

Multivessel Coronary Artery Disease: The Limitations of a “One-Size-Fits-All” Approach

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Multivessel coronary artery disease (MVD) is defined as luminal stenosis of at least 70% in at least two major coronary arteries or in one coronary artery in addition to a 50% or greater stenosis of the left main trunk. It is both common and deadly: 45% to 88% of men with angina have MVD, which carries a mortality hazard ratio of 3.14 compared to single-vessel disease.^{1,2} Given that percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) both effectively revascularize the myocardium, there has been ardent study of and debate over the optimal revascularization strategy for patients with MVD. In patients with MVD and diabetes, CABG is clearly superior to PCI³; however, in patients without diabetes, decision-making is more nuanced.

OPTIMAL REVASCUARIZATION STRATEGIES IN MULTIVESSEL DISEASE

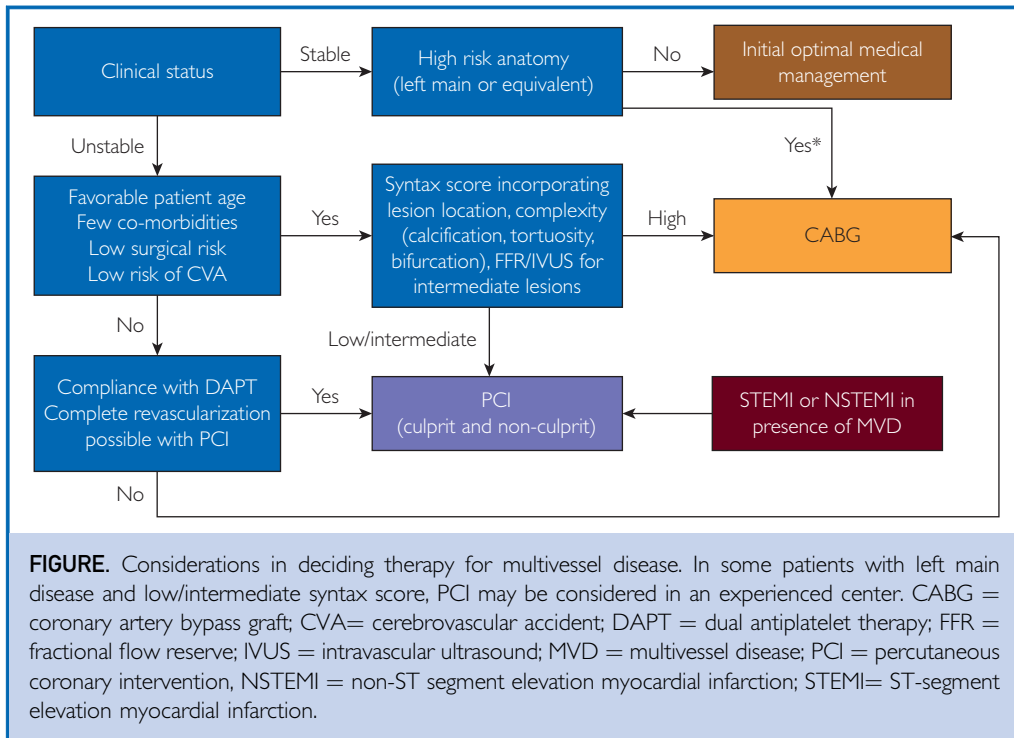
In 2011, the American Heart Association and American College of Cardiology Foundation suggest CABG as a class IB recommendation to improve survival in patients with MVD.⁴ This recommendation is based largely on the results of the 2009 Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial, which studied patients with previously untreated triple vessel and/or left main disease.⁵ Patients were assigned a SYNTAX score, a comprehensive angiographic assessment of coronary disease complexity with higher scores indicating more complex anatomy. At 12 months post-revascularization, patients with low and intermediate SYNTAX scores (<32) had no significant differences in major adverse cardiac or cerebrovascular outcomes after CABG versus PCI using paclitaxel drug-eluting stents (DES). However, in patients with higher SYNTAX

scores (>32), CABG was associated with lower rates of major adverse cardiac or cerebrovascular events at 1 year compared with PCI (10.9% versus 23.4%, respectively).⁵

Although the SYNTAX trial shows superior outcomes for CABG in patients with more complex anatomy, it must be realized that first-generation DES were used. These stents are no longer standard-of-care as they are associated with higher rates of restenosis and thrombosis compared to current-generation everolimus-eluting⁶ and zotarolimus-eluting⁷ stents. Compared to paclitaxel stents, everolimus stents reduce repeat revascularization by 40% to 50% of patients, whereas zotarolimus stents show a relative reduction in myocardial infarction (MI) and cardiac death (3.6% versus 7.1%, $P < .005$).^{7,8}

Importantly, the SYNTAX score is purely an anatomical assessment. More recently, fractional flow reserve — and its derivatives, instantaneous wave-free ratio (iFR) and diastolic hyperemia-free ratio (dFR) — have been used to augment the classic SYNTAX score by evaluating the physiologic severity of coronary lesions. In fact, using these physiologic indices rather than angiographic guidance alone is associated with better outcomes.^{9,10} The functional SYNTAX score decreases the total number of higher-risk patients and better determines risk for adverse events in patients with MVD undergoing PCI.¹¹

