Topics in Primary Care Medicine

Revascularization in Coronary Artery Disease
A Review of Randomized Trial Data

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Since the advent of bypass surgery in the late 1960s and catheter-based intervention in the late 1970s, the treatment of coronary artery disease has been revolutionized by the concept of revascularization. Surveys have demonstrated that the practice patterns around the world and within the US are inconsistent for these important treatment options and are often driven by availability and economics rather than evidence-based data. In addition, the studies examining the use of medical therapy, balloon angioplasty, atherectomy, coronary stenting, and bypass surgery are consistently lagging behind the technological advances in this field. This article reviews the data that randomized trials and meta-analyses provide to compare these modalities. We attempt to provide a framework for reasoned clinical decision making to help guide patient care. While the breakpoints between the medicine bottle, cath lab, and operating room will continue to evolve, we offer a revascularization strategy for patient subgroups based on what clinical data supports.

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The treatment of coronary artery disease changed drastically when the first coronary artery bypass graft (CABG) surgery was performed in 1968—an event that added coronary revascularization as an alternative to medical therapy alone.[1] Nine years later, the spectrum of treatment broadened even further with the introduction of percutaneous transluminal coronary balloon angioplasty (PTCA).[2] Further advances in catheter-based technology, including the recent introduction of coronary stenting and atherectomy, now provide clinicians with a range of revascularization options. At the same time, there have been many advances in the medical treatment of coronary disease. Choosing among the dizzying array of available therapeutic options can be a daunting task, particularly considering the wide range of clinical and angiographic presentations of coronary artery disease. In this article, we review the randomized trial data evaluating the many available therapies in an attempt to clarify when medical therapy, CABG, PTCA, or coronary stenting are appropriate or preferred.

Medical Therapy Versus CABG

The use of bypass surgery has expanded greatly since its introduction, with an estimated 501,000 performed in the US in 1994.[3] CABG now has a relatively low risk in most cases, with perioperative mortality rates of 1% to 3.7% and perioperative myocardial infarction (MI) rates of 6% to 8%.[4] The major conduits used for grafting, saphenous vein grafts and internal mammary artery grafts, have natural histories of their own, which are now well characterized. Saphenous vein grafts typically have a 12% to 20% closure rate after one year, with a slow attrition rate of 2% per year over the next four to five years. Thereafter, due to atherosclerosis of the grafts, the rate accelerates to 4% per year; this means that after 11 years, only 50% of the grafts remain patent. In contrast, the patency rate for internal mammary artery grafts to the left anterior descending coronary artery (LAD) is 90% after 10 years.[5] The difference in patency rates is clinically important, because patients receiving an internal mammary artery graft to the LAD have shown a long-term survival advantage over patients who received saphenous vein grafts only.[6] (It is important to note that all of the randomized trials comparing medical therapy to CABG took place before the widespread use of internal mammary artery grafts, which are now used in 75% to 80% of CABG cases.)

During the 1970s, seven randomized trials were performed to evaluate survival rates with medical versus surgical therapy for patients with stable coronary disease.[7–12] A meta-analysis using primary data from these trials was published by Yusuf and colleagues in 1994.[13] The seven trials tested the strategy of initial surgery ver-

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ABBREVIATIONS USED IN TEXT
CABG = coronary artery bypass graft
LAD = left anterior descending coronary artery
MI = myocardial infarction
PTCA = percutaneous transluminal coronary balloon angioplasty

sus that of initial medical therapy with the option to cross over to surgery for intractable anginal symptoms. One of the two typical indications for surgery was stable angina. The other was a recent MI with angiographic evidence of coronary artery disease, which was generally defined as 50% to 70% stenosis of either a major coronary artery or the left main coronary artery. The trials used mainly saphenous vein grafts; only 10% received internal mammary artery grafts. Three major trials—the VA Cooperative Study, the European Coronary Surgery Study, and the Coronary Artery Surgery Study—comprised 84% of the 2649 patients (about 2,225 patients) included in the meta-analysis.[7–9] Long-term survival data ranging from 10 to 18 years is now available for these three trials.

