Efficacy of Coronary Stenting Versus Balloon Angioplasty in Small Coronary Arteries

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Objectives. The goal of this study was to compare the efficacy of elective stent implantation and balloon angioplasty for new lesions in small coronary arteries.

Background. Palmaz-Schatz stents have been designed and approved by the Food and Drug Administration for use in coronary arteries with diameters ≥3.0 mm. The efficacy of elective stent placement in smaller vessels has not been determined.

Methods. By quantitative coronary angiography, 331 patients in the Stent Restenosis Study (STRESS) I–II were determined to have a reference vessel <3.0 mm in diameter. Of these, 163 patients were randomly assigned to stenting (mean diameter 2.69 ± 0.21 mm), and 168 patients were assigned to angioplasty (mean diameter 2.64 ± 0.24 mm). The primary end point was restenosis, defined as ≥50% diameter stenosis at 6-month follow-up angiography. Clinical event rates at 1 year were assessed.

Results. Baseline clinical and angiographic characteristics were similar in the two groups. Procedural success was achieved in 100% of patients assigned to stenting and in 92% of patients assigned to angioplasty (p < 0.001). Abrupt closure within 30 days occurred in 3.6% of patients in both groups. Compared with angioplasty, stenting conferred a significantly larger postprocedural lumen diameter (2.26 vs. 1.80 mm, p < 0.001) and a larger lumen at 6 months (1.54 vs. 1.27 mm, p < 0.001). Restenosis (≥50% diameter stenosis at follow-up) occurred in 34% of patients assigned to stenting and in 55% of patients assigned to angioplasty (p < 0.001). At 1 year, event-free survival was achieved in 78% of the stent group and in 67% of the angioplasty group (p = 0.019).

Conclusions. These findings suggest that elective stent placement provides superior angiographic and clinical outcomes than balloon angioplasty in vessels slightly smaller than 3 mm.

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Palmaz-Schatz stents have been developed and approved by the Food and Drug Administration (FDA) for use in large coronary arteries with diameters ≥3.0 mm (1–3). The goal of this Stent Restenosis Study (STRESS) substudy was to compare the efficacy of elective stent implantation and balloon angioplasty for new lesions in smaller vessels.

Methods

In the STRESS I–II trial, 598 patients with new lesions of native coronary arteries were randomly assigned to either elective placement of a Palmaz-Schatz stent or balloon angioplasty. Patient selection criteria, details of stent technique and primary outcomes have been previously reported for the initial 410 patients (known as STRESS I) (2). The "STRESS II" component of this trial represents the continuation of the original STRESS trial under an investigational device exemption mandated by the FDA. The participating centers and principal investigators are listed in the Appendix. The study protocol was approved by the Institutional Review Board at each site, and all patients gave written, informed consent. Angiography was performed in paired orthogonal views before and after intervention and at 6 months. Intracoronary nitro-

glycerin (200 μg) was given before all angiographic assessments. Quantitative angiographic analysis was performed in a core laboratory at Jefferson Medical College using a validated automatic edge-detection program (2,4–6). Vessel edges were determined by the computerized algorithm, and lumen dimensions were measured using the guiding catheter as a scaling reference. The diameters of the normal-appearing segments, proximal and distal to the lesions, were averaged to determine the reference vessel diameter. The minimal lumen diameter (MLD), reference diameter and percent diameter stenosis were calculated as the mean values from orthogonal projections.

By quantitative analysis, 331 patients were determined to have baseline reference vessels <3.0 mm in diameter. In this substudy analysis, the outcomes of stenting versus angioplasty in these patients with small vessels were compared. The primary angiographic end point of the trial was restenosis, defined as ≥50% diameter stenosis at follow-up. The primary clinical end point was defined as the occurrence of any of the following events: death, myocardial infarction, coronary artery bypass graft surgery or repeat angioplasty. Target lesion revascularization was defined as repeat angioplasty or bypass surgery performed because of restenosis.

Outcomes were analyzed by intention to treat. Results of continuous data were expressed as the mean value ± SD, and differences between groups were assessed by two-tailed t tests. Categoric data are presented as rates and comparisons made by chi-square tests. One-year clinical event rates were calculated by Kaplan-Meier curves, with differences between the treatment groups compared by log-rank tests. A p value <0.05 was considered significant.

Results

One hundred sixty-three patients were assigned to stent placement, and 168 patients were assigned to angioplasty. Baseline clinical and lesion characteristics were similar in the two groups (Table 1). The mean vessel size was 2.69 mm in the stent group and 2.64 mm in the angioplasty group (p = NS). Procedural success, defined as <50% residual stenosis, was achieved in 100% of patients assigned to stenting and in 92% of patients assigned to angioplasty (p < 0.001). Abrupt reclosure during the first 30 days was 3.6% in both groups. Vascular complications requiring transfusion or surgical treatment were also comparable (7.9% after stenting and 6.6% after angioplasty, p = NS).

