JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 80, NO. 22, 2022

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

A Practical Approach to Left Main Coronary Artery Disease

JACC State-of-the-Art Review

Laura J. Davidson, MD,[a,*] Joseph C. Cleveland, MD,[b,†] Frederick G. Welt, MD,[c,*] Saif Anwaruddin, MD,[d,*] Robert O. Bonow, MD,[a] Michael S. Firstenberg, MD,[e,†] Mario F. Gaudino, MD,[f,†] Bernard J. Gersh, MB ChB, DPhil,[g] Kendra J. Grubb, MD, MHA,[h,†] Ajay J. Kirtane, MD, SM,[i,*] Jacqueline E. Tamis-Holland, MD,[j] Alexander G. Truesdell, MD,[k,*] Stephan Windecker, MD,[l] Roza A. Taha, MBChB,[a] S. Chris Malaisrie, MD,[a,†]
On behalf of the ACC's Interventional and Cardiac Surgery Leadership Councils

ABSTRACT

The treatment of left main (LM) coronary artery disease (CAD) requires complex decision-making. Recent clinical practice guidelines provide clinicians with guidance; however, decisions regarding treatment for individual patients can still be difficult. The American College of Cardiology's Cardiac Surgery Team and Interventional Council joined together to develop a practical approach to the treatment of LM CAD, taking into account randomized clinical trial, meta-analyses, and clinical practice guidelines. The various presentations of LM CAD based on anatomy and physiology are presented. Recognizing the complexity of LM CAD, which rarely presents isolated and is often in combination with multivessel disease, a treatment algorithm with medical therapy alone or in conjunction with percutaneous coronary intervention or coronary artery bypass grafting is proposed. A heart team approach is recommended that accounts for clinical, procedural, operator, and institutional factors, and features shared decision-making that meets the needs and preferences of each patient and their specific clinical situation. (J Am Coll Cardiol 2022;80:2119–2134) © 2022 Published by Elsevier on behalf of the American College of Cardiology Foundation.

The natural history of medically treated left main (LM) disease has been associated with 73% mortality at 15 years, and historically, coronary artery bypass grafting (CABG) has been recommended in all patients with stable ischemic heart disease and significant LM disease to prevent fatal acute myocardial infarction (MI).[1] Randomized clinical trials on the survival benefit of CABG over medical therapy in that era showed a substantial treatment effect of CABG in the subset of LM stenosis,

From the [a]Divisions of Cardiology and Cardiac Surgery, Northwestern University, Chicago, Illinois, USA; [b]Department of Cardiothoracic Surgery, University of Colorado, Aurora, Colorado, USA; [c]Department of Cardiovascular Medicine, University of Utah, Salt Lake City, Utah, USA; [d]Department of Cardiology & Interventional Cardiology, St. Vincent Hospital, Worcester, Massachusetts, USA; [e]Department of Cardiothoracic Surgery, St. Elizabeth Medical Center, Appleton, Wisconsin, USA; [f]Department of Cardiothoracic Surgery, Weill Cornell Medicine, New York, New York, USA; [g]Department of Cardiovascular Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA; [h]Department of Surgery, Division of Cardiothoracic Surgery, Emory University, Atlanta, Georgia, USA; [i]Division of Cardiology and the Cardiovascular Research Foundation, Columbia University Irving Medical Center/NewYork-Presbyterian Hospital, New York, New York, USA; [j]Department of Cardiology, Mount Sinai, New York, New York, USA; [k]Department of Interventional Cardiology, Virginia Heart and the Inova Heart and Vascular Institute, Falls Church, Virginia, USA; and the [l]Department of Cardiology, Bern University Hospital, Inselspital, Bern, Switzerland. *American College of Cardiology Interventional Council. †American College of Cardiology Cardiac Surgery Team Council.

Habib Samady, MD, served as Guest Associate Editor for this paper. Javed Butler, MD, MPH, MBA, served as Guest Editor-in-Chief for this paper.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received August 10, 2022; accepted September 7, 2022.

Listen to this manuscript's audio summary by Editor-in-Chief Dr Valentin Fuster on www.jacc.org/journal/jacc.

ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2022.09.034

ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

AHA = American Heart Association

CABG = coronary artery bypass grafting

CAD = coronary artery disease

CTA = computed tomography angiography

EACTS = European Association for Cardio-Thoracic Surgery

ESC = European Society of Cardiology

FFR = fractional flow reserve

IVUS = intravascular ultrasound

LAD = left anterior descending

LCx = left circumflex coronary artery

LIMA = left internal mammary artery

LM = left main

LMB = left main bifurcation

LMCA = left main coronary artery

LOE = Level of Evidence

LV = left ventricular

MI = myocardial infarction

MVD = multivessel disease

PCI = percutaneous coronary intervention

RIMA = right internal mammary artery

SCAI = Society for Cardiovascular Angiography and Interventions

precluding any further studies involving medical treatment alone for patients with LM disease.[2-4] Unlike the other epicardial arteries in which significant stenosis is defined as diameter reduction >70%, the threshold for intervention in LM disease is set at 50% because of early observations that patients with 50% to 70% LM stenosis derive a survival benefit after CABG.[1,3,4] Revascularization, whether CABG or percutaneous coronary intervention (PCI), may be appropriate on an urgent basis for some patients with LM stenosis in whom hospital admission and subsequent revascularization may be preferred after diagnosis of LM disease.[5] LM disease is treated on a nonelective (urgent or emergent) basis in 17% to 59% of patients.[6]

The left main (LM) coronary artery arises from the aorta and branches into the left anterior descending (LAD) and left circumflex (LCx) coronary arteries. The LM coronary artery supplies circulation to a large portion (75% to 100%) of the left ventricular (LV) myocardium; as a result, significant LM stenosis places the left ventricle at considerable risk. MI after LM plaque rupture involves the entire left ventricle and the inferior wall of the right ventricle in patients with left dominant anatomy. LM stenosis can occur in the ostial (23%), mid-shaft (15%), and distal (61%) segments, and depending on the location and severity of the disease, treatment strategies may differ.[7] Patients with LM coronary artery disease (CAD) commonly have multivessel disease (MVD), and isolated LM stenosis occurs in only 4% to 6% of patients.[8] The historical gold standard for diagnosis of LM disease is coronary angiography, with significant stenosis defined as luminal diameter reduction of >50%[9]; within the category of severe disease, the stenosis severity can be further subclassified as intermediate (50% to 69%), severe (70% to 90%), and critical (>90%) (**Figure 1**).

In clinical practice, decisions regarding the choice of medical therapy alone, PCI, or CABG for LM disease require a tailored multidisciplinary team-based and patient-centered approach that integrates clinical factors,[10,11] procedural considerations,[12-14] operator and institution issues,[15,16] and clinical practice guideline recommendations (**Figure 2**). The revascularization guidelines provide an excellent framework for addressing these complex issues.[17,18] This paper represents a collaborative effort among cardiac surgeons, general cardiologists, and interventional cardiologists to provide a multidisciplinary review on the management of LM CAD. The goal is to decrease ambiguity and shed light on the spirited debate surrounding this complex topic. Optimal outcomes rely on the engagement with a heart team, composed at least of general cardiologists, interventional cardiologists, cardiac surgeons, anesthesiologists, and the patient/family with shared decision-making. It is important to recognize that LM disease is heterogeneous, and a single approach will not be applicable to each individual patient's circumstances. Specific patient characteristics will be addressed in this document.

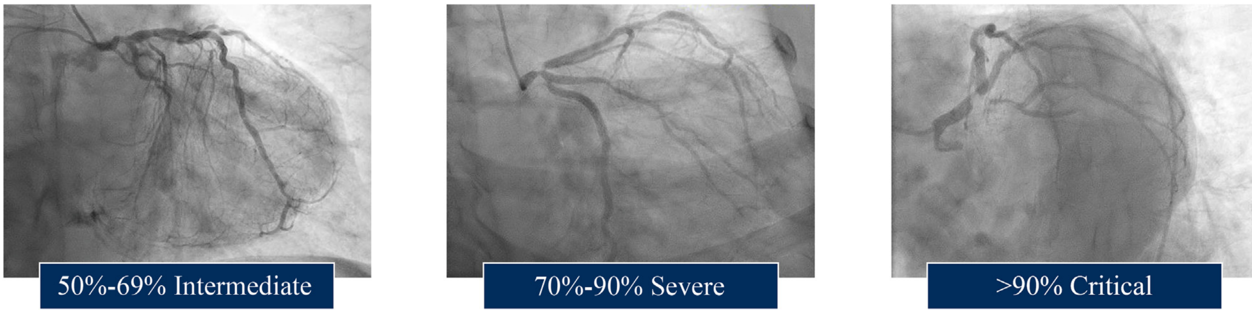
HIGHLIGHTS

- LM CAD can be categorized as ostial/shaft and distal lesions, and may be complicated by multivessel disease.
- Clinical, procedural, and institutional factors should be considered along with clinical practice guidelines in selecting the mode of revascularization for patients with LM CAD.
- Engagement of a multidisciplinary heart team and shared decision making are key components of management for patients with LM CAD.

CLINICAL FACTORS FOR DECISION-MAKING

When weighing the risks and benefits of PCI vs CABG for LM disease, it is important to take into account the factors that are important to the patient first and foremost, while also considering clinical factors that may affect optimal outcomes. From a patient perspective, factors that may be taken into consideration in the decision for revascularization method may include symptom relief, longevity, recovery time, and freedom from complications post-procedure. When reviewing these potential benefits with a patient, clinical factors must be thoroughly considered and discussed. Multiple methods have been validated to objectively determine patient outcomes with coronary revascularization, including the clinical risk scores of the STS (Society of Thoracic Surgeons), the EuroSCORE II (European System for Cardiac Operative Risk Evaluation), and the NCDR (National Cardiovascular Data Registry) CathPCI Registry.[19-21] Integrated anatomical and clinical scores such as the SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) score and the more recent SYNTAX II 2020 update provide additional

FIGURE 1 **Distal Left Main Coronary Artery Stenosis Severity**



Angiography demonstrating various degrees of significant distal left main coronary artery stenosis by quantitative categories. The severity of left main stenosis may influence clinical decisions regarding urgency of revascularization.

value in assessing the suitability for PCI vs CABG.[22-25] Overall, the purpose of a comprehensive preprocedural assessment is to delineate clinical, anatomical, and procedural factors most favorable or unfavorable for short-, medium-, and long-term outcomes for CABG, PCI, and medical therapy, identify where equipoise may exist, and assign comparative percentages to risk and success estimates, from which to best align physician and patient objectives. Unfortunately, most of these tools are limited in how they incorporate specific comorbidities. Furthermore, with the rapid pace of medical therapies, the impact of revascularization in a patient receiving guideline-directed medical therapy on short-term and long-term outcomes continues to be a moving target.

