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Effects of Coronary Stenting on Vessel Patency and Long-Term Clinical Outcome After Percutaneous Coronary Revascularization in Diabetic Patients

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OBJECTIVES We sought to compare coronary stent implantation with balloon angioplasty (BA), in a diabetic population, in terms of the six-month angiographic outcome and four-year clinical events.

BACKGROUND Diabetic patients have a poor angiographic and clinical outcome after standard coronary BA. To date, it is still unclear whether stent implantation may improve this outcome.

METHODS We investigated this issue by individual matching of 314 diabetic patients treated with either coronary stenting or standard BA. These two groups were derived from a population of consecutive diabetic patients (1993 to 1996). Matching criteria were gender, anti-diabetic regimen, stenosis location, reference diameter, and minimal luminal diameter (±0.4 mm). One lesion per patient was considered for matching.

RESULTS Baseline characteristics were similar between the two groups of 157 patients. At six months, the rates of restenosis (27% vs. 62%; $p < 0.0001$) and occlusion (4% vs. 13%; $p < 0.005$) were lower in the stent group than in the BA group. This was associated with a significant decrease in ejection fraction at six months in the BA group ($p = 0.02$) while, during the same period, no change was observed in the stent group (p = NS). Subgroup analysis demonstrated that angiographic benefit was consistent among the subgroups. At four years, the combined clinical end point of cardiac death and non-fatal myocardial infarction was lower in the stent group (14.8% vs. 26.0%; $p = 0.02$), as was the need for repeat revascularization (35.4% vs. 52.1%; $p = 0.001$).

CONCLUSIONS In a population of diabetic patients, coronary stent implantation was associated with a highly beneficial effect on the six-month angiographic outcome and four-year clinical events compared with standard BA. (J Am Coll Cardiol 2002;40:410–7) © 2002 by the American College of Cardiology Foundation

Diabetics currently comprise 15% to 25% of patients referred for coronary revascularization (1–4). Several studies reporting a high rate of cardiac events in diabetics treated-with standard balloon angioplasty (BA) (1,2,5–7) have generated concern regarding the use of percutaneous coronary revascularization (PCR) in this group of patients and have led to a general consensus that surgical revascularization may be preferable in this population (8).

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It is now well established that diabetics have unacceptably high rates of restenosis (~60%) after coronary BA (4,9,10), and more recent studies have shown dramatically higher rates of occlusive restenosis (13% to 14%) in diabetics than in non-diabetics (4,9). Recent studies investigating the effect of diabetes on restenosis after coronary stenting (11–14) have reported a more favorable angiographic outcome after stenting, although the degree of restenosis rates varied markedly among the studies (24% to 55%). The marked discrepancies between these study groups from different populations has led to continuing uncertainty regarding the potential beneficial effect of stent implantation on both the angiographic and clinical outcome in diabetic patients.

Thus, we designed our study to investigate the impact of coronary stenting on restenosis, late vessel occlusion, left ventricular (LV) function, and long-term clinical outcome in diabetic patients. These issues were investigated by individual matching of a consecutive series of diabetic patients treated with coronary stenting to a consecutive series of diabetics treated with BA.

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Abbreviations and Acronyms

ARTS	= Arterial Revascularization Therapy Study
BA	= balloon angioplasty
EPISTENT	= Evaluation of Platelet IIb/IIIa Inhibitor for Stenting
LV	= left ventricular, left ventricle
LVEF	= left ventricular ejection fraction
MI	= myocardial infarction
MLD	= minimal luminal diameter
PCR	= percutaneous coronary revascularization
PTCA	= percutaneous transluminal coronary angioplasty
SVG	= saphenous vein graft
TIMI	= Thrombolysis in Myocardial Infarction trial

METHODS

Stent and BA groups. We identified, from the records of our catheterization laboratory (1993 to 1996), 164 consecutive diabetic patients who underwent coronary stent implantation during a percutaneous transluminal coronary angioplasty (PTCA) procedure and 462 who underwent standard BA without adjunctive stent implantation.

