamin K Antagonist and Aspirin Versus Aspirin Placebo in Patients With Atrial Fibrillation and ACS and/or PCI) trial[1] and the ENTRUST-AF-PCI (Edoxaban–Based Versus Vitamin K Antagonist–Based Antithrombotic Regimen After Successful Coronary Stenting in Patients With Atrial Fibrillation) trial[4]—examined regimens of apixaban and edoxaban and supported earlier findings,[6,7] reporting lower bleeding rates in patients with atrial fibrillation who were treated with a non–vitamin K oral anticoagulant and P2Y12 inhibitor than in those treated with triple therapy after PCI. Although none of the trials was powered for ischemic endpoints, pooled data from these trials[1] have shown rates of death, MI, and stent thrombosis with dual therapy that are similar to those seen with triple therapy. All patients enrolled in these trials were briefly treated with triple therapy after PCI before the aspirin was discontinued. An analysis of stent thrombosis rates suggested that 80% of events occur within 30 days of PCI.[3] For this reason, it is possible that prolonging aspirin therapy to 1 month after PCI may reduce the risk of stent thrombosis.[3] Therefore, in patients deemed to be at high risk of stent thrombosis, aspirin could be maintained for up to 30 days.
2. The AUGUSTUS trial[2] randomized patients with atrial fibrillation undergoing PCI and found that apixaban, as compared with warfarin, reduced the rate of bleeding and was associated with a lower incidence of the combined endpoint of death or hospitalization. Compared with other treatment regimens, the combination of apixaban with a P2Y12 inhibitor was associated with the lowest rates of bleeding. The ENTRUST-AF-PCI trial[4] compared edoxaban and P2Y12 monotherapy with triple therapy with a vitamin K antagonist in patients with atrial fibrillation undergoing PCI. Although there were fewer bleeding events in the first 14 days in the vitamin K antagonist arm, a landmark analysis from 14 days onward demonstrated less bleeding in the dual-therapy group.

15. RECOMMENDATIONS FOR ADDRESSING PSYCHOSOCIAL FACTORS AND LIFESTYLE CHANGES AFTER REVASCULARIZATION

15.1. Cardiac Rehabilitation and Education

Recommendations for Cardiac Rehabilitation and Education
Referenced studies that support the recommendations are summarized in Online Data Supplement 49.

COR	LOE	Recommendations
1	A	1. In patients who have undergone revascularization, a comprehensive cardiac rehabilitation program (home based or center based) should be prescribed either before hospital discharge or during the first outpatient visit to reduce deaths and hospital readmissions and improve quality of life.[1-4]
1	C-LD	2. Patients who have undergone revascularization should be educated about CVD risk factors and their modification to reduce cardiovascular events.[5-7]

Synopsis

Cardiac rehabilitation is an evidence-based intervention comprising patient education, behavior modification, and exercise training to improve secondary prevention outcomes in patients with CVD.[8] Cardiac rehabilitation assists patients with adherence to healthy lifestyle habits; addresses comorbid conditions (eg, diabetes); monitors for safety issues, including new or recurrent symptoms; and facilitates adherence to evidence-based medical therapies.[9] Cardiac rehabilitation may include a center-based cardiac rehabilitation program that incorporates face-to-face supervised exercise or an alternative cardiac rehabilitation delivery model that meets criteria for safety and effectiveness, as specified by the cardiac rehabilitation guidelines of the American Association of Cardiovascular and Pulmonary Rehabilitation.[10]

Recommendation-Specific Supportive Text

1. The safety and effectiveness of the traditional, medically supervised center-based cardiac rehabilitation model are well established. Observational studies and RCTs have demonstrated that center-based cardiac rehabilitation is effective in reducing hospital readmissions, secondary events, and deaths in patients with CVD.[1,2,4,11] Guidelines and standards of care have been well defined for center-based cardiac rehabilitation, including core components,[10] core competencies,[12] clinical practice guidelines,[13] performance measures,[12] and certification (program and individual).[9] Home-based cardiac rehabilitation can help improve delivery of cardiac rehabilitation to eligible patients by overcoming common barriers that impede a patient's participation in center-based cardiac rehabilitation, including transportation challenges, competing time demands, and lack of a center-based cardiac rehabilitation program near the patient's home.[14] Core components of home-based cardiac rehabilitation are similar to those for center-based cardiac rehabilitation.[14] Cochrane reviews concluded that home- and center-based cardiac rehabilitation have similar effects on quality of life and costs among patients with recent MI or coronary revascularization.[15-17]
2. Patients and caregivers should receive a comprehensive plan of care and educational materials during the hospital stay that support adherence to evidence-based therapies. The "2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease"[18] provides comprehensive recommendations for improving risk factors for CVD (unhealthy dietary pattern, lack of exercise and physical activity, obesity, diabetes, high blood cholesterol, hypertension, and tobacco use). This information and management can be accomplished in a center-based or a home-based cardiac rehabilitation program and should be tailored to age, health literacy, cultural practices, and socioeconomic status.[7] The basic self-care activities important to CVD management are captured in the AHA's Life's Simple 7 program (eg, smoking cessation, maintenance of body mass index, physical activity, healthy diet, maintaining low cholesterol, maintaining normal blood pressure, and maintaining normal fasting plasma glucose).[19]

15.2. Smoking Cessation in Patients After Revascularization

Recommendations for Smoking Cessation in Patients After Revascularization
Referenced studies that support the recommendations are summarized in Online Data Supplement 50.