Regarding overall survival, the three major trials varied in their results. The Coronary Artery Surgery Study showed no difference between the two strategies; the VA Cooperative Study showed a short-lived survival advantage with CABG after seven years that was not evident after ten years; and the European Coronary Surgery Study showed a definite survival advantage with CABG beginning after five years and extending to the end of the trial at 12 years. Results of the meta-analysis, however, showed a significant survival advantage with CABG, lasting from year 5 (90% survival with CABG versus 84% with medical therapy, $P < 0.001$) to year 10 (74% with CABG versus 70% with medical therapy, $P = 0.04$).

Most clinicians who treat coronary artery disease accept the clear survival advantage with CABG shown in these trials for patients with left main coronary artery disease or with three-vessel disease and reduced left-ventricular function. A review of the data, however, identifies other subgroups that derive much benefit from CABG and still others that derive little or no benefit. We will concentrate on the subgroups that are commonly seen in clinical settings.

First, it appears that patients with proximal LAD stenosis have a survival advantage with CABG. The European Coronary Surgery Study, which only included patients with normal left-ventricular function and two- or three-vessel disease, showed no significant mortality difference between medical and surgical therapy in patients without proximal LAD disease (with a 10-year survival rate of 81% for CABG and 83% for medical therapy, P = NS). Patients with proximal LAD disease, however, did have a mortality benefit with surgery (a 10-year survival rate of 76% with CABG versus 65% with medical therapy, $P = 0.007$). The VA Cooperative Study did not analyze this subgroup, and the Coronary Artery Surgery Study showed no difference between therapies in these patients. The meta-analysis, however, showed that with CABG, patients with proximal LAD disease had a 42% decreased risk of death after five years ($P = 0.001$).

A second important subgroup involves the number of diseased vessels. In Yusuf's meta-analysis,[13] after five years, patients with one- and two-vessel disease showed a nonsignificant trend toward mortality reduction with CABG (as compared to medical therapy); they showed no mortality difference after 10 years. In contrast, patients with three-vessel disease had a decreased risk of mortality with CABG—42% after five years ($P = 0.001$) and 24% after 10 years ($P = 0.02$). The European Coronary Surgery Study, in which all patients had normal left ventricular function, showed similar results from surgery in patients with three-vessel disease (mortality rates after 10 years of 22% with CABG and 32% with medical therapy, $P = 0.01$). No significant difference in mortality was seen for patients with two-vessel disease. These data indicate that patients with three-vessel disease have a significant survival benefit with CABG.

The three major studies also analyzed the rate of nonfatal MI. In the European Coronary Surgery Study and the Coronary Artery Surgery Study, there were no significant differences in the rate of Q wave MI between the surgical and medical groups. The VA study, which examined both Q wave and non–Q wave infarctions, showed a significantly higher rate of MI in the surgical group at 10 and 18 years of follow-up. Interestingly, in this trial, of patients who had had an MI, surgically treated patients had better survival rates than medically treated patients.[14]

The randomized trial data comparing the strategy of initial CABG to initial medical therapy shows an overall survival advantage with CABG, even in time periods before the extensive use of internal mammary artery grafts. This survival advantage is most evident in certain high-risk subgroups—including left-main coronary artery disease, three-vessel disease with reduced left ventricular function, proximal LAD disease, and three-vessel coronary artery disease. The significant survival advantage was not seen in patients with one- and two-vessel disease. CABG decreases angina frequency and antianginal medication use, but it does not reduce the rate of nonfatal MI.

Standard PTCA versus Medical Therapy

In patients with lesions amenable to angioplasty, PTCA has a higher than 85% success rate with an associated 3% to 5% risk of procedural MI, 2% to 4% risk of emergency CABG, and less than 1% risk of death.[15] Most centers now perform PTCA as an outpatient procedure. Restenosis at the angioplasty site, however, occurs within 6 months in 25% to 35% of patients.[15] The occurrence of restenosis clearly plays an important role in examining the utility of PTCA and its long term efficacy.