All patients in whom the procedure was considered successful by the operator were included. Patients undergoing primary, rescue BA for acute myocardial infarction (MI) or rescue stent implantation for occlusive dissection were not included.

At the time of the initial procedure, the patients were asked to return for follow-up angiography at six months, regardless of their symptomatic status. Angiography was performed earlier if there was a clinical indication. Angiographic follow-up was actually performed in 138 patients (84%) in the stent group and in 377 patients (82%) in the BA group.

Matching process. In order to compare the results of coronary stenting and BA, 157 diabetic patients from the stent group were individually matched to 157 patients from the BA group; the matching characteristics were gender, anti-diabetic regimen, target lesion location, reference diameter (within ±0.4 mm), and minimal luminal diameter (MLD; within ±0.4 mm). Only one lesion per patient was considered for matching. At the end of the matching process, no suitable match was found for seven patients in the stent group. The matching process was performed by two investigators who were unaware of the angiographic and clinical outcomes of the patients.

Definition of diabetes mellitus. At the time of the initial procedure, patients were classified as diabetic if they were treated with oral hypoglycemic drugs or insulin or if they had a history, as documented in their medical records, of elevated (≥140 mg/dl) fasting blood glucose on at least two separate occasions in conjunction with ongoing dietary measures. They were classified in three categories depending on the anti-diabetic management at the time of the initial procedure: 1) diet alone; 2) oral hypoglycemic drugs (diet and oral hypoglycemic drugs but no insulin); and 3) insulin (irrespective of other therapy).

Baseline blood glucose and creatinine levels, as well as the presence of other organ damage (e.g., retinopathy, nephropathy, neuropathy), as documented in the medical records, were recorded.

Angioplasty procedure. Balloon angioplasty and coronary stenting were performed according to the standard technique in our laboratory (4,12). All patients received 300 mg/day of aspirin, and a bolus dose of heparin (10,000 IU) was administered just before PTCA. Patients who had conventional BA received aspirin alone, whereas patients who had coronary stent implantation received a combination of aspirin (325 mg/day) and ticlopidine (500 mg/day) for four to six weeks and then aspirin alone. None of the patients was treated with glycoprotein IIb/IIIa inhibitors.

Angiographic analyses. Qualitative analyses were performed independently by two experienced interventional cardiologists. Lesions were classified in accordance with the American Heart Association/American College of Cardiology classification, as modified by Ellis and colleagues (15). Anterograde blood flow was graded using the Thrombolysis in Myocardial Infarction (TIMI) trial classification (16).

Quantitative computer-assisted angiographic measurements were obtained, as previously described, from end-diastolic frames at maximal dilation, using the computer-assisted evaluation of stenosis and restenosis (CAESAR) system (4,12). The following definitions were used: "acute gain" was defined as the MLD after the index procedure, minus the MLD before the procedure; "late loss" was defined as the MLD after the index procedure, minus the MLD at follow-up; "net gain" was defined as the difference between acute gain and late loss; "restenosis" was defined as >50% diameter stenosis at follow-up; and finally, "complete vessel occlusion" was defined as TIMI flow grade 0 or 1.

The left ventricular ejection fraction (LVEF) was calculated on ventriculograms obtained before angioplasty and at follow-up.

Clinical follow-up. Long-term clinical follow-up beginning at the time of the index procedure was accomplished by a questionnaire completed by the patient or by telephone contact. Review of hospital records and contact with the referring physician enabled us to complete some missing information. The information obtained included the occurrence of MI since the initial PTCA procedure, subsequent need for additional revascularization, and death (cardiac or non-cardiac). Sudden death and death of unknown cause were classified as cardiac deaths. Clinical follow-up was obtained in all patients at an average of 3.8 ± 1.3 years.

