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Prospective, Multicenter Study of the Safety and Feasibility of Primary Stenting in Acute Myocardial Infarction: In-Hospital and 30-Day Results of the PAMI Stent Pilot Trial

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Objectives. **The goals of this study were to examine the safety and feasibility of a routine (primary) stent strategy in acute myocardial infarction (AMI).**

Background. **Limitations of reperfusion by primary percutaneous transluminal coronary angioplasty (PTCA) in AMI include in-hospital recurrent ischemia or reinfarction in 10% to 15% of patients, restenosis in 37% to 49% and late infarct-related artery reocclusion in 9% to 14%. By lowering the residual stenosis and sealing dissection planes created by PTCA, primary stenting may further improve short- and long-term outcomes after mechanical reperfusion.**

Methods. **Three hundred twelve consecutive patients treated with primary PTCA for AMI at nine international centers were prospectively enrolled. After PTCA, stenting was attempted in all eligible lesions (vessel size 3.0 to 4.0 mm; lesion length ≤2 stents; and the absence of giant thrombus burden after PTCA, major side branch jeopardy or excessive proximal tortuosity or calcification). Patients with stents were treated with aspirin, ticlopidine and a 60-h tapering heparin regimen.**

Results. **Stenting was attempted in 240 (77%) of 312 patients, successfully in 236 (98%), with Thrombolysis in Myocardial Infarction grade 3 flow restored in 230 patients (96%). Patients with stents had low rates of in-hospital death (0.8%), reinfarction (1.7%), recurrent ischemia (3.8%) and predischarge target vessel revascularization for ischemia (1.3%). At 30-day follow-up, no additional deaths or reinfarctions occurred among patients with stents, and target vessel revascularization was required in only one additional patient (0.4%).**

Conclusions. **Primary stenting is safe and feasible in the majority of patients with AMI and results in excellent short-term outcomes.**

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Prospective, randomized trials comparing thrombolytic therapy with primary percutaneous transluminal coronary angioplasty (PTCA) in patients with an acute myocardial infarction (AMI) have documented superior reperfusion rates and improved clinical outcomes with the invasive approach (1–5). However, several limitations of primary PTCA remain to be overcome. After successful PTCA, recurrent ischemia still occurs in 10% to 15% of patients (1–6), which results in hemodynamic and arrhythmic complications, necessitates repeat catheterization and revascularization procedures, prolongs the hospital stay and increases costs (6). Reinfarction develops in 3% to 5% of patients before hospital discharge, and infarct-related artery (IRA) reocclusion in 5% to 10% of vessels, which results in blunted myocardial recovery and excess mortality (1–17). Finally, angiographic restenosis has been documented in 37% to 49% of patients after primary PTCA, with late infarct-related vessel reocclusion in 9% to 14% (9,18–21). As a result, ~20% of patients require repeat PTCA or bypass surgery within 6 months after discharge (1–4,20).

Compared with PTCA, the implantation of coronary stents in the elective setting has been shown to reduce angiographic restenosis and improve late clinical outcomes (22–24). How-

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Abbreviations and Acronyms

ACT = activated clotting time
AMI = acute myocardial infarction
CK-MB = creatine kinase-MB fraction
ECG = electrocardiogram, electrocardiographic
IRA = infarct-related artery
PAMI = Primary Angioplasty in Myocardial Infarction (trial)
PTCA = percutaneous transluminal coronary angioplasty
TIMI = Thrombolysis in Myocardial Infarction

ever, stenting has historically been contraindicated in thrombus-containing lesions because of the risk of subacute thrombosis (25,26). With advances in stent implantation technique derived from intravascular ultrasound imaging (27,28), and the recognition of the importance of adequate platelet inhibition (29–31), the incidence of subacute thrombosis has progressively fallen despite stenting in increasingly complex subsets, including acute ischemic syndromes and thrombus-laden lesions (32,33). We therefore hypothesized that a routine (primary) stent strategy would be feasible in the majority of patients with AMI and would result in low rates of recurrent ischemia, reinfarction and late restenosis.

