

Multivessel coronary disease should be treated with coronary artery bypass grafting in all patients who are not (truly) high risk



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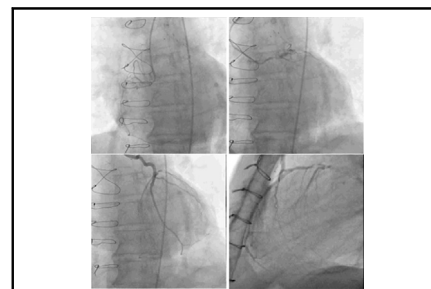
Patients with multivessel coronary artery disease (MVD) who undergo coronary artery bypass grafting (CABG) experience better long-term survival and lower risks of adverse cardiac events than those who do not.¹ Recent US guideline recommendations downgraded CABG relative to medical therapy for MVD with ejection fraction (EF) greater than 30%.² This review explains why MVD should be treated with CABG in all patients who are not truly high risk.

UNDERSTANDING MULTIVESSEL CORONARY ARTERY DISEASE AND GRAFTING

Coronary artery disease (CAD) results from atherosclerotic plaque development in the coronary vessels that ultimately stenose, leading to ischemia, or rupture, causing vessel occlusion and leading to acute myocardial infarction (MI). Treatment of CAD, which is aimed at alleviating symptoms and preventing MI or death, includes medical therapy and revascularization with percutaneous coronary intervention (PCI) or CABG.

MVD is present when a patient has significant stenosis (>70%) in 2 or more major coronary arteries.² The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score is used to grade anatomic complexity of CAD in patients with MVD and to guide revascularization decisions.³ CABG provides the best option for complete and durable revascularization. In stable CAD, CABG offers a survival advantage over medical therapy and can reduce the risk of new MI.¹

Most coronary infarcts occur as a result of nonflow-limiting stenoses resulting from eventual progression of the less-obstructive plaques.¹ Because PCI is focused on treating flow-limiting lesions, it does not significantly limit new infarcts; however, CABG provides flow distal to the



Coronary angiography of a 90-year-old patient 30 years after CABG for stable MVD and normal EF.

CENTRAL MESSAGE

CABG remains the gold standard for patients with complex multivessel disease and left main disease. High-risk patients who are not candidates for CABG are infrequently encountered.

vessel occlusion and may be more likely to limit new infarcts.¹ This concept of surgical collateralization and the importance of internal thoracic artery inflow are well illustrated when post-CABG patients undergo coronary angiography years later (Figure 1).

REVASCUARIZATION GUIDELINES

CABG has been a Class I recommendation for patients with MVD, regardless of EF, in all guidelines before 2021. The 2021 American College of Cardiology (ACC)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions (SCAI) Guidelines for Coronary Artery Revascularization downgraded CABG relative to medical therapy with survival as an end point in patients with stable ischemic heart disease with normal EF and severe 3-vessel disease.² Although CABG remained Class I in patients with MVD and severe left ventricular (LV) systolic dysfunction, it decreased to Class IIB for those patients with normal LV function (and stable MVD) and Class IIA for those patients with mild-to-moderate LV dysfunction.

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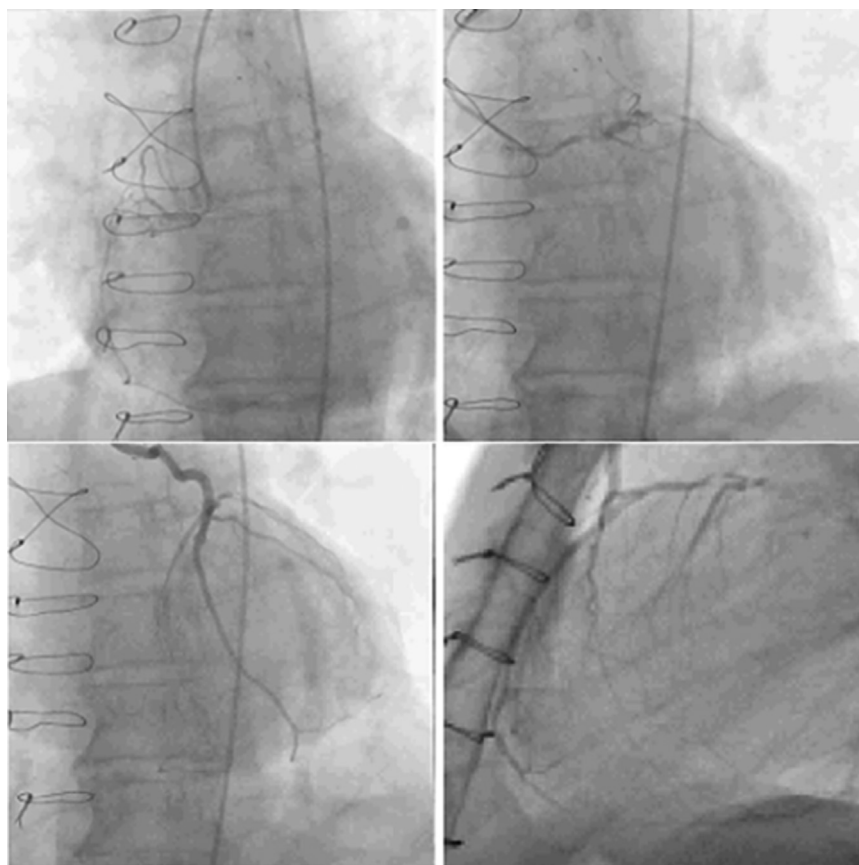


