Denton A. Cooley Cardiovascular Surgical Society

Stents or Surgery

The Case for Stents

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In Meredith Willson's "The Music Man," sleepy River City, Iowa, comes under musical assault from a smooth and self-assured confidence man, Professor Harold Hill. He declares that restless youth (who are not so restless) are in moral peril but may be saved through an effortless acquisition of musical skill requiring only the purchase of uniforms and instruments, and the use of the "think" method. Of course, the think method is a sham promulgated to convince these offbeat Iowans to enrich the good professor and gain little in return. Fortunately, the sham and its purveyor are very entertaining.

You may ask how this pertains to revascularization therapy. The common ground lies in the glee with which our surgical colleagues point to the application and failures of balloon angioplasty, which offers a comparison in which cardiologists are Professor Hill and percutaneous transluminal coronary angioplasty (PTCA) is the "think" method. In this scenario, the cardiologist identifies every coronary lesion as a source of peril. Salvation is offered, with less musical distraction but equal reward, in the form of morbidity-free angioplasty, and patients are diverted from a more effective means of revascularization.

There is a kernel of truth in this argument. Not every lesion requires revascularization. Angioplasty is not without risk and frequently fails within the first 6 months after the procedure. In populations whose survival is unlikely to be affected by any revascularization procedure, PTCA compares favorably to coronary bypass surgery, albeit with a substantially greater need for more procedures. Worse still, in the high-risk diabetic subpopulation with multivessel coronary stenosis, a 1st choice of PTCA carries a heavy toll in both the need for repeat procedures and, more importantly, survival. However, I hope to convince you that with the recent advances in stent-assisted angioplasty (recently acquiring the abbreviation PCI, for percutaneous coronary intervention) proper application now offers a very good alternative to surgery. But, as Professor Hill was admonished as he disembarked in River City to begin his confidence game, "you've gotta know the territory."

The introduction of coronary artery bypass grafting (CABG) was an enormous advance in the treatment of coronary artery disease. Successful bypass reduced angina and improved exercise capacity. When studied in randomized trials of early surgical referral (Fig. 1),[1-4] CABG proved effective in reducing mortality. However, 3 central principles of that survival impact quickly became apparent: 1) the amount of potential survival benefit was roughly proportional to the patient's risk of death from the next coronary event, whether estimated using clinical, angiographic, or physiological variables; 2) revascularization was not a treatment for atherosclerosis, but a means of reducing the impact of later disease progression; and 3) benefit lasted only as long as the grafts remained patent.

When we examine the outcome of the VA Cooperative trial,[4-6] these principles can be seen clearly (Fig. 1). Early on, procedural risk obscured the impact of successful revascularization; but by 5 years, improved survival in surgically treated patients was apparent. This apparent difference was statistically verified only in patients at high risk (3-vessel disease with low left ventricular ejection fraction [LVEF]), and it disappeared after 11 years.[5] In fact, follow-up out to 22 years showed that low-risk patients were harmed by an early referral for surgical therapy.[4] If we compare the survival curves from the VA study to a superimposed graph of saphenous vein graft (SVG) patency, it is apparent that the decline in benefit from early surgical referral follows the natural history of an SVG. If, instead, we compare the survival curves to a graph of internal mammary artery patency when the internal mammary artery (IMA) is used to bypass the left anterior descending coronary artery (LAD), we might imagine (in fact, we all believe it to be the case) that

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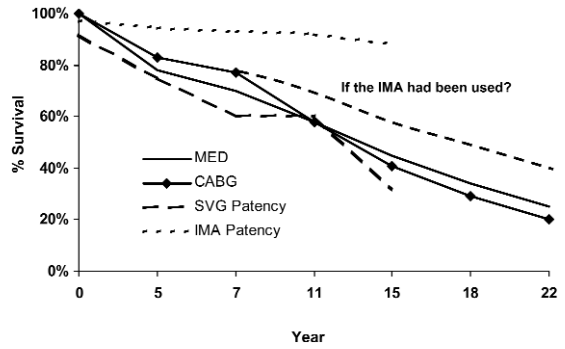

Fig. 1 *Survival curves from the VA Cooperative trial[6] compare early referral for CABG with an initial strategy of medical therapy. Superimposed on the survival curves are the long-term patency of SVGs and IMA-to-LAD bypass grafts. Extending from the surgical survival curve is an estimate of what might have been, had the usefulness of the internal mammary artery been recognized before the design of the VA Cooperative trial.*