Methods

Patients and clinical centers. To test the feasibility, safety and efficacy of a primary stent strategy in AMI, nine centers experienced in both stenting and primary PTCA (seven in North America, one in South America and one in Europe) were invited to participate in a large pilot experience. Patient entry criteria were deliberately chosen to be nonrestrictive. Thus, consecutive patients of any age with chest pain ≤12 h in duration, with any electrocardiographic (ECG) pattern of AMI were enrolled. Patients with previous bypass surgery and vein graft occlusion were included. Patients were excluded only for the presence of cardiogenic shock (systolic blood pressure <80 mm Hg for >30 min not responsive to fluids) and for absolute contraindications to heparin, aspirin or ticlopidine, including hemorrhagic diathesis, known allergy or thrombocytopenia. Patients were also excluded if they had previously received thrombolytic therapy during the same hospital period or were participating in other investigational studies. The protocol was approved by the investigational review board at each clinical site, and written informed consent was obtained from all patients before enrollment.

Study protocol. Patients were treated in the emergency room with 324 mg of chewable aspirin (500 mg of intravenous aspirin in France), 250 to 500 mg of oral ticlopidine and a 5,000- to 10,000-U bolus of intravenous heparin. Intravenous beta-blockade was administered in the absence of contraindications. Patients were then transferred emergently to the cardiac catheterization laboratory and underwent left ventriculography and coronary arteriography. Low osmolar, ionic contrast medium (Ioxaglate) was used to minimize the risk of thromboembolic complications (34,35). PTCA was then performed if appropriate. As previously described (1), PTCA was deferred for medical therapy if Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow was present with an IRA stenosis <70%, if a very small vessel was occluded or if the IRA could not be identified. PTCA was deferred for urgent or emergent bypass surgery if TIMI grade 3 flow was present in the infarct-related vessel, with either a left main stenosis >60%, severe triple-vessel disease or other lesion characteristics unfavorable for PTCA (1). All patients in whom primary PTCA was performed were formally entered into the study, and patients treated medically or surgically were excluded.

Before PTCA, additional heparin was given to achieve an activated clotting time of >350 s. PTCA was then performed using standard over the wire balloons and floppy guidewires as previously described (1) to restore patency and anterograde flow. After restoration of flow, the lesion was assessed for stent eligibility. Stent implantation was then attempted in all eligible lesions. The Johnson & Johnson Palmaz-Schatz stent was considered the stent of choice, given its proven ability to reduce restenosis in randomized trials (22–24). The sheath delivery system was used in all centers except in France, where stents were hand crimped onto high pressure balloons. For this pilot experience, stenting was deferred if the lesion would require three or more Palmaz-Schatz stents for coverage; if the reference segment was visually <3.0 mm or >4.0 mm in diameter such that 3.0- to 4.0-mm stents could not be used; if the infarct-related lesion was a true ostial left anterior descending or left circumflex coronary artery lesion; if a major side branch would be placed in jeopardy (≥3.0-mm diameter); or if excessive proximal tortuosity or lesion calcification was present, making it unlikely that the stent could be successfully delivered or fully expanded. No lesion was excluded because of the presence of thrombus before PTCA. However, if a large thrombus burden was present after PTCA refractory to repeat dilation or pharmacologic treatment (thrombus more than twice the vessel diameter), stenting was also deferred. However, stenting was routinely performed directly into small or moderate amounts of thrombus. Additional reasons for not stenting individual lesions were left to the discretion of the operator and were recorded.

After stent implantation, noncompliant balloons (balloon/artery ratio of 1 to 1.1:1) were used to fully deploy the stent or stents at high pressure (18 atm recommended). By protocol, any persistent dissection was treated with additional stents. An angiographic filling defect consistent with thrombus after stenting was treated with additional PTCA and, if still refractory, with intracoronary thrombolysis, intravenous abciximab or, conservatively, at the operator's discretion. All lesions with a stenosis ≥70% either proximal or distal to the infarct-related lesion that might represent a significant inflow or outflow obstruction were also stented.

After the procedure, sheaths were removed when the ACT fell below 170 s. Six hours later, a heparin drip was restarted

with a 2,500-U intravenous bolus and was adjusted to maintain the activated partial thromboplastin time at 60 to 85 s for 48 h, then reduced to half dose for 12 h to avoid a rebound hypercoagulable state (36), after which it was discontinued. All patients were treated with oral aspirin (325 mg/day), ticlopidine (250 mg twice daily), beta-adrenergic blocking agents and angiotensin-converting enzyme inhibitors if hypertension, heart failure or reduced left ventricular function was present. Initially, warfarin sodium (Coumadin) was recommended if an unfavorable stent result was obtained (>10% residual stenosis or a persistent filling defect or unstented dissection). However, shortly after enrollment commenced, with the demonstration by Schomig et al. (30) that adverse event rates after high risk stenting were lower with an aspirin and ticlopidine regimen than an aspirin and warfarin regimen, warfarin was no longer permitted (except for nonstent indications, such as valve prosthesis and atrial fibrillation). No patient received warfarin for stent anticoagulation.