FIGURE 1. Coronary angiography of a 90-year-old patient who underwent CABG for stable MVD and normal EF 30 years ago. *Top:* Occluded native circulation (right and left coronaries). *Bottom:* The importance of surgical collateralization that supplies blood to the entire heart. CABG, Coronary artery bypass grafting; MVD, multivessel disease; EF, ejection fraction.

Professional associations have challenged the scientific basis of the new controversial CABG recommendations. The Society of Thoracic Surgeons (STS) and the American Association for Thoracic Surgery (AATS) do not endorse these guidelines.

A recent editorial reviewed this downgrade by examining source data behind the guidelines.⁴ Only 4 studies supported the downgraded designation of Class IIB for CABG in patients with 3-vessel disease and normal EF. Of these, 2 studies demonstrated a survival advantage for CABG, and 2 studies were not designed to compare CABG with medical therapy. Only 6 studies supported the downgraded designation of Class IIA for CABG in patients with MVD and mild-to-moderate LV dysfunction. Four studies demonstrated a survival advantage for CABG. One was equivocal but designed to gauge the effect of myocardial viability, and another study was negative overall but positive for improved survival in a subset of patients with mild-to-moderate LV dysfunction.

To further support the downgrade to Class IIB, the guidelines cite the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches

(ISCHEMIA) trial,⁵ but this was a strategy trial examining initial conservative versus invasive strategies for stable coronary disease. To understand the appropriateness in applicability of this trial to its role in support of the guideline change, it is important to consider its specific aims and design.

The ISCHEMIA trial randomized 5179 patients with moderate-to-severe ischemia to an invasive strategy (angiography and revascularization) or a conservative strategy (medical therapy). The primary outcome was a composite of cardiovascular death, MI, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest.

Not one patient was initially randomized to CABG (or PCI). Additionally, CABG accounted for only 23.6% of the invasive study arm patients. The median follow-up of 3.2 years severely limits this trial's applicability to any evaluation of survival benefit in CABG.

Another study of the invasive arm of ISCHEMIA revealed that the rate of complete revascularization achieved with CABG was only 35.7%.⁶ This was just more than half of the completeness of revascularization rate in the SYNTAX trial and lower than any other published trial. This unusually low rate casts serious concern on the veracity of the

ISCHEMIA trial's ability to present meaningful data and conclusions about CABG.

The ISCHEMIA trial largely excluded patients with significant atherosclerotic burden and complex disease; therefore, the population included is not wholly representative of the typical CABG population. Even with the cutoff of 50% or greater, only 36.2% had proximal left anterior descending artery (LAD) lesions. It is rare for patients to undergo CABG in the absence of a significant proximal LAD lesion.

The lower atherosclerotic burden of the ISCHEMIA patient explains their more favorable risk compared with STS CABG patients (Table 1).^{7,8}

The 2021 guidelines pointed to other “new evidence” in support of the CABG downgrade. Namely, a systemic review and meta-analysis of randomized trials examining routine revascularization versus initial medical therapy for stable ischemic heart disease concluded that routine revascularization was not associated with improved survival.¹¹ In this meta-analysis of 14 trials, most patients enrolled had low ischemic burden. The majority of participants receiving revascularization had PCI, and only 16% received CABG. Half of the trials included no CABG cases.

