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CLINICAL RESEARCH **Clinical Trials**

The Medicine, Angioplasty, or Surgery Study (MASS-II): A Randomized, Controlled Clinical Trial of Three Therapeutic Strategies for Multivessel Coronary Artery Disease

One-Year Results

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OBJECTIVES We sought to evaluate the relative efficacies of three possible therapeutic strategies for patients with multivessel coronary artery disease (CAD), stable angina, and preserved ventricular function.

BACKGROUND Despite routine use of coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI), there is no conclusive evidence that either one is superior to medical therapy (MT) alone for the treatment of multivessel CAD.

METHODS The primary end point was defined as cardiac mortality, Q-wave myocardial infarction (MI), or refractory angina requiring revascularization. All data were analyzed according to the intention-to-treat principle.

RESULTS A total of 611 patients were randomly assigned to either a CABG (n = 203), PCI (n = 205), or MT (n = 203) group. The one-year survival rates were 96.0% for CABG, 95.6% for PCI, and 98.5% for MT. The rates for one-year survival free of Q-wave MI were 98% for CABG, 92% for PCI, and 97% for MT. After one-year follow-up, 8.3% of MT patients and 13.3% of PCI patients underwent to additional interventions, compared with only 0.5% of CABG patients. At one-year follow-up, 88% of the patients in the CABG group, 79% in the PCI group, and 46% in the MT group were free of angina ($p < 0.0001$).

CONCLUSIONS Medical therapy for multivessel CAD was associated with a lower incidence of short-term events and a reduced need for additional revascularization, compared with PCI. In addition, CABG was superior to MT for eliminating anginal symptoms. All three therapeutic regimens yielded relatively low rates of cardiac-related deaths. (J Am Coll Cardiol 2004;43:1743–51)

The most appropriate treatment for patients with multivessel stable coronary artery disease (CAD) remains unknown. There is no recent evaluation of medical therapy (MT) versus surgical therapy in the modern era of pharmacologic treatment, since novel surgical techniques have been performed. Furthermore, the use of percutaneous coronary intervention (PCI) is increasing more rapidly than surgery, despite a lack of evidence regarding its superiority to either MT or surgical approaches.

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Medical therapy for patients with multivessel CAD has changed considerably in recent years. Current therapeutic strategies, including aggressive modification of risk factors and intermittent use of nitrates, beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and more recently, 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors, have improved the outcomes of patients with CAD (1,2). Nonetheless, the rate of major cardiovascular events is considerable in medically treated patients, particularly those with multivessel disease (3).

For patients with multivessel disease, the benefits of coronary artery bypass graft surgery (CABG) are well documented with respect to symptoms and, in some groups, mortality and morbidity (4–6). Refinements in PCI have improved the treatment of patients with CAD (7,8). However, the rapidly expanding use of PCI is based on a perceived benefit in comparison with the use of CABG or MT, but these perceptions are from selected subsets of patients (9). In fact, no study has demonstrated a mortality benefit over MT in patients with stable CAD (10).

The specific question of whether PCI or surgical treatment offers any advantage over MT in patients with stable

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Abbreviations and Acronyms

CABG	= coronary artery bypass graft surgery
CAD	= coronary artery disease
CCS	= Canadian Cardiovascular Society
ECG	= electrocardiogram/electrocardiographic
MASS-II	= Medicine, Angioplasty, or Surgery Study-II
MI	= myocardial infarction
MT	= medical therapy
PCI	= percutaneous coronary intervention

angina and multivessel disease remains unanswered. Because PCI is unlikely to be more effective than CABG in reducing mortality or myocardial infarction (MI) in this patient population, its potential benefits are measured more readily in terms of symptomatic and functional outcomes. In this respect, several factors complicate the choices among patients who are appropriate candidates for all three therapies—namely, CABG, MT, or PCI. For example, the incidence of the most common adverse event—restenosis—remains high despite the reduction observed after stent placement in PCI patients (11,12). Thus, there is no objective comparison of the three therapeutic strategies for patients with multivessel disease (13). The Medicine, Angioplasty, or Surgery Study (MASS-II), a randomized trial, was therefore designed to compare the relative efficacy of either CABG, PCI, or MT in the management of patients with symptomatic multivessel CAD.

METHODS

Patient selection. Patients with angiographically documented proximal multivessel coronary stenosis of more than 70% by visual assessment and documented ischemia were considered for inclusion. Ischemia was documented by either stress testing or the typical stable angina assessment of the Canadian Cardiovascular Society (CCS) (class II or III). Patients were enrolled and randomized if there was agreement on the part of the surgeon and interventionist that revascularization could be attained by either strategy. Patients gave written, informed consent and were randomly assigned to a treatment group. The Ethics Committee of the Heart Institute approved the trial, and all procedures were performed in accordance with the Helsinki Declaration.