There have been only two small randomized trials comparing PTCA to medical therapy for stable angina. The first was the Angioplasty Compared to Medicine

TABLE 1.—*PTCA versus CABG: Mortality, Myocardial Infarction, Recurrent Angina, and Repeat Procedure Rates*

	Mortality (%)		Myocardial Infarction (%)		Recurrent Angina (%)		Repeat Procedure (%)	
Study	PTCA	CABG	PTCA	CABG	PTCA	CABG	PTCA	CABG
BARI[23] n = 1829 5.4 years	13.7	10.7	10.9	11.7	NA	NA	54	8
CABRI[22] n = 1054 1 year	3.9	2.7	4.9	3.5	13.9	10.1	36.5	3.5
RITA[21] n = 1011 2.5 years	3.1	3.6	6.7	5.2	31.3	21.5¶	37.1	5.0¶¶
EAST[20] n = 392 3 years	7.1	6.2	14.6	19.6	20	12¶	54	13¶¶
GABI[19] n = 359 1 year	2.2	4.9	3.8	7.3	29	26	44	6
ERACI[18] n = 127 3 years	3.2	0	3.2	1.8	32	18¶	32	3¶¶

¶ = $P < 0.05$

¶¶ = $P < 0.001$

study, which evaluated 212 male veterans (with either stable angina, an abnormal exercise test, or a recent MI) who had single-vessel coronary artery disease with 70% to 99% stenosis.[16] After randomization either to angioplasty or to standard medical therapy (consisting of aspirin, beta-blockers, nitrates, and calcium channel blockers), the patients were followed for six months and then subjected to a second exercise test. The results showed a significant reduction in angina in the angioplasty group—64% were free of angina versus 46% in the medical therapy group ($P < 0.01$). The patients who underwent PTCA also had a prolonged exercise time over baseline (an increase of 2.1 minutes versus 0.5 minutes for the medical therapy group, $P < 0.0001$). Sixteen percent of the angioplasty patients required repeated PTCA, and 7% went on to CABG during the six-month trial period. In the medical therapy group, only 10% underwent PTCA and none underwent CABG. Patients in the angioplasty group also had a greater improvement in measures of psychological well-being than did those in the medical group. No differences in mortality or MI were observed; however, the trial was not designed to evaluate these potential differences given the small number of study subjects and the short duration of follow-up.

The second trial—the Medicine, Angioplasty, or Surgery Study—randomized patients at a single center to medical therapy, balloon angioplasty (PTCA), or internal mammary CABG.[17] The patients had isolated lesions (more than 80% stenosis) in the proximal LAD and normal left ventricular function. The results of the trial showed that after a mean follow-up duration of 3 years with the 214 randomized patients, the surgical group was more likely to be free of angina than were the PTCA and medical therapy groups (98% versus 82% and 32%, respectively, $P < 0.05$). The CABG group was also less likely to have a primary event, defined as cardiac death, MI, or the need for further intervention with PTCA or surgery (3% CABG versus 17% PTCA and 24% medical therapy, $P < 0.01$). It should be noted that in these groups, the major difference was the need for either PTCA or CABG for symptom relief, with similar rates of MI and death in all of the groups.

These two trials—the Angioplasty Compared to Medicine study and the Medicine, Angioplasty, or Surgery Study—suggest that angioplasty is more efficacious at reducing angina than medical therapy alone. Angioplasty, however, often necessitates repeated procedures (PTCA or CABG) to sustain this benefit. Unfortunately, the two trials lack sufficient sample size and follow-up to evaluate potential differences in the rates of MI or death.