Factors that may favor CABG include diabetes mellitus (especially with concurrent significant MVD),[26,27] a contraindication to dual antiplatelet therapy, history of recurrent in-stent restenosis, or concomitant ascending aortic or valvular pathology with an independent indication for surgery.[28,29]

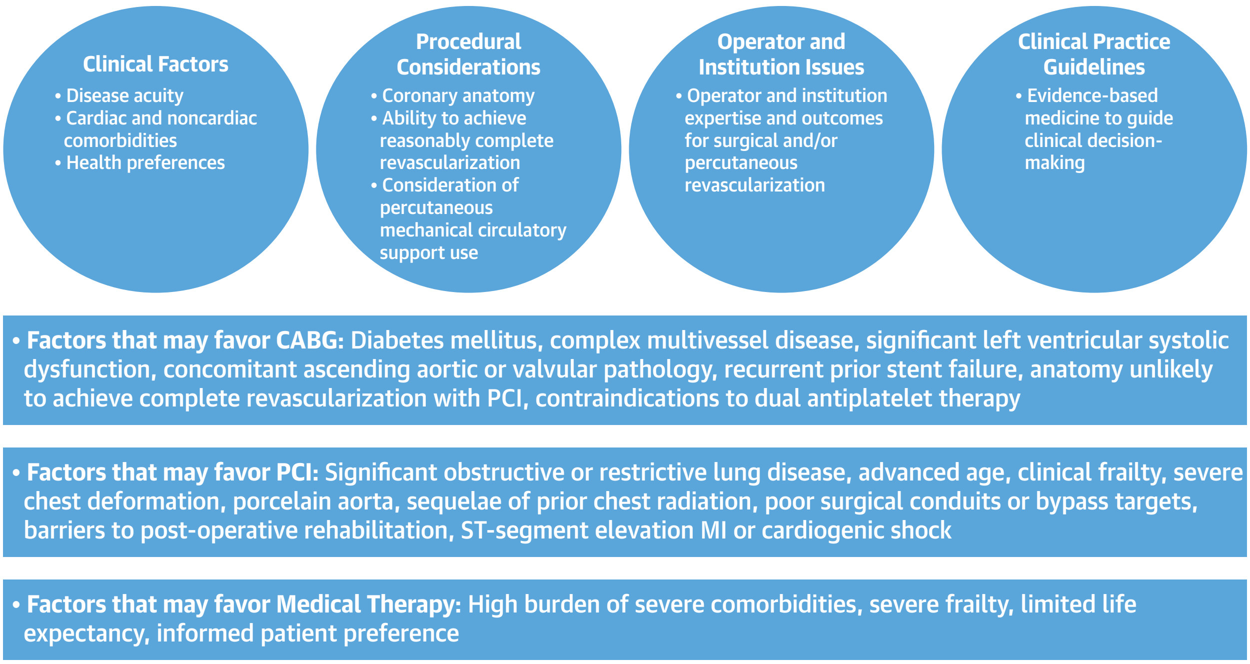
Clinical factors that may favor PCI include clinical frailty or severe comorbidities that may affect a patient's ability to rehabilitate after CABG. Some of these comorbidities are severe chronic obstructive pulmonary disease, severe chest deformity, prior sternotomy and/or lack of conduits, sequelae of prior chest radiation,[29] advanced chronic kidney disease,[30,31] immunosuppression, reduced life expectancy, or suboptimal psychosocial support.[32]

Despite the established benefits of revascularization for LM disease, medical therapy alone may be preferred if the weight of comorbidities is high, life expectancy or the likelihood of benefit is low,[4,33,34] or a fully informed patient desires this approach.[18,26,27] Increasing age is a predictor of adverse events, yet older adults are underrepresented in randomized clinical trials, and frailty is inadequately measured in current risk prediction models.[35-39] Age, comorbidity burden, and clinical frailty often travel together, affect both surgical and percutaneous outcomes, and should be considered in conjunction with traditional risk factors in the decision-making process when counseling patients regarding periprocedural risks associated with PCI or CABG.[40-43] Although CABG is feasible and may offer superior longer-term outcomes vs PCI in the elderly, postoperative stays, intensive care unit readmission, and hospital stays are all significantly higher compared with younger surgical patients and may influence patient-centered shared decision-making.[44] Octogenarians and nonagenarians are also more often focused on near-term risks and outcomes, in particular recovery time and short-term relative risks of stroke, atrial fibrillation, acute kidney injury, and physical debility, and may thus favor less invasive therapeutic options.[45] For similar reasons, the long-term benefits of revascularization for an asymptomatic patient with LM disease may be less relevant in the elderly, and therefore, the benefits of revascularization over medical therapy alone for LM disease should also be considered before entertaining revascularization for the sole purpose of improving survival.

Special consideration should be given to patients with LV systolic dysfunction and decompensated heart failure as these conditions increase the short-term risks of both surgical and percutaneous approaches; however, in observational studies, CABG appears superior to PCI for patients with LM disease and severe LV systolic dysfunction.[46,47] The absence of myocardial viability on noninvasive testing in patients with ischemic cardiomyopathy is not necessarily a contraindication to revascularization.[48] Finally, when mechanical support is necessary to

JACC VOL. 80, NO. 22, 2022
NOVEMBER 29, 2022:2119–2134

FIGURE 2 **Heart Team Considerations for Left Main Coronary Artery Disease**



The heart team must consider clinical factors, procedural considerations, operator and institution issues, and clinical practice guidelines to inform decision making on the optimal treatment of left main coronary artery disease for each individual patient. If clinically feasible, a multidisciplinary heart team approach to each patient is imperative when making decisions regarding treatment strategies for left main disease. CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

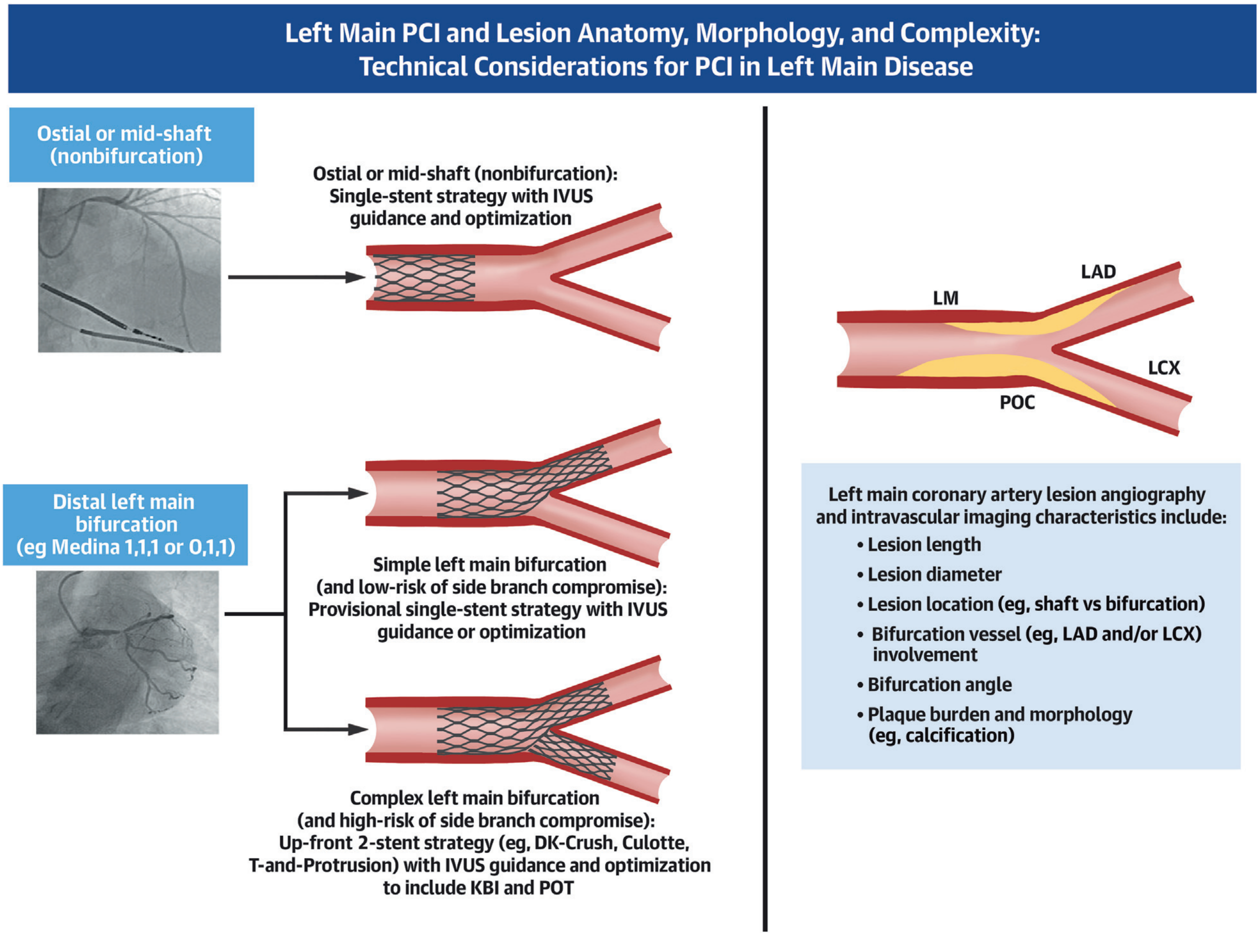
perform PCI, the elevated risks of vascular complications and major bleeding with current percutaneous mechanical support devices in this patient population should be factored into the assessment of the relative risk of CABG vs PCI.[49,50] Decision-making regarding the options for pursuing nonrevascularization therapies, such as long-term ventricular assist devices or transplants, should be considered in such high-risk patients, and although such protocols and options are beyond the scope of this paper, early engagement with a heart team should be encouraged for patients with advanced cardiomyopathies that are not anticipated to improve with standard recommended therapies.