COR	LOE	Recommendations
1	A	1. In patients who use tobacco and have undergone coronary revascularization, a combination of behavioral interventions plus pharmacotherapy is recommended to maximize cessation and reduce adverse cardiac events.[1-3]
1	A	2. In patients who use tobacco and have undergone coronary revascularization, smoking cessation interventions are recommended during hospitalization and should include supportive follow-up for at least 1 month after discharge to facilitate tobacco cessation and reduce morbidity and mortality.[4-6]

Synopsis

Tobacco use, especially cigarette smoking, is a major risk factor for cardiovascular morbidity and mortality and is the leading preventable cause of death worldwide.[6,7] Among patients with coronary heart disease, continued cigarette smoking after revascularization is associated with adverse clinical outcomes,[8] particularly stent thrombosis.[9] Electronic nicotine delivery systems or e-cigarettes[10] are a class of tobacco product that emit aerosol containing fine and ultrafine particulates, nicotine, and toxic gases that may increase risk of CVD and pulmonary disease.[11-13] The dominant pattern of e-cigarette use in adults is dual use of both combustible cigarettes and e-cigarettes.[14,15] When patients are counseled about risk factor management after revascularization, the topic of tobacco abuse is paramount and timely, because patients who are hospitalized after revascularization are often at their most attentive state. The recommendations for smoking cessation counseling and treatment are outlined in the "2019 ACC/AHA Guideline on the Primary Prevention

of Cardiovascular Disease"[16] and are also applicable to the secondary prevention of patients after coronary artery revascularization.

Recommendation-Specific Supportive Text

1. The US Public Health Service's *Clinical Practice Guideline for Smoking Cessation* recommends smoking-cessation pharmacotherapy for all smokers attempting to quit.[17] The most effective smoking-cessation therapies include both behavioral and pharmacological interventions.[1,6] High-quality evidence showed that using a combination of behavioral support and medication increases the chances of successfully quitting for at least 6 months.[2,5] Moreover, the chance of success was increased by 70% to 100% compared with just brief advice or support. Among patients with CVD who were motivated to quit smoking, varenicline and bupropion are efficacious for smoking cessation, as are individual and telephone counseling.[2,5] Varenicline was the most efficacious of therapies in patients with stable CVD who were motivated to quit smoking.[2,5,18,19] In 1 study, abstinence rates in the group of patients treated with varenicline were higher than in those treated with placebo, a result that persisted for 52 weeks.[19] Given the uncertainties of the long-term effects of e-cigarettes on health, clinicians have been urged to advise cigarette smokers seeking to quit to use evidence-based, US Food and Drug Administration–approved, safe and effective smoking cessation pharmacotherapies as first-line treatments in preference to e-cigarettes.[7]
2. Studies have shown that when hospitalized tobacco users receive counseling with supportive follow-up for ≥1 month after discharge, smoking cessation rates increase by 37% at 6 to 12 months after discharge.[4] Varenicline use for hospitalized smokers with ACS who were motivated to quit significantly increased abstinence versus placebo at 1 year after discharge.[20-22] At week 24, using varenicline increased smoking abstinence and reduced cigarette use by ≥50%. There is no evidence that pharmacotherapies (varenicline, bupropion, and nicotine replacement versus placebo) increase the risk of cardiovascular adverse events during or after treatment.[19,21,23] The EAGLES (Neuropsychiatric Safety and Efficacy of Varenicline, Bupropion, and Nicotine Patch in Smokers With and Without Psychiatric Disorders) trial showed that pharmacotherapies do not increase the risk of cardiovascular or neuropsychiatric adverse events compared with nicotine patch or placebo in smokers with and without psychiatric disorders.[18,23]

