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Fate of Lesion-Related Side Branches After Coronary Artery Stenting

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Objectives. **The aim of this study was to assess the immediate and long-term patency of lesion-associated side branches after coronary artery stenting.**

Background. **The possible adverse effects related to implantation of coronary stents are not completely known. An important potential complication of stenting is side branch occlusion due to mechanical obstruction or thrombosis.**

Methods. **Serial coronary angiography was performed in 153 patients (167 lesions) at baseline, after conventional balloon angioplasty, immediately after Palmaz-Schatz stent placement and at 6 months. The patency of side branches, where present, was analyzed at each of these points.**

Results. **Of 167 lesions stented, 57 stent placements spanned 66 side branches with a diameter ≥1 mm. Twenty-seven (41%) of these side branches had ≥50% ostial stenosis before standard balloon angioplasty. Six side branches became occluded after standard balloon angioplasty and remained occluded after stenting. Of the 60 side branches patent after conventional angioplasty, 57 (95%) remained patent immediately after stenting. All three side branches that became occluded after stenting had ≥50% ostial stenosis at baseline. All 60 side branches, including the 3 initially occluded after stenting, were patent at 6-month follow-up.**

Conclusions. **These findings demonstrate that 1) acute side branch occlusion due to coronary stenting occurs infrequently; 2) when side branch occlusion occurs, it is associated with intrinsic ostial disease; and 3) the patency of side branch ostia is well maintained at long-term follow-up.**

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Preliminary reports have shown that the Palmaz-Schatz stent may be effective in addressing two of the major challenges of coronary angioplasty: treatment of a suboptimal result due to intimal dissection (1) and prevention of late restenosis (2). However, the possible adverse effects related to implantation of this device are not completely known. An important potential complication of stenting is side branch occlusion due to mechanical obstruction or thrombosis. Therefore, the aim of this study was to assess the immediate and long-term patency of lesion-associated side branches after coronary artery stenting.

Methods

Patients. The study group comprised 153 consecutive patients who 1) underwent coronary angioplasty followed by stent implantation between December 21, 1987 and November 8, 1990 at one of eight participating centers (see Appendix), and 2) whose films were sent to the core angiographic laboratory for analysis. All patients met the following inclusion criteria: presence of single-vessel disease (stenosis ≥70%) with objective evidence of ischemia and preserved left ventricular function (ejection fraction ≥50%).

All patients signed written informed consent to a protocol approved by the Institutional Review Board of each center. All cineangiograms were forwarded to a central angiographic laboratory at Thomas Jefferson University Hospital for qualitative and quantitative analysis. For purposes of the present study, we analyzed the immediate and long-term effects of intracoronary stenting on lesion-associated side branches.

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JACC Vol. 22, No. 6
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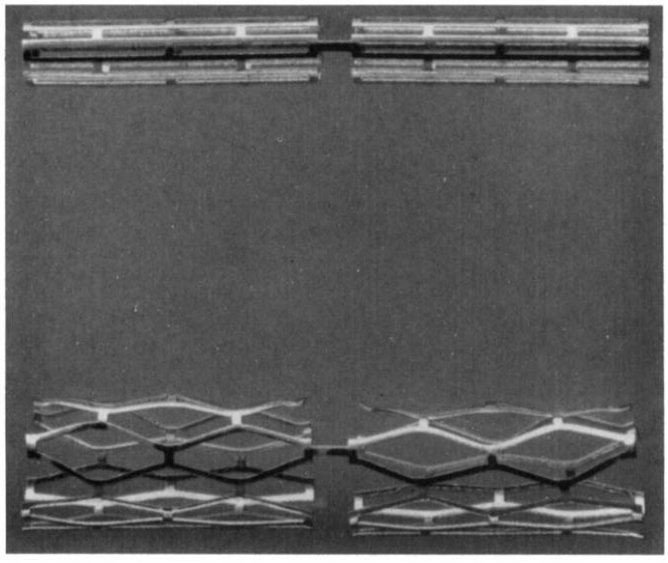


Figure 1. The Palmaz-Schatz stent.