CABG = coronary artery bypass grafting; IMA = internal mammary artery graft; LAD = left anterior descending coronary artery; MED = medical therapy alone; SVG = saphenous vein graft; VA = Veterans Administration

the outcome of this and other trials might have been very different (Fig. 1). In a small subgroup of patients from the Coronary Artery Surgery Study who received an IMA, this suspicion was borne out.[7] The lessons of the randomized trials and the outcome differences when using the IMA as a bypass conduit are that the untreated natural history of a patient's disease determines the acceptable procedural risk and the possibility of obtaining a survival benefit from revascularization, and that benefit is afforded by an open vessel. The contention of advocates of PCI borrows a phrase from golf's 19th hole, "it's not how, it's how many"—and our way is safer.

Gary, Indiana

When questioned about his musical credentials, the erstwhile Professor Hill claimed matriculation from "the Gary Conservatory, class of '05." In '05, the conservatory didn't exist, but most of the players were either ignorant of or oblivious to that fact. When engineering advances made PTCA an easier procedure, one that could be used in attempts to treat multivessel disease, the hope was to apply a safer, easier procedure to the task of repairing native vessels, thus obviating the need for CABG with its temporally limited SVGs. However, with a procedural mortality rate of 1% and a 6-month restenosis rate after PTCA that is conservatively estimated at 40%, we encountered a problem with one of the 3 principles of revascularization: benefit lasts only as long as the vessel is open. In short, most patients will need multiple procedures to maintain patency, thus being exposed to an aggregate procedural risk of death that is essentially the equivalent of a single bypass procedure, or their protection from angina and death will be inferior. Like the class of '05, the grounds upon which PTCA was held to be superior to surgery didn't exist. This was put to the test in the BARI[8,9] (Bypass Angioplasty Revascularization Investigation) trial, in which patients with multivessel disease amenable to either procedure were randomized to CABG or PTCA.

There are a couple of caveats about BARI . First, almost all of the patients in the trial had normal left ventricular systolic function. Therefore, with respect to survival, the gain from a revascularization procedure may have been difficult to detect had either procedure been compared with medical therapy. Second, the interventionalist's eyes may have been bigger than his balloons. In patients who had an average of 3.5 treatable lesions, only 1.9 were successfully treated in the PTCA arm of the trial. Meanwhile, 3.1 lesions were treated in the surgical arm. Fortunately, in nondiabetic patients, no apparent harm came of 1st referral for PTCA. In diabetics, the outcome was quite different. Patients randomized to CABG who got a left internal mammary artery (LIMA) graft to the LAD fared far better than their counterparts who were treated by means of PTCA.[9]

In a very interesting post-hoc analysis of both the trial and the accompanying registry, Detre and colleagues[10] examined the impact of revascularization upon the outcome of the next myocardial infarction (MI). In diabetic patients who did not receive CABG either primarily or later when problems resurfaced, there was a 10-fold increase in mortality after any subsequent MI. Performance of coronary bypass surgery at any time after entry into the study allowed a patient to be considered among the CABG group. After 5 years, 64% of diabetic patients initially treated with PTCA underwent CABG. Therefore, it is possible that Darwinian bias, or surgery for the fittest, resulted in overestimation of the relative impact of CABG. However, it is very unlikely that bias is responsible for all of the rather dramatic difference between the groups. The observed difference between PTCA and CABG in the frequency of potentially significant coronary stenoses, implying less effective revascularization with PTCA, is a more likely explanation.[11]

A registry of eligible patients who underwent the procedure of their own or their physicians' choice accompanied the BARI randomized trial. The overall survival of patients in the registry was slightly but not significantly better than among the randomized patients. Unlike patients in the randomized trial, registry diabetic patients enjoyed the same survival probability whether treated with surgery or PTCA (Table I).[12]

However, patients referred for surgery had more LAD lesions, more type-C lesions, and just plain more lesions. More patients referred for surgery had 3-vessel disease and diffuse disease. In addition, some patients were treated medically.[12] The natural conclusion drawn from these observations is that the cardiologists cherry-picked their patients, saving the easy lesions for themselves. They did, but they did so to the patients' benefit. They chose patients whom they could treat well and did so, with all the weaknesses of PTCA, without adverse performance compared with surgery. The real conclusion is that PTCA can be used safely and well in comparison with bypass surgery. But because of its weaknesses, as well as the risk of failure of emergency surgical referral and the risk of restenosis within 6 months, choosing the right patient and lesion is of supreme importance.

