Coronary Artery Bypass Grafting Versus Stenting for Unprotected Left Main Coronary Artery Disease
Where Lies the Body of Proof?
Richard J. Shemin, MD

The standard of care for left main coronary artery disease is coronary bypass surgery (CABG). The efficacy and survival advantage of CABG have resulted in CABG being established practice since the 1970s. Further improvements in late survival have been achieved with arterial grafting, which is practiced routinely even in patients more than 80 years of age.

Technical advances in percutaneous coronary interventions (PCIs) and stent technology have emboldened the interventional cardiology community to test the feasibility of and document the procedural results for stenting the left main coronary artery. Surgical approaches have a distinct advantage in that they can ignore the complexity and location of the left main coronary lesion, because bypass grafts are placed distally to the left anterior descending and circumflex coronary arteries. In addition, complete revascularization is easily accomplished.

The feasibility and success of PCI require an evaluation of lesion complexity. The probability of procedural success requires a consideration of whether the obstructing plaque involves the ostium of the coronary artery, the body of the left main, or the length of the left main and whether disease involves the bifurcation with or without extension into the left anterior descending or circumflex coronary arteries. Ostial or body obstructions in a long left main vessel are more desirable to stent than bifurcation or trifurcation lesions. An additional consideration is the possibility of sudden stent thrombosis early or late after the use of drug-eluting stents (DES) or bare-metal stents. Such events in the left main coronary artery would have catastrophic consequences that most likely would result in sudden death. Current recommendations for DES are to continue dual-antiplatelet therapy for prolonged periods of time (>6 months or indefinitely), because stent healing with endothelium is incomplete. This protocol may be particularly risky in elderly patients. The therapy is costly, and serious consequences can ensue if unrelated medical problems require discontinuation of the platelet therapy. CABG procedures avoid not only the technical factors of the obstructing lesion but require only low-dose aspirin therapy.

Survival advantages of stent therapy for coronary artery disease over medical therapy have not been a consistent result in clinical trials. Most trials of PCI have used a composite end point (major adverse cardiac events) as the primary end point. These trials have limited follow-up, usually no more than 2 years. The use of major adverse cardiac events as an end point, the small number of patients, and the limited duration of follow-up have biased the randomized trials that compare PCI and CABG. The randomized clinical trial screens large numbers of patients to randomize a small subset of eligible patients. There is no bias regarding assigned treatment. There is bias to entry into the trial, which is a major limitation after the trial is over and the physician needs to extrapolate the data to clinical practice. In addition, intention-to-treat analysis and crossovers make the results misleading. A short duration of follow-up adversely affects CABG when an end point of major adverse cardiac events is used; 5 years of follow-up is necessary in PCI versus CABG trials.

Results from real-world therapy can be found in the analysis of large observational databases. In spite of bias to treatment, there is no bias to entry into the data set. Several published large observational studies have used the Duke, Society of Thoracic Surgeons, New York State, and Northern New England databases. These studies have consistently shown a survival advantage for CABG over PCI.

The results of the SYNTAX (Synergy between PCI with TAXUS drug-eluting stent and cardiac surgery) Trial, reported at the European Society of Cardiology Congress 2008 in Munich, Germany, showed that DES placement was inferior to CABG surgery as a treatment option for patients with multivessel and left main coronary disease. The SYNTAX study randomized 1800 patients with 3-vessel and left main disease to PCI with DES versus CABG. The study found that at the 1-year end point, PCI was inferior to CABG for major adverse cardiovascular or cerebrovascular events (death, heart attack, stroke, or repeat revascularization; 17.8% versus 12.1%).

The SYNTAX trial also provided supportive data regarding the survival benefit of CABG relative to stenting. The study results showed that CABG had a strong trend toward better survival at 1 year, with a 23% relative mortality benefit,
consistent with other studies of DES versus CABG. For example, a larger study of DES versus CABG from New York State data presented by Hannan et al44 showed a significant mortality benefit of CABG versus DES at 18 months, with a 21% relative mortality benefit in 3-vessel disease and a 35% relative mortality benefit in 2-vessel disease.