Statistical analysis. Data are presented as the mean value ± SD. Comparisons between groups for continuous data were performed with the paired or unpaired Student *t* test. Differences between proportions were assessed by chi-square analysis. Survival without an event was estimated using the Kaplan-Meier method. Differences were tested using the log-rank test. Multivariate correlates of events

Table 1. Baseline Clinical Characteristics of the 314 Diabetic Patients

	All Patients (n = 314)	Balloon Angioplasty Group (n = 157)	Stenting Group (n = 157)	p Value
Age (yrs)	61 ± 10	62 ± 9	61 ± 11	0.63
Males	240 (76%)	120 (76%)	120 (76%)	1
Smokers	154 (49%)	75 (48%)	79 (50%)	0.65
Hypertension	196 (62%)	104 (66%)	92 (59%)	0.42
Hypercholesterolemia	142 (45%)	76 (49%)	66 (43%)	0.26
Family history of CAD medications	132 (42)	61 (39)	71 (45)	0.26
Oral antiplatelet drugs	313 (99%)	156 (99%)	157 (100%)	0.99
Beta-blockers	229 (73%)	118 (75%)	111 (70%)	0.45
Calcium channel antagonists	96 (31%)	45 (29%)	51 (32%)	0.54
ACE inhibitors	141 (31%)	71 (45%)	70 (45%)	0.99
Lipid-lowering agents	140 (45%)	71 (45%)	69 (44%)	0.91
Statins	111 (35%)	52 (33%)	59 (38%)	0.48
Fibrates	30 (9%)	19 (12%)	11 (7%)	0.18
Antidiabetic management				
Diet alone	58 (18%)	29 (18%)	29 (18%)	
Oral hypoglycemic drugs	214 (68%)	107 (68%)	107 (68%)	1
Insulin	42 (14%)	21 (14%)	21 (14%)	
Glucose (mmol/l)	9.00 ± 3.39	8.94 ± 3.17	9.06 ± 3.61	0.78
Creatinine (μmol/l)	97 ± 39	101 ± 49	94 ± 27	0.21
End-organ damage				
Retinopathy	27 (9%)	15 (10%)	12 (8%)	0.55
Nephropathy	51 (16%)	25 (16%)	26 (17%)	0.88
Neuropathy	12 (4%)	6 (4%)	6 (4%)	1
At least one of the above	76 (24%)	38 (24%)	38 (24%)	1
Previous PTCA	106 (34%)	58 (37%)	48 (31%)	0.23
Previous CABG	27 (9%)	14 (9%)	13 (8%)	0.84
Recent (<1 month) MI	84 (27%)	43 (27%)	41 (26%)	0.80
Unstable angina	82 (26%)	37 (24%)	45 (27%)	0.52
Multiple vessel disease	177 (56%)	86 (55%)	91 (58%)	0.57
No. of dilated vessels	1.20 ± 0.42	1.20 ± 0.42	1.20 ± 0.41	0.89
LVEF (%)	58.6 ± 14.8	58.7 ± 14.3	58.5 ± 15.2	0.78

Data are presented as the mean value ± SD or number (%) of patients.
ACE = angiotensin-converting enzyme; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

were analyzed using the Cox proportional hazards model. A value of $p < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline characteristics. The adequacy of the matching process was confirmed by the lack of difference between the groups with respect to major baseline patient and lesion characteristics (Tables 1 and 2). Most of the 314 diabetics were male (76%; mean age 61 ± 10 years). Twenty-four percent had a documented complication of diabetes other than atherosclerosis (e.g., nephropathy, neuropathy, retinopathy). Twenty-six percent of the patients had unstable angina, and 27% had experienced a recent (<1 month) MI. Eighteen percent of the patients were treated with diet alone, 68% were treated with oral hypoglycemic drugs, and 14% with insulin.

Percutaneous coronary revascularization was performed for a recent infarct-related lesion in 24% of cases and for restenosis in 20% of cases (Table 2). The dilated lesion was most often located in the left anterior descending coronary artery (45%) and less frequently in the right coronary artery (31%), left circumflex coronary artery (19%), or saphenous vein graft (SVG; 5%). Nineteen percent of the lesions had TIMI flow grade <3.