TABLE I. Survival of Patients in the BARI Trial12

Subgroup	CABG (%)	PCI (%)	*P* Value*
Overall	85.8	86.1	0.86
Diabetic	74	74	0.8
Low LVEF	83	80	0.8
3-Vessel disease	83.3	83.6	0.3
3-Vessel with low LVEF	76.3	72.4	0.51

CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention

**P* value after adjustment for differences in baseline variables

Data from: Feit F, et al.[12]

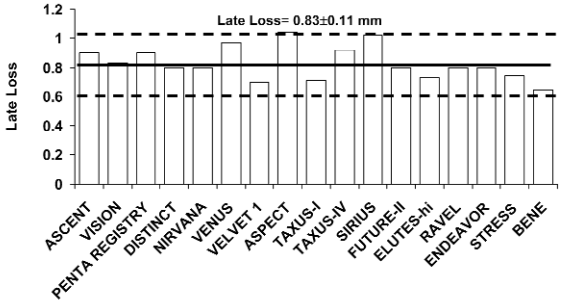

Fig. 2 *The angiographic loss in luminal diameter after 6 or 9 months is a measure of the severity of intimal hyperplasia after stent placement. The late loss reported for various forms of bare-metal stent is shown with their average value (solid line) ± 2 standard deviations.*[15-30]

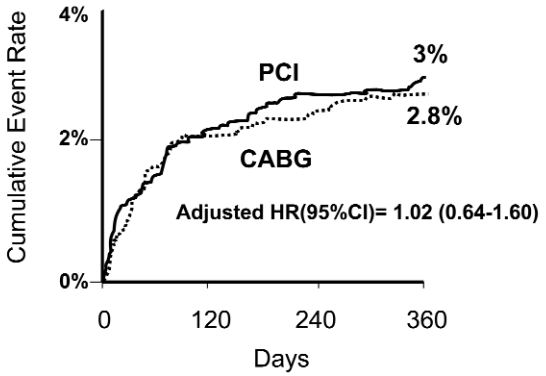

Fig. 3 *Survival curves from a meta-analysis compare the outcomes after an initial revascularization strategy of PCI-stent vs coronary artery bypass grafting (CABG).*[31]

HR = hazard ratio; PCI - percutaneous coronary intervention

Marian

But . . . then along came stents. The good professor's undoing as a confidence man begins with his attraction to a spinster, Marian the librarian. His pursuit of her is not only the source of a whimsical, musical alliteration but also the beginning of attempts to truly fulfill his promises. Unfortunately for him, the wherewithal is lacking.

While not proved in a randomized trial, it is pretty clear that stents make a PCI procedure safer by affording the interventionalist the capacity to get out of trouble and avoid emergency surgical referral and its attendant risks.[13,14] Stents are also highly touted for their ability to reduce the risk of restenosis after angioplasty but, in fact, their effect is rather small. There are 2 reasons. Stents actually worsen intimal hyperplasia, which is the major determinant of restenosis. Using the loss in lumen diameter at 6 months after stent implantation as a measure of intimal hyperplasia, if even the newest stents are compared to PTCA, it is apparent that all stents fall in the same range, at a loss of about 0.8 mm —and that's worse than PTCA, at a loss of 0.32 mm (Fig. 2[12-27,15-30]). Second, with a lower likelihood of early procedural failure, the interventionalist can be a bit more daring and attempt to tackle longer, more complex lesions, thus nullifying any potential gain in terms of restenosis.

How then do stents compare to CABG? The same as PTCA, of course (Fig. 3).[31] Several trials have been performed. Their data were recently compiled in a meta-analysis[28] that reported a virtually identical 3-year survival expectation after either procedure, with the exception, at least in the population studied in one of the trials, of diabetic patients, who did not do quite as well when treated with PCI.[32] With the protection of a stent, the interventionalist now will not give up on tougher lesions and leave them untreated, as was done in BARI. But, by extending our reach, we further expose the Achilles' heel of PCI: restenosis, the need for repeat procedures, and less effective revascularization.