Integrating a multidisciplinary heart team into institutional practice provides a formalized approach to evaluate complex LM disease and to best ensure standardized and equitable care delivery.[51,52] Conversations with the patient and designated family members should be conducted in the patient's native language to both maximize understanding of the issues and minimize health care disparities. The patient should be informed of the clinical relevance of LM disease, the possible treatment options, as well as the anticipated risks and benefits of each approach. Consideration must also be given to patients who cannot, or will not, be adherent to recommended postprocedure therapies (ie, sternal precautions after CABG or the need for dual antiplatelet therapies after PCI). Patient preferences are important, but patients must understand when such preferences are not aligned with current guidelines or the recommendations of the heart team.[17] Presently, a detailed, but understandable, highly visual, and standardized decision aid, aimed to provide the patient with a detailed understanding of all options, which can be used by all members of the heart team to consistently convey individualized and weighted risks and benefits to all patients is strongly needed.[53,54]

PROCEDURAL CONSIDERATIONS FOR PCI AND CABG IN LM DISEASE

When evaluating revascularization strategies for unprotected LM disease, it is important to consider that isolated LM disease is an uncommon issue. Concomitant severe MVD should weigh in as a technical

FIGURE 3 **Left Main PCI Technical Considerations**



Left main percutaneous coronary intervention (PCI) requires careful consideration of lesion characteristics, including lesion length, bifurcation angle, plaque burden, and morphology. For left main shaft and simple bifurcation lesions, a provisional single-stent strategy may be preferred, and for more complex bifurcation lesions, a 2-stent strategy may be required. Intravascular ultrasound (IVUS) should be used for preintervention lesion and vessel assessment, periprocedural guidance of lesion preparation and stent deployment, and postintervention assessment of optimal endpoints and exclusion of complications.

consideration in the decision to pursue percutaneous vs surgical treatment with the goal of complete revascularization. Technical considerations should be factored into the decision-making process as optimal results will be influenced not only by operator experience, but also by technical feasibility. Consideration should also be given to hybrid or staged therapies when neither CABG nor PCI is ideal—especially, as discussed in the preceding text, when patients present with acute symptoms.

TECHNICAL CONSIDERATIONS FOR PCI IN LM DISEASE. Anatomy of LM disease can add technical challenges to PCI and should weigh on the decision to pursue PCI vs CABG (Figure 3). The majority of LM stenoses involve the LM bifurcation (LMB), and this location has important implications for performing PCI compared with patients with ostial and mid-vessel stenosis.[55] The use of intravascular imaging remains an important and necessary adjunct for assessing lesion severity, technical PCI approach, proper stent sizing, and stent apposition in both non-LMB and LMB anatomy, whereas functional testing can help to assess hemodynamic significance of LM stenosis and to evaluate side branch compromise if a provisional stenting strategy is being considered. For angiographically intermediate lesions, intravascular ultrasound (IVUS) is commonly used to determine significance of a stenosis, and revascularization is generally accepted to be safe to defer if IVUS reveals a minimum lumen area of 6 mm^2 or greater.[56] In Asian populations, a smaller minimum lumen area cutoff of 4.5 mm^2 may be acceptable.[57] One type of functional testing, fractional flow reserve (FFR), has also been useful in deciding whether revascularization is indicated, with FFR values of $>$0.8, representing an acceptable number to defer PCI.

In LMB PCI, several technical considerations should be considered when deciding on stenting strategies. The first is a provisional single-stent strategy vs an upfront dedicated 2-stent strategy. Although the vast majority of LMB PCIs can be performed using a provisional single-stent strategy, sometimes an anatomically complex lesion will require the use of a dedicated 2-stent strategy.[58,59] Second, with regard to bifurcation techniques for a dedicated 2-stent strategy, double kiss crush stenting appears superior to culotte stenting with lower rates of target vessel revascularization.[60]

Lesion complexity in LMB PCI is an important consideration in deciding on anatomical feasibility and the decision to pursue a provisional vs a dedicated 2-stent strategy. The utility of the SYNTAX score, as a predictor of adverse outcomes, typically used to assess lesion complexity, has not been borne out in the 2 most recent trials of LM stenting.[61,62] However, the DEFINITION (Definitions and impact of complEx biFurcation lesIons on clinical outcomes after percutaNeous coronary intervenTION using drug-eluting steNts) trial investigators proposed criteria for simple vs complex bifurcations based on anatomical criteria and demonstrated that 30% of patients had complex bifurcations. Not only did these patients have higher rates of adverse events than those with simple LMB lesions, but they also had better outcomes with a 2-stent strategy.[12] The multicenter randomized DEFINITION II trial demonstrated that a 2-stent strategy compared with a provisional approach was associated with improved outcomes, and the EBC MAIN (European Bifurcation Club Left Main Coronary Stent) trial demonstrated further major cardiac events with a provisional approach vs a 2-stent strategy, but did not reach statistical significance.[59,63] Therefore, studies have been contradictory with regard to 2-stent vs provisional strategies for LM PCI, and lack of standardization between studies prevents definitive conclusions regarding superiority.

The use of adjunctive mechanical circulatory support devices, such as Impella (Abiomed) or the intra-aortic balloon pump, can be of value in carefully selected patients. In patients with LM disease, particularly those with LMB disease and unstable hemodynamics or depressed ejection fraction who might not be able to tolerate the ischemic insult of complex PCI, the use of circulatory devices can provide essential hemodynamic support. Ensuring adequate arterial access (either femoral, axillary, or transcaval) to facilitate support should be an important consideration.

TECHNICAL CONSIDERATIONS FOR CABG IN LM DISEASE. The nature of isolated LM lesions is an irrelevant issue for CABG, because distal epicardial vessels almost always prove to be appropriate bypass targets unless there is concomitant severe diffuse distal disease. For patients with LM CAD and concomitant MVD, complete revascularization is achievable with adequate (minimum 1.5 mm) distal target vessels. Epicardial vessels with smaller caliber targets, calcified walls, or intramyocardial course increase CABG complexity, but are challenges encountered more often in MVD without LM coronary artery (LMCA) involvement.

Several technical considerations are unique to CABG for LM disease (Figure 4). Cardioplegic arrest of the heart during on-pump CABG may be hindered by severe LM stenosis. In cases of critical LMCA disease, patients may become unstable during induction of anesthesia, so careful attention should be paid upon induction with less cardiodepressive agents; in some cases, preinduction use of hemodynamic support (eg, with an intra-aortic balloon pump) may mitigate this issue. Inadequate myocardial protection using solely antegrade cardioplegia may result in a poor distribution of cardioplegia and failure to arrest the heart. The addition of retrograde cardioplegia to facilitate adequate distribution during CABG is a simple solution for myocardial protection.[64] Porcelain aorta or aorta with atheroma can be addressed via off-pump CABG and avoidance of aortic cannulation, aortic cross-clamping, and graft anastomosis to the aorta to avoid embolic stroke.[65,66] However, surgeon experience with off-pump CABG is necessary to achieve the best results. Minimally invasive and hybrid revascularization strategies, to avoid a sternotomy, have been described and are an area of active investigation.[67,68]

Complete surgical revascularization with durable bypass grafts is the objective of CABG. Utilization of the left internal mammary artery (LIMA) is the gold standard in modern CABG and provides both graft durability and superior patient survival.[69,70] Use of multiarterial grafting has been associated with improved outcomes in some series.[69,71,72] Choices for the second arterial graft include the right internal mammary artery (RIMA) and the radial artery. The RIMA can be taken in situ from the subclavian artery, routed either anterior or posterior to the aorta, and grafted to a second left-sided epicardial vessel. In situ

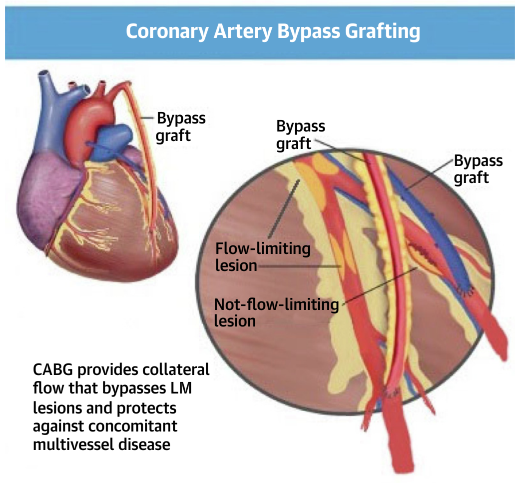
RIMA grafts necessarily cross midline, and the prospect of reoperative surgery must be factored into decision-making. Both the RIMA and radial artery grafts can be grafted to the aorta or from another bypass graft in a Y or T configuration. Sequencing arterial grafts to multiple bypass targets increases the flow through the conduit and may improve long-term patency. Finally, devascularization of vascular beds are concerns during both RIMA and radial artery harvest. However, the risk of deep-sternal wound infection secondary to sternal devascularization can be mitigated by harvesting the RIMA from the chest wall as a skeletonized graft as opposed to a pedicled graft but may come at the cost of reduced graft patency.[73,74] Similarly, hand devascularization after radial artery harvest can be minimized by selecting the nondominant hand and evaluating for sufficient ulnar blood flow into the palmar arch; hand neuropathy is an infrequent and generally transitory complication.[75]

An unanswered question regarding CABG for LM disease is the revascularization strategy when the lesion does not involve the LM bifurcation. The traditional teaching is to bypass both the LAD and LCx distribution, selecting the largest obtuse marginal branch as the distal target on the lateral wall. However, concern arises for competitive flow between the larger vein graft to the circumflex and the LIMA graft to the LAD. On the other hand, a single-vessel bypass, LIMA to LAD, can be considered for patients with small nondominant circumflex distributions. There remain concerns that the flow in the LIMA may be inadequate to supply the entire left ventricle and does not address the potential evolution of proximal LM disease into the bifurcation. Multiarterial grafting with bilateral internal mammary artery grafts might be considered the ideal compromise, avoiding competitive flow from a high-flow vein graft while providing blood flow to both LAD and LCx territories.