Results of quantitative coronary angiography are shown in Table 2. At baseline, there were no differences in stenosis severity or MLD between the two groups. After the procedure,

Table 1. Baseline Clinical and Angiographic Characteristics*

Characteristic	Stent Group (n = 163)	Angioplasty Group (n = 168)
Age (yr)	59 ± 10	61 ± 11
Male	74%	68%
Hypertension	53%	52%
Hyperlipidemia	52%	57%
Current smoker	25%	20%
Diabetes	17%	16%
Unstable angina	56%	48%
MI within 6 wk	19%	25%
Vessel location		
LAD	59%	58%
LCx	14%	10%
RCA	27%	32%
Vessel size (mm)	2.69 ± 0.21	2.64 ± 0.24
Range	2.05 − 2.99	1.93 − 2.99
Lesion length (mm)	8.9 ± 3.0	8.5 ± 2.5
Eccentric	58%	54%
Calcified	17%	18%
Ulcerated	18%	14%
Bend >45°	7%	14%
Thrombus		
Definite	3%	1%
Possible	11%	10%

*p = NS for all comparisons. Data presented are mean value ± SD or percent of patients. LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; MI = myocardial infarction; RCA = right coronary artery.

a larger acute gain was achieved with stent placement, resulting in a larger mean MLD in the stent group (2.26 vs. 1.80 mm, p < 0.001). Follow-up angiography was performed in 84% of eligible patients. The stent group had a greater late loss in MLD (0.75 vs. 0.56 mm, p = 0.005) but greater overall net gain (0.84 vs. 0.57 mm, p < 0.001), resulting in a larger MLD at 6 months (1.54 vs. 1.27 mm, p < 0.001). Cumulative frequency curves of MLD at baseline, after the procedure and at follow-up are plotted in Figure 1.

Table 2. Results of Quantitative Coronary Angiography

Variable	Stent Group (n = 163)	Angioplasty Group (n = 168)	p Value
% DS			
Baseline	75 ± 9	74 ± 9	NS
After procedure	17 ± 11	34 ± 15	< 0.001
At 6 mo	44 ± 19	54 ± 20	< 0.001
MLD (mm)			
Baseline	0.69 ± 0.25	0.68 ± 0.24	NS
After procedure	2.26 ± 0.36	1.80 ± 0.36	< 0.001
At 6 mo	1.54 ± 0.54	1.27 ± 0.53	< 0.001
Change in lumen diameter (mm)			
Acute gain	1.58 ± 0.41	1.11 ± 0.40	< 0.001
Late loss	0.75 ± 0.55	0.56 ± 0.55	0.005
Net gain	0.84 ± 0.58	0.57 ± 0.58	< 0.001

Data presented are mean value ± SD. DS = diameter stenosis; MLD = minimal lumen diameter.
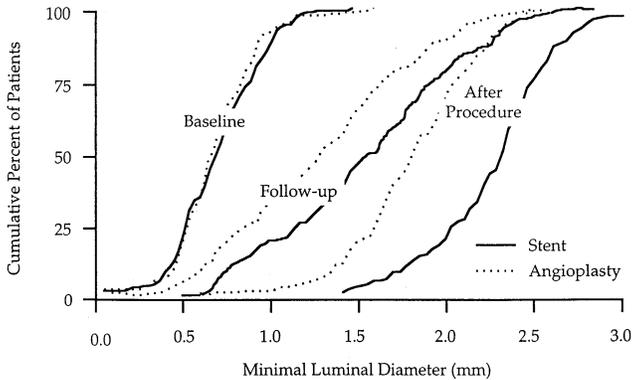
Figure 1. Cumulative frequency curves of MLD at baseline, immediately after the intervention and at follow-up. At baseline, there was no difference between the stent and angioplasty groups. Immediately after the procedure, a larger MLD was observed in the stent group. Six months later, a larger lumen persisted in the stent group.

The comparative effects of stenting and angioplasty as a function of vessel size are shown in Figure 2. When compared in arteries 2.75 to 2.99, 2.50 to 2.74 and ≤2.49 mm, stenting conferred a significantly larger lumen at follow-up than did balloon angioplasty. Six-month MLDs for stenting and angioplasty, respectively, were 1.60 versus 1.40 mm for 2.75 to 2.99 mm arteries, 1.55 versus 1.20 mm for 2.50 to 2.74 mm arteries and 1.39 versus 1.14 mm for ≤2.49 mm arteries (all $p < 0.05$). Thus, stenting conferred a significantly larger lumen across all vessel sizes.