76 Trombones

The thrilling musical conclusion of "The Music Man" follows the near exposure of Professor Hill's duplicity and an essentially magical transformation of the town's youth into a talented marching band. So too—even as the disappointments of stent-assisted PCI were looming—interventional cardiologists were given the drug-eluting stent (Fig. 4).[16,19,23-28,33-36]

Using a polymer-based drug delivery system that enables high local drug concentration but avoids systemic toxicity, sirolimus- and paclitaxel-eluting stents have been used to reduce the growth of intimal hyperplasia. The impact is really rather striking. If we use late lumen loss after angioplasty as our measure of intimal hyperplasia, drug-eluting stents reduce the primary determinant of restenosis by 50% to 100% (Fig. 5).[24-28,37,38] In large-scale clinical trials, this corresponds to an angiographic restenosis rate of 4% to 6% and a very low likelihood of a repeat procedure on the same lesion.[22,23] We can assume that a lasting, successful resolution of occlusive lesions will provide lasting relief from angina and protection from death in the event of a future MI. Building upon the results of prior trials comparing PCI to CABG, we can surmise that the comparison between drug-eluting stents and surgery will be much more favorable for stents, if the proper lesions are chosen.

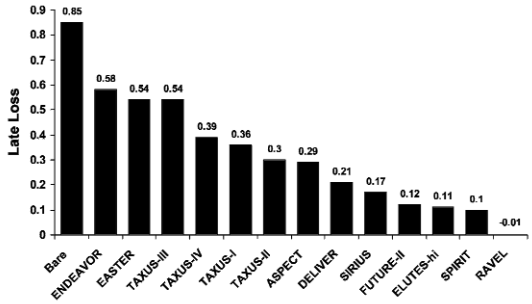

Fig. 4 *The late loss in luminal diameter after trials of various forms of drug-eluting stent, compared with bare-metal stent.*

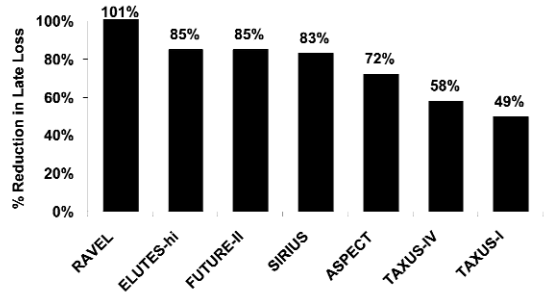

Fig. 5 *Populations and lesion characteristics differ between trials of drug-eluting stents. Therefore, the percent reduction (Control Late Loss – Experimental Late Loss/Control Late Loss) in late loss from several reported trials of drug-eluting stents is shown.*[24-28,37,38]

Let's try to get a peek at the future, drawing from a recent article by Sawhney's group[39] (Table II[39-42]). Three studies[40-42] have compared stent-PCI to the real gold standard procedure, LIMA-to-LAD bypass. By enrolling patients with disease limited to the LAD, we can get a look at the performance of the methods. Each of the studies has used slightly different endpoints to perform their comparisons. Diegeler and associates[40] used cardiac death, MI, and target-lesion revascularization. Drenth and coworkers[41] used all-cause death, MI, and target-vessel revascularization, but added stroke. Goy and colleagues[42] used cardiac death, MI, and any repeat revascularization. Surely there is no surprise that the stented population did not do quite as well as the LIMA population. Stented patients were roughly 2 to 3 times more likely to have a bad outcome—a result driven mostly by repeat revascularization. The drug-eluting stent trials have used some different definitions to look at outcomes after implantation of a bare-metal stent or a drug-eluting stent. One of the terms is target-vessel failure, which is defined as death, MI, or target-vessel revascularization. Because this definition is pretty comparable to the outcomes used for the stent versus LIMA trials, we can estimate what may come of a comparison between drug-eluting stents and LIMA bypass. In the SIRIUS trial of the sirolimus-eluting CYPHER™ stent,[39] a small subgroup of patients with isolated proximal LAD stenosis was treated. Their target-vessel failure rate of 10% compares very favorably to the reported event rates for LIMA bypass.[39]

Why should we pursue stents as the 1st option for revascularization? Coronary bypass surgery has been historically plagued by the invasive nature of the sternotomy and its attendant risk of infection, the need to manipulate the aorta (producing risk of stroke), the finite lifespan of an SVG, and the many problems associated with cardiopulmonary bypass. The wound after a stent procedure is minimal, the stroke risk small, and the promised success rate equal to or better than that of an SVG. Some may argue that surgical techniques are improving to minimize risks, and they are. Recently performed surgical trials suggest that new techniques, including limited sternotomy and warm-heart surgery, are a significant advance. Difficulties with the creation of the graft anastomosis and with graft failure must still be conquered, however. The oft-heralded weakness of the SVG has been partially overcome by vigorous risk-factor management and by the increasingly popular use of all-arterial-conduit bypass procedures. However, the free radial grafts have patency rates that are eerily similar to those of SVGs, and even the mammary, when not directed to the high flow region of the LAD, is less than perfect.[43-45] At the same