COMPARATIVE TRIALS OF CABG VS PCI

Several randomized clinical trials have studied the comparative effectiveness of CABG and PCI for LM CAD (**Table 1**).[24,62,76,77] In these 4 major studies, LM stenosis was defined visually as >50%, but EXCEL (Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) included patients with lesions ≤70% only if hemodynamically significant as determined by additional hemodynamic testing. Another notable difference between the earlier trials and more recent trials is that the EXCEL

FIGURE 4 **CABG Technical Considerations in LM Disease**



Coronary artery bypass grafting (CABG) provides collateral flow that addresses left main (LM) lesions regardless of complexity and protects against multivessel disease by bypassing both current and future upstream-limiting lesions.

and NOBLE (Nordic-Baltic-British Left Main Revascularization Study) trials recommended an IVUS-guided PCI strategy. Although IVUS has not been formally studied in these trials, subset analyses have indicated that use of IVUS is associated with reduced target lesion revascularization.[78]

Published outcomes of LM disease have generated controversy.[79-82] However, several meta-analyses have been conducted analyzing the 4 major LM PCI vs CABG trials; the most recent of which is a collaborative, individual patient-level analysis that seeks to critically evaluate the available data (**Table 2**). These meta-analyses consistently have demonstrated a lack of significant mortality difference between CABG and PCI.[83-86] In, Bayesian analysis, there was an 85.7% probability that death at 5 years was greater with PCI than with CABG; however, this difference was more likely than not <0.2% per year.[86] In another analysis, it was shown that the estimated posterior probability (ie, of any) excess mortality with PCI over CABG was 85% with a 47% probability of exceeding 1 event per 100 treated.[87] Although differences in the rates of procedural MI depended upon the ascertainment of biomarkers (and definition of MI) used within the specific trials, the incidence of spontaneous MI was lower with CABG compared with PCI. With respect to other outcomes, stroke was found to be similar between PCI and CABG and repeat revascularization was consistently less after CABG.

TABLE 1 LM CAD Randomized Clinical Trials Compared by Primary Composite Endpoint

	SYNTAX[24] Serruys 2009	PRECOMBAT[77] Park 2011	EXCEL[62] Stone 2016	NOBLE[61,76] Holm 2020
Sponsor	Boston Scientific	Cardiovascular Research Foundation	Abbott Vascular	Aarhus University Hospital
Trial design	RCT, subset analysis, 1-year	RCT, noninferiority, 1-year	RCT, noninferiority, 3-year	RCT, noninferiority, 5-year
N	705	600	1,905	1,201
Anatomy	>50% stenosis	>50% stenosis	>70% stenosis or 50%-70% hemodynamically significant	>50% stenosis or FFR ≤0.80
Primary composite endpoint	1. death 2. stroke 3. MI 4. repeat revascularization	1. death 2. stroke 3. MI 4. repeat revascularization	1. death 2. stroke 3. MI—SCAI	1. death 2. stroke 3. MI—nonprocedural 4. repeat revascularization
Results	15.8% PCI vs 13.7% CABG	8.7% PCI vs 6.7% CABG	15.4% PCI vs 14.7% CABG	28% PCI vs 19% CABG
Conclusions	Hypothesis generating	Hypothesis generating	PCI noninferior to CABG	PCI inferior to CABG

CABG = coronary artery bypass grafting; EXCEL = Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization; FFR = fractional flow reserve; MI = myocardial infarction; NOBLE = Nordic-Baltic-British Left Main Revascularization Study; PCI = percutaneous coronary intervention; PRECOMBAT = Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease; RCT = randomized clinical trial; SCAI = Society for Cardiovascular Angiography and Interventions; SYNTAX = Synergy Between PCI With TAXUS and Cardiac Surgery.

The comparative studies of CABG and PCI on LM CAD differ by trial design, inclusion criteria, primary composite endpoints, length of follow-up, and even types of stents and adjunctive techniques (eg, IVUS) used. Table 3 contains data on the longest available follow-up from these trials.

CURRENT GUIDELINE RECOMMENDATIONS FOR MANAGING PATIENTS WITH LM DISEASE

Recent guidelines committees have considered the evidence base for LMCA revascularization and formulated recommendations broadly. When considering patients with LM disease, the 2021 American College of Cardiology (ACC)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions (SCAI) guidelines for coronary artery revascularization focus on several key issues: 1) the importance of shared decision-making incorporating the patient's preferences and beliefs; 2) the role of the heart team in facilitating these decisions; 3) the indications for revascularization to improve survival; 4) situations in which one therapy is preferred over another; and 5) the use of intravascular imaging to assess patients with intermediate disease and, when PCI is planned, the use of imaging to guide PCI (Table 4).[17] The 2018 European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) guidelines on myocardial revascularization emphasize: 1) the use of established risk scores to estimate operative risk (STS Class I, Level of Evidence [LOE]: B; EuroSCORE II Class II, LOE: B); 2) the calculation of the SYNTAX score (Class I, LOE: B) to determine anatomical complexity; 3) the importance to achieve complete revascularization (Class IIa, LOE: B); and 4) the heart team (Class I, LOE: C).[18]

Shared decision-making is one of the most important take-home points of the 2021 ACC/AHA/SCAI guidelines for coronary artery revascularization. As mentioned earlier, and as is critical in all cases of coronary revascularization, a patient's own beliefs and preferences must be considered when deciding whether to proceed with revascularization and when contemplating the mode of revascularization. The discussion should be fully transparent, highlighting the institutional volume and expertise with each method of revascularization. Educational tools including illustrations or videos are strongly encouraged.[88,89] The goal is to provide the patient with sufficient information and appropriate time to make an educated decision.

Both guidelines emphasize the importance of the heart team in cases where there is uncertainty regarding the optimal approach to revascularization. This is imperative because by design, randomized trials include patients that meet very stringent enrollment criteria, and in clinical practice, many patients will fall outside of the exact patient population that is studied in an individual trial. In addition to general cardiologists, cardiac surgeons, interventional cardiologists, and anesthesiologists, in many situations, the heart team may include internists, geriatricians, vascular specialists, neurologists, nephrologists, oncologists, pulmonologists, and nursing and/or social workers. They should consider the indications for revascularization, disease complexity, mode of revascularization, anticipated risks/benefits of revascularization strategies, and the patient's preferences. Risk assessment should not solely focus on complexity of disease, STS risk score, or other scoring systems, but should also incorporate other relevant clinical factors that are not

TABLE 2 Meta-Analyses Comparison of Primary Endpoints

	Ahmad 2020[83] RR (95% CI)	Gallo 2020[84] OR (95% CI)	Kuno 2020[85] HR (95% CI)	Sabatine 2021[86] HR (95% CI)
Journal	*European Heart Journal*	*Journal of Thoracic and Cardiovascular Surgery*	*American Heart Journal*	*Lancet*
Death	1.03 (0.82-1.30)	1.13 (0.57-1.38)	1.11 (0.91-1.35)	1.10 (0.91-1.32)
Stroke	0.74 (0.36-1.50)	0.88 (0.61-1.28)	0.81 (0.42-1.53)	0.84 (0.59-1.21)
MI	1.22 (0.96-1.56)	**1.43 (1.13-1.79) $P = 0.003$**	1.48 (0.88-2.48)	**1.34 (1.08-1.67) $P = 0.0087$**
Revascularization	**1.73 (1.49-2.02) $P < 0.001$**	**1.89 (1.58-2.26) $P < 0.0001$**	**1.80 (1.52-2.13) $P < 0.01$**	**1.78 (1.51-2.10) $P < 0.0001$**

Statistically significant values are in **bold**.
MI = myocardial infarction.

always included in risk scores. Similarly, the 2018 ESC/EACTS guidelines on myocardial revascularization highlight the importance of the multidisciplinary heart team to guide a balanced, multidisciplinary decision-making process and establish institutional protocols to implement the appropriate revascularization strategy in accordance with current guidelines (Class I, LOE: C).[18]

The 2021 ACC/AHA/SCAI guidelines provide specific recommendations for proceeding with revascularization in stable patients to improve survival. In stable patients, revascularization of significant LM disease with CABG has been shown to improve survival compared with medical therapy, and therefore, revascularization with CABG to treat LM disease is recommended.[3,17,90] There is a Class I, LOE: B recommendation for revascularization with CABG.[3,34,90] The guidelines also recommend revascularization with PCI to improve mortality compared with medical therapy as a reasonable strategy if revascularization with PCI can provide similar results to that seen with CABG. This is based on a network meta-analysis demonstrating that the survival advantage with PCI compared with medical therapy was similar to that achieved with CABG.[3,34,90,91] It is important to note that the randomized trials showing a survival advantage with CABG were performed at a time before the use of antiplatelet therapies and statins. Although medical therapy has evolved dramatically since that time, newer surgical techniques including the use of arterial grafting have also improved the safety and success of CABG. The 2018 ESC/EACTS guidelines on myocardial revascularization distinguish between prognostic and symptomatic indications for revascularization in patients with stable angina or silent ischemia, and allocate a Class Ia indication for revascularization in patients with LM stenosis >50% in the presence of documented ischemia or hemodynamically relevant stenoses defined by a positive instantaneous wave-free ratio or FFR or lesions with angiographic stenosis >90%.