Exclusion criteria included unstable angina or acute MI requiring emergency revascularization, ventricular aneurysm requiring surgical repair, left ventricular ejection fraction of <40%, a history of PCI or CABG, and single-vessel disease. Patients were also excluded: if they had a history of congenital heart disease, valvular heart disease, or cardiomyopathy; if they were unable to understand or cooperate with the protocol requirements or to return for follow-up; or if they had left main coronary artery stenosis of 50% or more, or suspected or known pregnancy or another coexisting condition that was a contraindication to CABG or PCI.

Treatment intervention. In this trial, all patients were placed on an optimal medical regiment consisting of a stepped-care approach using nitrates, aspirin, beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, or a combination of these drugs, unless contraindicated. Hydroxymethylglutaryl-coenzyme A reductase inhibitors were also prescribed, along with a low-fat diet on an individual basis. The medications were provided for free by the Heart Institute. Patients were then randomized to continue with aggressive medical therapy alone or to undergo PCI or CABG concurrently with MT.

Trial operators were required to perform optimum coronary revascularization in accordance with current best practice. Equivalent revascularization was encouraged but not mandatory.

For patients assigned to PCI, the procedure was available within three weeks after the assignment. Devices used for catheter-based therapeutic strategies, including stents, lasers, directional atherectomy, and balloon angioplasty, were available to the interventionist. Angioplasty was performed according to a standard protocol (14). Glycoprotein IIb/IIa agents were not used. Successful revascularization in the PCI group was defined as a residual stenosis of <50% reduction in luminal diameter with Thrombolysis In Myocardial Infarction (TIMI) flow grade 3.

Patients assigned to the CABG group underwent the operation within 12 weeks after assignment. Complete revascularization was accomplished, if technically feasible, with saphenous vein grafts, internal mammary arteries, and other conduits such as radial or gastroepiploic arteries. Standard surgical techniques (15) were used under hypothermic arrest with blood cardioplegia. No off-pump CABG was performed.

Follow-up. Adverse and other clinical events were tracked from randomization. Patients were assessed with follow-up visits every three months until one year at the Heart Institute. Patients underwent a symptom-limited treadmill exercise test, according to a modified Bruce protocol, at baseline and by the end of one year, unless contraindicated. We considered exercise test results as positive when exertional angina developed or when we observed an ST-segment with an abnormal depression (horizontal or downsloping of 1 mm for men and 2 mm for women) at 0.08 s after the J point. Routine examinations included electrocardiography at rest, echocardiography, and routine blood tests every six months. Patients assigned to the PCI group also underwent routine coronary angiography at six months.

Coronary arteriography was performed by use of the Sones or Seldinger technique. For assessment of ventricular function, patients underwent contrast left ventriculography at baseline in the right anterior oblique projection, and ejection fraction was calculated by the Dodge formula (16).

Symptoms of angina were graded according to severity, from 1 to 4, as previously defined (17). Angina was considered refractory only when patients had been treated with full anti-ischemic therapies to their level of tolerance. Myocardial infarction was defined as the presence of signif-

icant new Q waves in at least two electrocardiographic (ECG) leads or symptoms compatible with MI associated with creatine kinase, MB fraction concentrations that were more than three times the upper limit of the reference range.

The predefined primary end point was the incidence of cardiac mortality, MI, or refractory angina requiring revascularization. The performance of a revascularization procedure was considered an end point for patients in any group, except for those assigned to PCI, who had additional routine coronary angioplasty. All patients in the PCI group had routine planned angiograms at six months. These angiograms were not considered to be end points because they were done independently of symptoms. However, therapeutic PCI or CABG performed during an episode of unstable angina at any time during follow-up was considered to be an end point and was applied equally across all three arms of therapy. Secondary end points included angina status and stroke or cerebrovascular accident.

Statistical analyses. The sample size was calculated to detect a two-fold difference of event rates between any two groups, with a power of 80% and a two-sided level of significance of 0.05%. On the basis of the two-year event rate of 8.58% from the Randomized Intervention Treatment of Angina (RITA) trial (18), assumptions included 41 composite events for each group to be reached during follow-up. It was determined that a minimum of 191 patients in each group was necessary to conduct this study, using the formula of Makuch and Simon (19). All data were analyzed according to the intention-to-treat principle rather than treatment received.