Patients were progressively ambulated and discharged when stable, as in the Primary Angioplasty in Myocardial Infarction (PAMI) 2 study (12,13). Thus, stable low risk patients were generally discharged on hospital day 3 to 4, and stable high risk patients were discharged on day 5 to 7. After discharge, follow-up visits were performed at 1 and 6 months. Aspirin was continued indefinitely, and ticlopidine was maintained for 4 weeks and then discontinued. Complete blood counts were checked at 2 and 4 weeks after discharge. Other medications were used as clinically indicated.

Definitions. Anterograde flow was assessed by TIMI flow grade (37). *TIMI grade 3 flow* was defined by the core angiographic laboratory as complete opacification of the distal coronary bed by the third cardiac cycle. *IRA reocclusion* was present when follow-up angiography of a previously patent vessel demonstrated ≥90% stenosis and TIMI grade 0 to 1 flow. *Recurrent ischemia* was defined as recurrent symptoms consistent with angina plus new ECG changes, new sustained hypotension or pulmonary edema, a new loud systolic murmur, creatine kinase-MB fraction (CK-MB) reelevation or the need for IRA revascularization with either repeat PTCA or stenting or bypass surgery. *Reinfarction* was defined as recurrent ischemic symptoms or ECG changes, with any CK-MB reelevation. *Congestive heart failure* was defined as Killip class III to IV and sustained hypotension as systolic blood pressure <90 mm Hg for >30 min, unresponsive to fluids or pressor dependent.

Data collection and statistical analysis. Detailed in-hospital and 1-month follow-up case report forms were prospectively completed for each patient and were confirmed at the data coordinating center by separate review of catheterization reports, ECGs, laboratory tests and discharge summaries. Adverse events were reported to the clinical coordinating center within 24 h of occurrence. Quantitative coronary analysis was performed by an independent core angiographic laboratory at the Washington Hospital Center using previously validated methodology (38). Of 312 index films, 300 (96%) were technically able to be analyzed; the remainder were recorded on a CD-ROM format that presented an incompatible synchronization signal and could not be acquired. Data were entered into a computerized database, and statistical analysis was performed with a commercially available package (Statview 4.5, Abacus Concepts).

By intention to treat analysis, unless otherwise stated, the "stent" group comprised all patients in whom stenting was attempted, even if the stent was not ultimately implanted. Categoric variables were compared with chi-square or Fisher exact tests, whereas continuous variables were compared with the unpaired Student *t* test. A p value <0.05 was required for statistical significance.

Table 1. Baseline Clinical and Angiographic Features in 312 Patients

	Stent (n = 240)	PTCA Only (n = 72)	p Value
Age (yr)	61 ± 12	61 ± 11	0.90
Women	61 (25.4%)	22 (30.6%)	0.39
Hypertension	107 (44.6%)	32 (44.4%)	0.97
Diabetes mellitus	37 (15.4%)	11 (15.3%)	0.98
Current cigarette smoking	96 (40.0%)	30 (41.7%)	0.80
Prior MI	31 (12.9%)	11 (15.3%)	0.61
Prior PTCA	24 (10.0%)	8 (11.1%)	0.79
Prior CABG	15 (6.3%)	4 (5.6%)	0.83
Prior stroke or TIA	17 (7.1%)	6 (8.3%)	0.72
ECG infarct location			
Anterior	88 (36.7%)	20 (27.8%)	0.15
Inferior	126 (52.5%)	44 (61.1%)	0.22
Posterior	7 (2.9%)	0	0.59
Lateral	6 (2.5%)	3 (4.2%)	0.70
Subendocardial	13 (5.4%)	5 (6.9%)	0.52
Admission Killip class ≥II	30 (12.5%)	7 (9.7%)	0.52
Symptom onset to ER arrival (min)	174 ± 190	169 ± 157	0.84

Data presented are mean value ± SD or number (%) of patients. CABG = coronary artery bypass graft surgery; ECG = electrocardiographic; ER = emergency room; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; TIA = transient ischemic attack.