Table 1. Lesion-Associated Branches

Stented Vessel and Branch	No.
LMCA	
LAD	1
LCx	2
Ramus	1
LAD	
Diagonal	13
Septal	9
LCx	
Marginal	5
Atrial	1
RCA	
Right ventricular branch	29
Sinoatrial node	3
Posterior descending coronary artery	2

LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; RCA = right coronary artery.

Description of the device and implantation protocol. The stent used in this study was the Palmaz-Schatz balloon-expandable intracoronary stent (Fig. 1). The stent is a monoconstructed, two-segmented slotted tube of stainless steel with a central articulation strut. In the first 30 patients, a prototype device without a central strut was used. The device measures 15 mm in length, with an outer diameter of 1.6 mm in the unexpanded state. When fully expanded, the stent takes on a diamond mesh configuration with a low metal/surface area ratio of approximately 10%. The diameter of individual metal strands is 0.075 mm. The cross-sectional area is 0.00039 cm^2. Standard balloon angioplasty using over-the-wire catheter systems was performed in all patients immediately before stent implantation. After balloon dilation, an exchange guide wire was left in place, and coronary angiography was repeated. The stent was then delivered over a standard angioplasty balloon.

Premedication included aspirin (325 mg/day), dipyridamole (225 mg/day) and a calcium antagonist for at least 48 h before stent implantation. Intravenous heparin (10,000 U) was administered before conventional angioplasty, followed by intermittent boluses of 2,500 to 5,000 U to maintain activated clotting time at >300 s. In addition, each patient received a 1-liter infusion of low molecular weight dextran (dextran 40) that was begun 3 h before the procedure and was infused for 12 to 24 h. After stent implantation, all patients were given warfarin and maintained on intravenous heparin therapy in the hospital until the prothrombin time was 16 to 18 s. After hospital discharge, warfarin therapy was continued for 1 to 3 months. In addition, each patient was treated with a calcium antagonist for 6 months, dipyridamole for 3 months and aspirin indefinitely.

Side branch analysis. Coronary angiography was performed at baseline, after conventional balloon angioplasty, immediately after stent implantation and at 6-month follow-up. Detailed morphologic analysis of the cineangiograms was performed at the core angiographic laboratory by a panel of experienced angiographers. For purposes of this analysis, side branches that were bridged by the stent and that had an estimated diameter ≥1 mm were prospectively evaluated. Patency of side branches and severity of ostial disease were assessed at baseline, after conventional angioplasty, after stent implantation and at 6-month follow-up. Occlusion of a side branch was defined as development of Thrombolysis in Myocardial Infarction (TIMI) trial perfusion grade 0 or 1 in a previously patent vessel (TIMI perfusion grade 2 or 3). Quantitative coronary analysis of all side branches to determine actual branch vessel diameter was performed using a validated computer-based coronary angiography analysis system (1–3).

Statistical analysis. All numeric data are expressed as mean value ± SD. The chi-square test was used to compare the incidence of side branch occlusion in patients with and without preexistent ostial disease. Differences were considered statistically significant at a $p < 0.05$.

Results

Patient demographics. One hundred fifty-three patients underwent intracoronary stenting of 167 lesions. There were 119 men and 34 women with a mean age of 59 years (range 26 to 86).

Side branch characteristics. A total of 66 side branches in 57 lesions were bridged by stent implantation. Table 1 illustrates the distribution of stented lesions and their associated side branches. The mean reference vessel size of the stented lesions was 3.16 ± 0.51 mm. The mean diameter of these side branches was 1.7 ± 0.4 mm (range 1.0 to 2.6). Intrinsic ostial stenosis ≥50% was present in 27 (41%) of 66 side branches.

Effect of stenting on side branches. The outcome of stenting in the 66 side branches at jeopardy is depicted in