The event-free survival time was defined as the interval between random assignment and the occurrence of a primary end point or the latest follow-up. Event-free survival was estimated by the Kaplan-Meier method, and differences among groups were assessed by means of the log-rank test. Continuous variables were estimated as the mean value ± SD and compared among the three groups by one-way analysis of variance followed by the multiple comparisons test. The chi-square and Fisher exact tests were used to compare qualitative variables among the three groups. All tests were two-tailed, and $p \leq 0.05$ was considered statistically significant. Statistical analysis was performed with the Statistical Analysis System (SAS Institute, Cary, North Carolina).

RESULTS

Baseline variables. A total of 20,769 patients who had a presumptive clinical diagnosis of CAD and who underwent coronary arteriography were screened at the Heart Institute between May 1995 and May 2000. Of these, 18,692 (90%) patients either refused to participate or refused a specific treatment or did not meet the clinical or angiographic requirements for study inclusion. The most frequent reasons for exclusion were single-vessel disease, unstable angina, stenosis <70%, previous PCI or CABG, and valvular disease. The remaining 2,077 (10%) patients who had indications for revascularization were enrolled. Of these patients, 1,466 (71%) could not be randomly assigned because of specific protocol restrictions. Of these, 991 (68%) patients refused to participate in this trial, and 474 (32%) patients specifically refused the surgical procedure. The remaining eligible 611 (29%) patients who met all entry criteria were randomly assigned to one of three groups: CABG (n = 203; 33%), PCI (n = 205; 34%), or MT (n = 203; 33%). A total of 254 (42%) randomly assigned patients had double-vessel disease, and 357 (58%) had triple-vessel disease.

The vital status of all randomly assigned patients was ascertained in May 2001. The minimal duration of follow-up was one year. Randomization created balanced treatment groups with respect to important prognostic characteristics, as depicted in Table 1. That is, patients in all three therapeutic groups were similar with respect to age, gender, employment status, severity of angina, use of medication, and history of MI, diabetes mellitus, or hypertension. Patients assigned to the three groups were also similar in terms of resting and exercise ECG findings, as well as arteriographic and ventriculographic characteristics.

At study entry, 79% of the participating patients had CCS class II or III angina, 268 (43.9%) had a history of MI, 167 (27.3%) showed ECG evidence of previous MI, 183 (30.0%) smoked cigarettes, and 487 (79.7%) were receiving beta-blockers (Tables 1 and 2).

Treatment outcomes. There were no significant differences in in-hospital major complications among the three groups. The hospital mortality rates of patients in the CABG group were similar. The same result was observed in relation to Q-wave MI. No patient in the CABG group needed in-hospital angioplasty or emergency bypass grafting. On the other hand, major abnormalities of respiratory function were observed in 10 (5%) patients; 5 (2.5%) patients had mediastinitis; and 2 (1%) patients required a thoracotomy for reasons other than revascularization. There were six strokes (3%) in the CABG group and two strokes (1%) in the PCI group (Table 3).

MEDICAL THERAPY. During the one-year follow-up, of the 203 patients assigned to receive MT, 10 (5%) had an uncomplicated MI, 12 (6%) were referred for CABG, and 4 (1.97%) were referred for angioplasty because of refractory angina. During the follow-up period, three (1.5%) patients died of MI and three (1.5%) other patients had a cerebrovascular accident. No patient in this group was lost to follow-up.

SURGICAL THERAPY. Of the 203 patients assigned to the CABG group, 198 (98%) received the assigned treatment. However, four (2.0%) patients received MT because they refused the surgical procedure; these patients were alive at the end of the first year of follow-up. Initial revascularization was performed within three weeks of assigned treatment in 47% of the patients. The remaining 53% received the assigned treatment within 12 weeks (mean 7 weeks).

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Table 1. Characteristics of 611 Patients Assigned to One of Three Groups for Multivessel Disease

Characteristic	MT (n = 203)	PCI (n = 205)	CABG (n = 203)
Demographic profile			
Age (yrs)	60 ± 9	60 ± 9	60 ± 9
Age ≥65 yrs	36	38	34
Female	31	33	28
Employed	29	27	24
Current or past smoker	33	27	32
Medical history			
Myocardial infarction	39	52	41
Hypertension	55	61	63
Diabetes mellitus	36	23	29
CCS class II or III angina	78	78	86
Laboratory values (mmol/l)			
Total cholesterol	5.74 ± 1.01	5.69 ± 1.06	5.53 ± 1.09
LDL cholesterol	3.83 ± 0.88	3.80 ± 0.93	3.70 ± 0.93
HDL cholesterol	0.96 ± 0.26	0.98 ± 0.26	0.96 ± 0.26
Triglycerides	2.01 ± 0.93	2.04 ± 0.82	1.91 ± 0.95
Positive treadmill test	47	33	56
Angiographic findings			
Mean ejection fraction (%)	68 ± 7	67 ± 8	67 ± 9
Double-vessel disease	41	42	42
Triple-vessel disease	59	58	58
LAD disease	89	93	93

Data are presented as the mean value ± SD or % of patients. Some patients had both angina and positive treadmill test or abnormal rest electrocardiogram.