The majority of studies comparing PCI to CABG in patients with LM disease excluded patients with complex disease, such as SYNTAX score ≥33.[76,92,93] Pooled data from these and other randomized trials did not demonstrate a clear survival advantage of CABG over PCI in patients with low-to-intermediate complexity of LM stenosis.[83,84,86] With this in mind, the guidelines do not provide comparative recommendations to favor one mode of revascularization over another when treating patients with low-to-intermediate complexity LM disease. On the other hand, in patients with complex disease, the SYNTAX trial showed clear superiority of CABG over PCI.[94-96] For this reason, in patients with complex LM disease, CABG is recommended over PCI as a Class I recommendation with a goal toward improving survival for high-complexity CAD.[17] The 2018 ESC/EACTS guidelines mention the significant interaction with time that is notable in randomized clinical trials suggesting early benefit for PCI in terms of periprocedural stroke and MI, which is subsequently offset by a higher risk of spontaneous MI and the consistent observation of more frequent revascularization with PCI than CABG, pointing to the need for individual decision-making taking a patient-centered approach. The recommendations to choose between PCI and CABG in the specific setting of LM stenosis have been guided by underlying disease complexity as estimated by the SYNTAX score. Whereas CABG assumes a Class I, LOE: A indication irrespective of disease complexity in patients at low predicted surgical risk, PCI is contraindicated in patients with LM disease and high complexity (SYNTAX score ≥33, Class III, LOE: B) owing to the low number of patients included in randomized clinical trials, as well as the improved long-term outcomes in patients with high-complexity MVD undergoing CABG. Conversely, PCI has been considered an alternative to CABG among patients with LM disease and low (SYNTAX score ≤22; Class Ia) or intermediate (SYNTAX score 23-32; Class IIa, LOE: A) disease complexity. Of note,

TABLE 3 LM Randomized Clinical Trials Compared by Individual Endpoints and Longest Reported Follow-Up

	EXCEL[93]	NOBLE[76]	SYNTAX[94,96]	PRECOMBAT[92]
Follow-up	5 y	5 y	10 y[a]	10 y
Published	2019	2019	2014/2019	2020
N	1,905	1,186	1,800	600
Death	13% PCI vs 9.9% CABG; **OR: 1.38 (1.03-1.85)**	9% PCI vs 9% CABG; HR: 1.08 (0.74-1.59); $P = 0.68$	27% PCI vs 28% CABG; HR: 0.92 (0.69-1.22)	14.5% PCI vs 13.8% CABG; HR: 1.13 (0.75-1.70)
Stroke	2.9% PCI vs 3.7% CABG; OR: 0.78 (0.46-1.31)	4% PCI vs 2% CABG; HR: 1.75 (0.86-3.55); $P = 0.11$	2.4% PCI vs 3.7% CABG; $P = 0.09$	1.9% PCI vs 2.2% CABG; HR: 0.71 (0.22-2.23)
MI	10.6% PCI vs 9.1% CABG; OR: 1.14 (0.84-1.55)[b]	8% PCI vs 3% CABG; **HR: 2.99 (1.66-5.39); $P = 0.0002$**	9.7% PCI vs 3.8% CABG; **$P < 0.001$**	3.2% PCI vs 2.8% CABG; HR: 0.76 (0.32-1.82)
Revascularization	17.2% PCI vs 10.5% CABG; **OR: 1.79 (1.36-2.36)**	17% PCI vs 10% CABG; **HR: 1.73 (1.25-2.40); $P = 0.0009$**	25.9% PCI vs 13.7% CABG; **$P < 0.0001$**	16.1% PCI vs 8.0% CABG; **HR: 1.98 (1.21-3.21)**

Values in parenthesis are 95% CI. [a]10 years for mortality only, 5 years for other endpoints. [b]Using the Universal Definition of Myocardial Infarction, 9.6% PCI vs 4.7% CABG (95% CI: 2.6%-7.2%).[105] **Bold** indicates statistically significant results.

Abbreviations as in Tables 1 and 2.

the latter recommendation is currently not supported by EACTS and is being reviewed.[18]

Intravascular imaging is useful in patients with LM disease. For this reason, the 2021 ACC/AHA/SCAI guidelines recommend IVUS as a reasonable option for evaluating patients with intermediate LM disease.[17] In patients with LM disease in whom PCI is planned, IVUS or optical coherence tomography can provide useful information related to degree of calcium, volume and extent of plaque, and vessel size. Poststent imaging can also be useful to identify geographic miss, or peristent dissection or thrombus and to assess for adequate stent expansion. The ULTIMATE (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-Comers" Coronary Lesions) trial demonstrated that IVUS-guided PCI resulted in a lower rate of target vessel failure at 1 and 3 years, and a lower rate of stent thrombosis at 3 years.[97,98] Additionally, meta-analyses of studies evaluating IVUS-guided PCI, including the Ultimate trial, have shown a lower cardiac mortality with IVUS-guided PCI.[99] Both sets of guidelines recommend the use of IVUS as a useful tool for procedural guidance for LM PCI (Class IIa, LOE B).[17,18]

PRACTICAL APPROACH TO LM DISEASE

LM disease is the CAD subset with the strongest evidence that revascularization provides survival benefit over medical treatment alone in stable patients.[91] As such, for practicing clinicians, it is important to ascertain an individual patient's likelihood of LM disease as part of risk stratification. In the ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial, in which mildly symptomatic and stable patients with moderate-severe ischemia on noninvasive stress testing were randomized to an invasive vs conservative strategy, screening computed tomography angiography (CTA) was performed before randomization in patients with uncompromised renal function. Among this cohort, significant LM disease was identified in 8% of patients.[100] With the mortality advantage afforded by revascularization, missing the diagnosis of a significant LM disease may be lethal, especially given the association of LM lesions with significant MVD. On the other hand, a shift toward calcium scoring and/or CTA for risk stratification may enrich the population of patients diagnosed with either calcified or noncalcified LM plaques, necessitating a careful assessment of the clinical indications for further workup and testing (eg, cardiac catheterization).

Beyond the upstream consideration of the presence (or absence) of LM disease in the outpatient setting, within the cardiac catheterization laboratory, the angiographic assessment of LM stenosis can be challenging. Coronary angiography has been demonstrated to both underestimate and overestimate the significance of LM stenoses when compared with either invasive imaging (eg, IVUS) or physiological assessment (eg, FFR). Thus, especially for intermediate LM stenoses, a complete assessment using intravascular imaging or physiology is reasonable.

With respect to in-lab decision-making, in patients with stable disease and symptoms, ad hoc intervention is strongly discouraged. In more urgent situations, rapid collaborative multidisciplinary team consultation may be preferred if immediately available on-site or via virtual consultation.[101] In contemporary practice, owing to persistently high operative risks, few patients with ST-segment elevation MI or cardiogenic shock are presently managed

TABLE 4 Recommendations From the 2021 ACC-AHA-SCAI and 2018 ESC-EACTS Relevant to Patients With Left Main Disease

Focus Area	ACC-AHA-SCAI Recommendation	COR, LOE	ESC-EACTS Recommendation	COR, LOE
Shared decision-making	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. 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.	I, C—LD I, C—LD		
The heart team	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.	I, B—NR	It is recommended that institutional protocols are developed by the heart team to implement the appropriate revascularization strategy in accordance with current guidelines.	I, C
Assessing lesion severity in intermediate left main disease	In patients with intermediate stenosis of the LM artery, intravascular ultrasound is reasonable to help define lesion severity.	IIa, B—NR	IVUS should be considered to assess the severity of unprotected LM lesions.	IIa, B
Indications for revascularization to improve survival compared with medical therapy	In patients with SIHD and significant LM stenosis, CABG is recommended to improve survival. In selected patients with SIHD and significant LM stenosis for whom PCI can provide equivalent revascularization to that possible with CABG, PCI is reasonable to improve survival.	I, B IIa, B—NR	In patients with stable angina or silent ischemia and LM disease with stenosis >50% in the presence of documented ischemia or hemodynamically significant coronary stenosis (FFR ≤0.80 or iwFR ≤0.89 or >90% stenosis), treatment with revascularization is recommended.	I, A
Situations in which PCI or CABG would be preferred	In patients who require revascularization for significant LM CAD with high-complexity CAD it is recommended to choose CABG over PCI to improve survival.	I, B—R	In LM disease with intermediate SYNTAX score (0-22), CABG and PCI are equally recommended[a] In LM disease with intermediate SYNTAX score (23-32), CABG is recommended over PCI. In LM disease with high (≥33) SYNTAX score, CABG is recommended but not PCI.	I, A vs I, A I, A vs IIa, A I, A vs III, B
Use of intravascular imaging to guide PCI	In patients undergoing coronary stent implantation, IVUS can be useful for procedural guidance, particularly in cases of LM or complex PCI, to reduce ischemic events.	IIa, B—R	IVUS should be considered to assess the severity of unprotected LM stenoses.	IIa, B
Operator/institutional volume in myocardial revascularization			It should be considered that CABG be performed at institutions with annual institutional volumes of ≥200 CABG cases. It should be considered that PCI for LM be performed by trained operators with an annual volume of ≥25 LM PCI cases per year.	IIa, C IIa, C

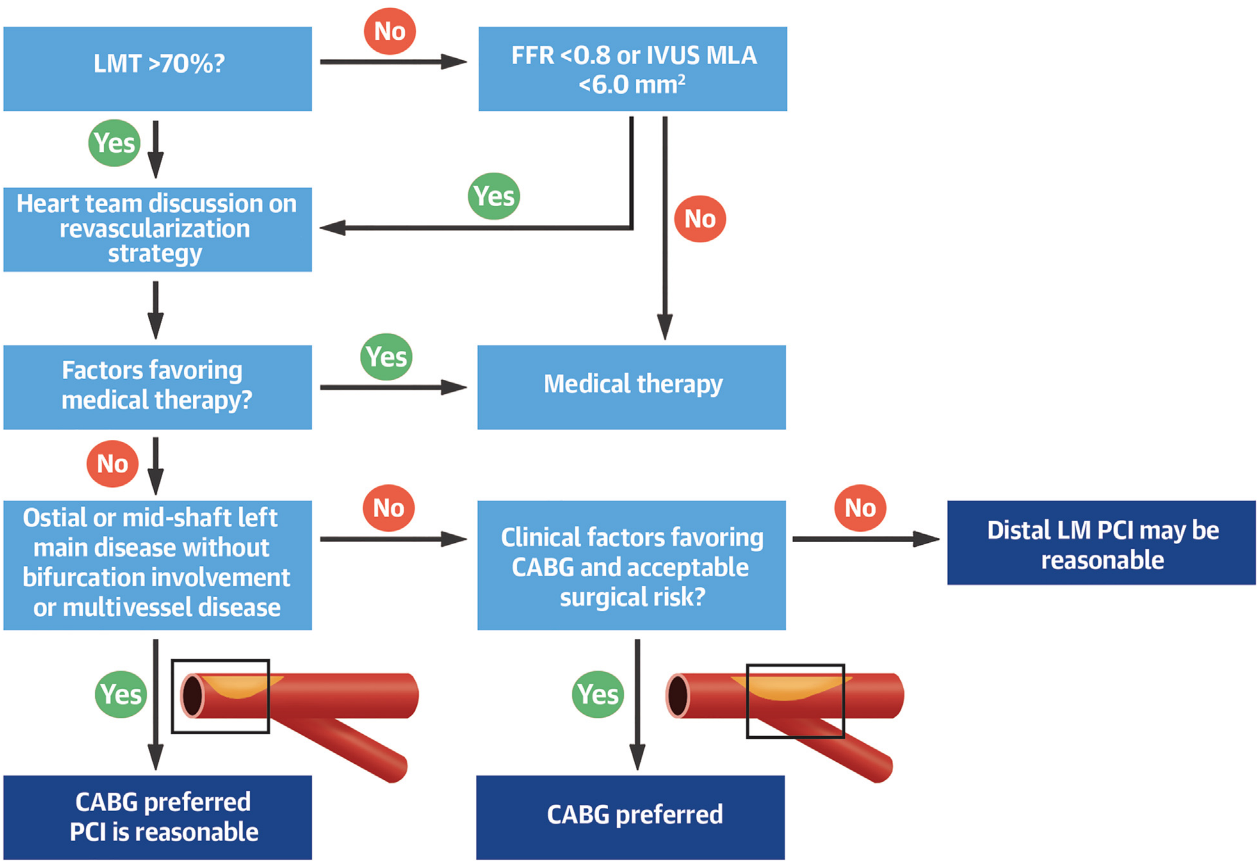
[a]The European Association for Cardio-Thoracic Surgery (EACTS) has withdrawn support of the guideline due to this recommendation.[81,82]