In the stent group, a single stent was implanted in 80% of cases; the most frequently used stent was the Palmaz-Schatz (65%). The maximal balloon size was 3.2 ± 0.4 mm, and the maximal inflation pressure was 15 ± 3 atm.

Angiographic outcome. Angiographic follow-up was obtained in 134 patients in the BA group (85%) and in 133 patients in the stent group (85%). The results of quantitative angiography are presented in Table 3. The immediate angiographic outcome was significantly better in stented patients (MLD; 2.70 ± 0.46 mm) than in BA patients (MLD; 1.99 ± 0.47 mm) ($p < 0.0001$). At follow-up angiography, patients in the stent group had a larger net gain (1.08 ± 0.82 vs. 0.47 ± 0.73 mm; $p < 0.0001$) and thus a significantly greater MLD at follow-up (1.81 ± 0.83 vs. 1.20 ± 0.76 mm; $p < 0.0001$). When analyzed by the categorical approach with >50% diameter stenosis as the criterion for restenosis, 27% of the stent group and 62% of

Table 2. Baseline Lesion Characteristics

	All Lesions (n = 314)	Balloon Angioplasty Group (n = 157)	Stenting Group (n = 157)	p Value
Infarct-related (<1 month) lesion	77 (24%)	39 (25%)	38 (24%)	0.90
Previous PTCA at same site	64 (20%)	36 (23%)	28 (18%)	0.26
Site of angioplasty				
RCA	96 (31%)	48 (31%)	48 (31%)	
LAD	142 (45%)	71 (45%)	71 (45%)	1
LCx	60 (19%)	30 (19%)	30 (19%)	
SVG	16 (5%)	8 (5%)	8 (5%)	
AHA/ACC classification				
A	69 (22%)	42 (27%)	27 (17%)	
B1	90 (29%)	44 (28%)	46 (29%)	0.22
B2	125 (40%)	57 (36%)	68 (43%)	
C	30 (9%)	14 (9%)	16 (10%)	
TIMI flow grade				
0	23 (7%)	11 (7%)	12 (8%)	
1	10 (3%)	5 (3%)	5 (3%)	0.76
2	25 (8%)	10 (6%)	15 (9%)	
3	256 (82%)	131 (83%)	125 (80%)	
Lesion length (mm)	8.6 ± 4.2	8.4 ± 3.8	8.8 ± 4.7	0.42
Reference diameter (mm)	3.06 ± 0.50	3.06 ± 0.48	3.06 ± 0.51	0.98
Minimal luminal diameter (mm)	0.73 ± 0.39	0.74 ± 0.38	0.72 ± 0.40	0.76
Diameter stenosis (%)	75 ± 13	75 ± 13	76 ± 13	0.72

Data are presented as the number (%) of patients or mean value ± SD.
AHA/ACC = American Heart Association/American College of Cardiology; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; PTCA = percutaneous transluminal coronary angioplasty; RCA = right coronary artery; SVG = saphenous vein graft; TIMI = Thrombolysis in Myocardial Infarction trial.

the BA group had restenosis ($p < 0.0001$). Total occlusion of the dilated site at follow-up occurred in only 4% of the stent group and in 13% of the BA group ($p < 0.005$).

Subgroup analyses based on the anti-diabetic regimen, presence of end-organ damage, site of angioplasty, vessel size, lesion length, or TIMI flow grade at baseline were performed (data not shown). In each of these subgroups, stent implantation was associated with a significant reduction in the rate of restenosis and/or late occlusion. However, stent implantation in a long lesion or SVG was still associated with a restenosis rate of 34% to 40%, and stent implantation in a vessel <3 mm in diameter or with TIMI flow grade <3 was associated with an occlusion rate of 6% to 7%.