Standard PTCA versus CABG Surgery

Along with the Medicine, Angioplasty, or Surgery Study trial described above, there have been six major randomized trials reported since 1993 that compare standard PTCA to CABG. These trials have had over 4700 patients enrolled with follow-up from 1 to 5.4 years.[18–23] Of note, these trials included a substantial proportion of patients with unstable angina and did not include coronary stents. All six of the trials evaluated patients with

multivessel coronary artery disease with the exception of the Randomized Intervention Treatment of Angina trial, which also included patients with single-vessel disease. Notably, a large proportion of patients screened for these trials were shown to be ineligible for inclusion in this study, often because multivessel angioplasty was not feasible secondary to angiographic features.

In five of the six trials there were no differences between CABG and PTCA in either mortality or MI rates (Table 1). The exception was the German Angioplasty Bypass Surgery Investigation trial, in which the combined endpoint of mortality and myocardial infarction was significantly higher in the CABG group (13% versus 7%, $P = 0.02$). This difference was largely due to the high rate of perioperative MI in the surgery group (8%), a factor not observed in the other trials. In the Bypass Angioplasty Revascularization Investigation trial, the investigators also looked at the subset of patients with diabetes mellitus. They found that these patients apparently have a survival advantage with CABG—an 80.6% survival rate versus a 65.5% survival rate with PTCA ($P = 0.003$)—at a mean follow-up of 5.4 years. The diabetes subgroup was not specifically analyzed in the other trials, and this finding needs further validation.

Of the five trials that reported on angina recurrence rates, four demonstrated that CABG results in a significant reduction in angina recurrence. The remaining study, the German Angioplasty Bypass Surgery Investigation, showed only a nonsignificant trend favoring CABG. The largest trial, the Bypass Angioplasty Revascularization Investigation, did not report on angina recurrence.

The most noticeable difference seen in these trials was the high incidence of repeated revascularization procedures, either angioplasty or CABG, in patients randomized to PTCA. For example, during an average follow-up of 5.4 years, 54% of the angioplasty group in the Bypass Angioplasty Revascularization Investigation had repeated revascularization (23% PTCA, 20% CABG, and 11% both PTCA and CABG). In the surgical group, only 8% needed a repeat procedure (7% PTCA and 1% CABG). It should be noted that many patients in the PTCA groups had to have staged, multiple angioplasties to achieve initial revascularization; these cases are *not* included in the repeat revascularization numbers. Cost-effectiveness analyses, however, suggest that a strategy of initial angioplasty, even with such high recurrent procedure rates, is less costly than receiving an initial CABG.[18,24]

To summarize, the randomized trial data comparing PTCA to CABG indicate that there is no significant difference in mortality or MI rates during the short-term follow-up period of one to five years. Patients with diabetes may have a survival advantage with surgery, as demonstrated in the Bypass Angioplasty Revascularization Investigation trial, but this was a post-hoc subgroup analysis and needs further validation. Surgery appears to be the best way to relieve angina and greatly reduce the need for repeated revascularization procedures for both single- and multivessel coronary artery disease, but it may be more costly than other options.

Given that these studies show no clear survival advantage for either treatment strategy, patient preferences become paramount in the choice of a revascularization procedure. Surgery is more efficacious at relieving symptoms, but it has a higher perioperative risk and requires more rehabilitation time than angioplasty. Angioplasty recipients, however, might expect a greater than 50% chance of requiring another revascularization during the first five years, as well as more noninvasive studies and a diagnostic coronary angiography—with their accompanying costs and risks. Patients with significant comorbid diseases (such as chronic obstructive pulmonary disease) have higher incidences of perioperative complications, and they may select PTCA to minimize these risks. Lastly, some (particularly younger) patients may consider using PTCA for symptom relief and thus delay CABG to an older age, given the propensity for graft stenosis and recurrent symptoms after surgery. Careful discussion with patients and their families will help in selecting the best option for a given person.