Therefore, this “new” evidence does not support the change from a Class I recommendation for CABG relative to medical therapy in MVD with survival as an end point. At best, it supports an initial approach of conservative medical therapy only in patients with stable CAD, normal EF, and low-to-moderate atherosclerotic burden.⁴ Evidence has shown the long-term benefits of CABG in MVD. A systematic review of 10-year results from randomized trials of CABG showed significant reduction in all-cause mortality risk with CABG compared with medical therapy at 5 years (39%), 7 years (32%), and 10 years (17%).⁹ This survival benefit was seen in patients with both normal and abnormal EF. No new trial has contradicted this finding.

After a critical review of the best available evidence, the 2024 European Society of Cardiology guidelines for the management of chronic coronary syndromes reaffirmed CABG as a Class I recommendation in patients with

3-vessel CAD regardless of LVEF, thus validating the concerns about the ACC/AHA guidelines.¹⁰

Regarding CABG versus PCI in patients with MVD, the SYNTAX trial found that CABG provides a significant survival benefit in patients with 3-vessel disease,³ an advantage that continues after 10 years of follow-up.¹² This mortality benefit was greater in patients with diabetes and higher coronary complexity. A systematic review of 11 trials comparing CABG with PCI examined all-cause mortality in patients with MVD or left main CAD without acute MI and more than 1 year of follow-up.¹³ This report also showed CABG had a survival benefit over PCI in patients with MVD, which was greater in patients with diabetes and higher coronary complexity.

Additionally, the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial found that CABG was superior to PCI for patients with diabetes and advanced CAD, with significantly reduced rates of death and MI, and 10-year follow-up showing a survival benefit to CABG.¹⁴

Modern-day CABG is a safe procedure. The STS National Database data show that perioperative morbidity for all-comers in 2021 is quite low. CABG has an in-hospital mortality of less than 2.1%, with centers of excellence achieving a rate less than 1%.^{15,16} The Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) III trial's 30-day mortality of CABG was 0.3% and identical to that of PCI.¹⁷

NEW PRIORITIES OF CORONARY ARTERY BYPASS GRAFTING: LESS INVASIVENESS, ENHANCED RECOVERY, AND QUALITY OF LIFE

Recent innovations in cardiac surgery, including implementation of enhanced recovery pathways and a less-invasive procedure, have improved patient outcomes and experience.^{18,19} Minimally invasive coronary surgery and robotic-assisted CABG allow for the avoidance of a sternotomy and often cardiopulmonary bypass. These options involve access through a left anterior small thoracotomy or thoracoscopy.¹⁸ Hybrid revascularization refers to a combination of sternal-sparing left internal thoracic artery LAD grafting with PCI of non-LAD vessels with stenosis.²⁰ Despite the low adoption rate of less-invasive CABG techniques,²¹ it is anticipated that their use will increase over time in select patients and in experienced hands with careful quality assurance.

Finally, in addition to improving survival relative to these therapies, CABG has a proven track record of improving the quality of life in patients with CAD, and this is a focus of ongoing and future trials.²²

DECISION-MAKING

The decision-making process about the management of MVD is ideally undertaken by a heart team and requires good judgment and attention to the patient's informed

TABLE 1. Comparison of International Study of Comparative Health Effectiveness with Medical and Invasive Approaches trial patients versus Society of Thoracic Surgeons database patients^{9,10}

Comorbidities of included patients	ISCHEMIA	STS
Diabetes	41.8%	47.9%
Hypertension	73.4%	88.7%
Current smoker	12.4%	22.6%
Cerebrovascular disease	7.3%	18.6%
Peripheral vascular disease	3.9%	13.8%
Heart failure	4.0%	17.6%

ISCHEMIA, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches; STS, Society of Thoracic Surgeons.

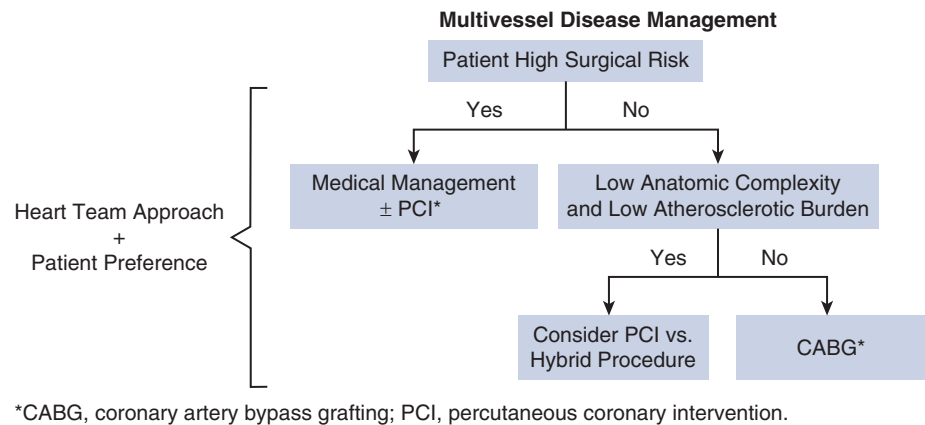


FIGURE 2. A heart team approach to multivessel disease management.