LV function at angiographic follow-up. Among the 267 patients with angiographic follow-up, 226 (85%) had ventriculograms obtained before PTCA and at follow-up that were suitable for determination of ventricular function. Total occlusion of the dilated site at follow-up was associated with a significant decrease in LVEF between baseline and follow-up (−9.9 ± 11.2%; $p = 0.001$) that was not seen in patients without restenosis or with non-occlusive reste-

Table 3. Quantitative Angiographic Analysis in the 267 Patients With Angiographic Follow-Up

	Balloon Angioplasty Group (n = 134)	Stenting Group (n = 133)	p Value
Reference diameter (mm)			
Before	3.06 ± 0.47	3.06 ± 0.49	0.98
After	3.05 ± 0.49	3.11 ± 0.49	0.32
Follow-up	3.07 ± 0.50	3.07 ± 0.49	0.94
Minimal luminal diameter (mm)			
Before	0.73 ± 0.38	0.72 ± 0.41	0.82
After	1.99 ± 0.47	2.70 ± 0.46	0.0001
Follow-up	1.20 ± 0.76	1.81 ± 0.83	0.0001
Diameter stenosis (%)			
Before	75 ± 12	75 ± 13	0.75
After	33 ± 12	8 ± 9	0.0001
Follow-up	61 ± 23	38 ± 25	0.0001
Acute gain (mm)	1.25 ± 0.50	1.98 ± 0.51	0.0001
Late loss (mm)	0.78 ± 0.78	0.89 ± 0.75	0.25
Net gain (mm)	0.47 ± 0.73	1.08 ± 0.82	0.0001
Diameter stenosis >50% at follow-up	82 (62%)	36 (27%)	0.0001
Total occlusion at follow-up	18 (13%)	5 (4%)	0.005

Data are presented as the mean value ± SD or number (%) of patients.

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nosis ($-0.8 \pm 11.3\%$; $p = 0.42$). Because total occlusion of dilated sites was frequent in BA patients, a significant decrease in LVEF was observed in the entire BA group ($-2.4 \pm 10.9\%$; $p = 0.02$). Conversely, because occlusion of dilated sites was quite rare in patients treated with coronary stent implantation, no significant change in LVEF was observed in the stent group ($-0.5 \pm 12.2\%$; $p = 0.60$).

Clinical end points at four years. The actuarial rates of clinical events are presented at four years. At this time point, trends toward a lower total mortality rate (13.5% vs. 19.2%; $p = 0.20$), lower cardiac mortality rate (6.6% vs. 14.6%; $p = 0.07$) (Fig. 1A), and lower rate of MI (9.9% vs. 16.0%; $p = 0.06$) (Fig. 1B) were observed in the stent group compared with the BA group. The incidence of the composite end point of cardiac death and non-fatal MI was significantly lower in the stent group than in the BA group (14.8% vs. 26.0%; $p = 0.02$) (Fig. 1C). Repeat revascularization (PTCA or coronary artery bypass graft surgery) was performed in 35.4% of patients in the stent group compared with 52.1% in the BA group ($p = 0.001$) (Fig. 1D). This reduction reflected a lower rate of target vessel revascularization in the stent group (21.0% vs. 40.6%; $p = 0.0002$) (Fig. 1E). The composite end point of cardiac death, non-fatal MI, and repeat revascularization was significantly lower in the stent group than in the BA group (41.2% vs. 63.1%; $p < 0.0001$) (Fig. 1F).

In an attempt to elucidate whether the reduction in the incidence of the composite end point of cardiac death and non-fatal MI observed in the stent group was mainly related to the reduction in restenosis, multivariate analysis (Cox proportional hazards model) was performed in patients with six-month angiographic follow-up. The technique of revascularization (stent or balloon) and the restenosis status were entered into the model. Restenosis was found to be the key predictor of the composite end point of cardiac death and non-fatal MI (restenosis vs. no restenosis: hazard ratio [HR] = 2.39, 95% confidence interval [CI] = 1.32 to 4.35, $p = 0.004$; stent vs. balloon: HR = 0.67, 95% CI = 0.36 to 1.23, $p = 0.20$).

DISCUSSION

The findings of the present study comparing coronary stent implantation with standard BA in diabetic patients matched for five major patient and lesion characteristics clearly demonstrate that coronary stent implantation was associated with a highly beneficial effect on both the six-month angiographic outcome and four-year clinical events, compared with standard BA, and strongly suggest that stent implantation should be the preferred strategy when PCR is performed in diabetic patients.