ACC = American College of Cardiology; AHA = American Heart Association; COR = class of recommendation; ESC = European Society of Cardiology; IVUS = intravascular ultrasound; iwFR = instantaneous wave-free ratio; LD = limited data; LM = left main; LOE = level of evidence; NR = nonrandomized data; R = randomized data; SIHD = stable ischemic heart disease; other abbreviations as in Table 1.

acutely with CABG.[102,103] Because both CABG and PCI have important roles in the treatment of LM CAD, a thoughtful heart team-based approach is preferred, especially if the patient is stable. Most patients with critical and/or severe LM stenosis should undergo expedited surgical evaluations, typically before discharge, but for selected and truly stable patients, an expedited outpatient evaluation with close follow-up may be reasonable. Another key principle relating to the multidisciplinary management of LM disease is that for patients who are too high risk for CABG, a review of the feasibility of PCI should be performed by an experienced interventional team rather than simply relegating the patient to a strategy of medical therapy alone. Finally, if a patient is deemed prohibitive risk, a referral to centers specializing in the treatment of complex CAD patients (both surgical and interventional) may allow patients who are deemed inoperable at a local center to be evaluated and treated successfully.

It is important to explicitly state that the optimal revascularization strategy for a given patient can vary, based upon the expertise, experience, and outcomes of the specific surgical and interventional teams at a given institution. The complexity of performing CABG for a distal LM lesion with associated MVD, for example, is typically less for the "average" surgeon performing CABG than the complexity of PCI in the same patient for the "average" interventional cardiologist performing PCI in the United States.

CENTRAL ILLUSTRATION Left Main Coronary Artery Disease Clinical Decision-Making Algorithm



Davidson LJ, et al. J Am Coll Cardiol. 2022;80(22):2119–2134.

This algorithm outlines a clinical approach that may be utilized by clinicians to assist with decision-making for patients who present with left main coronary artery disease. Medical therapy, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) may be reasonable strategies depending on each patient's clinical history, anatomy, and preferences.

When invoking the results of head-to-head clinical trials of CABG vs PCI in order to guide clinical decision-making, the optimized strategies for coronary revascularization used in these trials need to be taken into account. Further, some institutions are not facile with performing LM interventions; a survey of the NCDR demonstrated that the average hospital in the United States performed <5 LM PCIs per year. Irrespective of operator experience, if the institutional support is inadequate, outcomes will likely suffer.

The best revascularization strategy chosen for an individual patient should therefore reflect input from several domains including: 1) patient characteristics including patient preference for one strategy vs another; 2) procedural considerations; 3) operator and institutional experience with the offered procedure (eg, does an interventional cardiologist have sufficient volume and experience to treat LM disease using the best possible PCI technique such as routine intravascular imaging, comfort with plaque modification strategies, familiarity with bifurcation stenting techniques, and safe and especially judicious use of mechanical circulatory support?; and 4) the clinical evidence base for a specific revascularization strategy (eg, data favoring CABG in reduction of especially late MI and repeat revascularization offset by the upfront greater invasiveness of the operation) (Central Illustration).

A careful assessment of both the short- and longer-term goals for the patient is necessary when determining the best treatment options for the patient. A vibrant and independent octogenarian may not wish to undergo the up-front morbidity and recovery following a CABG operation and would accept the tradeoff of a high-quality LM PCI, despite a greater risk for repeat revascularization and/or late MI. On the other hand, a 50-year-old diabetic patient with an ejection fraction of 45% would likely live long enough to realize these late benefits and would be done a disservice if a PCI was performed, especially by a less experienced operator not using imaging guidance or using a poorly indicated hemodynamic support device due to discomfort performing a higher-risk procedure. In making these decisions collectively at an institutional level, it is important to be objective and circumspect, and to place the patient's best interests at the forefront of clinical decision-making.

Finally, it is important to consider the long-term follow-up of patients who undergo LM revascularization and the prompt initiation of proper medical therapy following both revascularization strategies. In the case of patients who undergo LM PCI, dual antiplatelet therapy must be initiated, and patients must understand the importance of compliance with dual antiplatelet therapy to avoid such complications as in-stent thrombosis. For those that undergo CABG, sternotomy precautions must be discussed thoroughly with patients and their families. All patients with LM disease will also require aggressive, disease-modifying guideline-directed medical therapy including high-intensity statins, lifestyle modification (eg, smoking cessation and exercise), and control of hypertension (including beta-blockers and angiotensin-converting enzyme inhibitor/angiotensin receptor blockers), diabetes mellitus, and other cardiovascular risk factors.[104] For those with LV dysfunction, maximizing guideline-directed medical therapy is also imperative. It is also standard for patients to be referred to a cardiac rehabilitation program where efforts at lifestyle management can be implemented. Patients must understand that adherence to medical therapy following revascularization with regular follow-up is imperative to their long-term success.

CONCLUSIONS

The issue of LM artery revascularization has emerged as a topic of considerable debate within our professional societies. Although the clinical trial data and recent guidelines are crucial to understand and to inform clinical decisions, the patients included in these clinical trials reflect only a small portion of the patients encountered in clinical practice. LM disease is a complex clinical process that can be treated with medical therapy alone, PCI, or CABG. The clinical circumstances accompanying LM disease are difficult to quantify. These clinical differences in presentation and anatomy are crucial in decision-making. Thus, it is for that reason that ultimately, a heart team approach, which includes specific, individualized attention to each patient's clinical circumstances, preferences, and goals, is imperative when choosing treatment strategies for LM CAD. In institutions where the heart team approach is embraced, it is our experience and hope that the divisions manifest in the recent literature will be rare. Our paradigm, as outlined, can hopefully serve as a template for such a program. Moving forward, there is a need for professional societies to come together and agree upon mutually acceptable clinical endpoints in order to allow meaningful research to continue on this important topic.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Davidson is a co-investigator for Edwards Lifesciences and Abbott clinical trials. Dr Cleveland has received research grants from Medtronic and Abbott; has served on research committees for Abbott; has been a consultant for and received honoraria from ConneX Biomedical and Medtronic; and has received honoraria from Edwards Lifesciences. Dr Welt has been a consultant for and received honoraria from Medtronic; and holds stock in Xenter, Inc. Dr Anwaruddin has been a consultant and proctor for Edwards Lifesciences and Medtronic; has served on a steering committee for Boston Scientific; and holds equity in East End Medical. Dr Grubb has been a speaker for Edwards Lifesciences, Boston Scientific, and Medtronic; has been a proctor for Edwards Lifesciences and Medtronic; has served on advisory boards for Medtronic and Abbott; has been a principal investigator for trials sponsored by Edwards Lifesciences and Medtronic; and has been a consultant for Gore. Dr Kirtane has been a consultant for IMDS; has received travel expenses/meals from Medtronic, Boston Scientific, Abbott Vascular, CSI, Siemens, Philips, ReCor Medical, Chiesi, OpSens, Zoll, and Regeneron; and has received research grants from, been a consultant for, an/or received speaker fees from Medtronic, Boston Scientific, Abbott Vascular, Amgen, CSI, Philips, ReCor Medical, Neurotronic, Biotronik, Chiesi, Bolt Medical, Magenta Medical, Canon, and SoniVie, paid to his institution. Dr Truesdell has received consultant and speaker fees, paid to his institution, from Abiomed Inc. Dr Windecker has received research and educational grants paid to employer from Abbott, Abiomed, Amgen, AstraZeneca, Bayer, Biotronik, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardinal Health, CardioValve, Corflow Therapeutics, CSL Behring, Daiichi-Sankyo, Edwards Lifesciences, Guerbet, InfraRedx, Janssen-Cilag, Johnson & Johnson, Medicure, Medtronic, Merck Sharp & Dohm, Miracor Medical, Novartis, Novo Nordisk, Organon, OrPha Suisse, Pfizer, Polares, Regeneron, Sanofi, Servier, Sinomed, Terumo, Vifor, V-Wave; has served as advisory board member and/or member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, AstraZeneca, Bayer, Boston Scientific, Biotronik, Bristol Myers Squibb, Edwards Lifesciences, Janssen, MedAlliance, Medtronic, Novartis, Polares, Recardio, Sinomed, Terumo, V-Wave, and Xeltis with payments to employer but no personal payments; and has been a member of the steering/executive committee group of several investigator-initiated

trials that receive funding by industry without impact on his personal remuneration. Dr Malaisrie has been a consultant for and received research funding from Edwards Lifesciences, Medtronic, Terumo Aortic, and Artivion. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr S. Chris Malaisrie, Department of Cardiac Surgery, Northwestern University, 676 North St. Clair, Suite 730, Chicago, Illinois 60611, USA. E-mail: chris.malaisrie@nm.org.

REFERENCES

1. Campeau L, Corbara F, Crochet D, Petitclerc R. Left main coronary artery stenosis: the influence of aortocoronary bypass surgery on survival. *Circulation*. 1978;57:1111–1115.

2. European Coronary Surgery Study Group. Long-term results of prospective randomised study of coronary artery bypass surgery in stable angina pectoris. *Lancet*. 1982;2:1173–1180.

3. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main coronary artery disease. Long-term CASS experience. *Circulation*. 1995;91:2325–2334.

4. Takaro T, Peduzzi P, Detre KM, et al. Survival in subgroups of patients with left main coronary artery disease. Veterans Administration Cooperative Study of Surgery for Coronary Arterial Occlusive Disease. *Circulation*. 1982;66:14–22.