Results

Enrollment and stent eligibility. Between June 1995 and July 1996, primary PTCA was performed in 312 consecutive patients with an AMI meeting the enrollment criteria at nine clinical centers. After initial PTCA, stenting was attempted in 240 patients (77%). In 72 patients, stenting was not considered feasible; these patients were treated by primary PTCA alone. The baseline demographic, admission and angiographic features of patients in whom stenting was or was not attempted appear in Tables 1 and 2. The major reasons given by the investigators for not attempting to stent are shown in Table 3. Compared with lesions in which stenting was attempted, lesions in which stenting was not attempted were located more distally in the coronary tree and had smaller reference segment diameters. Stenting was performed more frequently in patients with single-vessel disease, and PTCA only was more common in patients with triple-vessel disease.

Table 2. Angiographic Characteristics of Patients in Whom Stenting Was or Was Not Attempted

	Stent (n = 240)	PTCA Only (n = 72)	p Value
LVEF (%)	48 ± 13	51 ± 11	0.08
No. of diseased epicardial vessels			
One	119 (49.6%)	27 (37.5%)	0.009
Two	70 (29.2%)	22 (30.6%)	0.82
Three	51 (21.2%)	23 (31.9%)	0.01
Infarct-related vessel type			
Native coronary artery	231 (96.2%)	68 (94.4%)	0.50
Saphenous vein bypass graft	7 (2.9%)	4 (5.6%)	0.29
Internal mammary artery graft	2 (0.8%)	0	0.99
Infarct-related artery distribution			
LMCA	1 (0.4%)	0	0.99
LAD	88 (36.7%)	24 (33.3%)	0.61
LCx	38 (15.8%)	15 (20.8%)	0.32
RCA	113 (47.1%)	33 (45.9%)	0.85
Infarct-related lesion location			
Proximal vessel	125 (52.1%)	31 (43.1%)	0.18
Mid vessel	93 (38.8%)	17 (23.6%)	0.01
Distal vessel or branch	22 (9.1%)	24 (33.3%)	< 0.0001
Ref segment diam (mm)*	3.17 ± 0.53	2.80 ± 0.71	< 0.0001
Lesion MLD (mm)*	0.28 ± 0.46	0.38 ± 0.62	0.14
Lesion DS (%)*	90.7 ± 15.1	87.0 ±18.4	0.09

*Core laboratory analysis (n = 300). Data presented are mean value ± SD or number (%) of patients. diam = diameter; DS = diameter stenosis; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MLD = minimal lumen diameter; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery; Ref = reference.

Stent deployment. Stents were successfully delivered to the lesion and deployed in 236 (98%) of 240 patients. In four patients, the Palmaz-Schatz stent with sheath delivery system would not reach or cross the lesion, and the stent was successfully withdrawn without being lost. Among stent group patients, a mean (±SD) of 1.4 ± 0.7 stents (range 1 to 7) were implanted per patient (97% JJIS, 1% Cook, 1% Schneider, 1% AVE). The mean stent size was 3.4 ± 0.5 mm (median 3.5), and 17.3 ± 2.4 atm of pressure was used for postimplantation stent expansion. By quantitative coronary analysis, the final measured mean balloon/artery ratio was 1.08 ± 0.14. Intravascular ultrasound guidance was used in 48 stent group patients (20%) and in 3 with PTCA only (4%). Adjunctive antiplatelet and thrombolytic drug use in the catheterization laboratory was infrequent; intravenous abciximab was given to 21 patients (6.7%) (including 13 stent group patients [5.4%] and 8 with PTCA only [11.1%]), and intracoronary urokinase was used in only 4 patients (1.3%) (3 stent group patients [1.2%] and 1 with PTCA only [1.4%]).

Core laboratory angiographic analysis appears in Figure 1. The comparison of the site and core laboratory angiographic assessment is shown in Table 4. By core laboratory analysis, TIMI grade 3 flow was present at the end of the procedure in 92.7% of patients (94.4% of stent group patients vs. 87.3% of patients with PTCA only, p = 0.04). The mean postprocedural residual stenosis was 12.1% ± 16.2% in the stent group versus 33.3% ± 14.3% in the PTCA-only group (p < 0.0001) (Fig. 1). Thus, a <50% residual stenosis with TIMI grade 3 flow was obtained in 93.7% of the stent group versus 77.3% of the PTCA-only group (p < 0.0001).