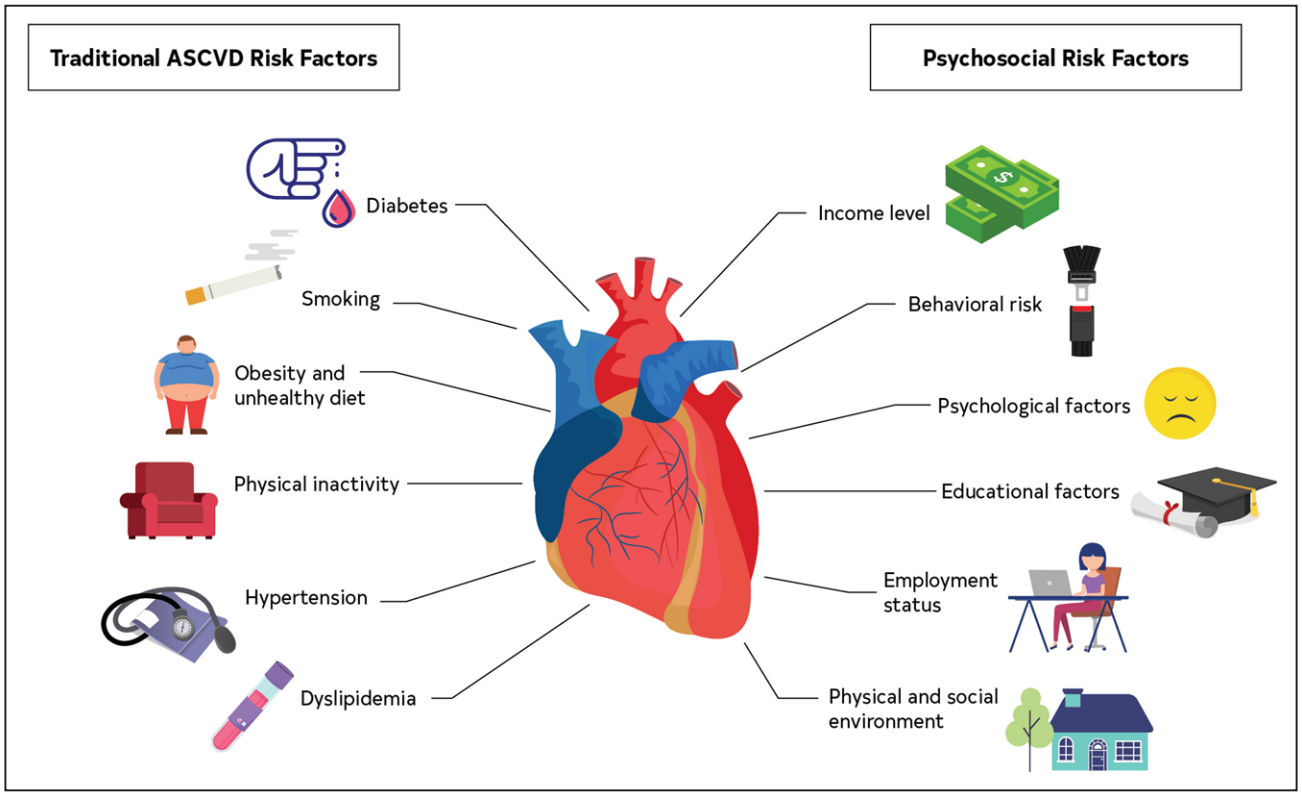

Figure 8. Traditional and Psychosocial Risk Factors for ASCVD.
ASCVD indicates atherosclerotic cardiovascular disease.

15.3. Psychological Interventions in Patients After Revascularization

Recommendations for Psychological Interventions in Patients After Revascularization Referenced studies that support the recommendations are summarized in Online Data Supplement 51.		
COR	**LOE**	**Recommendations**
1	**B-R**	1. In patients who have undergone coronary revascularization who have symptoms of depression, anxiety, or stress, treatment with cognitive behavioral therapy, psychological counseling, and/or pharmacological interventions is beneficial to improve quality of life and cardiac outcomes.[1-7]
2b	**C-LD**	2. In patients who have undergone coronary revascularization, it may be reasonable to screen for depression and refer or treat when it is indicated to improve quality of life and recovery.[8,9]

Synopsis

Cardiac events and coronary revascularization can be distressing life events that lead to psychosocial morbidity.[10-13] Anxiety, depression, and stress are associated with poor adherence to healthy behaviors and prescribed medications, compromised quality of life, increased health care costs, and increased recurrent cardiac events[12,14-18] and are independent risk factors for CVD morbidity and mortality[19-24] (Figure 8). Presurgery estimates of depression in patients undergoing CABG range from 14% to 43%,[23,25-27] and depression increases length of hospital stay[28] and mortality rate.[14,23,29] About 20% of patients who undergo CABG remain depressed postoperatively.[30] Several psychological therapies have been used as part of secondary prevention to improve psychological outcomes. These include relaxation and stress management, enhancement of coping skills, and cognitive behavioral therapy, many of which are incorporated into cardiac rehabilitation programs.[3,31]

Recommendation-Specific Supportive Text

1. In the EsDEPACS (Escitalopram for Depression in Acute Coronary Syndrome) trial, escitalopram was superior to placebo in reducing depression during the 24-week trial.[32] Long-term follow-up showed that escitalopram resulted in a significantly lower risk of MACE and MI but not death.[2] The ENRICHD (Enhancing Recovery in Coronary Heart Disease Patients) trial demonstrated that therapy with counseling or selective serotonin reuptake inhibitors was associated with improved depression but not event-free survival after 24 months of follow-up.[5] A subgroup analysis of this study, however, found a 42% lower risk of death or MI in patients treated with a selective serotonin reuptake inhibitor.[33] The Bypassing the Blues trial randomized depressed patients undergoing CABG to 8 months of collaborative care or usual care and demonstrated a 50% reduction in depression scores and improved quality of life in the collaborative care group.[7,34] A meta-analysis of these trials reported a reduction in cardiovascular deaths but not overall deaths, MI, or revascularization with psychological interventions.[1] These interventions also improved depression, anxiety, and stress as compared with controls.[1]
2. Depression remains an important comorbidity after revascularization, and treatment options are underused. On the basis of observational data and the availability of effective depression treatments,[35] multiple professional societies recommend depression screening for patients with ACS, followed by treatment when depression is identified.[8,19,36,37] Programs combining depression screening, with support systems in place, improve clinical outcomes in adults.[1] However, in the CODIACS-QoL (Comparison of Depression Interventions After Acute Coronary Syndrome: Quality of Life) trial evaluating 1500 patients with ACS without a history of depression, providing universal depression screening and notifying treating clinicians of positive results of screening, either with or without provision of enhanced depression care, did not alter quality of life, depression-free days, depressive symptoms, mortality rate, or patient-reported harms in patients with ACS.[9] In this trial, a smaller-than-expected proportion of patients with screening were found to have depression.

16. REVASCULARIZATION OUTCOMES

16.1. Assessment of Outcomes in Patients After Revascularization

Recommendations for Assessment of Outcomes in Patients After Revascularization Referenced studies that support the recommendations are summarized in Online Data Supplement 52.		
COR	**LOE**	**Recommendations**
1	**B-NR**	1. With the goal of improving patient outcomes, it is recommended that cardiac surgery and PCI programs participate in state, regional, or national clinical data registries and receive periodic reports of their risk-adjusted outcomes as a quality assessment and improvement strategy.[1-8]
2a	**C-LD**	2. With the goal of improving patient outcomes, it is reasonable for cardiac surgery and PCI programs to have a quality improvement program that routinely 1) reviews institutional quality programs and outcomes, 2) reviews individual operator outcomes, 3) provides peer review of difficult or complicated cases, and 4) performs random case reviews.[9,10]
2b	**C-EO**	3. Smaller volume cardiac surgery and PCI programs may consider affiliating with a high-volume center to improve patient care.

Synopsis

Centers that provide coronary revascularization should participate in clinical data registries with the intent to review and continuously improve patient outcomes. Comparison of outcomes through the use of national databases allows individual- and program-level assessment of the care provided and the opportunity to enhance care with quality improvement initiatives. Collaboration with other centers allows peer review and discussion, as well as sharing and adoption of effective quality improvement measures.