Previous studies. Restenosis in diabetic patients is considered to be related to enhanced neointimal hyperplasia (17), an accelerated fibrotic response (18), and an enhanced predisposition to vascular thrombosis (19). Previously published studies have yielded conflicting results on the potential benefit of coronary stent implantation in diabetic patients. Data on angiographic outcomes are derived from studies investigating the effect of diabetes on restenosis either in patients treated with standard BA (4,9,10) or in those treated with coronary stent implantation (11–14). These studies included patients with differing clinical characteristics, and they reported a wide range of restenosis rates after BA (35% to 71%) (4,9,10) and stent implantation (24% to 55%) (11–14). Carrozza et al. (11) reported a restenosis rate of 55% in a population of diabetic patients treated at a saphenous vein graft lesion in more than half of cases, Elezi et al. (14) reported a restenosis rate of 37% in a diabetic population in whom multiple overlapping-stenting was common (44% of cases), while we previously reported (12) a 24% restenosis rate in patients exclusively treated on native coronary artery lesions and in whom multiple overlapping-stenting was rare (20% of cases).

Data on clinical outcomes are even more difficult to compare. Although extensive data on the 5- to 10-year clinical outcomes of diabetic patients treated with standard BA are available (1,2,5–7,20), data focused on the outcomes of diabetic patients treated with coronary stenting are limited (14,21,22).

Coronary stenting and angiographic outcome. The present study is the first study that attempts to directly compare the effects of stent implantation and standard BA in diabetic patients undergoing PCR without any pharmacologic adjunct. The matching process, using five major criteria (i.e., gender, anti-diabetic regimen, vessel location, vessel size, MLD), allowed us to select a group of patients treated with standard BA with characteristics very similar to the group of patients treated with coronary stent implantation. These patients were optimal candidates for stent implantation or BA: they were treated on relatively large vessels (mean reference diameter of 3.06 mm) and short lesions (9 mm in length) that were covered with a single stent in the vast majority of cases (80%).

As illustrated by a higher net gain (1.08 vs. 0.47 mm) and a lower restenosis rate (27% vs. 62%), coronary stent implantation was associated with a better six-month angiographic outcome, compared with BA, in our population of diabetic patients. These results strengthen some trends that were seen in a subgroup analysis of previous randomized studies. Indeed, diabetic patients in the STent REStenosis Study (STRESS I-II) trials ($n = 92$) had a lower restenosis rate after coronary stenting than after standard BA (24% vs. 60%) (23). Similarly, among diabetic patients receiving the antiplatelet agent abciximab in the Evaluation of Platelet IIb/IIIa Inhibitor for STENTing (EPISTENT) trial, those randomized to coronary stenting had a higher net gain at six months than those treated with BA (0.88 vs. 0.43 mm; $p = 0.001$) (24).

Additional information is provided by analysis of the angiographic data of the present study. First, coronary stent implantation reduces the rate of occlusive restenosis (4% vs. 13%) and partly prevents the deterioration of LV function

