Patients with multivessel coronary artery disease (CAD) are now faced with a number of treatment choices, including coronary artery bypass graft surgery, medical therapy, and percutaneous coronary interventions (using bare-metal or drug-eluting stents). Each carries certain benefits and risks: bypass surgery is favored in the subset of patients with multivessel disease and diabetes or impaired left ventricular systolic function who are able to receive a left internal mammary artery graft; medical therapy consisting of β-blockers, angiotensin-converting enzyme inhibitors, statins, aspirin, and nitrates is offered to patients with stable angina. Percutaneous procedures have previously been limited in their efficacy by restenosis and resulting morbidity, but contemporary stenting procedures appear to show equivalent mortality and morbidity outcomes (to bypass surgery) at 5 years. Drug-eluting stents are the newest percutaneous technique and show significant reduction in restenosis compared with older catheter-based therapies, but further investigation is needed to definitively define the role of drug-eluting stents in the treatment of multivessel CAD. This review summarizes the data comparing medical, surgical, and percutaneous treatment approaches for patients with multivessel CAD.

Introduction
Coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention (PCI) are widely utilized revascularization therapies for the treatment of atherosclerotic coronary artery disease (CAD). Current clinical practice favors CABG in the treatment of select patient populations with multivessel CAD, and PCI is the more common therapy in the setting of single-vessel CAD or acute coronary syndromes. Recommendations favoring CABG in the treatment of multivessel CAD are driven by the long-term morbidity and mortality benefit of this therapy, especially in certain patient populations, such as those with diabetes, impaired left ventricular (LV) systolic function, and those who can receive a left internal mammary artery (LIMA) or other arterial graft. Emerging data have suggested that the benefit of CABG may not be as robust in the era of newer percutaneous techniques such as bare-metal stents (BMS) and drug-eluting stents (DES), and with advances in medical therapy. In this review, we examine the historic data that led to current practice patterns, the impact of BMS and DES on patient outcomes, and the role of more aggressive medical therapy in the treatment of multivessel CAD.

CABG Versus Medical Therapy: Historic Data
CASS [1–7] enrolled patients at 15 centers, between 1974 and 1979. Inclusion in the study required at least one coronary segment with more than 70% stenosis. Patients were treated with medical therapy, limited mostly to β-blockers and nitrates at the time [1], or CABG. Only those patients with Class I or II angina were randomized, due to the already-known benefits of CABG in the treatment of medication-refractory angina [2–4]. Within the cohort of patients with stable Class I or II angina, at 5-year follow-up, there was no difference in mortality between the medically treated patients and surgically treated patients, regardless of severity of CAD or degree of LV dysfunction [5,6,8]. At 7-year follow-up, there was no difference in mortality between the two groups, but subset analysis began to show improved mortality in patients randomized to CABG who had LV ejection fractions (LVEF) of less than 50%, especially with three-vessel CAD [8]. At 10-year follow-up, there remained no statistical difference in mortality in the overall cohort. However, survival was improved in surgically treated patients with stable angina plus LVEF of less than 50% (80% CABG, 59% medical;
artery (LAD) stenosis regardless of severity of other epicardial CAD, or any patient with proximal left anterior descending artery graft. Patients were assessed with follow-up visits every 3 months until 1 year, and underwent symptom-limited treadmill exercise testing at baseline and at 1 year. Repeat angiography in the medical therapy and CABG arms was based on assessment of symptoms or positive stress test result at 1 year.

One-year follow-up in the MASS-II trial [11•] showed no significant difference between medical therapy and CABG in the composite incidence of cardiac mortality, myocardial infarction (MI), or refractory angina requiring revascularization. The individual endpoint of cardiac mortality was also similar between medical therapy and CABG. However, the medical therapy arm had a higher incidence of recurrent angina requiring additional interventions. At the end of 1 year, 6% patients in the medical therapy arm required CABG and 1.97% required PCI, whereas no patients in the CABG arm required repeat surgical procedures and only one patient required PCI. In terms of symptom control, only 36% patients in the medical therapy arm were angina-free at 1 year, compared with 59% in the CABG arm (P < 0.0001).

CABG Versus Medical Therapy: Contemporary Data

More recent data comparing treatment options for stable CAD are available in MASS-II [11•], which randomized 611 patients to medical therapy (n = 203), CABG (n = 203), or PCI (n = 205). Inclusion criteria were documented ischemia by stress testing or Canadian Cardiovascular Society Class II or III angina, and angiographically documented multivessel CAD (> 70% stenosis in multiple proximal coronary vessels). Equivalent revascularization was deemed achievable by consensus between the cardiac surgeon and interventional cardiologist, but was not mandated as part of the study design. All patients (including those in the CABG and PCI arms) received medical therapy consisting of a combination of nitrates (42%), aspirin (77%), β-blockers (58%), calcium channel blockers (45%), angiotensin-converting enzyme (ACE) inhibitors (27%), statins (63%), and low-fat diet.

Patients enrolled in the CABG arm of this trial underwent surgery within 12 weeks of randomization. No patients underwent off-pump CABG, and 92% patients in the CABG arm received at least one internal mammary artery graft. Patients were assessed with follow-up visits every 3 months until 1 year, and underwent symptom-limited treadmill exercise testing at baseline and at 1 year. Repeat angiography in the medical therapy and CABG arms was based on assessment of symptoms or positive stress test result at 1 year.

Summary

From the early randomized trials, CABG was found to be superior to available medical therapy in the treatment of multivessel CAD, especially in patients with depressed LV function. This benefit was greater in patients with more severe impairment in LV function, or patients with severe angina regardless of LV function. The mortality benefit of CABG surgery appears time-limited, as the natural history of atherosclerosis leads to graft closure and late mortality in surgically treated patients. Additionally, medically treated patients had significant need for subsequent CABG surgery, which may contribute to the eventual equivalence between medical and surgical arms. Only 13% patients in the CABG cohort within CASS received LIMA grafts [3], and arterial grafting was noted to confer longer mortality benefit than conventional saphenous vein grafting [7].

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