Recommendation-Specific Supporting Text

1. Participation in regional, state, or national registries that provide regular, risk-adjusted outcomes is beneficial in quality assessment and improvement. It allows participants to compare their performance to regional or national validated benchmarks, identify opportunities for improvement, and disseminate best practices.[1-8]
2. Quality and performance measures are defined by attributes related to structure, processes, and risk-adjusted outcomes. Structural attributes include elements such as equipment, supplies, staffing, institution- and operator-level volumes, and electronic health records. Processes include strategies for appropriate patient selection; protocols for pre- and postprocedural care, procedural execution, and management of complications; and participation in databases and registries for benchmarking the performance of the program and individual operator. Risk-adjusted outcomes are the end result of these structures and processes of care, and when available, they may be more reliable measures of quality than the institutional-level and individual operator–level volumes.[9-11]
3. Smaller-volume coronary revascularization programs may benefit from affiliation and collaboration with larger volume programs. Standardized processes from both centers may be shared bidirectionally, and periodic exchange of staff will facilitate the transfer of best practices. Teaching conferences, as well as conferences on morbidity and mortality in both centers, may be shared via videoconferencing. In addition, residents and fellows may rotate between programs. Program size is typically defined by the specific database.

17. UNANSWERED QUESTIONS AND FUTURE DIRECTIONS

The indications for revascularization and the approach to treatment in patients with CAD are generally based on evidence supporting benefit or lack thereof. Many recommendations for revascularization are derived from the results of RCTs or observational studies of large registries or cohorts of patients that show consistent trends in outcomes. However, there are some patient subgroups and clinical scenarios for which there is a paucity of evidence to support a formal recommendation. In addition, in some circumstances, it is inappropriate or unethical to perform a randomized trial comparing 2 treatments. Furthermore, in some situations, even in the absence of strong evidence, recommendations are created on the basis of experiential consensus on best practices for the delivery of care. In these cases, further research is needed to inform practice, which would enable updated recommendations based on clinical trial results.

17.1. Special Populations

17.1.1. Underrepresented Racial and Ethnic Groups

Despite advances in the identification of risk factors for CVD and the widespread use of evidence-based strategies to manage CVD, there are persistent sex, racial, and ethnic disparities in the delivery of care and in morbidity and mortality.[1-8] Studies have shown that Black patients and patients of South Asian descent with CAD have worse outcomes than do White patients.[2,4] Additionally, studies have reported worse outcomes in women than in men, although this finding is largely attenuated after adjustment for differences in baseline presentation and treatment.[9] Recommendations for care in patients with CAD are often derived from RCT data with an unequal representation of women and racial and ethnic groups.[10] Although a study's findings might be extrapolated to such populations, it is unclear whether similar outcomes can be assumed from the reported trial results across all populations of patients. For this reason, in the planning of clinical trials, measures to ensure the enrollment of underrepresented racial and ethnic groups should be implemented to inform better care of patients.[11]

17.2. Special Clinical Situations

17.2.1. Left Ventricular Dysfunction

RCT data support the use of CABG for the treatment of patients with coronary heart disease and left ventricular dysfunction to improve survival.[12-14] Although the STICH trial reported improved outcomes with CABG compared with medical therapy, the advantage of CABG over medical therapy was independent of the presence or absence of myocardial viability.[15-17] Critics have argued that the lack of a relative benefit of myocardial viability in predicting outcome with CABG was largely a result of the type of testing used.[18] Many surgeons still use viability testing to guide decisions about revascularization in patients with severe left ventricular dysfunction. Nevertheless, in view of the lack of association of myocar-

dial viability with derived benefit from revascularization, it remains unclear whether viability studies should be used to inform clinical practice, and if they are used, it remains unclear which method of assessment provides the most useful information.

There are currently insufficient data on the role of PCI in patients with left ventricular dysfunction to improve survival or cardiovascular outcomes. To address this gap in evidence, the ongoing REVIVED-BCIS2 (Percutaneous Revascularization for Ischemic Ventricular Dysfunction)[19] study will evaluate the benefits of PCI versus medical therapy in reducing the combined endpoint of death or hospitalization for heart failure at 2 years' follow-up. Additional studies are also currently under way, including the ISCHEMIA–Heart Failure Planning Study,[20] which is expected to pave the way for a larger phase 3 trial of PCI in patients with systolic heart failure.

17.2.2. SCAD

SCAD is increasingly recognized as a cause of ACS in young patients, particularly women, and is present in roughly one-fourth of women ≤50 years of age presenting with AMI.[21] The management of SCAD has evolved over the years toward a more cautious use of PCI after various case series demonstrated low success rates and higher rates of complications with PCI for SCAD, as well as good long-term outcomes in conservatively treated patients.[22] For this reason, expert consensus statements emphasize conservative care in most patients.[23] However, managing patients with SCAD who have ongoing symptoms, hemodynamic instability, or severely compromised blood flow of an artery subtending a large amount of myocardium (ie, the proximal LAD or left main lesions) is particularly problematic, as conservative care may not be a good option. Further investigation therefore is needed to understand the ideal scenarios for proceeding with revascularization and the optimal techniques for revascularization in SCAD.

17.2.3. Coronary Artery Aneurysm

Coronary artery aneurysms and fistulas are uncommon findings on coronary angiography, with a reported prevalence of 0.02% to 0.2%.[24,25] Most patients with coronary artery aneurysms are asymptomatic, but coronary artery aneurysms can lead to ischemia, vessel thrombosis, fistula formation, or rupture.[24-27] There are no randomized studies evaluating the most effective therapy for these patients. Case reports and case series have described various methods for repair of aneurysms or fistulas, including covered stenting, coil embolization, Amplatzer device implantation, and surgical bypass with exclusion of the aneurysm.[24-27] Because many patients remain asymptomatic and treatments for aneurysms or fistulas are not well defined, information on the timing of intervention (with respect to size and/or symptoms) and the ideal approach to treatment (surgical excision versus percutaneous therapies) is strongly needed.