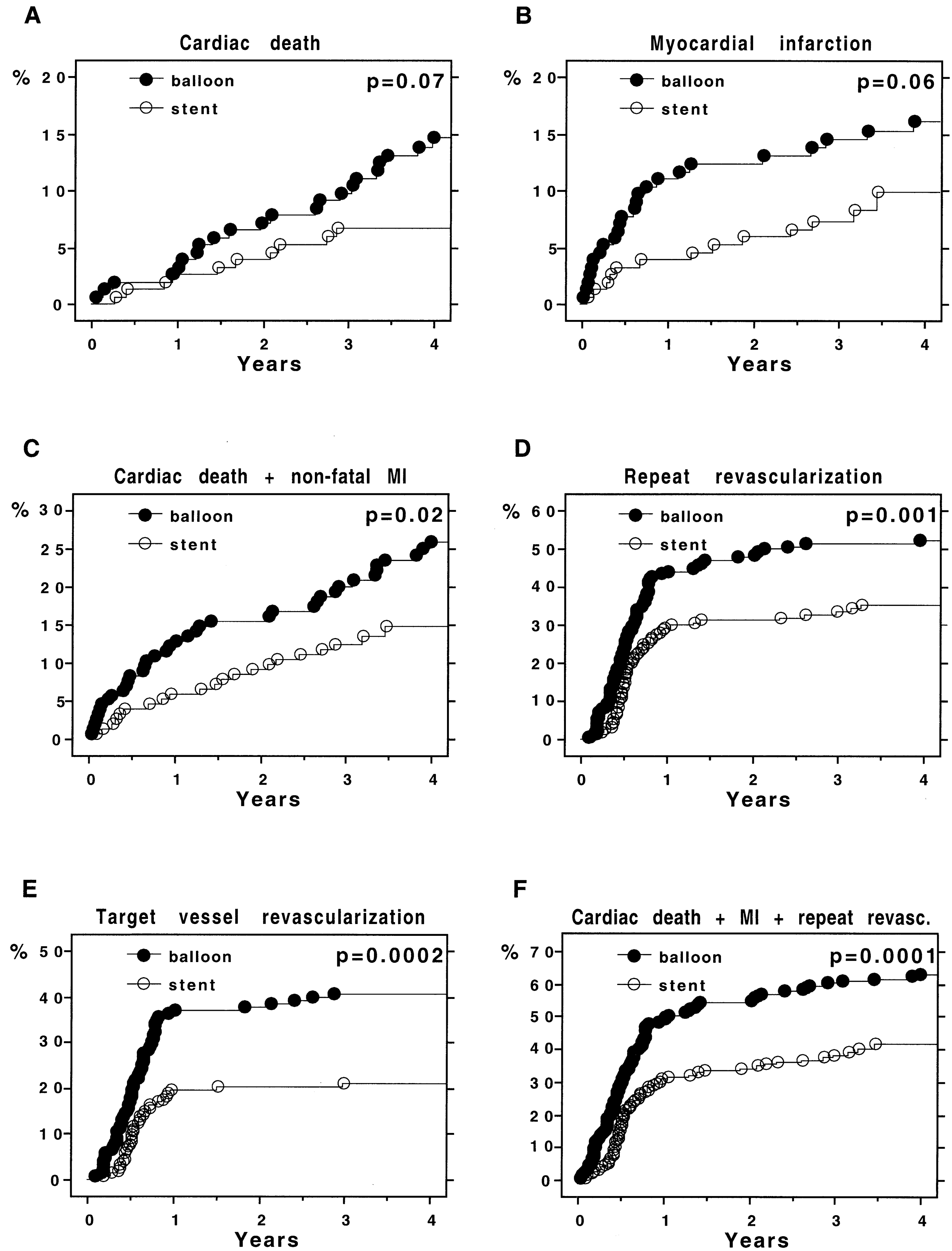

Figure 1. Four-year Kaplan-Meier curves for cardiac mortality **(A)**; myocardial infarction (MI) **(B)**; the composite end point of cardiac death and non-fatal MI **(C)**; repeat revascularization **(D)**; target vessel revascularization **(E)**; and the composite end point of cardiac death, non-fatal MI, and repeat revascularization **(F)**.

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observed at six months in diabetics treated with BA. Second, although the risk of occlusive or non-occlusive restenosis may vary between subgroups, the beneficial effect of coronary stent implantation is consistent among these subgroups. Finally, this study also shows that stent implantation is not a panacea for restenosis in diabetic patients. Restenosis, particularly in its occlusive form, is still a major concern when angioplasty is performed in SVG lesions, small vessels (≤3.0 mm), long lesions (>8.0 mm), or vessels with TIMI flow grade <3.