TABLE II. Trials of Stent Implantation for Isolated Proximal LAD Stenosis[39]

Trial	Design	N	Endpoint	Stent (%)	Surgery (%)	*P* Value
Diegeler, et al[40]	BMS vs LIMA	220	CD, MI, TLR	31	15	0.02
Drenth, et al[41]	BMS vs LIMA	102	D, MI, CVA, TVR	24	10	0.07
Goy, et al[42]	BMS vs LIMA	123	CD, MI, RR	31	7	<0.001
SIRIUS[39]	BMS vs DES	459	CD, MI, TVR	12	—	—

BMS = bare-metal stent; CD = cardiac death; CVA = cerebrovascular accident; D = death; DES = drug-eluting stent; LIMA = left internal mammary artery; MI = myocardial infarction; RR = repeat revascularization; TLR = target-lesion revascularization; TVR = target-vessel revascularization

Adapted from: Sawhney N, Moses JW, Leon MB, Kuntz RE, Popma JJ, Bachinsky W, et al. Treatment of left anterior descending coronary artery disease with sirolimus-eluting stents. Circulation 2004;110:374-9. Used by permission of the American Heart Association.

time that surgical technique is evolving, PCI technique is evolving as well. Techniques of groin management are improving to reduce the risk of access complications after stent placement. Restenosis, although not completely conquered, will be drastically reduced by drug-eluting stents, and the risk of stent-procedural MI is falling with improved antithrombotic therapy and the introduction of distal protection devices—a risk that has not been confronted surgically. The main point of difference between the procedures, and perhaps the most important difference, is the nature of the procedure. After PCI, recovery time is a matter of days. And if the lasting success that is promised by the early results of drug-eluting stents can be delivered, there is no reason for patients to undergo the more intrusive surgical procedure.

However, in keeping with good debate technique, I will point out some of the weaknesses of PCI when drug-eluting stents are used. First and foremost, certain lesion characteristics carry a high risk of procedural complication and eventual failure. Most prominent among these is a bifurcation lesion with large daughter vessels. A bifurcation lesion increases the likelihood of procedural failure. If both daughter vessels receive a bare-metal stent, the risk of any adverse event, either immediately or within 6 months, is greater than 50%.[46] Drug-eluting stents reduce the risk of restenosis after stent placement in this situation, but not to the extraordinary extent reported for simpler lesions. Rather than a rate of 4% or 5%, the risk is 26% and the incidence of out-of-laboratory thrombosis of the lesion is increased by about 3-fold.[47]

In truth, the major areas of weakness for bare-metal stents—diabetes, long lesions, small vessels, and final result—plague drug-eluting stents as well, although the impact is somewhat diminished. In a nondiabetic patient with a lesion 10- to 15-mm long in a vessel of 3-mm or greater diameter, the likelihood of target-vessel failure is very low, less than 5%. This failure rate compares very favorably to the expected failure rate of a bypass conduit and argues that treatment of multivessel disease can be performed with the expectation of excellent outcome in terms of both survival and repeat revascularization. But failure rates are higher in diabetic patients (12%), in long lesions (12%), and in small vessels (18%).[48-50] Therefore, if we approach a patient who has several characteristics suggestive of an early or late suboptimal result, we clearly cannot expect the excellent outcomes reported for lower-risk patients or lesions, and comparisons with CABG are likely to echo the outcomes of BARI and ARTS.[8,32]

An unrelated and fortunately uncommon point of concern is the need for coronary revascularization before a patient undergoes a noncardiac surgical procedure that requires general anesthesia. The only patient truly in need of revascularization in this setting is one who has the anatomic and physiologic characteristics that indicate a survival benefit from CABG. Meanwhile, the application of stent-assisted angioplasty in this setting meets with difficulty when the surgical procedure demands the withdrawal of antiplatelet therapy. When patients who have received coronary stents undergo a surgical procedure, the risk for stent thrombosis, myocardial infarction, and death is substantially increased.[51,52] A minimum waiting time of 6 weeks has been recommended after placement of bare-metal stents before surgery.[52] The safe waiting time after placement of a drug-eluting stent is unknown.