preference (Figure 2). Careful patient selection is instrumental in ensuring good, durable outcomes. The anatomic complexity of the CAD and patient risk profile are important considerations.

CORONARY ARTERY DISEASE COMPLEXITY

As outlined above, the benefits of CABG over medical therapy and PCI are most manifest in the patient with complex MVD. In patients with less complex disease, PCI may be a reasonable treatment modality with an ACC/AHA guideline designation of Class IIA.²

PATIENTS (TRULY) AT HIGH RISK FOR CORONARY ARTERY BYPASS GRAFTING

There will be some patients who are truly high risk for CABG; however, careful evaluation of the evidence reveals that this number is small.

In the registry data of the SYNTAX trial,²³ patients were more than 5 times more likely to be assigned to PCI than CABG (35% vs 6.4%). Interestingly, patients who could not undergo surgery had high major adverse cardiovascular and cerebrovascular events rates, whereas those who were deemed not suitable for PCI (largely due to coronary anatomic complexity) had excellent results.

More than 70% of those patients who were deemed ineligible were identified as too high risk for CABG; however, there was no granularity within SYNTAX to actually qualify high risk. The Outcomes of Percutaneous Revascularization for Management of Surgically Ineligible Patients with Multivessel or Left Main Coronary Artery Disease (OPTIMUM) Registry aimed to examine this question (Table 2).²⁴ Factors listed as prohibitive surgical risk include poor targets or conduits (18.9%), prior sternotomies (8.7%), and severe systolic dysfunction or cardiomyopathy (14.6%).

The issue of poor conduits and targets is clearly subjective, and it is not uncommon for tertiary referral centers to operate on CABG patients who were declined for surgery or referred from other cardiac centers because of these factors. With respect to prior sternotomies, we know that with

experience, the risk of redo CABG is identical to primary CABG.²⁵ Thus, redo CABG should not automatically make a patient too high risk for CABG.

Categorizing patients with severe systolic dysfunction as “prohibitive risk” to undergo CABG should raise concern,

TABLE 2. Outcomes of Percutaneous Revascularization for Management of Surgically Ineligible Patients with Multivessel or Left Main Coronary Artery Disease trial variables to categorize patients as high or prohibitive risk for coronary artery bypass grafting²⁴

Surgical risk determinants	Percentage (N = 726)
Poor targets or conduits	18.9%
Severe systolic dysfunction/ cardiomyopathy	14.6%
Severe lung disease	10.1%
Prior sternotomies	8.7%
Other	7.4%
Frailty	6.5%
Advanced age	6.1%
High predicted operative risk	4.7%
Prior stroke or severe cerebrovascular disease	3.9%
Severe aortic calcification or plaque	3.4%
Immobility or neuromuscular disease	3.2%
Renal insufficiency	3.2%
Extensive nonviable myocardium	2.2%
End-stage liver disease	2.2%
Morbid obesity	1.9%
Malignancy	1.5%
Systemic infection	1.4%
Cognitive impairment or dementia	0.3%

because this is precisely the population who stands to benefit the most from the procedure. This was evidenced by the Surgical Treatment for Ischemic Heart Failure (STICH) trial, with extended follow-up showing survival advantage for CABG over medical therapy in this population starting at 3 years postprocedure and increasing to 10 years.²⁶ Conversely, the Revascularization for Ischemic Ventricular Dysfunction (REVIVED-BCIS2) trial, which looked at PCI versus medical therapy in patients with ischemic cardiomyopathy, showed no advantage to PCI over medical therapy in this population.²⁷

Thus, a significant subset of the patients considered to be too high risk for CABG are not truly so and, in fact, warrant CABG consideration under the current body of evidence.

CONCLUSIONS

The evidence shows CABG is the only revascularization procedure to offer a survival advantage and reduced spontaneous MI over medical therapy in stable complex MVD. Patients with 3-vessel CAD should be offered CABG unless it is truly high risk within the context of a heart team approach and consideration of the patient's informed preference.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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