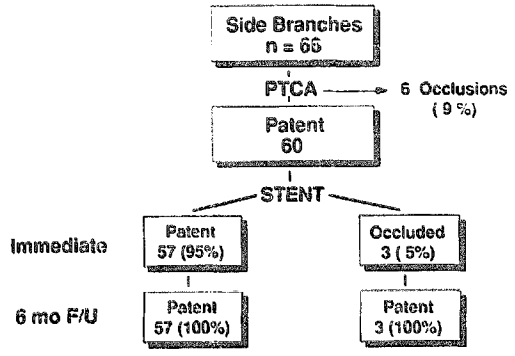
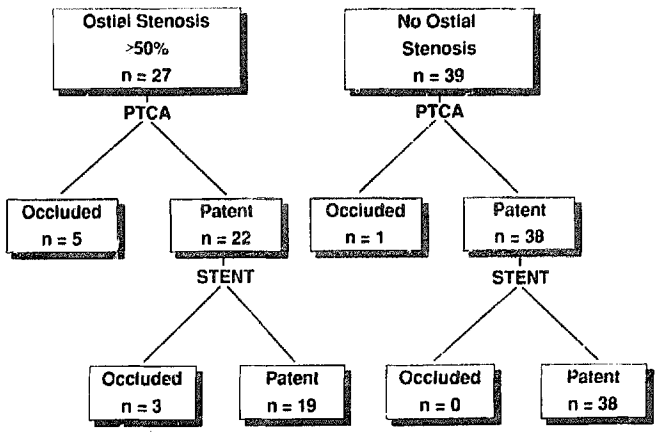


Figure 2. Outcome of side branches after stenting. F/U = follow-up; PTCA = percutaneous transluminal coronary angioplasty.

Figure 2. Of the initial 66 side branches, 6 branches (9%) became occluded after conventional angioplasty. Of the 60 side branches patent before stent implantation, 57 (95%) remained patent immediately after stenting and at long-term follow-up. Three side branches (5%) became occluded immediately after stenting. These occlusions were uncomplicated, and no patient developed electrocardiographic changes or serum creatine kinase elevations. At 6-month follow-up, all 60 side branches were patent, including the three branches that were occluded immediately after stent placement.

Significance of ostial branch disease. Figure 3 illustrates the effect of ostial disease on the outcome of side branches after angioplasty and stent implantation. Of the 27 side branches with ostial stenoses ≥50%, 5 became occluded after standard angioplasty and remained so after stenting. Of the 22 residual side branches patent after conventional dilation, 3 became occluded after stenting. Of the 39 side branches without ostial disease before balloon dilation, 1 became occluded after conventional angioplasty and remained occluded after stenting. All of the 38 remaining side branches patent after angioplasty, remained patent after stenting. Thus, 8 (30%) of 27 side branches with ostial disease were occluded after angioplasty or stenting, or both, compared with 1 (3%) of 39 without ostial disease ($p < 0.01$).

Figure 3. Effect of ostial disease on the outcome of side branches after stenting. PTCA = percutaneous transluminal coronary angioplasty.



Illustrative cases. Figure 4 illustrates the effect of stenting on a nondiseased side branch. The baseline angiogram (Fig. 4A) of a 65-year old man reveals critical lesions of the proximal and mid-right coronary arteries. There is a large right ventricular branch arising just beyond the distal lesion (Fig. 4A, arrow) that is subsequently bridged by stent implantation. Figure 4B illustrates the angiogram immediately after stent placement. The right ventricular branch is spanned by the second of two implanted stents and remains widely patent. At 6 months the right ventricular branch remains widely patent (Fig. 4C).

Figure 5 demonstrates the effect of stent placement on a small branch vessel arising from within the lesion. The baseline angiogram (Fig. 5A) of a 47-year old man reveals a critical stenosis of the proximal left anterior descending coronary artery. Originating within this lesion is a small diagonal branch (Fig. 5A, arrow). After stenting (Fig. 5B), the diagonal vessel is widely patent and remains so at 6-month follow-up (Fig. 5C).

Discussion

The major findings of this study are that 1) coronary stenting only minimally increases the risk of acute side branch occlusion over that associated with conventional angioplasty; 2) when side branch occlusion occurs, it is usually in the presence of underlying branch ostial disease; and 3) the patency of side branch ostia is maintained at long-term follow-up.