5. Ramadan R, Boden WE, Kinlay S. Management of left main coronary artery disease. *J Am Heart Assoc*. 2018;7(7):e008151. https://doi.org/10.1161/JAHA.117.008151

6. Park DW, Park SJ. Percutaneous coronary intervention of left main disease: pre- and post-EXCEL (Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) and NOBLE (Nordic-Baltic-British Left Main Revascularization Study) era. *Circ Cardiovasc Interv*. 2017;10(6):e004792. https://doi.org/10.1161/CIRCINTERVENTIONS.117.004792

7. Morice MC, Serruys PW, Kappetein AP, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. *Circulation*. 2010;121:2645–2653.

8. Ragosta M. Left main coronary artery disease: importance, diagnosis, assessment, and management. *Curr Probl Cardiol*. 2015;40:93–126.

9. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol*. 2011;58(24):e44–e122. https://doi.org/10.1016/j.jacc.2011.08.007

10. Bourantas CV, Zhang YJ, Garg S, et al. Prognostic implications of severe coronary calcification in patients undergoing coronary artery bypass surgery: an analysis of the SYNTAX study. *Catheter Cardiovasc Interv*. 2015;85:199–206.

11. Huisman J, van der Heijden LC, Kok MM, et al. Impact of severe lesion calcification on clinical outcome of patients with stable angina, treated with newer generation permanent polymer-coated drug-eluting stents: a patient-level pooled analysis from TWENTE and DUTCH PEERS (TWENTE II). *Am Heart J*. 2016;175:121–129.

12. Chen SL, Sheiban I, Xu B, et al. Impact of the complexity of bifurcation lesions treated with drug-eluting stents: the DEFINITION study (Definitions and impact of complEx biFurcation lesIons on clinical outcomes after percutaNeous coronary IntervenTIOn using drug-eluting steNts). *J Am Coll Cardiol Intv*. 2014;7:1266–1276.

13. Gossl M, Faxon DP, Bell MR, Holmes DR, Gersh BJ. Complete versus incomplete revascularization with coronary artery bypass graft or percutaneous intervention in stable coronary artery disease. *Circ Cardiovasc Interv*. 2012;5:597–604.

14. Malkin CJ, George V, Ghobrial MS, et al. Residual SYNTAX score after PCI for triple vessel coronary artery disease: quantifying the adverse effect of incomplete revascularisation. *EuroIntervention*. 2013;8:1286–1295.

15. Benedetto U, Lau C, Caputo M, et al. Comparison of outcomes for off-pump versus on-pump coronary artery bypass grafting in low-volume and high-volume centers and by low-volume and high-volume surgeons. *Am J Cardiol*. 2018;121:552–557.

16. Gaudino M, Bakaeen F, Benedetto U, et al. Use rate and outcome in bilateral internal thoracic artery grafting: insights from a systematic review and meta-analysis. *J Am Heart Assoc*. 2018;77(11):e009361. https://doi.org/10.1161/JAHA.118.009361

17. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 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. *J Am Coll Cardiol*. 2022;79:e21–e129.

18. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J*. 2019;40:87–165.

19. Brennan JM, Curtis JP, Dai D, et al. Enhanced mortality risk prediction with a focus on high-risk percutaneous coronary intervention: results from 1,208,137 procedures in the NCDR (National Cardiovascular Data Registry). *J Am Coll Cardiol Intv*. 2013;6:790–799.

20. Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734–744. discussion 744-745.

21. O'Brien SM, Feng L, He X, et al. The Society of Thoracic Surgeons 2018 adult cardiac surgery risk models: part 2-statistical methods and results. *Ann Thorac Surg*. 2018;105:1419–1428.

22. Escaned J, Collet C, Ryan N, et al. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. *Eur Heart J*. 2017;38:3124–3134.

23. Farooq V, van Klaveren D, Steyerberg EW, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet*. 2013;381:639–650.

24. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–972.

25. Takahashi K, Serruys PW, Fuster V, et al. Redevelopment and validation of the SYNTAX score II to individualise decision making between percutaneous and surgical revascularisation in patients with complex coronary artery disease: secondary analysis of the multicentre randomised controlled SYNTAXES trial with external cohort validation. *Lancet*. 2020;396:1399–1412.

26. The BARI Investigators. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: the Bypass Angioplasty Revascularization Investigation (BARI). *Circulation*. 1997;96:1761–1769.

27. Lee K, Ahn JM, Yoon YH, et al. Long-term (10-year) outcomes of stenting or bypass surgery for left main coronary artery disease in patients with and without diabetes mellitus. *J Am Heart Assoc*. 2020;9:e015372.

28. Gaba P, Gersh BJ, Ali ZA, Moses JW, Stone GW. Complete versus incomplete coronary revascularization: definitions, assessment and outcomes. *Nat Rev Cardiol*. 2021;18:155–168.

29. Leonardi S, Capodanno D, Sousa-Uva M, et al. Composition, structure, and function of heart teams: a joint position paper of the ACVC, EAPCI, EACTS, and EACTA focused on the management of patients with complex coronary artery disease requiring myocardial revascularization. *Eur J Cardiothorac Surg*. 2021;59:522–531.

30. Ali ZA, Karimi Galougahi K, Nazif T, et al. Imaging- and physiology-guided percutaneous coronary intervention without contrast administration in advanced renal failure: a feasibility, safety, and outcome study. *Eur Heart J*. 2016;37:3090–3095.

31. Giustino G, Mehran R, Serruys PW, et al. Left main revascularization with PCI or CABG in patients with chronic kidney disease: EXCEL trial. *J Am Coll Cardiol*. 2018;72:754–765.

32. Doenst T, Haverich A, Serruys P, et al. PCI and CABG for treating stable coronary artery disease: JACC review topic of the week. *J Am Coll Cardiol*. 2019;73:964–976.

33. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007;356:1503–1516.

34. Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet*. 1994;344:563–570.

35. Afilalo J, Alexander KP, Mack MJ, et al. Frailty assessment in the cardiovascular care of older adults. *J Am Coll Cardiol*. 2014;63:747–762.

36. Lemaire A, Soto C, Salgueiro L, Ikegami H, Russo MJ, Lee LY. The impact of age on outcomes of coronary artery bypass grafting. *J Cardiothorac Surg*. 2020;15:158.

37. Madhavan MV, Gersh BJ, Alexander KP, Granger CB, Stone GW. Coronary artery disease in patients >/=80 years of age. *J Am Coll Cardiol*. 2018;71:2015–2040.

38. McNulty EJ, Ng W, Spertus JA, et al. Surgical candidacy and selection biases in nonemergent left main stenting: implications for observational studies. *J Am Coll Cardiol Intv*. 2011;4:1020–1027.

39. Waldo SW, Secemsky EA, O'Brien C, et al. Surgical ineligibility and mortality among patients with unprotected left main or multivessel coronary artery disease undergoing percutaneous coronary intervention. *Circulation*. 2014;130:2295–2301.

40. Kumar S, McDaniel M, Samady H, Forouzandeh F. Contemporary revascularization dilemmas in older adults. *J Am Heart Assoc*. 2020;9:e014477.

41. Mamas MA, Fath-Ordoubadi F, Danzi GB, et al. Prevalence and impact of co-morbidity burden as defined by the Charlson co-morbidity index on 30-day and 1- and 5-year outcomes after coronary stent implantation (from the Nobori-2 study). *Am J Cardiol*. 2015;116:364–371.

42. Potts J, Nagaraja V, Al Suwaidi J, et al. The influence of Elixhauser comorbidity index on percutaneous coronary intervention outcomes. *Catheter Cardiovasc Interv*. 2019;94:195–203.

43. Reichart D, Rosato S, Nammas W, et al. Clinical frailty scale and outcome after coronary artery bypass grafting. *Eur J Cardiothorac Surg*. 2018;54:1102–1109.

44. Wang W, Bagshaw SM, Norris CM, et al. Association between older age and outcome after cardiac surgery: a population-based cohort study. *J Cardiothorac Surg*. 2014;9:177.

45. Kok MM, von Birgelen C. Involving the patient's perspective and preferences concerning coronary angiography and percutaneous coronary intervention. *EuroIntervention*. 2020;15:1228–1231.

46. Cui K, Zhang D, Lyu S, et al. Meta-analysis comparing percutaneous coronary revascularization using drug-eluting stent versus coronary artery bypass grafting in patients with left ventricular systolic dysfunction. *Am J Cardiol*. 2018;122:1670–1676.

47. Sun LY, Gaudino M, Chen RJ, Bader Eddeen A, Ruel M. Long-term outcomes in patients with severely reduced left ventricular ejection fraction undergoing percutaneous coronary intervention vs coronary artery bypass grafting. *JAMA Cardiol*. 2020;5:631–641.

48. Panza JA, Ellis AM, Al-Khalidi HR, et al. Myocardial Viability and Long-Term Outcomes in Ischemic Cardiomyopathy. *N Engl J Med*. 2019;381:739–748.

49. Atkinson TM, Ohman EM, O'Neill WW, Rab T, Cigarroa JE. Interventional Scientific Council of the American College of Cardiology. A practical approach to mechanical circulatory support in patients undergoing percutaneous coronary intervention: an interventional perspective. *J Am Coll Cardiol Intv*. 2016;9:871–883.

50. Patel N, Sharma A, Dalia T, et al. Vascular complications associated with percutaneous left ventricular assist device placement: a 10-year US perspective. *Catheter Cardiovasc Interv*. 2020;95:309–316.

51. Holmes DR Jr, Rich JB, Zoghbi WA, Mack MJ. The heart team of cardiovascular care. *J Am Coll Cardiol*. 2013;61:903–907.

52. Luckraz H, Norell M, Buch M, James R, Cooper G. Structure and functioning of a multidisciplinary 'Heart Team' for patients with coronary artery disease: rationale and recommendations from a joint BCS/BCIS/SCTS working group. *Eur J Cardiothorac Surg*. 2015;48:524–529.

53. Chhatriwalla AK, Decker C, Gialde E, et al. Developing and testing a personalized, evidence-based, shared decision-making tool for stent selection in percutaneous coronary intervention using a pre-post study design. *Circ Cardiovasc Qual Outcomes*. 2019;12:e005139.

54. Doll JA, Jones WS, Lokhnygina Y, et al. PREPARED Study: A Study of Shared Decision-Making for Coronary Artery Disease. *Circ Cardiovasc Qual Outcomes*. 2019;12:e005244.