17.2.4. Myocardial Bridging

Myocardial bridging occurs when there is systolic compression of a coronary artery because of a segmental intramyocardial course of the vessel, and it is seen in up to 25% of patients undergoing coronary angiography.[28] Although most myocardial bridging is clinically insignificant, severe bridging has been inferred to produce myocardial ischemia, coronary thrombosis, AMI, and stress cardiomyopathy.[28] In patients with ischemic pain and a myocardial bridge, provocative testing can be performed by measuring FFR under baseline conditions and during dobutamine stress or by obtaining positron emission tomographic imaging during adenosine vasodilator challenge.[29] If a patient has evidence of severe ischemia and a significant myocardial bridge, surgical approaches are available; small studies have reported subsequent improvement in angina, as documented by the Seattle Angina Questionnaire.[30] Although these data appear promising, the long-term risks and benefits of surgery for myocardial bridging are uncertain, and larger studies are needed to define best practices in these circumstances.

17.2.5. Treatment of Graft Failure

Robust data are also lacking for recommendations for clinical situations that include acute graft failure after CABG, the percutaneous treatment of significant arterial graft disease after CABG, and percutaneous interventions via an arterial graft after CABG. Such circumstances warrant discussion with a Heart Team and further investigation.

17.2.6. Antiplatelet Therapy in Patients With ACS After CABG With an Indication for Anticoagulation

Although antiplatelet therapy in patients with atrial fibrillation who are on anticoagulation after PCI is detailed in Section 14.5., there are no data to inform the treatment of patients after ACS who undergo CABG and also have an indication for anticoagulation (atrial fibrillation or mechanical valve). Care in such patients requires further study and careful consideration of bleeding risks, recurrent ischemic events, graft patency, and risk of thromboembolic events.

17.3. Revascularization Considerations

17.3.1. Use of the Radial Artery for a Conduit After Radial Artery Catheterization

The number of patients undergoing radial artery catheterization has increased exponentially over the years.[31] Some patients undergoing radial artery catheterization will ultimately require CABG. In patients undergoing CABG, the radial artery is the preferred conduit after the use of the LIMA.[32] However, if the radial artery has been manipulated (eg, for access to perform coronary angiography or intervention), there is informal agreement among surgeons to generally avoid the use of this artery as a conduit for grafting, because of the findings of

reduced acute and long-term graft patency in such patients.[33,34] Intimal tears, medial dissections, and increased intimal thickness are frequently found after radial artery catheterization,[35] and greater intimal hyperplasia was noted in the radial artery in pathology studies after radial artery catheterization.[34] The studies, which evaluated the integrity of the radial artery early after radial artery catheterization, were generally performed within 6 weeks of the radial artery procedure. The persistence of these abnormal findings in the radial artery in longer-term follow-up is uncertain. Given the increase in the use of radial access for coronary angiography and intervention, it would be important to know whether these pathological findings remain over time. Further research is needed to determine whether there is healing of the radial artery and, if so, whether the radial artery might be considered suitable for graft harvesting after a prespecified period of time that allows for resumption of normal endothelial integrity.

17.3.2. Completeness of Revascularization in Multivessel Disease

In patients with multivessel disease, when feasible, operators often attempt to treat all vessels to allow for a complete revascularization. There are no randomized studies prospectively comparing planned complete versus incomplete revascularization in SIHD, but several observational studies have concluded that patients who undergo CABG or PCI have worse outcomes if major epicardial vessels with significant stenoses are not revascularized during the index procedure.[36-41] In the SYNTAX trial, in which complete revascularization was attempted in all patients, patients who underwent CABG or PCI with incomplete revascularization had worse cardiovascular outcomes at long-term follow-up.[42] Nevertheless, patients who have incomplete revascularization are more likely to have a greater burden of comorbidities, including older age, diabetes, renal failure, previous MI, lower left ventricular function, and more extensive and complex coronary anatomy, that may also impact the completeness of revascularization. The observational studies comparing patients who receive complete or incomplete revascularization cannot fully account for the underlying reasons why an operator might choose to revascularize only a limited area. It is reasonable to rationalize that complete revascularization to improve perfusion of as large an amount of myocardium as possible is a good strategy and likely improves patient outcomes. Nevertheless, the ISCHEMIA trial, which encouraged complete revascularization (especially if the arteries supplied areas in which there was ischemia on stress testing), did not demonstrate improved cardiovascular outcomes with revascularization. As such, when considering multivessel PCI or additional bypass grafting during a CABG procedure, one must be mindful of the theoretical benefits of complete revascularization for the individual patient. RCTs are needed to examine the benefits of complete revascularization in SIHD, with trial designs that mimic the trials performed on patients with STEMI and multivessel disease.[43]

17.3.3. Hybrid Coronary Surgery

The hybrid approach to coronary revascularization (which combines minimally invasive off-pump grafting of the LIMA to the LAD, with PCI of the remaining vessels) has gained increasing popularity in recent years, although it is still performed by few select centers in the United States.[44] Small RCTs and observational studies with propensity-matching of hybrid revascularization versus conventional CABG[45-47] have found similar rates of death, MI, stroke, and repeat revascularization. Unfortunately, the Hybrid Coronary Revascularization trial, a phase 3, large-scale, randomized trial designed to compare multivessel PCI with hybrid coronary surgery in patients with disease of the LAD and ≥1 additional stenoses, was terminated early because of low enrollment (ClinicalTrials.gov identifier: NCT03089398). For this reason, the role of hybrid surgery as an alternative to multivessel PCI for patients with multivessel disease involving the LAD remains unclear. Furthermore, the Hybrid Coronary Revascularization trial did not compare hybrid surgery as an alternative to traditional CABG and, as such, additional studies to evaluate the use of hybrid surgery in these circumstances are needed. Other areas in need of further research include the use of non-sternotomy coronary artery revascularization.