Clinical outcomes. Major in-hospital adverse outcomes are presented in Table 5. Repeat predischarge catheterization (which was not required by the protocol) was performed in 18% of patients, usually for physician preference or recurrent atypical chest pain without ECG changes (Table 6). Among stent group patients, stent occlusion was documented in two (0.8%). In two additional patients with reinfarction, recatheterization revealed moderate stenoses with peristent dissection in one and in-stent thrombus in the other. One additional stent group patient who did not undergo repeat catheterization had a major reinfarction on day 7, presumably due to stent thrombosis.

The mean hospital stay was 6.2 ± 3.7 days among stent group patients versus 7.1 ± 6.4 days in patients undergoing PTCA only (p = 0.11). Among stent group patients, 98% were discharged with aspirin or ticlopidine (with lovenox in 1%), or both, and 2% were discharged with warfarin with or without aspirin. One-month follow-up data were complete for 309 (99.7%) of 310 discharged patients. Adverse events occurring within the first 30 days after discharge were infrequent among stent group patients and appear in Table 7.

Discussion

The present study demonstrates that a primary stent strategy is safe and feasible in the majority of patients with an AMI undergoing mechanical reperfusion. With the routine use of high pressure implantation techniques and a post-stent anticoagulation regimen of aspirin, ticlopidine and a 60-h heparin taper, reinfarction occurred in only four stent group patients

Table 3. Operator Reasons for Not Stenting 72 Lesions*

Vessel too small for ≥3.0-mm diam stent	30 (9.6%)
Lesion length ≥3 stents	8 (2.6%)
Excessive proximal tortuosity	7 (2.2%)
Major side branch jeopardy	6 (1.9%)
Large thrombus burden	5 (1.6%)
Poor distal runoff (diffuse disease)	4 (1.3%)
Vessel diam >4.0 mm	2 (0.6%)
Unresolved no reflow after PTCA	2 (0.6%)
Predischarge elective CABG planned	2 (0.6%)
Heavy calcification	2 (0.6%)
Bleeding diathesis	2 (0.6%)
Diffuse ectasia	2 (0.6%)
Additional reasons	
Ostial LAD	1 (0.3%)
VSD identified	1 (0.3%)
Accordian RCA	1 (0.3%)
Unsure of culprit lesion	1 (0.3%)

*More than one reason was present in some patients. Data presented are number (%) of patients. VSD = ventricular septal defect; other abbreviations as in Tables 1 and 2.

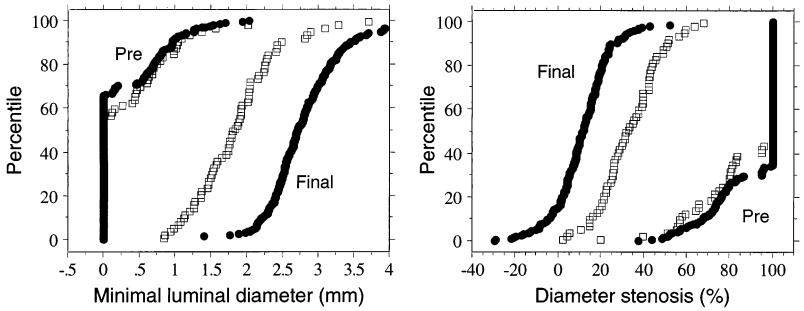

Figure 1. Minimal lumen diameter **(left)** and percent diameter stenosis **(right)** before and after intervention, expressed as a cumulative distribution function. **Solid circles** = patients in whom stenting was attempted; **open squares** = patients treated with PTCA only.

(1.7%), despite the known presence of thrombus in most patients with AMI (39,40). Furthermore, recurrent ischemia occurred in only 3.8% of stent group patients, strikingly less common than the 10% to 15% incidence observed after primary PTCA in our previous PAMI trials (1,2,6,12,13). The low observed rates of subacute thrombosis and 30-day target vessel revascularization are also encouraging. Thus, a strategy of stenting all eligible lesions (achievable in 77% of patients) would appear to result in at least equivalent and possibly superior short-term outcomes than balloon dilation alone (1–6,12,13).