CABG = coronary artery bypass graft surgery; CCS = Canadian Cardiovascular Society; HDL and LDL = high- and low-density lipoprotein, respectively; LAD = left anterior descending coronary artery; MT = medical therapy; PCI = percutaneous coronary intervention.

Each patient who underwent CABG had an average of 3.3 ± 0.8 vessels bypassed. All intended vessels were grafted in 74% of patients. At least one internal thoracic artery was used for grafting in 92% of patients, and two internal thoracic arteries and a radial artery were used in 36% of patients. The epigastric artery was used in 10% of patients.

The median hospital stay after CABG was 10 days. During follow-up, only one patient in this group underwent PCI, and four (2%) patients had an uncomplicated MI. Nevertheless, in this follow-up period, eight (4%) patients died of MI, and three (1.5%) other patients had a cerebrovascular accident.

CORONARY ANGIOPLASTY. Among the 205 patients assigned to the PCI group, 194 (95%) received the assigned treatment, 6 (3%) underwent CABG as their initial treatment, and 2 (0.98%) died before treatment. The deaths were due to automobile and occupational accidents. In addition, three (1.5%) patients received MT because they refused the PCI procedure; these patients were alive at the end of the first year of follow-up.

Angioplasty as the initial revascularization was performed within three weeks of treatment assignment in 70% of patients (mean 2.7 weeks). Each patient who underwent PCI had an average of 2.1 ± 0.7 vessels dilated. Multivessel PCI was performed in 141 (73%) patients.

Immediate angiographic success was achieved in 92% of patients in whom PCI was attempted, and at least one stent was implanted in 140 (72%) patients. Complete revascularization (as defined by successful intervention in all major

Table 2. Use of Medications During Follow-Up by Patients Assigned to One of Three Groups

Medication	MT (n = 203)	PCI (n = 205)	CABG (n = 203)	Mean Value	p Value
Aspirin	80%	80%	70%	77%	0.024
Long-acting nitrates	73%	41%	12%	42%	<0.0001
Beta-blockers	68%	61%	44%	58%	<0.0001
Calcium channel antagonists	61%	30%	44%	45%	<0.0001
HMG-CoA reductase inhibitors	68%	73%	49%	63%	0.00001
ACE inhibitors	29%	30%	21%	27%	0.085
Insulin	13%	9%	11%	11%	0.424
Oral hypoglycemic agents	22%	14%	35%	37%	<0.0001

ACE = angiotensin-converting enzyme; HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A; other abbreviations as in Table 1.

Table 3. Frequency of Major In-Hospital Events

	PCI (n = 205)	CABG (n = 203)
Death	5 (2.4%)	5 (2.5%)
Q-wave MI	2 (1.0%)	2 (1.0%)
Emergency CABG	2 (1.0%)	—
Emergency PCI	2 (1.0%)	—
Stroke	2 (1.0%)	6 (3.0%)

No differences between groups were significant.
MI = myocardial infarction; other abbreviations as in Table 1.

vessels with at least 70% stenosis) was achieved in 41% of patients. Two (1.03%) additional patients in whom PCI was uncomplicated but unsuccessful were referred for elective CABG during the initial hospitalization; two (1.03%) patients required repeat PCI before discharge.

During follow-up, 18 (8.78%) patients underwent further PCI and 7 (3.4%) underwent CABG. Nevertheless, in this follow-up period, 9 (4.5%) patients died of MI, 16 (8.3%) had an uncomplicated MI, and 2 had a cerebrovascular accident (Table 4).

EVENT-FREE SURVIVAL. The rates of event-free survival—namely, the combined incidence of cardiac mortality, MI, or refractory angina requiring revascularization—were significantly different among patients in the three therapeutic groups ($p < 0.0001$). Patients assigned to the PCI group had more events (n = 50) than did patients in the MT (n = 29) or CABG (n = 13) groups, despite the fact that repeat PCI was not considered as an end point, except when the patients had unstable angina (Fig. 1).

CARDIAC-RELATED MORTALITY. There were no significant differences among the cumulative cardiac-related mortality curves associated with the three therapeutic strategies (Fig. 2). There were nine deaths in the PCI group, eight deaths in the CABG group, and three deaths in the MT group ($p = 0.23$). The cumulative survival rates at one year for patients assigned to each group were 96% for PCI, 96% for CABG, and 98% for MT.