Conclusion

As the techniques for surgical and percutaneous revascularization have been refined and their long-term outcomes better understood, surgeons and interventional cardiologists have begun to treat different patient populations, and appropriately so. In a low- or intermediate-risk patient pool that requires revascu-

larization primarily for the treatment of angina, a 1st choice of PCI—assuming the reasonable evaluation of lesions and the likelihood of success—results in a survival expectation that does not differ from that for a surgically treated patient. The introduction of drug-eluting stents will certainly reduce the problematic need for repeat procedures. Meanwhile, in a patient with a potential survival benefit from revascularization and a greater risk of treatment failure even when treated with drug-eluting stents, surgery is, and will remain the preferred treatment. Specifically, patients with long lesions, diffuse disease, bifurcation lesions, heavy calcification, insulin-treated diabetes mellitus, or another surgical lesion remain within the realm of surgery. However, patients with focal lesions, no bifurcations, and large vessels can and should be safely treated with PCI (Table III). Moreover, the population at high risk for surgical complications, a population that includes comorbidities such as severe chronic obstructive pulmonary disease or patients who have previously undergone sternotomy, may be more safely treated with PCI and with reasonable efficacy.

TABLE III. Some of the Factors Now Affecting Choice between Surgery and Stents

Factors Favoring CABG	Factors Favoring PCI
Diabetes mellitus	Focal lesions
Diffuse disease	No bifurcation lesions
Bifurcation lesions	No IMA available
Heavy calcification	Prior cardiac surgery
Other lesion requiring surgery; urgent need for noncardiac surgery	Comorbid conditions (e.g., severe COPD)

CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; IMA = internal mammary artery; PCI = percutaneous coronary intervention

Clearly, technological advances, most notably the drug-eluting stents, have improved both the safety and the efficacy of PCI. But in regard to the question "Will stents replace surgery?" I would suggest a change. We should instead ask, "Are stents now a good alternative to surgery in the right circumstances?" The answer, at long last, is "Yes."

References

1. Detre KM, Takaro T, Hultgren H, Peduzzi P. Long-term mortality and morbidity results of the Veterans Administration randomized trial of coronary artery bypass surgery. Circulation 1985;72(6 Pt 2):V84-9.
2. Passamani E, Davis KB, Gillespie MJ, Killip T. A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction. N Engl J Med 1985;312:1665-71.
3. Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med 1988;319:332-7.
4. Peduzzi P, Kamina A, Detre K. Twenty-two-year follow-up in the VA Cooperative Study of Coronary Artery Bypass Surgery for Stable Angina. Am J Cardiol 1998;81:1393-9.
5. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. The Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. N Engl J Med 1984;311:1333-9.
6. Eighteen-year follow-up in the Veterans Affairs Cooperative Study of Coronary Artery Bypass Surgery for stable angina. The VA Coronary Artery Bypass Surgery Cooperative Study Group. Circulation 1992;86:121-30.
7. Cameron A, Davis KB, Green GE, Myers WO, Pettinger M. Clinical implications of internal mammary artery bypass grafts: the Coronary Artery Surgery Study experience. Circulation 1988;77:815-9.
8. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators [published erratum appears in N Engl J Med 1997;336:147]. N Engl J Med 1996;335:217-25.
9. 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;96:1761-9.
10. Detre KM, Guo P, Holubkov R, Califf RM, Sopko G, Bach R, et al. Coronary revascularization in diabetic patients: a comparison of the randomized and observational components of the Bypass Angioplasty Revascularization Investigation (BARI). Circulation 1999;99:633-40.
11. Whitlow PL, Dimas AP, Bashore TM, Califf RM, Bourassa MG, Chaitman BR, et al. Relationship of extent of revascularization with angina at 1 year in the Bypass Angioplasty Revascularization Investigation (BARI). J Am Coll Cardiol 1999;34:1750-9.
12. Feit F, Brooks MM, Sopko G, Keller NM, Rosen A, Krone R, et al. Long-term clinical outcome in the Bypass Angioplasty Revascularization Investigation Registry: comparison with the randomized trial. BARI Investigators. Circulation 2000;101:2795-802.
13. Al Suwaidi J, Holmes DR Jr, Salam AM, Lennon R, Berger PB. Impact of coronary artery stents on mortality and nonfatal myocardial infarction: meta-analysis of randomized trials comparing a strategy of routine stenting with that of balloon angioplasty. Am Heart J 2004;147:815-22.
14. Brophy JM, Belisle P, Joseph L. Evidence for use of coronary stents. A hierarchical bayesian meta-analysis. Ann Intern Med 2003;138:777-86.
15. Kereiakes DJ, Midei M, Hermiller J, O'Shaughnessy C, Schlofmitz R, Yakubov S, et al. Procedural and late outcomes following MULTI-LINK DUET coronary stent deployment. Am J Cardiol 1999;84:1385-90.
16. Serruys PW. SPIRIT FIRST: Everolimus-eluting durable polymer on the ML VISION platform — baseline and 6-month follow-up. Presented at Transcatheter Cardiovascular Therapeutics 2004; 2004 Sep 27–Oct 1; Washington, DC. Available from: http://www.medscape.com/viewarticle/491699. Accessed on 3/24/05.
17. Fischman DL, Leon MB, Baim DS, Schatz RA, Savage MP, Penn I, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. Stent Restenosis Study Investigators. N Engl J Med 1994;331:496-501.
18. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, et al. A comparison of balloon-expand-