17.3.4. Revascularization Before Percutaneous Valve Procedures

The presence of CAD in patients referred for TAVR is variable, with 15% to 81% of patients enrolled in the landmark trials of TAVR having obstructive CAD.[48] Although the presence of CAD, particularly complex CAD, is associated with worse outcomes after TAVR,[49] observational studies have not demonstrated improved outcomes when PCI is performed before TAVR.[50] The RCT that evaluated TAVR versus surgical AVR advised that PCI be performed before TAVR in patients with proximal obstruction of large vessels.[51] For this reason, PCI is often planned before valve procedures, and guidelines indicate that PCI may be reasonable in patients with severe disease of the proximal arteries.[52] Nevertheless, this recommendation is based on limited data, and therefore, further research is needed to determine whether the routine use of PCI before percutaneous valve procedures improves outcomes.

17.3.5. Revascularization Before Organ Transplantation

There are currently no RCTs evaluating the role of revascularization before solid organ transplantation, although

the RCT of revascularization before vascular surgery did not report improved outcomes with PCI.[53] Nonetheless, because of the increased risk of cardiovascular events among renal transplant recipients,[54] routine risk assessment is often performed before consideration for transplantation. When obstructive CAD is noted, many transplantation surgeons are hesitant to proceed with surgery in this complex group of patients without revascularization; therefore, it is common for a patient to be referred for revascularization in preparation for organ transplantation. In the Ischemia CKD trial, there were no differences in outcomes with routine revascularization even in the presence of severe ischemia, although only about 10% of enrolled patients were on the waitlist for transplantation. Even less is known about revascularization before liver transplantation. For this reason, it remains unclear whether revascularization before organ transplantation imparts a better outcome, and RCTs are needed to further inform care in this complex group of patients.

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ARTICLE INFORMATION

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APPENDIX

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)–2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Jennifer S. Lawton, Chair	Johns Hopkins Medicine–Professor and Chief of Cardiac Surgery	None	None	None	None	None	None
Jacqueline E. Tamis-Holland Vice-Chair/JCPG liaison	Mount Sinai Morningside Hospital–Associate Director, Cardiac Catheterization Laboratory; Icahn School of Medicine at Mount Sinai–Professor of Medicine	None	None	None	None	None	None
Sripal Bangalore	New York University School of Medicine, The Leon H. Charney Division of Cardiology–Professor of Medicine and Director, Complex Coronary Intervention; Director of Research, Cardiac Catheterization Laboratory and Director, Cardiovascular Outcomes Group	• Abbott* • Amgen* • Biotronik • Meril • Pfizer • Reata • SMT	None	None	• Abbott* • Reata*	None	None
Eric R. Bates	University of Michigan Department of Internal Medicine–Professor of Internal Medicine	None	None	None	None	None	None
Theresa M. Beckie	University of South Florida, Tampa–Professor and Associate Dean PhD Program, College of Nursing Professor, College of Medicine, Division of Cardiovascular Sciences	None	None	None	None	None	None
James M. Bischoff	AHA Volunteer (Patient Representative)	None	None	None	None	None	None
John A. Bittl	Advent Health Ocala, Interventional Cardiology– Chief of Staff, Medical Director of Surgical Services, Research, and Education	None	None	None	None	None	None
Mauricio G. Cohen (TFDS liaison)	University of Miami Hospital and Clinics–Professor of Medicine and Director, Cardiac Catheterization Laboratory	• Abiomed* • AstraZeneca* • Medtronic* • Merit Medical* • Terumo Medical • Zoll	None	• Accumed Radial Systems	None	None	None
J. Michael DiMaio	Baylor Scott & White Health System–Medical Director of Surgical Services	None	None	None	None	None	None
Creighton W. Don (SCAI representative)	VA Puget Sound Medical Center–Associate Professor of Medicine and Section Chief Cardiology; University of Washington Division of Cardiology–Director of the Interventional Cardiology and Structural Heart Fellowships	• Siemens	None	None	None	• Abbott* • Boston Scientific* • CSI* • Medtronic* • Spectranetics*	None
Stephen E. Fremes (AATS representative)	University of Toronto Schulich Heart Centre–Cardiovascular Surgery Professor	None	None	None	None	• Bayer†,‡ • Edwards‡ • Medtronic‡	None
Mario F. Gaudino	Weill Cornell Medicine Professor/Surgeon–Cardiothoracic Surgery	None	None	None	None	None	None
Zachary D. Goldberger	University of Wisconsin School of Medicine and Public Health–Associate Professor of Medicine, Division of Cardiovascular Medicine/Electrophysiology; University of Wisconsin School of Medicine and Public Health–Associate Program Director, Clinical Electrophysiology Fellowship	None	None	None	None	None	None
Michael C. Grant	The Johns Hopkins Medical Institutions, The Armstrong Institute for Patient Safety and Quality–Associate Professor, Divisions of Cardiothoracic Anesthesia, Surgical Critical Care and Acute Care Surgery and Core Faculty, Departments of Anesthesiology/ Critical Care Medicine and Surgery	None	None	None	None	None	None