Effect of angioplasty on side branches. Previous studies have shown that more than half of the patients who undergo percutaneous transluminal coronary angioplasty have side branches at risk for iatrogenic occlusion. In a study of 557 patients who had standard balloon angioplasty, 54% had side branches in jeopardy of occlusion (4). Overall, 20 (5%) of 365 side branches became occluded after standard balloon dilation. Furthermore, side branches originating from a severely diseased segment of a coronary artery had a 14% incidence of occlusion, whereas side branches not directly involved in the lesion (but within the segment encompassed by the dilating balloon) had only a 1% incidence of occlusion. In a study of 100 patients with 109 dilated lesions, Vetrovec et al. (5) reported the presence of 97 lesion-associated side branches in 76 dilated stenoses. After successful balloon angioplasty, six side branches (6%) became totally or subtotally occluded. In addition, nonocclusive progression of branch ostial disease was noted in 16 (16%) of the side branches. A decrease in the caliber of the ostial lumen occurred more frequently in branches with preexisting ostial disease (14 [27%] of 52) compared with 2 (5%) of 44 nondiseased branches. In a similar study, Boxt et al. (6) reported a 17% overall incidence of occlusion or compromise of branch vessels as a result of angioplasty, with a

JACC Vol. 22, No. 6
November 15, 1993:1641–6

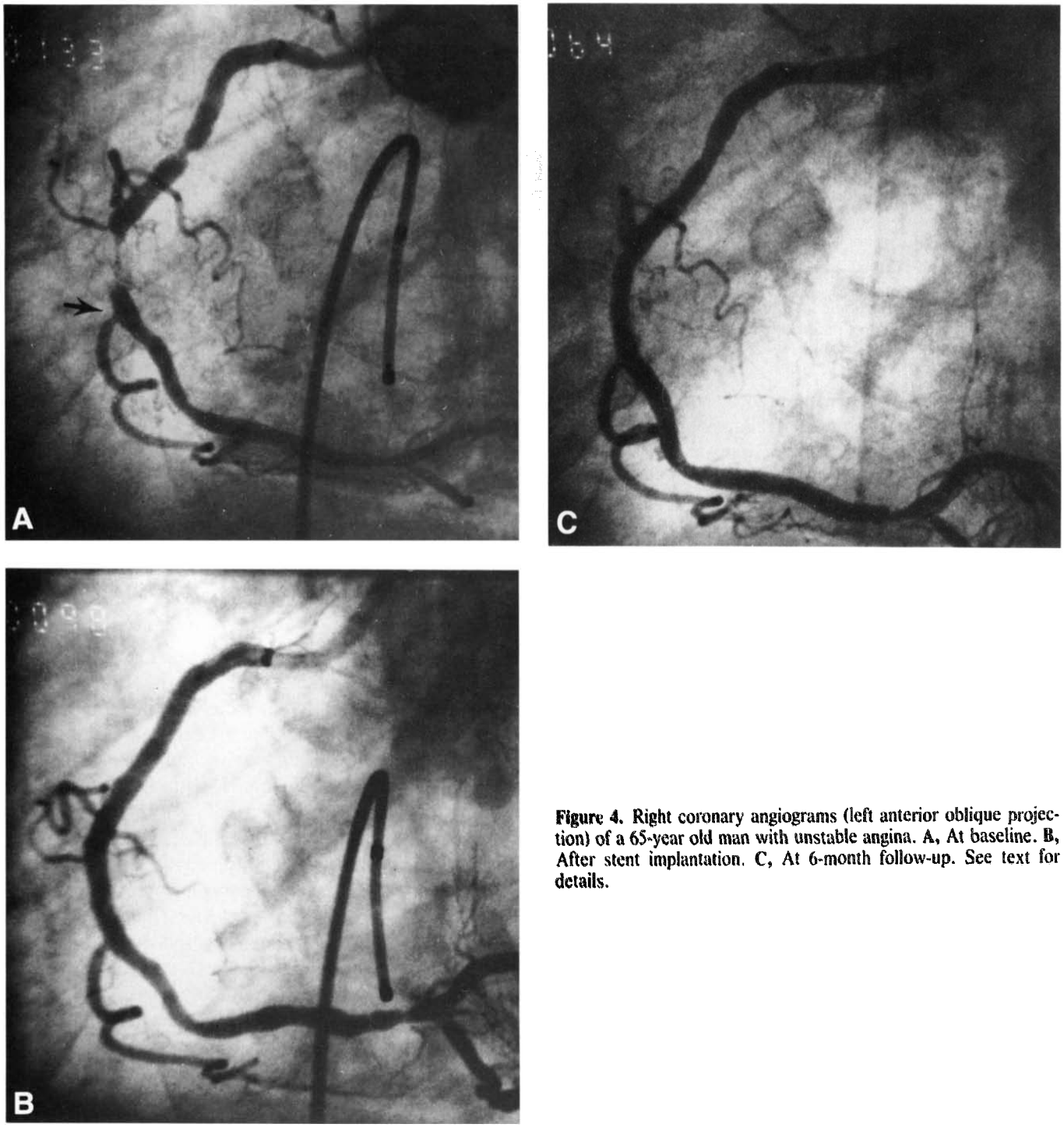


Figure 4. Right coronary angiograms (left anterior oblique projection) of a 65-year old man with unstable angina. **A,** At baseline. **B,** After stent implantation. **C,** At 6-month follow-up. See text for details.

greater than threefold increase in the incidence in side branches with preexisting ostial disease.

Effect of stenting in animal models. In preliminary studies in the animal model, Schatz et al. (7) showed that the balloon-expandable stent could be placed in the normal canine coronary artery without immediate or long-term compromise of side branches. A total of 20 stents were placed in 20 dogs, with angiography performed at 1, 3, 6 and 12 months. In addition, the dogs were killed in groups of three at 1, 3, 8 and 32 weeks for gross, light and electron microscopic analysis. In no instance was a side branch orifice compromised by stent placement.

Present study. This study demonstrates that placement of the Palmaz-Schatz stent does not produce significant side branch compromise despite the permanent implantation of a metallic intravascular prosthesis. Side branch occlusion occurred more commonly after standard balloon angioplasty and, when it occurred after stenting, it did so in the presence of branch ostial disease. This finding is similar to previous observations with conventional balloon angioplasty. In ad-