It should no longer be considered that there is equipoise for PCI and CABG for this complex, higher-risk group of patients. In previous trials, trial design and eligibility criteria prevented high-risk patients who would benefit most from CABG from participating; therefore, no definitive conclusion could be made for the effectiveness of CABG.

With these new results, it is critical that before stenting is performed, clinicians provide patients with full and complete disclosure of the risks and benefits of both DES and bare-metal stents, including the possibilities of decreased survival, risk of stent thrombosis, and increased reintervention. In left main disease, stent thrombosis causes sudden complete closure of a major coronary vessel, and 40% of stent thromboses are fatal. Coronary artery graft closure may cause angina, but rarely does it cause myocardial infarction or muscle loss, because the native vessel is still open with graft failure.36,37

The use of major adverse cardiac events as the primary end point allows fewer patients to be randomized to adequately power the study. In addition, it reduces the cost for performing the trial. Inappropriate subset analyses are often performed; however, the subset findings are often reported as factual. This was the case in the SYNTAX trial, in which the primary end point was negative. Underpowered subset analyses were performed and are often quoted as the trial result. These analyses should only be hypothesis generating for future studies, not interpreted as clinically proven fact.

A current study of CABG versus PCI in octogenarians in the present issue of Circulation18 suffers from the well-recognized limitations of nonrandomized, retrospective studies. The decision to perform PCI versus CABG is biased by the clinicians, referring doctors, or the patient. In the PCI group, the location, extent, and complexity of the left main lesion will often exclude a patient from treatment, thereby adding procedural bias. As noted previously, lesion complexity rarely affects inclusion into the surgical group. Comorbidities in nonrandomized studies are often increased in the PCI group, as was the case in the present study. Propensity analysis attempts to deal with these differences statistically, but imperfectly. The present study had a complex definition of major adverse cardiac or cerebrovascular events (cardiac death, myocardial infarction, cardiovascular event, or repeat revascularization), with an extremely limited mean follow-up of less than 2 years. Surgery patients will always have a higher procedural morbidity. Most studies have shown that a follow-up of >2 years is necessary to discern the advantages of surgery when major adverse cardiac and cerebrovascular events are used as the primary end point.

The most unambiguous end point and perhaps the most important is patient survival. In the present study,38 procedural (30 days) mortality was similar in both groups (CABG 8.3%, PCI 6.7%); however, late mortality (mean follow-up of 23±16 months) was 10.3% for PCI and 4.5% for CABG. The CABG patients were more likely to have revascularization (87% versus 57%), less likely to require repeat revascularization (2.3% versus 10.3%), and less likely to experience late myocardial infarctions (2.3% versus 11.3%) and cerebral vascular events (0.8% versus 8.2%). The overall rate of post-procedural major adverse cardiac or cerebrovascular events was 9% for CABG versus 30.9% for PCI.

The most useful information from the study by Rodés-Cabau et al18 is found in the results that can be obtained when surgery is not offered because the risk is prohibitive owing to noncardiac risk factors. Interestingly, these authors found the procedural risk prediction euroSCORE (European System for Cardiac Operative Risk Evaluation) overpredicted the observed procedural risk.

Therefore, the present study has useful data but does not provide evidence supporting a change from the current recommendation that left main disease requires treatment with a surgical approach.3,39–41 The cardiovascular community requires a study that is multicentered, randomized, and adequately powered to address survival as a primary end point. Such a study is essential to guide therapy for this anatomically critical lesion. The trial must be of adequate duration and contain sufficient subjects to allow adequate power for subset analysis. The results of such a trial will become increasingly relevant as the clinical burden of coronary artery disease and left main lesions increases as the “baby boomers” grow exponentially as a percentage of the US population. Cost analyses must be an important component of these studies, because healthcare budgets are further strained by this demographic change and technological advances.

Disclosures

None.

References


KEY WORDS: Editorials ● coronary artery bypass grafting ● stents
Coronary Artery Bypass Grafting Versus Stenting for Unprotected Left Main Coronary Artery Disease: Where Lies the Body of Proof?
Richard J. Shemin

_Circulation._ 2008;118:2326-2329
doi: 10.1161/CIRCULATIONAHA.108.820324
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/118/23/2326

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/