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Jang B. Jaswal	National Ambassador for AHA (Patient Representative)	None	None	None	None	None	None
Paul A. Kurlansky	Columbia University College of Physicians and Surgeons–Associate Professor of Surgery, Division of Cardiothoracic Surgery; Columbia HeartSource–Director of Research, Recruitment and CQI; Center for Innovation and Outcomes Research–Associate Director	None	None	None	None	None	None
Roxana Mehran	Mount Sinai–Professor in Cardiovascular Clinical Research and Outcomes, Professor of Medicine (Cardiology); Icahn School of Medicine at Mount Sinai Population Health Science and Policy–Director of Interventional Cardiovascular Research and Clinical Trials	• Bayer • Boston Scientific • Janssen Pharmaceuticals	None	• Claret* • Boston Scientific* • Controlrad* • Elixir Medical*	• Abbott* • Abiomed* • AstraZeneca* • Bayer*	None	None
Thomas S. Metkus	Johns Hopkins University School of Medicine–Assistant Professor of Medicine and Surgery, Division of Cardiology, Department of Medicine and Division of Cardiac Surgery Department of Surgery	None	None	None	None	None	None
Lorraine C. Nnacheta§	American Heart Association/American College of Cardiology–Guideline Advisor	None	None	None	None	• AHA/ACC salaried employee	None
Sunil V. Rao	Duke University Health System–Professor of Medicine and Section Chief, Cardiology	None	None	None	• Amgen* • Bayer • Shockwave Medical • Svelte Medical	None	None
Frank W. Sellke	Alpert Medical School of Brown University and Rhode Island Hospital–Director of the Cardiovascular Institute and Karl Karlson Professor and Chief of Cardiothoracic Surgery	• Stryker	None	None	• Bayer†	None	None
Garima Sharma	Johns Hopkins University School of Medicine, Department of Medicine, Ciccarone Center for the Prevention of Cardiovascular Disease, Division of Cardiology–Assistant Professor of Medicine and Director of Cardio-Obstetrics Program	None	None	None	None	None	None
Celina M. Yong	Stanford University School of Medicine–Assistant Professor, Division of Cardiovascular Medicine; VA Palo Alto Health care System–Director of Interventional Cardiology	None	None	None	None	None	None
Brittany A. Zwischenberger	Duke University–Assistant Professor, Division of Cardiothoracic Surgery	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACC/AHA, a person has a *relevant* relationship IF: a) the *relationship or interest* relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the *document;* or b) the *company/entity* (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document* or makes a competing drug or device addressed in the *document*; or c) the *person or a member of the person's household*, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the *document*. Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply.

*Significant relationship.

†No financial benefit.

‡This disclosure was entered under the Clinical Trial Enroller category in the ACC's disclosure system. To appear in this category, the author acknowledges that there is no *direct* or *institutional* relationship with the trial sponsor as defined in the (ACCF or ACC/AHA) Disclosure Policy for Writing Committees.

§Lorraine Nnacheta is an AHA/ACC joint staff member and acts as the guideline advisor for the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization." No relevant relationships to report. Non-voting author on recommendations and not included/counted in the RWI balance for this committee.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; AHA, American Heart Association; CQI, Continuous Quality Improvement; JCPG, Joint Committee on Clinical Practice Guidelines; RWI, relationships with industry and other entities; SCAI, Society for Cardiovascular Angiography and Interventions; TFDS, ACC/AHA Task Force for Clinical Data Standards; and VA, Veterans Affairs.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Comprehensive)–2021 ACC/AHA/SCAI Guideline for Coronary Revascularization (January 2021)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Anastasia L. Armbruster	Content Reviewer–Joint Committee on Clinical Practice Guidelines	University of Health Sciences and Pharmacy in St. Louis	None	• AstraZeneca	None	None	None	None
Joshua A. Beckman	Official Reviewer–Joint Committee on Clinical Practice Guidelines	Vanderbilt University Medical Center	• Amgen • JanOne • Janssen Pharmaceuticals*	None	• EMX† • JanaCare† • VIA*	• Bayer (DSMB) • Novartis (DSMB)	• Amgen	None
Kim K. Birtcher	Content Reviewer–Joint Committee on Clinical Practice Guidelines	University of Houston College of Pharmacy	• Jones & Bartlett Learning	None	None	None	None	None
Lynne T. Braun	Content Reviewer–ACC/AHA	Rush University (Retired)	None	None	None	None	• AHA† • PCNA† • UptoDate	None
Edward Butler	Lay Reviewer	Lay Stakeholder Representative Retired, Mint Hill, NC	None	None	None	None	None	None
Anita Deswal	Content Reviewer–Joint Committee on Clinical Practice Guidelines	University of Texas MD Anderson Cancer Center	None	None	None	None	• ACC • AHA	None
Dave L. Dixon	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Virginia Commonwealth University School of Pharmacy	• American Pharmacists Association	None	None	• Centers for Disease Control and Prevention* • Community Pharmacy Foundation*	• Accreditation Council for Lipidology† • American College of Pharmacy Cardiology Practice Research Network† • National Lipid Association†	None
David Faxon	Content Reviewer–ACC/AHA	Brigham and Women's Hospital	• Boston Scientific • CSL Behring*	None	None	• Boston Scientific (DSMB) • CSL Behring (DSMB) • Medtronic†	• Akenia Therapeutics* • Medtronic • REVA Medical	None
Lisa de las Fuentes	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Washington University in St. Louis	• Acceleron • Altavant • Arena • Bayer • Express Scripts • Gossamer • Johnson & Johnson • Phase Bio • V-wave • Vaderis • WebMD*	• Simply Speaking*	None	• Acceleron* • Altavant* • Bayer • Complexa* • Foundation for the National Institutes of Health • Johnson & Johnson* • Liquidia* • Medtronic* • NIH* • Reata* • Trio Analytics • United Therapeutics* • University of Kentucky (DSMB)† • University of Toronto (DSMB)†	• ACC† • AHA† • *Circulation* Journals • Pulmonary Hypertension Association	None
Kirk N. Garratt	Official Reviewer–SCAI	ChristianaCare	None	None	• LifeCuff Technologies*	• Abbott (DSMB)* • Jarvik Heart (DSMB)	None	None
Zachary D. Goldberger	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Associate Professor, University of Wisconsin-Madison, School of Medicine and Public Health	None	None	None	None	None	None
Bulent Gorenek	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Eskisehir Osmangazi University	• AstraZeneca • Sandoz	None	None	None	None	None
Robert Guyton	Official Reviewer–STS	Emory University	• Edwards Lifesciences	None	None	• Edwards Lifesciences† • NIH†	• Boston Scientific* • Edwards Lifesciences*‡ • Medtronic‡	None
Norissa Haynes	Content Reviewer–Joint Committee on Clinical Practice Guidelines	University of Pennsylvania	None	None	None	None	None	None