Restenosis rates are shown in Figure 3. For the entire cohort of patients, restenosis was observed in 47 (34%) of 139 lesions in the stent group and in 66 (55%) of 121 lesions in the angioplasty group ($p < 0.001$). Compared as a function of the reference vessel size, the restenosis rates for stenting and angioplasty, respectively, were 36% versus 50% in 2.75 to 2.99 mm arteries ($p = 0.125$), 34% versus 59% in 2.50 to 2.74 mm arteries ($p = 0.024$) and 30% versus 57% in ≤2.49 mm arteries ($p = 0.028$).

Rates of major cardiac events at 1 year are shown in Table 3. One-year survival was excellent in both groups: 99.4% in the stent cohort and 98.2% in the angioplasty cohort ($p = NS$).

Figure 2. Minimal lumen diameter 6 months after the intervention as a function of reference vessel size. Note that stenting (**open bars**) conferred a significantly larger lumen irrespective of vessel size. **Hatched bars** = percutaneous transluminal coronary angioplasty.
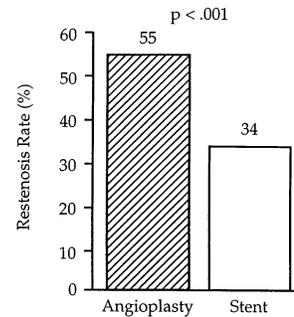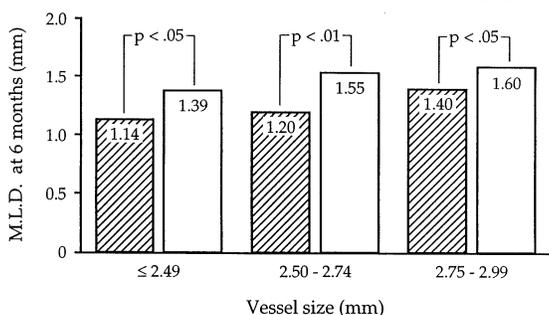

Figure 3. Restenosis rates after balloon angioplasty and coronary stenting for all patients with small coronary arteries.

Repeat target lesion revascularization was significantly less frequent in the stent group (16.1% vs. 26.6%, $p = 0.015$). Event-free survival (Fig. 4) was 77.9% in the stent group and 67.3% in the angioplasty group ($p = 0.019$). Thus, stenting conferred a 33% reduction in cardiac events compared with balloon angioplasty.

Discussion

The complex, vexing problem of restenosis after balloon angioplasty is influenced by a variety of clinical and anatomic factors. One important anatomic factor is vessel size, because the restenosis rate is inversely rated to the reference vessel diameter (7,8). In the Multi-Hospital Eastern Atlantic Restenosis Trial (M-HEART) of 598 patients undergoing conventional balloon angioplasty, Hirshfeld et al. (7) reported a significantly higher restenosis rate of 44% in vessels <2.9 mm compared with a restenosis rate of 34% in vessels >2.9 mm. A similar relation between vessel size and restenosis was observed in the angioplasty arm of the STRESS trial (2). Accordingly, interventions designed to ameliorate restenosis would have a greater relative impact if applicable to smaller vessels.

Elective stenting in small vessels. The Palmaz-Schatz stent was designed to reduce restenosis in large arteries with diameters ≥3 mm. The present study suggests that elective stent placement may be highly effective for smaller vessels. Compared with balloon angioplasty, stent placement was associated with a 38% relative reduction in restenosis and a 33% reduction in clinical events. These results have potentially far-

Table 3. Clinical Events at 1 Year

Event	Stent Group (n = 163)	Angioplasty Group (n = 168)	p Value
Death	0.6	1.8	NS
MI	6.1	8.3	NS
CABG	6.7	11.9	NS
Repeat PTCA	16.6	21.4	NS
TLR	16.1	26.6	0.015
Any event	22.1	32.7	0.019

Data presented are percent of patients. CABG = coronary artery bypass graft surgery; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; TLR = target lesion revascularization.
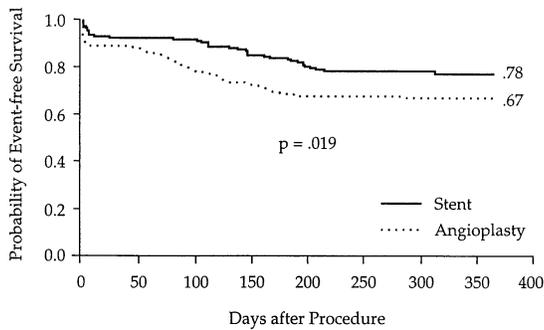
Figure 4. Kaplan-Meier curves of event-free survival after angioplasty and stenting at 1 year.

reaching implications, because the routine use of stents in small vessels would significantly enlarge the population of patients who would be candidates for this breakthrough technology. Approximately one-half of coronary interventions involve vessels <3.0 mm in diameter, with 30% of procedures performed in 2.5 to 2.9 mm vessels (9).