ADDITIONAL REVASCULARIZATION. The greatest difference among the three groups was the frequency of additional interventions (surgery or angioplasty) required during the first year of follow-up. Only one additional intervention was required among patients in the CABG group, but 16 additional interventions were required for patients in the MT group and 25 for patients in the PCI group with unstable angina ($p = 0.000015$) (Fig. 3). This proportion includes patients undergoing another PCI after six-month angiography. Even though this was not considered in the primary end-point analysis, PCI was considered an end point if it was performed in patients with unstable angina at any time.

After one year of follow-up, additional surgical revascularization had been performed in no patients in the CABG group, in 12 (6%) patients in the MT group, and in 7 (3.4%) patients in the PCI group ($p = 0.008$) (Fig. 4). Also during this period, only one patient in the CABG group and four patients (1.97%) in the MT group underwent subsequent angioplasty, as compared with 18 (8.78%) patients in the PCI group ($p = 0.0001$) (Fig. 5). It should be emphasized that subsequent angioplasty in the PCI group was performed on the basis of restenosis with persistent ischemia, as evidenced by either angina or positive scintigraphic findings, and not merely on the basis of anatomic findings at the time of the protocol-driven angiogram.

Secondary end points. Patients treated with surgical revascularization were most likely to be free of anginal symptoms after one year of follow-up. In contrast, a marked presence of anginal symptoms was observed among patients randomly assigned to the MT group. More specifically, only 74 (36%) patients in the MT group were free of anginal symptoms after one year of follow-up, as compared with 120 (59%) patients in the CABG group and 107 (52%) patients in the PCI group. A statistically significant benefit was found for the CABG group compared with the MT group ($p < 0.0001$), as well as for the PCI compared with MT group ($p = 0.001$), but not for the CABG compared with PCI group ($p = 0.16$). None of the study patients in any treatment group had refractory angina (CCS class III or IV); moreover, we observed a reduction in the rates of positive exercise tests at the end of follow-up for all patients. However, this reduction was greater in the CABG group (36%) ($p < 0.0001$) and PCI group (18%) ($p = 0.0005$) than in the MT group (5%) ($p = 0.45$).

DISCUSSION

The largest randomized trial performed at a single institution, MASS-II, compared the relative efficacy of three current therapeutic strategies for patients with symptomatic multivessel CAD. We found no significant difference between the CABG, PCI, and MT groups with regard to

Table 4. One-Year Outcomes of the Randomized Groups

	MT (n = 203)	PCI (n = 205)	CABG (n = 203)	p Value
Death	3 (1.5%)	9 (4.5%)	8 (4.0%)	0.23
Q-wave MI	10 (5.0%)	16 (8.3%)	4 (2.0%)	0.01
CCS class II or III angina	126 (63.6)	87 (45.3%)	75 (39%)	<0.0001
CVA	3 (1.5%)	2 (1.0%)	3 (1.5%)	0.29
CABG	12 (6.0%)	7 (3.5%)	—	<0.0001
PCI	4 (1.97%)	18 (8.78%)	1 (0.5%)	0.008

CVA = cerebrovascular accident; other abbreviations as in Tables 1 and 3.

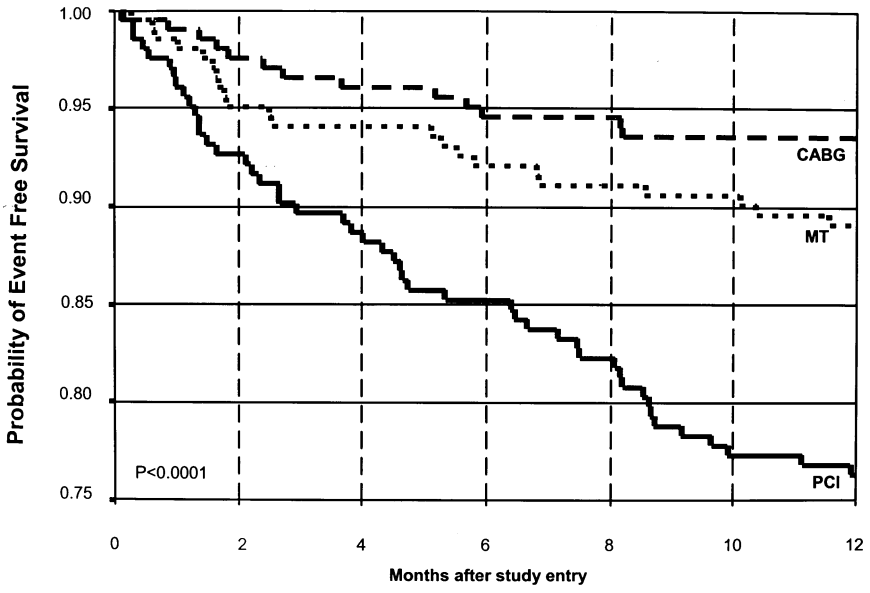

Figure 1. Probability of survival free of cardiac mortality, unstable angina requiring revascularization, and myocardial infarction among patients in the three treatment groups: medical therapy (MT), coronary artery bypass graft surgery (CABG), and percutaneous coronary intervention (PCI).