Rationale for the safety of stenting in AMI. The predominant mechanism of coronary occlusion in AMI is thrombotic closure of a ruptured atherosclerotic plaque (39,40), and thus concern has appropriately been expressed that stenting during the acute phase of myocardial infarction may increase the risk of stent thrombosis. In contrast, occlusive stent thrombosis occurred in only three (1.3%) patients with AMI in the present study. Several possible explanations may underlie the apparent safety of stenting in an obviously thrombotic environment. After primary PTCA for AMI, the presence of dissection and a residual stenosis >30% have been shown to be major predictors of recurrent ischemia and IRA reocclusion (41–43), both limitations of balloon dilation that are routinely overcome by stenting. Reinfarction after primary stenting may therefore be less common than after primary PTCA (as this study suggests), even if subacute thrombosis does rarely occur. Furthermore, the establishment by the stent of a wide lumen channel with brisk anterograde flow and no dissection planes may facilitate natural clot resolution by endogenous fibrinolysis (with aspirin, ticlopidine and heparin inhibiting new thrombus formation). Although it is possible that vessel occlusion after stenting in AMI may be asymptomatic and therefore undetected without routine repeat catheterization, TIMI grade 3 flow was present in all 39 patients without recurrent ischemia who underwent predischarge angiography, suggesting that silent stent occlusion occurs infrequently. Late patency of the infarct-related vessel will be assessed with protocol angiography during the 6-month follow-up phase of this study.

Technical issues. Stenting is technically more demanding than PTCA, and meticulous attention to detail is mandatory to reproduce these results. Stents must not be underdeployed or incompletely opposed to the vessel wall; because the vessel "grows" with improving anterograde flow, stent expansion may need to be increased with larger balloons to ensure a stent/artery ratio >1:1. The routine use of high pressure is recommended to ensure vessel wall apposition of the stent and adequate expansion, which may reduce subacute thrombosis

Table 4. Site and Core Laboratory Angiographic Measures

	Site Assessment			Core Laboratory Assessment		
	Stent (n = 240)	PTCA (n = 72)	Total (n = 312)	Stent (n = 231)	PTCA (n = 69)	Total (n = 300)
TIMI flow grade						
Initial						
0/1	79%	79%	79%	72%	64%	70%
2	14%	10%	13%	11%	10%	11%
3	7%	11%	8%	17%	26%	19%
Final						
0/1	1%	4%	2%	2%	3%	2%
2	3%	1%	2%	4%	10%	5%
3	96%	95%	96%	94%	87%	93%
Initial MLD (mm)	—	—	—	0.28 ± 0.46	0.38 ± 0.62	0.30 ± 0.50
Final MLD (mm)	—	—	—	2.77 ± 0.59	1.86 ± 0.61	2.56 ± 0.70
Initial %DS	99 ± 4	98 ± 5	99 ± 5	91 ± 15	87 ± 18	90 ± 16
Final %DS	3 ± 11	24 ± 17	8 ± 16	12 ± 16	33 ± 14	17 ± 18

Data presented are mean value ± SD or percent of patients. TIMI = Thrombolysis in Myocardial Infarction; other abbreviations as in Table 2.

Table 5. Major In-Hospital Adverse Effects in 312 Patients

	Stent (n = 240)	PTCA Only (n = 72)	p Value
Death	2 (0.8%)	0	0.99
Reinfarction	4 (1.7%)	0	0.58
Recurrent ischemia	9 (3.8%)	2 (2.9%)	0.69
Repeat PTCA	12 (5.0%)	6 (8.3%)	0.29
Of infarct-related vessel	5 (2.1%)	4 (5.6%)	0.13
Of non–infarct-related vessel	9 (3.8%)	2 (2.8%)	0.69
CABG	7 (2.9%)	9 (12.5%)	0.001
Emergent from cath lab	1 (0.4%)	0	0.99
Urgent or emergent from outside cath lab	3 (1.3%)	4 (5.6%)	0.03
Elective	3 (1.3%)	5 (6.9%)	0.007
Target vessel revasc for ischemia	3 (1.3%)	2 (2.9%)	0.37
Stroke	1 (0.4%)	0	0.99
Hemorrhagic	0	0	0.99
Nonhemorrhagic	1 (0.4%)	0	0.99
New-onset congestive heart failure	10 (4.2%)	3 (4.2%)	0.99
New-onset sustained hypotension	6 (2.5%)	5 (6.9%)	0.07
Blood transfusion	5 (2.1%)	7 (9.7%)	0.003
Groin complication*	6 (2.5%)	0	0.34
Requiring US compression or surgical repair	3 (1.3%)	0	0.99