In addition to the SYNTAX trial, other landmark studies, including Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM), Arterial Revascularization Therapies Study (ARTS), Medicine, Angioplasty, or Surgery Study (MASSII), Stent or Surgery (SoS), and Coronary Artery Revascularization in Diabetes Trial (CARDia), which



compared CABG with PCI in MVD also used first-generation stents and suggest the superiority of CABG in MVD.¹² However, much of the excess hazard of PCI versus CABG stems from the need for reintervention.¹³ As stenting technology improves, the rate of reintervention may decrease as has already been shown with everolimus compared to paclitaxel stents.⁶ In addition, the risk of needing a repeat PCI procedure (for a nonurgent reason) may outweigh the increased short-term morbidity of surgery and risk of stroke associated with CABG.⁵

Finally, while a meta-analysis by Sipahi et al¹⁴ concludes that there is a mortality benefit in favor CABG for MVD, the included studies are heterogenous, and single studies are typically underpowered for the detection of a mortality difference between CABG and PCI. Moreover, longer-term follow-up is necessary as it averages only 4.1 years in head-to-head trials.¹⁴

THE ROLE OF COMPLETENESS OF REVASCULARIZATION

Bangalore et al¹⁵ compared all-cause mortality, MI, stroke, and repeat revascularization in patients with MVD who received PCI versus

CABG.¹⁵ Patients who underwent revascularization with PCI with everolimus DES had a lower risk of stroke compared with CABG. Compared to CABG, there was a higher risk of MI in patients who received PCI with incomplete revascularization but not with complete revascularization. The study found comparable risks of death between the PCI group and the CABG group. The selection of therapy (PCI versus CABG) in MVD should consider the feasibility for complete revascularization with PCI and weigh the risks of death and stroke with CABG versus repeat revascularization with PCI. A 5-year follow-up from the SYNTAX study conducted in 2016 by Milojevic et al¹⁶ comparing PCI and CABG in MVD revealed that, among patients in the PCI arm, incomplete revascularization was an independent predictor of mortality.

This finding holds true for patients with MVD who are suffering from acute MI. Rathod et al showed that among patients with non-ST segment elevation myocardial infarction complete revascularization was superior to culprit-lesion-only PCI in reducing long term but not in-hospital mortality.¹⁷ The COMPLETE trial extended these findings to patients

with ST-segment elevation myocardial infarction not in cardiogenic shock. This randomized study found that complete revascularization reduced the risk of death, MI, or ischemia-driven revascularization.¹⁸ Non-culprit vessel PCI may be performed during the index procedure or soon after hospital discharge.¹⁸ The timing of non-culprit PCI is dependent on ease of the culprit lesion revascularization procedure, dye and radiation load, and complexity of the non-culprit lesion(s).

TO REVASCULARIZE OR NOT TO REVASCULARIZE?

The presence of multivessel disease alone is not an indication for revascularization (Figure). As the ISCHEMIA trial showed, stable MVD even with moderate-to-severe ischemia can be initially managed with optimal medical therapy as opposed to revascularization.¹⁹ However, patients with greater than 50% left main disease, ejection fraction <35%, New York Heart Association functional class III or IV heart failure, and significant angina were excluded from ISCHEMIA. Moreover, previous observational studies of patients with left main disease, the majority of whom also have MVD, show that patients with severe stenoses and evidence of left ventricular dysfunction show a survival benefit with surgical revascularization versus medical management.²⁰ These data suggest that the severity and location of disease, failure of medical therapy, the amount of vulnerable myocardium, and refractory angina should be crucial elements in the decision of whether to revascularize MVD by surgery or PCI.

CONCLUSION

Revascularization decisions should be made in the context of an integrated heart team, including a cardiothoracic surgeon, an interventional cardiologist, and very importantly, the patient. Percutaneous coronary intervention may be a preferable revascularization strategy in MVD patients with low-to-moderate SYNTAX score who do not have diabetes if and only if PCI can achieve revascularization as completely as CABG. Other features that should guide the decision include technical feasibility, surgical

risk (ie, Society of Thoracic Surgery score), presence of renal dysfunction, estimated dye load, planned concomitant cardiothoracic surgery, patient compliance, and patient preference. Patients should be informed about the relative technical feasibility, survival and mortality, MI risk, repeat procedure risk, need for antiplatelet therapy, and stroke risk by the heart team so that they can weigh the risks and benefits with their families. When all things are equal or the decision is complicated by an array of factors, patient preference should be strongly considered. Regardless of the choice, aggressive optimal medical therapy, tobacco cessation, exercise, and weight loss/maintenance are mandatory following a revascularization procedure.

In the current era, individualized decisions about optimal revascularization strategy, taking into consideration the complexity of coronary anatomy, patient comorbidities, the experience of the operator, and the preference as well as expectations of the patient, are mandatory; a “one-size-fits-all” approach to reflexively treat MVD is no longer justified.

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