Stent thrombosis. The potential for stent thrombosis remains an important concern for stents in small vessels. Previous studies of both the Palmaz-Schatz and Gianturco-Roubin stents have demonstrated an inverse relation between vessel size and the risk of stent thrombosis and early ischemic complications (10,11). Although the present study was performed using an anticoagulation regimen consisting of aspirin and warfarin (Coumadin) without routine high pressure stent deployment, the rate of abrupt reclosure was the same for the stent and angioplasty groups. Nevertheless, the results of the large French Multicenter Registry suggest that small vessel size remains an important risk factor for stent thrombosis in the current era of adjunctive aspirin and ticlopidine therapy without Coumadin (12). In this prospective registry of 2,900 patients, thrombosis occurred in 10% of vessels treated with stents sized ≤2.5 mm versus 1.5% of vessels treated with stents sized ≥3.0 mm.

Study limitations. Although the current findings were based on quantitative coronary analysis, the STRESS trial protocol included only patients with vessels of ~3 mm (or larger) in diameter by visual estimate. Accordingly, the trial was not designed to test the efficacy of stenting in arteries that the investigator subjectively perceived to be small. It should be noted in this regard that the mean vessel size by quantitative analysis in our study was >2.6 mm. However, even in the cohort of patients with the smallest vessels (<2.5 mm), stenting conferred a significant benefit on the 6-month angiographic results. It is also important to note that the STRESS trial was restricted to new focal lesions in the native circulation. These results cannot be extrapolated to patient groups excluded from the trial, including those with long, diffuse lesions or restenotic lesions.

A final limitation of this study is the lack of cost-effectiveness data. The routine use of stents in small vessel intervention could potentially have significant economic con-

sequences. Procedural expenses would increase owing to the additional costs associated with stent implantation. In contrast, the reduction in repeat revascularization procedures would provide a significant cost savings. Future studies will be needed to assess the economic implications of elective stent placement in the treatment of smaller coronary arteries.

Conclusions. This study suggests that elective stent placement provides superior angiographic and clinical outcomes to balloon angioplasty in vessels slightly smaller than 3 mm. However, the study is limited by the retrospective nature of the analysis. These promising results will be reassessed by the STRESS IV trial, a prospective comparison of stent placement and balloon angioplasty for small coronary arteries, using a customized slotted tube stent designed for vessels 2.25 to 2.75 mm in diameter.

Appendix

STRESS I–II Principal Investigators and Sites

Sheldon Goldberg, MD, Michael P. Savage, MD, *Thomas Jefferson University, Philadelphia, Pennsylvania*; Ian Penn, MD, Brendon Foley, MD, *Victoria Hospital, London, Ontario, Canada*; Michael Clemen, MD, *Yale University, New Haven, Connecticut*; Donald Baim, MD, *Beth Israel Hospital, Boston, Massachusetts*; Richard Stack, MD, James Zider, MD, *Duke University, Durham, North Carolina*; Martin B. Leon, MD, *Washington Hospital Center, Washington, D.C.*; Jeffrey Brinker, MD, *Johns Hopkins Hospital, Baltimore, Maryland*; David Fish, MD, *Texas Heart Institute, Houston, Texas*; Richard A. Schatz, MD, Paul Teirstein, MD, *Scripps Clinic, La Jolla, California*; Richard Heuser, MD, *Arizona Heart Institute, Phoenix, Arizona*; Masakiyo Nobuyoshi, MD, *Kokura Memorial Hospital, Kitakyushu, Japan*; Jeffrey Moses, MD, *Lenox Hill Hospital, New York, New York*; Don Ricci, MD, *Vancouver General Hospital, Vancouver, British Columbia, Canada*; John Hirshfeld, MD, *Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania*; Antonio Columbo, MD, Yaron Almagor, MD, *Centro Cuore Columbus, Milan, Italy*; David Almond, MD, *Toronto General Hospital, Toronto, Ontario, Canada*; Steven Bailey, MD, *University of Texas, San Antonio, Texas*; Stephen Ellis, MD, *Cleveland Clinic Foundation, Cleveland, Ohio*; Spencer B. King III, MD, *Emory University, Atlanta, Georgia*; Charles Curry, MD, *Florida Heart Group, Orlando, Florida*; Blair O'Neil, MD, *Victoria General Hospital, Halifax, Nova Scotia, Canada*; Paul Overlie, MD, *Cardiology Association of Lubbock, Lubbock, Texas*; David L. Fischman, MD, Randal Rake, BS, Diane Rehmann, *Core Laboratory, Thomas Jefferson University, Philadelphia, Pennsylvania*.

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