*Major hematoma, limb ischemia, arteriovenous fistula or pseudoaneurysm. Data presented are number (%) of patients. Cath lab = catheterization laboratory; revasc = revascularization; US compression = ultrasound-guided compression; other abbreviations as in Table 1.

(27,28). Eighteen atmospheres was chosen for the present study because the Palmaz-Schatz stent continues to expand as implantation pressure is increased from 12 to 18 atm (44). The use of low osmolar ionic contrast medium (Ioxaglate) is strongly recommended to reduce thromboembolic complications while at the same time producing minimal hemodynamic disturbance (34,35). Ticlopidine (in addition to aspirin) is mandatory (29–31) and may be given as a loading regimen of 500 mg twice daily for 48 h, which achieves significant antiplatelet activity more rapidly than standard dosing (45). Warfarin should be avoided because of its lack of efficacy, increased vascular and hemorrhagic complications and the possible induction of a prothrombotic state from protein C and S inhibition (22,23,29–31,46). With these guidelines, recurrent ischemia and reinfarction after stenting in AMI occurred rarely despite the infrequent use of intravenous abciximab and intracoronary thrombolytic therapy.

Table 6. Predischarge Cardiac Catheterization: Indications and Findings

	Stent (n = 240)	PTCA Only (n = 72)	p Value
Predischarge recath performed	43 (17.9%)	13 (18.1%)	0.99
Indication			
Recurrent ischemia	4 (1.7%)	1 (1.4%)	0.99
Chest pain without ECG changes	10 (4.2%)	3 (4.2%)	0.99
Recurrent ventricular arrhythmias	1 (0.4%)	0	0.99
Physician preference	22 (9.2%)	6 (8.3%)	0.83
For staged PTCA of noninfarct-related vessel	6 (2.5%)	3 (4.2%)	0.44
Status of infarct-related vessel			
Stenosis ≥50%	5 (2.1%)	6 (8.3%)	0.01
Reocclusion	2 (0.8%)	1 (1.4%)	0.54

Data presented are number (%) of patients. recath = recatheterization; other abbreviations as in Table 1.

Table 7. Adverse Events Occurring Within 30 Days After Hospital Discharge

	Stent (n = 237)	PTCA Only (n = 72)	p Value
Death	0	0	0.99
Reinfarction	0	1 (1.4%)	0.99
Revasc procedures	8 (3.4%)	9 (12.5%)	0.003
PTCA/atherectomy/stent	7 (3.0%)	6 (8.3%)	0.05
CABG	1 (0.4%)	3 (4.2%)	0.04
Target vessel revasc	1 (0.4%)	5 (6.9%)	0.0004
Ticlopidine side effects*	10 (4.2%)	0	0.07

*Rash (n = 6), dyspepsia (n = 2), neutropenia (n = 1), thrombocytopenia (n = 1). Data presented are number (%) of patients. Abbreviations as in Tables 1 and 5.

Nonetheless, despite the expertise of the operators participating in this study, several stent-related complications occurred, some of which may be preventable with increasing operator experience. Of note, one patient required emergency bypass surgery after a major stent-induced dissection, whereas additional unplanned stents were required in seven patients (3%) to treat peristent dissection not present after PTCA. The importance of scaffolding all margin dissections is also evidenced by the fact that two patients developed recurrent ischemia related to peristent edge tears that were left unstented (against protocol), only to resurface as an extensive propagating dissection 1 to 3 days after the initial procedure. Two patients also had partial stent thrombosis related to underdeployment (one stent undersized, one stent implanted at low pressure), both successfully treated with repeat PTCA and more optimal stent expansion. With improved operator technique, new stent designs soon to be available (including stents coated with thromboresistant materials such as heparin and phosphorylcholine [47–49]), and the possible adjunctive use of parenteral, local or stent-bonded glycoprotein IIb/IIIa inhibitors (50,51), the safety profile of stenting in AMI may be further enhanced.