cardiac death or acute MI during one-year follow-up. However, angina requiring new revascularization was higher in the PCI group compared with the other treatments. The CABG-treated patients had better symptomatic relief than patients who underwent the PCI or MT strategy.

Our results are consistent with the Coronary Artery Surgery Study (CASS) trial, in which no difference was seen between patients in the surgical and medical groups in terms of mortality, Q-wave MI, or event-free survival rates after five years of follow-up. In the CASS trial, a subgroup of patients with preserved ventricular function and mild stable angina was more likely to experience event-free survival with MT alone, even in the presence of three-vessel CAD.

After one-year follow-up study in the Asymptomatic Cardiac Ischemia Pilot (ACIP) (20) trial, better outcomes were observed in patients treated with surgical revascularization, even though this trial had different inclusion criteria. Mortality and morbidity, as well as MI, were less common in patients assigned to the revascularization treatment strategy than in patients in the angina-guided group, but not less common than in patients in the ischemia-guided group.

Compared with other therapeutic strategies, surgical therapy was superior in MASS-II in improving event-free survival. This superiority probably reflected a low perioperative complication rate, symptomatic improvement, and the

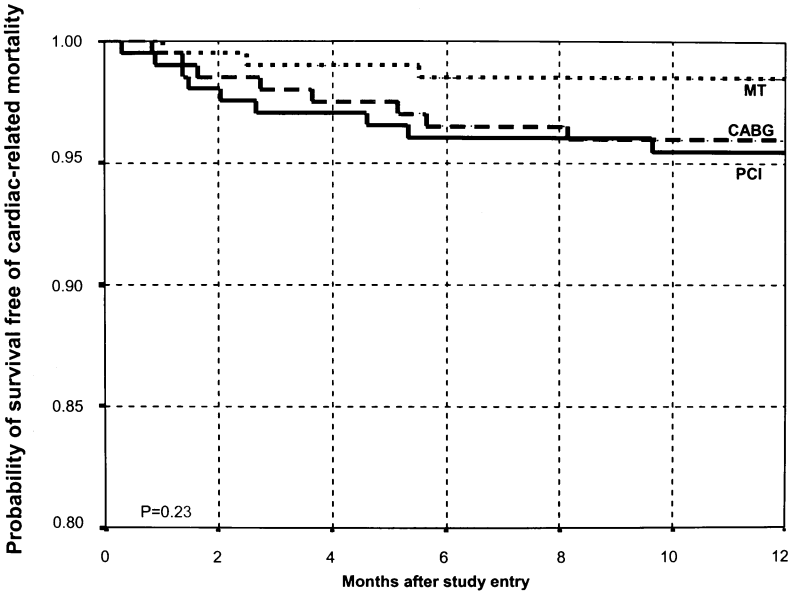

Figure 2. Probability of survival free of cardiac-related mortality among patients in the three treatment groups: MT, CABG, and PCI. Abbreviations as in Figure 1.