Coronary Stents versus Standard PTCA

Much of the need for repeat procedures after angioplasty comes from restenosis of the treated segment, which occurs in 25% to 35% of patients after six months. One development designed to combat this problem is the balloon-expandable intracoronary stent. The results of two large randomized trials comparing conventional balloon angioplasty to implantation of the Palmaz-Schatz stent for single vessel coronary artery disease were recently published.[25–27] The Benestent study randomized 520 patients with stable angina and a single new lesion to either PTCA or stent implantation and followed the patients for one year. The other study, the Stent Restenosis Study, randomized 410 patients with stable and unstable angina and a single new lesion. These trials showed that at seven months' follow-up, stents had angiographic restenosis rates of only 22% to 32%, compared to the 32% to 42% that resulted with standard balloon angioplasty (PTCA). The Benestent trial showed that stenting led to a significant reduction (after one year) in the combined primary endpoint of MI, stroke, death, or the need for CABG or repeat PTCA. This difference, however, was almost entirely attributable to the increased rate of repeat angioplasty in the PTCA group. The Stent Restenosis Study showed no difference after seven months between the groups in reaching a similar combined primary endpoint or in the rate of repeat revascularization.

These two trials favored stents for reducing restenosis. Three drawbacks of stent therapy were demonstrated, however. First, the stent groups had a higher incidence of bleeding and vascular complications, which included hemorrhages, hematomas, and pseudoaneurysms. Both trials used oral anticoagulation with warfarin for one to

TABLE 2.—*Options for Treatment*

CAD Subset	Intervention
Left main disease	CABG
3-vessel disease with decreased LV function	CABG > PTCA
3-vessel disease with normal LV function	CABG or PTCA
Proximal LAD disease	CABG or PTCA/Stent
1- or 2-vessel disease without proximal LAD disease, angina	Medical therapy or PTCA/Stent
1- or 2-vessel disease without proximal LAD disease, asymptomatic	Medical therapy

LAD = left anterior descending coronary artery; PTCA = percutaneous transluminal coronary balloon angioplasty; CABG = coronary artery bypass graft; LV = left ventricular

three months after stent placement to reduce the risk of stent thrombosis. The Benestent trial showed a significant increase in bleeding and vascular incidents with stenting (13.5% using stent and 3.1% using PTCA, $P < 0.001$), and the Stent Restenosis Study showed only a trend (7.3% using stent and 4% using PTCA, $P = 0.14$). Second, stent therapy led to a significantly longer length of hospitalization required to achieve adequate anticoagulation with warfarin before discharge. Third, the use of stents is associated with higher costs: the cost of the stent itself, the need for prolonged anticoagulation, and the additional days of hospitalization needed. A recent study of economic outcomes, based on in-patient cost data from the Stent Restenosis Study over one year, estimated that although stenting reduces restenosis, it costs approximately 7% more that standard angioplasty.[28] Even after the authors excluded from consideration the costs of vascular complications in the stent group, standard angioplasty still cost 3% less than stenting. Longer-term cost analyses are not yet available.

Of note is the fact that recent data suggest oral anticoagulation following stent placement is not necessary, which may minimize problems with cost and complications. A recent randomized trial compared oral anticoagulation with warfarin to combined antiplatelet therapy with aspirin and ticlopidine after Palmaz-Schatz stent placement. The results showed a lower rate of the combined endpoint (MI and the need for repeat revascularization with PTCA or CABG) in the antiplatelet group—1.6% versus 6.2%, $P = 0.01$.[29] The risk of stent occlusion was 5.4% in the warfarin group and only 0.8% in the antiplatelet group ($P = 0.004$). Importantly, the rate of hemorrhagic complications was significantly reduced (6.5% warfarin versus 0% antiplatelet, $P < 0.001$), as was the rate of peripheral vascular events including pseudoaneurysm formation (6.2% warfarin versus 0.8% antiplatelet, $P = 0.001$). Thus, the degree of anticoagulation that led to more bleeding and vascular complications in the Benestent and Stent Restenosis Study trials appears unwarranted. Additionally, the Benestent II trial is under way. This trial evaluates a heparin-coated Palmaz-Schatz stent, and preliminary results suggest that oral anticoagulation may not be needed with this stent design.[30]

There are over 20 different coronary stents in various stages of development that will reach the American market during the next five years. The different designs may improve stent efficacy. In addition, improved delivery and implantation systems and developments involving stent coatings will likely lead to further decreases in restenosis and complications that result from these devices.