Limitations of the study. Although the present prospective, multicenter trial is the largest series to date of primary stenting in AMI, all the caveats of comparing data from a registry series to historical control subjects apply, including the possibility of selection bias. Specifically, the outcomes of the 23% of patients in the present study in whom PTCA only was performed were better than might otherwise have been expected. Although this most likely reflects the fact that the PTCA-only group represented a lower risk subset with smaller vessels and less myocardium at risk than the stent group (Tables 2 and 3), the possibility of improved outcomes due to

evolving PTCA technique or selection bias cannot be totally discounted. Thus, firm conclusions regarding the superiority of primary stenting in eligible patients over primary PTCA cannot be made from this study. Furthermore, the favorable results of stenting during AMI in this report cannot be generalized to patient and lesion subsets that were excluded, such as small vessels and diffuse disease. As new, smaller stents for 2.0- to 2.5-mm vessels and longer stents are introduced, their safety and efficacy profiles in AMI will need to be established. Finally, because this study was designed to examine the feasibility and efficacy of a primary stent strategy in patients undergoing primary PTCA, we did not collect outcomes data for those patients undergoing angiography in whom PTCA was not performed, which in the previous PAMI studies has averaged 10% of patients with AMI (1,12,13).

Although the present study suggests that stenting is safe and feasible in the majority of patients with AMI over the short term, and results in excellent clinical outcomes, no inferences from this report can be drawn about late clinical events and restenosis, nor about the relative cost-effectiveness of a primary stent strategy relative to PTCA (52). Future studies must also address possible synergy between platelet glycoprotein IIb/IIIa receptor blockade and stenting in AMI. Large-scale, randomized, multicenter trials are thus mandated to establish the role of a primary stent strategy in patients with AMI. Nonetheless, given the impressive short-term results of the present study, if randomized trials demonstrate that stenting can reduce the high rates of restenosis and adverse clinical events otherwise present after primary PTCA, stenting has the potential to be the next major breakthrough in the mechanical reperfusion therapy of AMI.

Appendix

Participating Institutions and Investigators for the Primary Angioplasty in Myocardial Infarction Stent Pilot Trial

Clinical and Data Coordinating Centers. *The Cardiovascular Institute, El Camino Hospital*: Gregg W. Stone, JoAnn McDonnell, Nancy Richardson. *William Beaumont Hospital*: Cindy L. Grines, William W. O'Neill, Denise Jones.

Clinical Centers. *El Camino Hospital, Mountain View, California*: Gregg W. Stone (Principal Investigator), Frederick G. St. Goar, Clayton Bavor, Edward Bough, Robert Constantino, Martin Klughaupt, Ibrahim Saah, Robert Master, Robert Ratshin. *The Moses H. Cone Memorial Hospital, Greensboro, North Carolina*: Bruce R. Brodie (Principal Investigator), Denise Muncy, Thomas Stuckey, Richard Weintraub, Thomas Kelly, Jonathan Berry. *Virginia Beach General Hospital, Virginia Beach, Virginia*: John J. Griffin (Principal Investigator), John Kenerson, Sherry Theodosiou. *Institut Cardiovasculaire Paris Sud, Antony, France*: Marie Claude Morice (Principal Investigator), Pierre Dumas, Yves Louvard, Gaetan Karrillon, Thierry Lefevre, Dominique Robert, Mireille Simon. *Hospital Santa Case de Misericordia, Curitiba, Brazil*: Costantino Costantini (Principal Investigator), Sergio Tarbine. *St. Mary of the Plains, Lubbock, Texas*: Paul A. Overlie (Principal Investigator), Fawwaz M. Shoukfeh, Marc J. Levine, Karen E. Moore, Deenie Stone. *St. Vincent's Hospital, Indianapolis, Indiana*: Thomas J. Linnemeier (Principal Investigator), Donald A. Rothbaum, Janice Coverdale. *Lenox Hill Hospital, New York, New York*: Jeffrey A. Moses (Principal Investigator), Antonio Colombo. *St. Lukes Hospital, Kansas City, Missouri*: Tom Shimshak (Principal Investigator).

Core Angiographic Laboratory. *Cardiology Research Foundation, Washington Hospital Center, Washington, D.C.*: Jeffrey J. Popma (Director), Alexandra Lansky, Alan J. Merritt.

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