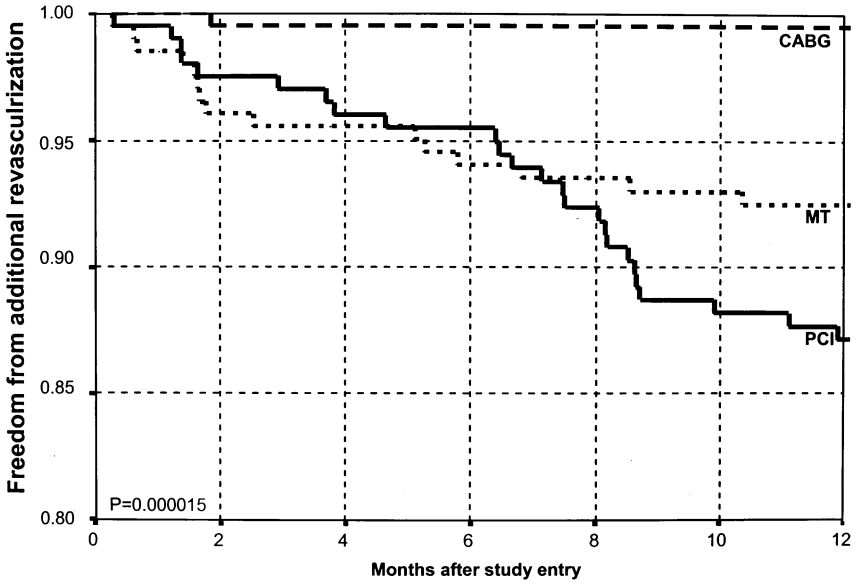

Figure 3. Freedom from additional revascularization after study entry among patients in the three treatment groups: MT, CABG, and PCI. Abbreviations as in Figure 1.

completeness of revascularization, as well as the use of arterial conduits. This eliminates the need for repeat intervention, at least during the one-year follow-up period.

In major trials (21–26) that enrolled about 4,130 patients with stable multivessel CAD who were followed up from one to five years, data showed no differences in mortality between patients in the PCI group and those in the CABG group. These trials were similar to MASS-II, except that a third randomized arm—MT alone—was not included as a treatment strategy. In contrast, in the RITA-2 trial (25), among patients with CAD considered suitable for either PCI or MT, and especially among patients with more severe angina, early intervention with PCI was associated with greater symptomatic improvement. However, nonfatal MI and cardiac-related death were more common in the PCI arm, although many of the infarcts were deferred by periprocedural enzyme leaks. In the Bypass Angioplasty Revascularization Investigation (BARI) trial (26), a worse prognosis was documented in patients who had diabetes, a finding that we did not observe in MASS-II, but our study included only a few diabetic patients.

More recently, in the Arterial Revascularization Therapy Study (ARTS), data were analyzed from one year of follow-up of 1,205 patients who were randomly assigned to undergo stent implantation or CABG (27). In ARTS, there was no statistically significant difference between the two

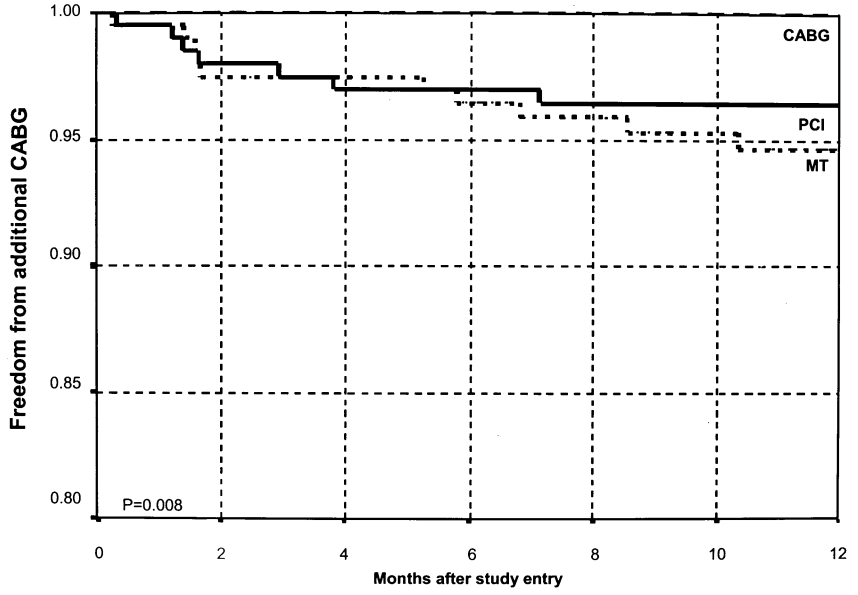

Figure 4. Freedom from additional CABG after study entry among patients in the three treatment groups: MT, CABG, and PCI. Abbreviations as in Figure 1.