In summary, the available data for Palmaz-Schatz stents show a lower angiographic restenosis rate over the first seven months of follow-up than that of standard PTCA. The Benestent trial showed decreased clinical event rates—particularly those of repeat procedures. The number of vascular complications and bleeding incidents seen in these studies has been reduced by using combined antiplatelet therapy or heparin-coated stents, and more trial data using these strategies are forthcoming. There are no randomized trials using stents in multivessel coronary artery disease; their role thus remains undefined in this clinical setting. The issue of the expanding role of stents for "rescue" in acute vessel closure complicating PTCA and for vein graft stenosis is beyond the scope of this article.

Overall Strategy

All patients with coronary artery disease should undergo aggressive risk reduction therapy, including aspirin, beta-blocker use in post-MI patients, and lipid-lowering if indicated. A suggested revascularization strategy based upon the randomized trial data for patients with certain subgroups of coronary artery disease is shown in Table 2. This is a general guideline; individual patient characteristics and preferences play important roles in choosing a specific strategy.

For patients with left-main coronary disease, CABG is clearly the therapy of choice. In patients with proximal LAD disease or with three-vessel disease and a normal ejection fraction, CABG has proven to be effective in lowering mortality risk; however, PTCA is also an option, based on short-term comparisons of these two strategies. With three-vessel disease and reduced left-ventricular function, CABG has more data showing a survival advantage than does PTCA, although angioplasty is also an option in patients wishing to avoid surgery. For patients with one- or two-vessel disease and without proximal LAD disease, the best options are medical therapy alone or PTCA, with angioplasty the better choice for relieving symptoms in the short-term. Coronary stenting as an alternative to standard PTCA can be considered in any patient who is planning to undergo angioplasty, particularly those with single-vessel lesions, but its role in multivessel disease is not yet clearly defined.

REFERENCES

1. Favorolo RG. Saphenous vein autograft replacement of severe segmental coronary artery occlusion: operative technique. Ann Thorac Surg 1968; 5:334–339

2. Gruntzig AR, Senning A, Seigenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. N Engl J Med 1979; 301:61–68

3. American Heart Association. 1997 Heart and Stroke Statistical Update. Dallas, TX: American Heart Association, 1996

4. Leape LL, Hilborne LH, Kahan JP, Stason WB, Park RE, Kamberg CJ, Brook RH. Coronary Artery Bypass Graft. Santa Monica, CA: RAND, 1991, pp 34–49

5. Nwasokwa ON. Coronary artery bypass graft disease. Ann Intern Med 1995; 123:528–545

6. Cameron A, Davis KB, Green G, Schaff HV. Coronary artery bypass surgery with internal-thoracic-artery grafts—effects on survival over a 15-year period. N Engl J Med 1996; 334:216–219

7. VA Coronary Artery Bypass Surgery Cooperative Study Group. Eighteen-year follow-up in the Veterans Affairs Cooperative Study of coronary artery bypass surgery for stable angina. Circulation 1992; 86:121–130

8. Varnauskas E and the European Coronary Surgery Study Group. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med 1988; 319:332–337

9. Alderman EL, Bourassa MG, Cohen LS, Davis KB, Kaiser GG, Killip T, et al. Ten-year follow-up of survival and myocardial infarction in the randomized Coronary Artery Surgery Study. Circulation 1990; 82:1629–1646

10. Norris RM, Agnew TM, Brandt PWT, Graham KJ, Hill DG, Kerr AR, et al. Coronary surgery after recurrent myocardial infarction: progress of a trial comparing surgical with nonsurgical management for asymptomatic patients with advanced coronary disease. Circulation 1981; 63:785–792