able-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group. N Engl J Med 1994;331:489-95.
19. Buellesfeld L, Grube E. ABT-578-eluting stents. The promising successor of sirolimus- and paclitaxel-eluting stent concepts? Herz 2004;29:167-70.
20. Boland JL, Corbeij HA, Van Der Giessen W, Seabra-Gomes R, Suyapranata H, Wijns W, et al. Multicenter evaluation of the phosphorylcholine-coated biodivYsio stent in short de novo coronary lesions: The SOPHOS study. Int J Cardiovasc Intervent 2000;3:215-25.
21. Baim DS, Cutlip DE, O'Shaughnessy CD, Hermiller JB, Kereiakes DJ, Giambartolomei A, et al. Final results of a randomized trial comparing the NIR stent to the Palmaz-Schatz stent for narrowings in native coronary arteries. Am J Cardiol 2001;87:152-6.
22. Serruys PW, IJsselmuiden S, Hout B, Vermeersch P, Bramucci E, Legrand V, et al. Direct stenting with the Bx VELOCITY balloon-expandable stent mounted on the Raptor rapid exchange delivery system versus predilatation in a European randomized Trial: the VELVET trial. Int J Cardiovasc Intervent 2003;5:17-26.
23. Hong MK, Mintz GS, Lee CW, Song JM, Han KH, Kang DH, et al. Paclitaxel coating reduces in-stent intimal hyperplasia in human coronary arteries: a serial volumetric intravascular ultrasound analysis from the Asian Paclitaxel-Eluting Stent Clinical Trial (ASPECT). Circulation 2003;107:517-20.
24. Grube E, Silber S, Hauptmann KE, Mueller R, Buellesfeld L, Gerckens U, Russell ME. TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. Circulation 2003;107:38-42.
25. Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. N Engl J Med 2004; 350:221-31.
26. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med 2003;349:1315-23.
27. Grube E. FUTURE II: Multicenter Evaluation of the Bioabsorbable Polymer-Based Everolimus-Eluting Stent. Presented at the 15th Annual Transcatheter Cardiovascular Therapeutics; 2003 Sep 15–19; Washington, DC. Available from: http://www.medscape.com/viewarticle/462169. Accessed on 3/24/05.
28. Gershlick A, De Scheerder I, Chevalier B, Stephens-Lloyd A, Camenzind E, Vrints C, et al. Inhibition of restenosis with a paclitaxel-eluting, polymer-free coronary stent: the European evaLUation of pacliTaxel Eluting Stent (ELUTES) trial. Circulation 2004;109:487-93.
29. Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002;346:1773-80.
30. Zidar JP, Fry E, Lambert C, Rubinstein R, Raizner AE, Fischell TA, et al. The VENUS trial: a multi-center registry of the Cordis Bx VELOCITY Stent. Am J Cardiol 2000;86(8 Suppl 1):17i.
31. Biondi-Zoccai GG, Abbate A, Agostoni P, Parisi Q, Turri M, Anselmi M, et al. Stenting versus surgical bypass grafting for coronary artery disease: systematic overview and meta-analysis of randomized trials. Ital Heart J 2003;4:271-80.
32. Legrand VM, Serruys PW, Unger F, van Hout BA, Vrolix MC, Fransen GM, et al. Three-year outcome after coronary stenting versus bypass surgery for the treatment of multivessel disease. Circulation 2004;109:1114-20.
33. Lansky AJ, Costa RA, Mintz GS, Tsuchiya Y, Midei M, Cox DA, et al. Non-polymer-based paclitaxel-coated coronary stents for the treatment of patients with de novo coronary lesions: angiographic follow-up of the DELIVER clinical trial. Circulation 2004;109:1948-54.
34. Abizaid A, Albertal M, Costa MA, Abizaid AS, Staico R, Feres F, et al. First human experience with the 17-beta-estradiol-eluting stent: the Estrogen And Stents To Eliminate Restenosis (EASTER) trial. J Am Coll Cardiol 2004;43:1118-21.
35. Tanabe K, Seruys PW, Grube E, Smits PC, Selbach G, van der Giessen WJ, et al. TAXUS III Trial: in-stent restenosis treated with stent-based delivery of paclitaxel incorporated in a slow-release polymer formulation. Circulation 2003; 107:559-64.
36. Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, et al. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. Circulation 2003;108:788-94.
37. Regar E, Serruys PW, Bode C, Holubarsch C, Guermonprez JL, Wijns W, et al. Angiographic findings of the multicenter Randomized Study With the Sirolimus-Eluting Bx Velocity Balloon-Expandable Stent (RAVEL): sirolimus-eluting stents inhibit restenosis irrespective of the vessel size. Circulation 2002;106:1949-56.
38. Park SJ, Shim WH, Ho DS, Raizner AE, Park SW, Hong MK, et al. A paclitaxel-eluting stent for the prevention of coronary restenosis. N Engl J Med 2003;348:1537-45.
39. Sawhney N, Moses JW, Leon MB, Kuntz RE, Popma JJ, Bachinsky W, et al. Treatment of left anterior descending coronary artery disease with sirolimus-eluting stents. Circulation 2004;110:374-9.
40. Diegeler A, Thiele H, Falk V, Hambrecht R, Spyrantis N, Sick P, et al. Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. N Engl J Med 2002;347:561-6.
41. Drenth DJ, Veeger NJ, Winter JB, Grandjean JG, Mariani MA, Boven van AJ, Boonstra PW. A prospective randomized trial comparing stenting with off-pump coronary surgery for high-grade stenosis in the proximal left anterior descending coronary artery: three-year follow-up. J Am Coll Cardiol 2002;40:1955-60.
42. Goy JJ, Kaufmann U, Goy-Eggenberger D, Garachemani A, Hurni M, Carrel T, et al. A prospective randomized trial comparing stenting to internal mammary artery grafting for proximal, isolated de novo left anterior coronary artery stenosis: the SIMA trial. Stenting vs Internal Mammary Artery. Mayo Clin Proc 2000;75:1116-23.
43. Buxton BF, Raman JS, Ruengsakulrach P, Gordon I, Rosalion A, Bellomo R, et al. Radial artery patency and clinical outcomes: five-year interim results of a randomized trial. J Thorac Cardiovasc Surg 2003;125:1363-71.
44. Khot UN, Friedman DT, Pettersson G, Smedira NG, Li J, Ellis SG. Radial artery bypass grafts have an increased occurrence of angiographically severe stenosis and occlusion compared with left internal mammary arteries and saphenous vein grafts. Circulation 2004;109:2086-91.
45. Chow MS, Sim E, Orszulak TA, Schaff HV. Patency of internal thoracic artery grafts: comparison of right versus left and importance of vessel grafted. Circulation 1994;90(5 Pt 2):II129-32.
46. Yamashita T, Nishida T, Adamian MG, Briguori C, Vaghetti M, Corvaja N, et al. Bifurcation lesions: two stents versus one stent—immediate and follow-up results. J Am Coll Cardiol 2000;35:1145-51.
47. Colombo A, Moses JW, Morice MC, Ludwig J, Holmes DR Jr, Spanos V, et al. Randomized study to evaluate sirolimus-

eluting stents implanted at coronary bifurcation lesions. Circulation 2004;109:1244-9.
48. Moussa I, Leon MB, Baim DS, O'Neill WW, Popma JJ, Buchbinder M, et al. Impact of sirolimus-eluting stents on outcome in diabetic patients: a SIRIUS (SIRolImUS-coated Bx Velocity balloon-expandable stent in the treatment of patients with de novo coronary artery lesions) substudy. Circulation 2004;109:2273-8.
49. Ardissino D, Cavallini C, Bramucci E, Indolfi C, Marzocchi A, Manari A, et al. Sirolimus-eluting vs uncoated stents for prevention of restenosis in small coronary arteries: a randomized trial. JAMA 2004;292:2727-34.
50. Lemos PA, Hoye A, Goedhart D, Arampatzis CA, Saia F, van der Giessen WJ, et al. Clinical, angiographic, and procedural predictors of angiographic restenosis after sirolimus-eluting stent implantation in complex patients: an evaluation from the Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) study. Circulation 2004; 109:1366-70.
51. Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol 2000;35:1288-94.
52. Wilson SH, Fasseas P, Orford JL, Lennon RJ, Horlocker T, Charnoff NE, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. J Am Coll Cardiol 2003;42:234-40.