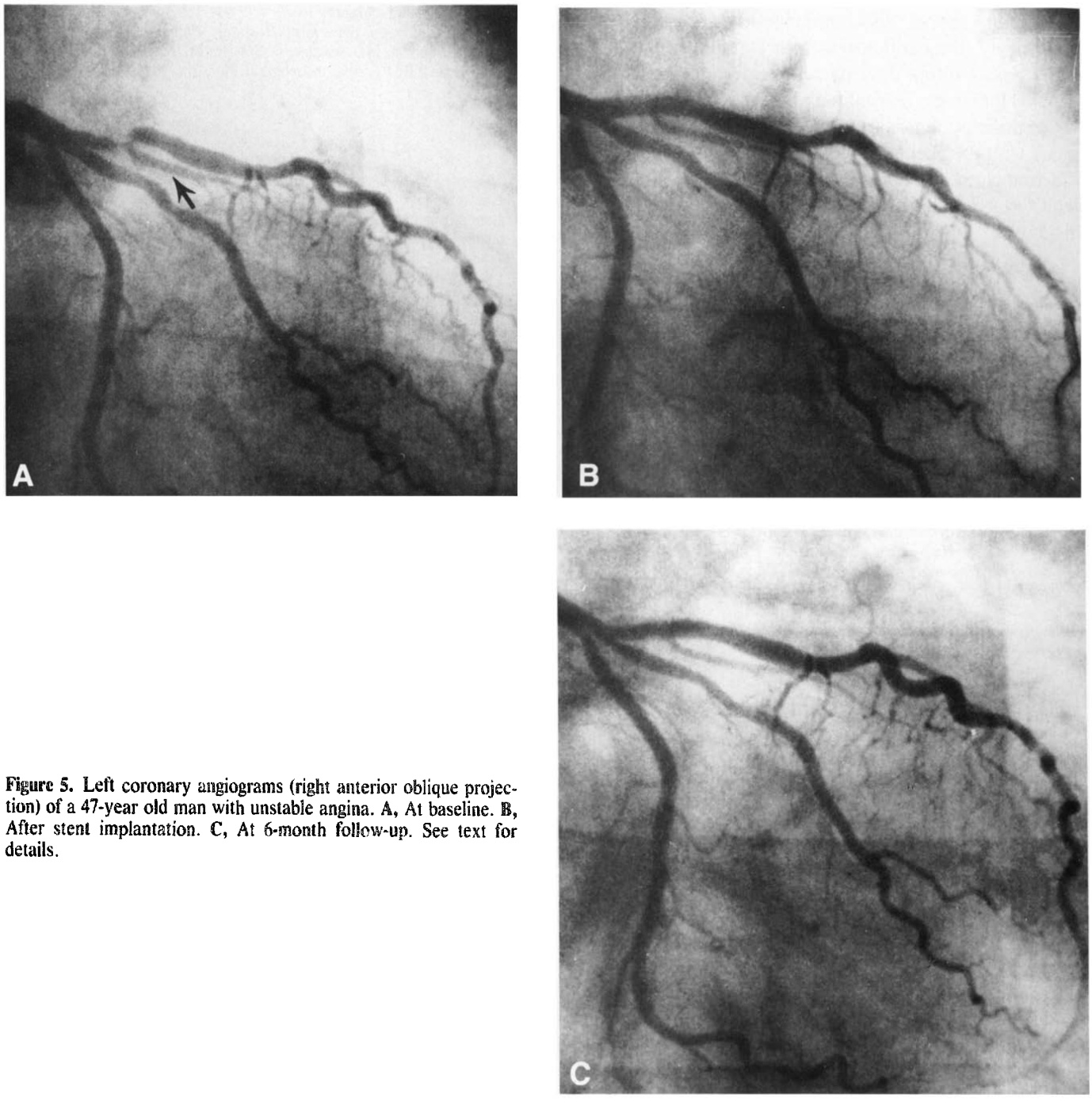


Figure 5. Left coronary angiograms (right anterior oblique projection) of a 47-year old man with unstable angina. A, At baseline. B, After stent implantation. C, At 6-month follow-up. See text for details.

dition, the patency of side branch ostia was well maintained at long-term follow-up. This stent's low ratio of metal to free space area may be an important factor contributing to these favorable results.

Study limitations. The patient group in this study represents a prospective consecutive series of patients with cineangiograms analyzed by the core angiographic laboratory rather than a universally consecutive series of patients undergoing stenting. The latter series was not available because of differences in technique among individual sites participating in this multicenter experience. For example, some centers did not routinely perform cineangiography after conventional balloon angioplasty and before stent placement. Their patients were therefore not eligible for this substudy analysis, which required angiograms after both balloon angioplasty and stent placement for comparative analysis.

Clinical implications. This study demonstrates that side branch patency is maintained up to 6 months after coronary stenting. Therefore, the presence of a small nondiseased side branch in the vicinity of a stenosis does not prohibit the use of a stent. Nevertheless, a large side branch should still be considered a relative contraindication because side branches spanned by the stent will not be accessible to catheter

JACC Vol. 22, No. 6