11. Mathur VS, Guinn GA. Prospective randomized study of the surgical therapy of stable angina. Cardiovasc Clin 1977; 8:131–144

12. Koster FE, Kremkau EL, Ritzman LW, Rahimtoola SH, Rosch J, Kanarek PH. Coronary bypass for stable angina. N Engl J Med 1979; 300:149–157

13. Yusuf S, Zucker D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet 1994; 344:563–570

14. Peduzzi P, Detre K, Murphy ML, Thomsen J, Hultgren H, Takaro T, et al. Ten-year incidence of myocardial infarction and prognosis after infarction. Circulation 1991; 83:747–755

15. Hilborne LH, Leape LL, Kahan JP, Park RE, Kamberg CJ, Brook RH. Percutaneous Transluminal Coronary Angioplasty. Santa Monica, CA: RAND, 1991, pp v–vii

16. Parisi AF, Folland ED, Hartigan P (for the ACME Investigators). A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. N Engl J Med 1992; 326:10–16

17. Hueb WA, Bellotti G, Almeida de Oliveira S, Arie S, Piva de Albuquerque C, Jatene AD, Pileggi F. The Medicine, Angioplasty, or Surgery Study (MASS): a prospective randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995; 26:1600–1605

18. Rodriguez A, Mele E, Peyregne E, Bullon F, Perez-Balino N, Sosa Liprandi MI, et al. Three-year follow-up of the Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI). J Am Coll Cardiol 1996; 27:1178–1184

19. Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. (for the German Angioplasty Bypass Surgery Investigation). A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. N Engl J Med 1994; 331:1037–1043

20. King SB III, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, et al. (for the Emory Angioplasty versus Surgery Trial [EAST]). A randomized trial comparing coronary angioplasty with coronary bypass surgery. N Engl J Med 1994; 331:1044–1050

21. RITA Trial participants. Coronary angioplasty versus coronary artery bypass surgery: the Randomized Intervention Treatment of Angina (RITA) Trial. Lancet 1993; 341:573–580

22. CABRI Trial participants. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularization Investigation). Lancet 1995; 346:1179–1184

23. Bypass Angioplasty Revascularization Investigation (BARI) investigators. Comparison of coronary artery bypass surgery with angioplasty in patients with multivessel disease. N Engl J Med 1996; 335:217–225

24. Weintraub WS, Mauldin PD, Becker E, Kosinski AS, King SB III. A comparison of the costs of and quality of life after coronary angioplasty or coronary surgery for multivessel coronary artery disease. Circulation 1995; 92:2831–2840

25. Fischman DL, Leon MB, Bairn DS, Schatz RA, Savage MP, Penn I, et al (for the Stent Restenosis Study Investigators). A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994; 331:496–501

26. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, et al (for the Benestent Study Group). A comparison of balloon-expandable stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994; 334:489–495

27. Macaya C, Serruys PW, Ruygrok P, Suryapranata H, Mast G, Klugmann S, et al (for the Benestent Study Group). Continued benefit of coronary stenting versus balloon angioplasty: one-year clinical follow-up of Benestent trial. J Am Coll Cardiol 1996; 27:255–261

28. Cohen DJ, Krumholz HM, Sukin CA, Ho KKL, Siegrist RB, Cleman M, et al (for the Stent Restenosis Study investigators). In-hospital and one-year economic outcomes after coronary stenting or balloon angioplasty. Circulation 1995; 92:2480–2487

29. Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med 1996; 334:1084–1089

30. Surruys PW, Emanuelsson H, van der Giessen W, Lunn AC, Kiemeneij F, Macaya C, et al (for the Benestent-II Study Group). Heparin-coated Palmaz-Schatz stents in human coronary arteries: early outcome of the Benestent-II pilot study. Circulation 1996; 93:412–422