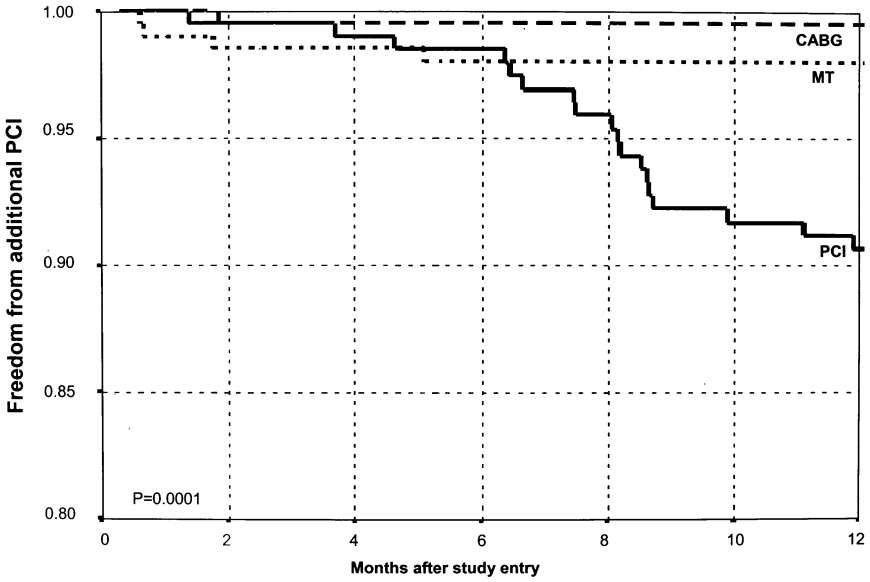

Figure 5. Freedom from additional PCI after study entry among patients in the three treatment groups: MT, CABG, and PCI. Abbreviations as in Figure 1.

groups regarding the rates of death, stroke, or MI. However, the stent group was associated with a greater need for repeat revascularization. Similarly, in our study, only one patient in the CABG group required further revascularization, and 12% of those in the PCI group underwent a second revascularization. The need for repeat revascularization was the greatest difference among our groups.

Furthermore, after a minimum of one year of follow-up in the Stent or Surgery (SoS) trial (28), the use of stents reduced the need for repeat revascularization, compared with previous studies that used balloon angioplasty, although the rate remained significantly higher than that in patients managed with CABG. Medical therapy reduces MI and death in patients with stable CAD. Four randomized, controlled trials have compared PCI with MT. These studies have demonstrated that PCI resulted in an improvement in angina and exercise tolerance compared with MT, but they also suggest that MT may be preferable to PCI with respect to the risk of cardiac events.

Nonetheless, the Atorvastatin Versus Revascularization Treatment trial (29) showed that in low-risk patients with stable CAD, aggressive lipid-lowering therapy is at least as effective as angioplasty and usual care in reducing the incidence of major cardiac events.

On the other hand, ongoing efforts toward a better definition of the role of PCI in the treatment of stable CAD will be addressed by the Clinic Outcomes Utilizing Revascularization and Aggressive druG Evaluation (COURAGE) trial, which compares aggressive MT with aggressive MT plus PCI during three to seven years of follow-up in patients with document myocardial ischemia. The hypothesis is that PCI plus MT is superior to MT alone for a primary end point of death or MI.

Despite the larger number of procedures performed in the PCI group, patients in the CABG group had a greater degree of revascularization and somewhat more favorable status with respect to anginal symptoms. The fact that surgeons grafted more vessels than were dilated by interventional cardiologists reflects conceptual differences between the two therapeutic strategies. Cardiologists performing angioplasty procedures have an opportunity to revise their initial decision on the basis of the clinical and angiographic outcomes of each lesion attempted or considered for intervention. Surgeons tend to use grafts for arteries with less stenosis (<50%), as well as for those with more stenosis. Not surprisingly, on the basis of the number of vessels treated, the degree of revascularization achieved surgically appeared to be more complete than that achieved with coronary angioplasty ($p < 0.0001$). Other ongoing trials of PCI involving patients with multivessel disease have also shown a frequent need for CABG in the angioplasty groups, ranging from 19% to 31% (18,23–25).

Although many new trials are being performed to elucidate the best therapeutic option for stable CAD with multivessel disease, we distinguished and contrasted the MASS-II trial from ongoing trials. Ours is the only one that will be able to compare PCI, CABG, or MT for the management of these patients, and our results should help to determine which one would be the best approach in long-term follow-up.

Conclusions and clinical implications. The MASS-II trial showed no difference in cardiac death or acute MI among patients in the CABG, PCI, or MT group. However, it did show a significantly greater need for additional revascularization procedures in patients who underwent PCI. Our finding of comparable mortality and morbidity rates for patients who underwent CABG or MT suggests that MT is a reasonable alternative for patients with

multivessel CAD who refuse surgical therapy. Therefore, the patient must be made aware of the possibility that further revascularization procedures may be required during the follow-up period.

Moreover, important developments in PCI have taken place since this trial was started. The use of glycoprotein IIb/IIa antiplatelet agents, the long-term use of the oral antiplatelet agent clopidogrel, and the development and more widespread application of a drug-eluting stent hold the promise of a significant reduction in restenosis and revascularization rates. In addition, surgery without cardiopulmonary bypass could have an important effect on surgical results in the future. Similarly, the aggressive MT and lifestyle prescriptions with comprehensive risk factor modification will also enhance the MT strategy.

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