55. Rab T, Sheiban I, Louvard Y, Sawaya FJ, Zhang JJ, Chen SL. Current Interventions for the Left Main Bifurcation. *J Am Coll Cardiol Intv*. 2017;10:849–865.

56. de la Torre Hernandez JM, Hernandez Hernandez F, Alfonso F, et al. Prospective application of pre-defined intravascular ultrasound criteria for assessment of intermediate left main coronary artery lesions results from the multicenter LITRO study. *J Am Coll Cardiol*. 2011;58:351–358.

57. Park SJ, Ahn JM, Kang SJ, et al. Intravascular ultrasound-derived minimal lumen area criteria for functionally significant left main coronary artery stenosis. *J Am Coll Cardiol Intv*. 2014;7:868–874.

58. Chen X, Li X, Zhang JJ, et al. 3-Year outcomes of the DKCRUSH-V trial comparing DK crush with provisional stenting for left main bifurcation lesions. *J Am Coll Cardiol Intv*. 2019;12:1927–1937.

59. Zhang JJ, Ye F, Xu K, et al. Multicentre, randomized comparison of two-stent and provisional stenting techniques in patients with complex coronary bifurcation lesions: the DEFINITION II trial. *Eur Heart J*. 2020;41:2523–2536.

60. Chen SL, Xu B, Han YL, et al. Comparison of double kissing crush versus Culotte stenting for unprotected distal left main bifurcation lesions: results from a multicenter, randomized, prospective DKCRUSH-III study. *J Am Coll Cardiol*. 2013;61:1482–1488.

61. Makikallio T, Holm NR, Lindsay M, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. *Lancet*. 2016;388:2743–2752.

62. Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. *N Engl J Med*. 2016;375:2223–2235.

63. Hildick-Smith D, Egred M, Banning A, et al. The European Bifurcation Club Left Main Coronary Stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN). *Eur Heart J*. 2021;42:3829–3839.

64. Buckberg GD. Antegrade/retrograde blood cardioplegia to ensure cardioplegic distribution: operative techniques and objectives. *J Card Surg*. 1989;4(37):216–238. https://doi.org/10.1093/eurheartj/ehab283

65. Dietl CA, Madigan NP, Laubach CA, et al. Myocardial revascularization using the "no-touch" technique, with mild systemic hypothermia, in patients with a calcified ascending aorta. *J Cardiovasc Surg (Torino)*. 1995;36:39–44.

66. Lev-Ran O, Ben-Gal Y, Matsa M, et al. 'No touch' techniques for porcelain ascending aorta: comparison between cardiopulmonary bypass with femoral artery cannulation and off-pump myocardial revascularization. *J Card Surg*. 2002;17:370–376.

67. Halkos ME, Rab ST, Vassiliades TA, et al. Hybrid coronary revascularization versus off-pump coronary artery bypass for the treatment of left main coronary stenosis. *Ann Thorac Surg*. 2011;92:2155–2160.

68. Harskamp RE, Bonatti JO, Zhao DX, et al. Standardizing definitions for hybrid coronary revascularization. *J Thorac Cardiovasc Surg*. 2014;147:556–560.

69. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts-effects on survival over a 15-year period. *N Engl J Med*. 1996;334:216–219.

70. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med*. 1986;314:1-6.

71. He GW. Arterial grafts for coronary artery bypass grafting: biological characteristics, functional classification, and clinical choice. *Ann Thorac Surg*. 1999;67:277–284.

72. Schwann TA, Yammine MB, El-Hage-Sleiman AM, Engoren MC, Bonnell MR, Habib RH. The effect of completeness of revascularization during CABG with single versus multiple arterial grafts. *J Card Surg*. 2018;33:620–628.

73. Gaudino M, Audisio K, Rahouma M, et al. Comparison of long-term clinical outcomes of skeletonized vs pedicled internal thoracic artery harvesting techniques in the arterial revascularization trial. *JAMA Cardiol*. 2021;6:1380–1386.

74. Lamy A, Browne A, Sheth T, et al. Skeletonized vs pedicled internal mammary artery graft harvesting in coronary artery bypass surgery: a post hoc analysis from the COMPASS trial. *JAMA Cardiol*. 2021;6(9):1042–1049. https://doi.org/10.1001/jamacardio.2021.1686

75. Holman WL, Davies JE, Lin JY, et al. Consequences of radial artery harvest: results of a prospective, randomized, multicenter trial. *JAMA Surg*. 2013;148:1020–1023.

76. Holm NR, Makikallio T, Lindsay MM, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. *Lancet*. 2020;395:191–199.

77. Park SJ, Kim YH, Park DW, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. *N Engl J Med*. 2011;364:1718–1727.

78. Ladwiniec A, Walsh SJ, Holm NR, et al. Intravascular ultrasound to guide left main stem intervention: a NOBLE trial substudy. *EuroIntervention*. 2020;16:201–209.

79. Gaudino M, Brophy JM. The controversy on the treatment of left main coronary artery disease. *J Thorac Cardiovasc Surg*. 2022;163(5):1864–1869. https://doi.org/10.1016/j.jtcvs.2020.08.122

80. Stone GW, Serruys PW, Sabik JF. PCI or CABG for left main coronary artery disease. reply. *N Engl J Med*. 2020;383:292–294.

81. Cohen D, Brown E. *Surgeons withdraw support for heart disease advice*. BBC Newsnight. BBC News: BBC; 2019. Accessed July 15, 2022. https://www.bbc.com/news/health-50715156

82. Pagano D. *Changing Evidence, Changing Practice. EACTS: EACTS*. 2019. Accessed July 15, 2022. https://www.eacts.org/changing-evidence-changing-practice/

83. Ahmad Y, Howard JP, Arnold AD, et al. Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials. *Eur Heart J*. 2020;41:3228–3235.

84. Gallo M, Blitzer D, Laforgia PL, et al. Percutaneous coronary intervention versus coronary artery bypass graft for left main coronary artery disease: a meta-analysis. J. *Thorac Cardiovasc Surg*. 2022;163:94–105. e15.

85. Kuno T, Ueyama H, Rao SV, et al. Percutaneous coronary intervention or coronary artery bypass graft surgery for left main coronary artery disease: a meta-analysis of randomized trials. *Am Heart J*. 2020;227:9–10.

86. Sabatine MS, Bergmark BA, Murphy SA, et al. Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data meta-analysis. *Lancet*. 2021;398:2247–2257.

87. Brophy JM. Bayesian interpretation of the EXCEL trial and other randomized clinical trials of left main coronary artery revascularization. *JAMA Intern Med*. 2020;180:986–992.

88. Coronary Artery Disease. The Patient Guide to Heart, Lung, and Esophageal Surgery. The Society of Thoracic Surgeons. Accessed July 15, 2022. https://ctsurgerypatients.org/adult-heart-disease/coronary-artery-disease

89. Coronary Artery Disease: CardioSmart. American College of Cardiology. Accessed July 15, 2022. https://www.cardiosmart.org/topics/coronary-artery-disease

90. Takaro T, Hultgren HN, Lipton MJ, Detre KM. The VA cooperative randomized study of surgery for coronary arterial occlusive disease II. Subgroup with significant left main lesions. *Circulation*. 1976;54:III107–III117.

91. Bittl JA, He Y, Jacobs AK, Yancy CW, Normand SL. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Bayesian methods affirm the use of percutaneous coronary intervention to improve survival in patients with unprotected left main coronary artery disease. *Circulation*. 2013;127:2177–2185.

92. Park DW, Ahn JM, Park H, et al. Ten-year outcomes after drug-eluting stents versus coronary artery bypass grafting for left main coronary disease: extended follow-up of the PRECOMBAT trial. *Circulation*. 2020;141:1437–1446.

93. Stone GW, Kappetein AP, Sabik JF, et al. Five-year outcomes after PCI or CABG for left main coronary disease. *N Engl J Med*. 2019;381:1820–1830.

94. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet*. 2013;381:629–638.

95. Morice MC, Serruys PW, Kappetein AP, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery trial. *Circulation*. 2014;129:2388–2394.

96. Thuijs D, Kappetein AP, Serruys PW, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. *Lancet*. 2019;394:1325–1334.

97. Gao XF, Ge Z, Kong XQ, et al. 3-Year outcomes of the ULTIMATE trial comparing intravascular ultrasound versus angiography-guided drug-eluting stent implantation. *J Am Coll Cardiol Intv*. 2021;14:247–257.

98. Zhang J, Gao X, Kan J, et al. Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: the ULTIMATE trial. *J Am Coll Cardiol*. 2018;72:3126–3137.

99. Darmoch F, Alraies MC, Al-Khadra Y, Moussa Pacha H, Pinto DS, Osborn EA. Intravascular ultrasound imaging-guided versus coronary angiography-guided percutaneous coronary intervention: a systematic review and meta-analysis. *J Am Heart Assoc*. 2020;9:e013678.

100. Hochman JS, Reynolds HR, Bangalore S, et al. Baseline characteristics and risk profiles of participants in the ISCHEMIA randomized clinical trial. *JAMA Cardiol*. 2019;4:273–286.

101. Blankenship JC, Gigliotti OS, Feldman DN, et al. Ad hoc percutaneous coronary intervention: a consensus statement from the Society for Cardiovascular Angiography and Interventions. *Catheter Cardiovasc Interv*. 2013;81:748–758.

102. Gu YL, van der Horst IC, Douglas YL, Svilaas T, Mariani MA, Zijlstra F. Role of coronary artery bypass grafting during the acute and subacute phase of ST-elevation myocardial infarction. *Neth Heart J*. 2010;18:348–354.

103. Mehta RH, Grab JD, O'Brien SM, et al. Clinical characteristics and in-hospital outcomes of patients with cardiogenic shock undergoing coronary artery bypass surgery: insights from the Society of Thoracic Surgeons National Cardiac Database. *Circulation*. 2008;117:876–885.

104. Kawashima H, Serruys PW, Ono M, et al. Impact of optimal medical therapy on 10-year mortality after coronary revascularization. *J Am Coll Cardiol*. 2021;78:27–38.

105. Lozano I, Rondan J, Vegas JM. PCI or CABG for left main coronary artery disease. *N Engl J Med*. 2020;383:290–291.

KEY WORDS coronary artery bypass grafting, coronary artery disease, left main coronary artery disease, myocardial revascularization, percutaneous coronary intervention