Coronary stenting and clinical outcome. This study is the first to demonstrate that the use of coronary stents may by itself improve the long-term clinical outcome of diabetic patients who have had PCR. Although the beneficial effect of coronary stenting was partly related to a decreased need for repeat revascularization (32% relative reduction), it is of potentially greater clinical relevance that it was also associated with a 43% reduction in the combined end point of cardiac death and MI at four years. The clinical benefit of coronary stent implantation in diabetic patients, as reported in the present study, is consistent with the recent observation of the EPISTENT trial, showing that among diabetics receiving abciximab, those randomized to coronary stent implantation had a trend toward a reduced rate of death and large MI at one year compared with those treated with BA (4.9% vs. 10.4%) (25). It is also consistent with the recently reported outcome of the Arterial Revascularization Therapy Study (ARTS) that compares stenting with coronary artery bypass graft surgery in patients with multi-vessel coronary artery disease (26) and shows that the mortality rate of diabetic patients who have had stent implantation (7%) was close to the mortality rate after bypass surgery (3%) and much lower than the mortality rate observed two years after BA in the Bypass Angioplasty Revascularization Investigation (BARI) trial (17%) (1).

When considered together, the angiographic and clinical data in our study suggest that a lower rate of occlusive restenosis and preserved LV function play key roles in the reduction in the combined end point of cardiac death and MI observed in patients treated with coronary stents. The previous demonstration that occlusive restenosis is associated with a significant decrease in ejection fraction (4) and poor long-term survival (27) in diabetic patients is also consistent with this hypothesis.

Need for further improvement. We have to acknowledge, however, that when used without pharmacologic adjunct, the rate of clinical events remains high in diabetic patients after coronary stent implantation. Elezi et al. (14) and Abizaid et al. (21) recently reported a trend toward a higher one-year mortality rate in diabetic patients than non-diabetic patients after coronary stent implantation, and the four-year mortality rate (13.5%) of diabetics treated with coronary stents in our study also seems high compared with the 9% mortality rate observed at three years by van Domburg et al. (22) in a contemporary series of 1,000 unselected patients treated with coronary stents. This may be partly explained by the persistently high rate of occlusive restenosis seen in some subgroups of diabetics after coronary stenting, as observed in the present study. In these subgroups of patients, coronary stenting should probably be performed with concomitant glycoprotein IIb/IIIa blockade, as recently suggested by the analysis of the one-year clinical follow-up of diabetic patients involved in the EPISTENT trial (25). The relatively high rate of events seen in diabetic patients after coronary stenting also warrants the need for more careful attention to secondary prevention in these patients.

Study limitations. This was a single-center study, and patient referral, technique of PTCA, and medical management may have influenced the results. In addition, the high rate of angiographic follow-up may have increased the target lesion revascularization rate in our population, as recently suggested by Ruygrok et al. (28). However, the combination of a high rate of angiographic (85%) and clinical (100%) follow-up allowed us to suggest a mechanism for the reduced rate of cardiac death and MI observed in our study after coronary stent implantation. Finally, it is evident that this retrospective study based on matching does not have the value of a randomized study. However, previous similar studies based on matching (29,30) have accurately predicted the results of prospective randomized trials (31–33).

Clinical implications. The present study demonstrates that coronary stent implantation may provide a significant benefit, compared with standard BA, in diabetic patients and suggests that coronary stents, alone or in combination with glycoprotein IIb/IIIa blockade, should be employed as a standard therapy for PCR in this group of patients, particularly when single-vessel revascularization needs to be performed.

Because long-term survival of diabetic patients who need multi-vessel revascularization is better after bypass surgery than after standard BA (1,6,7,20), surgery is currently the preferred revascularization technique in this group of patients. Our data, in conjunction with the data of the EPISTENT and ARTS studies (26), suggest that modern PCR with appropriate adjunctive pharmacotherapy (glycoprotein IIb/IIIa blockade) may become a viable alternative to bypass surgery in such patients. However, a prospective randomized trial is required before such an approach can be recommended in clinical practice. From this perspective, it is worth noting that the preliminary results achieved with drug-eluting stents (34) are encouraging.

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