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Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Adrian F. Hernandez	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Duke University	• Amgen • AstraZeneca* • Bayer • Biofourmis • Boehringer Ingelheim • Boston Scientific* • Cytokinetics • Daiichi Sankyo • Eli Lilly • Merck* • Myokardia • Novartis* • Pfizer • Relypsa • Sanofi-aventis* • Xogenex	None	None	• American Regent • AstraZeneca* • Eidos (DSMB) • Genentech • GlaxoSmithKline* • Janssen Pharmaceuticals • Merck • NIH† • Novartis* • PCORI† • Verily*	• AHA† • AstraZeneca • Boston Scientific • CSL Behring • Janssen Pharmaceuticals* • Merck • Novartis • Genentech* • Relypsa • Sanofi-aventis	• Defendant, Patent Dispute, 2019
Jose A. Joglar	Content Reviewer–Joint Committee on Clinical Practice Guidelines	UT Southwestern Medical Center	None	None	None	None	None	None
W. Schuyler Jones	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Duke University	• Amgen • Bayer • Janssen Pharmaceuticals* • Pfizer	None	None	• Bristol Myers-Squibb* • PCORI	• Abbott* • Amgen • AstraZeneca • Boehringer Ingelheim • Cardiovascular Systems Inc.* • Janssen Pharmaceuticals • ZOLL Medical	None
Andrew M. Kates	Content Reviewer–ACC/AHA	Washington University School of Medicine	None	None	None	None	None	None
Jim LoFaso	Lay Reviewer	Veeco; Solomon Page (Contactor)	None	None	None	None	None	None
Thomas MacGillivray	Content Reviewer–ACC/AHA	Houston Methodist Hospital	None	None	None	None	• Xylocor Therapeutics‡	None
Daniel B. Mark	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Duke University	None	None	None	• HeartFlow* • Merck	• HeartFlow* • Merck*	None
Sara C. Martinez	Content Reviewer–ACC	Providence Health and Services	None	None	None	None	• Abiomed • Boston Scientific • Novartis • Maquet Cardiovascular	None
Venu Menon	Content Reviewer–ACC/AHA	Cleveland Clinic	None	None	None	None	• Novartis†	None
L. Kristin Newby	Content Reviewer–ACC/AHA	Duke University	• Beckman-Coulter • Bristol Myers Squibb • CSL • Medtronic • NHLBI • Quidel • Roche Diagnostics	None	None	• BioKier • Boehringer Ingelheim • CDC • David H. Murdock Institute for Business and Culture • NIH* • North Carolina DHHS	• AHA† • ACC, Oregon Chapter • AstraZeneca† • Boehringer Ingelheim • David H. Murdock Research Institute† • *JACC*, Deputy Editor*	None
Michelle O'Donoghue	Content Reviewer–ACC/AHA	Brigham and Women's Hospital	• Amgen • CVS Caremark • Janssen Pharmaceuticals • Novartis	None	None	• Amgen* • AstraZeneca (DSMB)* • Eisai* • Intarcia* • Janssen Pharmaceuticals* • The Medicines Company/Novartis*	• Kowa Pharmaceuticals	None
Patrick T. O'Gara	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Brigham and Women's Hospital	None	None	None	None	• Edwards Lifesciences† • Medtrace† • Medtronic† • *JAMA Cardiology** • NIH*	None

(*Continued*)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Latha P. Palaniappan	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Stanford Concierge and Executive Medicine	• National Minority Cardiovascular Alliance	None	None	• NIH*	None	None
Mariann R. Piano	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Vanderbilt University	None	None	None	None	None	None
Marc Ruel	Official Reviewer–AHA	University of Ottawa Heart Institute	• Edwards Lifesciences • Medtronic	None	None	• Cryolife • Medtronic*	None	None
Jorge F. Saucedo	Official Reviewer–AHA	Medical College of Wisconsin	None	None	None	None	• B. Braun Interventional Systems Inc.	None
Erica S. Spatz	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Yale University School of Medicine	None	None	None	• FDA*	None	None
Elaine Tseng	Content Reviewer–ACC/AHA	University of California San Francisco and San Francisco VA Medical Center	None	None	• ReValve Med†	• NIH*	• AATS† • AHA† • Cryolife‡* • Edwards Lifesciences • *Journal of Heart Disease Valve*† • Medtronic • STS† • University of California • Zimmer Biomet	None
Saraschandra Vallabhajosyula	Content Reviewer–AHA	Emory University School of Medicine	None	None	None	None	None	None
Y. Joseph Woo	Content Reviewer–Joint Committee on Clinical Practice Guidelines	Stanford University School of Medicine	None	None	None	None	• NIH*	None
Marco Zenati	Official Reviewer–AATS	Harvard Medical School	None	None	None	• NIH*	None	None

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*Significant relationship.

†No financial benefit.

‡This disclosure was entered under the Clinical Trial Enroller category in the ACC's disclosure system. To appear in this category, the individual acknowledges that there is no direct or institutional relationship with the trial sponsor as defined in the (ACCF or AHA/ACC) Disclosure Policy for Writing Committees.

AATS indicates American Association for Thoracic Surgery; ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; AHA, American Heart Association; DSMB, Data and Safety Monitoring Board; FDA, US Food and Drug Administration; *JACC, Journal of the American College of Cardiology; JAMA, Journal of the American Medical Association*; NIH, National Institutes of Health; PCNA, Preventive Cardiovascular Nurses Association; PCORI, Patient-Centered Outcomes Research Institute; SCAI, Society for Cardiovascular Angiography and Interventions; STS, Society of Thoracic Surgeons; UT, University of Texas; and VA, Veterans Affairs.