November 15, 1993:1641–6

intervention should distal branch disease later develop. Accordingly, the cardiologist must carefully weigh the potential risk of future development of disease in a large side branch supplying a substantial amount of myocardium.

Conclusions. Coronary artery stent implantation is associated with excellent immediate and long-term patency of side branches. Therefore, lesion-related side branches of small to moderate size should not preclude implantation of this device.

Appendix

Study Participants

Clinical Sites and Investigators

Thomas Jefferson University Hospital, Philadelphia, Pennsylvania: Sheldon Goldberg, MD, Michael P. Savage, MD, David L. Fischman, MD. *Washington Hospital Center, Washington, D.C.:* Martin B. Leon, MD. *Scripps Clinic & Research Foundation, La Jolla, California:* Richard A. Schatz, MD, Paul Teirstein, MD. *Cleveland Clinic Research Foundation, Cleveland, Ohio:* Stephen Ellis, MD, Eric Topol, MD. *Yale University, New Haven, Connecticut:* Michael W. Cleman, MD, Henry S. Cabin, MD. *Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania:* John W. Hirshfeld Jr., MD. *The University of Texas Health Science Center at San Antonio, San Antonio, Texas:* Steven Bailey, MD. *Cardiac Institute of the South, Houma, Louisiana:* Craig M. Walker, MD, Jody Stagg, MD.

Core Angiographic Laboratory

Thomas Jefferson University Hospital, Philadelphia, Pennsylvania: David L. Fischman, MD, Michael P. Savage, MD, Sheldon Goldberg, MD, Glenn Morales, RCPT, Sharon Gebhardt, RN.

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