Repeat Coronary Angioplasty as Treatment for Restenosis

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Repeat coronary angioplasty has become the standard approach to a first restenosis. However, the long-term outcome of such a strategy is not well defined. In the present study, 465 patients (mean age 58 years [range 27 to 79], 53% with multivessel disease) underwent a second angioplasty procedure at the same site. The procedure was successful in 96.8% with a 1.5% rate of in-hospital bypass surgery, a 0.9% incidence rate of myocardial infarction and no procedural deaths. Four hundred sixty-three patients (99.6%) were followed up for a mean of 40.5 months. Forty-nine patients (10.6%) underwent a third angioplasty procedure at the same site, 55 (11.8%) had coronary bypass surgery and 33 (7.1%) underwent angioplasty at a different site. During follow-up, 89% of patients had sustained functional improvement and 78% were free of angina. The combined angiographic and clinical restenosis rate was 48%.

Even in the second decade of coronary angioplasty experience, restenosis remains an unresolved problem affecting about 30% of patients with successful dilation. Restenosis has a negative impact on the choice of angioplasty as a revascularization procedure by contributing to diminished efficacy, increased morbidity and unsatisfactory cost-effectiveness (1-12). Although repeat angioplasty at a site of recurrent stenosis is highly successful and has a low complication rate, the long-term results of such an approach are not well defined (13-15). This study reviews the characteristics and long-term outcome of a group of patients who underwent one or more angioplasty procedures as treatment for restenosis.

For the subgroup of 49 patients who had a third angioplasty procedure at the same site, the success rate was 93.9% with a 2% incidence rate of myocardial infarction. There were no in-hospital deaths or coronary artery bypass operations. The mean follow-up interval for this subgroup was 30.5 months with a 22.4% crossover rate to coronary bypass surgery, a 4.1% incidence rate of myocardial infarction and a 2% cardiac mortality rate. At last follow-up, 89% of patients had sustained functional improvement and 78% were free of angina. The combined angiographic and clinical restenosis rate was 48%. Repeat angioplasty as treatment for restenosis is an effective approach associated with a high success rate, low incidence of procedural complications, and sustained functional improvement in combination with an acceptable rate of bypass surgery. However, there is a trend toward diminished angioplasty efficacy after a second restenosis. Thus, decisions for further revascularization should be made after careful review of available options.

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Methods

Study patients. Review of the Cleveland Clinic Coronary Angioplasty Registry revealed that of 5,145 patients who underwent angioplasty between January 1983 and December 1987, 514 (9.4%) underwent repeat angioplasty at the same site. Forty-nine patients who had a repeat angioplasty procedure at the same site within 2 weeks of the initial procedure were considered to have had initial angioplasty failure and were excluded from analysis. The remaining 465 patients formed the study group. Clinical and angiographic characteristics, procedural details and complications were obtained from the Coronary Angioplasty Registry and verified by chart review.

Definitions. Extent of coronary artery disease was defined as the number of epicardial vessels (or major branches) with ≥50% lumen diameter stenosis. Successful balloon angioplasty was defined as <50% residual stenosis after angioplasty with a ≥20% reduction in the original stenosis without a major in-hospital complication (death, myocardial infarction, coronary bypass surgery). Restenosis was defined as ≥50% lumen narrowing at the site of the previous...
dilation. The degree of stenosis was assessed by caliper measurement in the view that demonstrated the maximal severity of the lesion.

Left ventricular dysfunction was assessed by contrast ventriculography and categorized as mild (ejection fraction 46% to 55%), moderate (31% to 45%) or severe (≤30%).

Unstable angina was defined as angina of recent onset in the presence of an accelerating pattern, progressive angina on effort or angina at rest.

Myocardial infarction was defined as a new significant Q wave or elevation of the creatine kinase MB fraction to >30 U/liter in association with ST and T wave changes (non-Q wave).

Angioplasty technique. Standard angioplasty techniques were utilized. Procedural medications included intravenous heparin, intracoronary or intravenous nitroglycerin, or both, antiplatelet therapy (aspirin with or without dipyridamole) and calcium channel blocking agents. Administration of the latter agents was continued for ≥6 months and nitrates were administered for ≥2 days after the procedure. Treatment with aspirin was continued indefinitely.

Follow-up data. Follow-up data were obtained during return visits of patients to the hospital, by contacting referring physicians and from interviews with patients by telephone or mail questionnaire. The follow-up questionnaire included information regarding symptomatic status after angioplasty, subsequent hospitalization, coronary angiography, occurrence of myocardial infarction, coronary bypass surgery, repeat angioplasty or death. In particular, patients were questioned about the presence or absence of symptoms suggestive of angina and categorization of their functional status as representing improvement, worsening or no change in comparison with their functional capacity before angioplasty.

Statistics. Statistical tests of the distribution of discrete variables were performed by chi-square or Fisher exact analysis. Continuous variables were analyzed by Student t test. Survival analysis was performed by the Kaplan-Meier method.

Results

Baseline characteristics. Four hundred sixty-five patients (mean age 58 years [range 27 to 79]) underwent angioplasty at a site of recurrent stenosis. Demographic and pertinent clinical and angiographic data at the time of repeat angioplasty are summarized in Table 1.

Angioplasty results (Table 2). During the first angioplasty procedure, 673 lesions (1.4 lesions/patient) were dilated. At repeat angioplasty for a first restenosis, 612 lesions were dilated (1.3 lesions/patient) including 505 redilated at sites of restenosis. Three patients presented with an evolving myocardial infarction, and in 27 the previously dilated vessel was totally occluded. The mean interval from the initial to the repeat angioplasty procedure was 5.8 months (range 0.5 to 40, median 5.1). Repeat angioplasty was performed ≥12 months after the initial procedure in 30 patients, including 3 patients who underwent repeat angioplasty 24 to 40 months after the initial procedure. The repeat procedure was successful in 96.8% of patients. Eight of the 15 unsuccessful procedures involved patients with a totally occluded vessel. Seven patients (1.5%) required pre-discharge coronary bypass surgery, which was performed electively in four patients and as an emergency procedure in three (0.6%). The four (0.9%) procedure-related myocardial infarctions included one Q wave (1.2%) and three non-Q wave (0.7%) infarctions. Three of these four infarctions were in patients

<table>
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<th>Event</th>
<th>No.</th>
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<tr>
<td>Death</td>
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<tr>
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<tr>
<td>Myocardial infarction</td>
<td>33</td>
<td>3.4</td>
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<tr>
<td>Emergency</td>
<td>3</td>
<td>0.6</td>
</tr>
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Table 2. Results of Angioplasty for a First Restenosis in 465 Patients
who underwent in-hospital coronary bypass surgery. There were no procedural deaths.

Follow-up data. Follow-up data were obtained in 463 patients (99.6%). The mean follow-up duration was 40.5 months (range 0.5 to 79). During follow-up, 125 patients (27%) required additional revascularization by either angioplasty or coronary bypass surgery (Fig. 1). Forty-nine patients (10.6%) had a third angioplasty procedure for a second restenosis at the same site a mean of 7.3 months (range 1 to 36) after the second angioplasty procedure. Thirty-three patients (7.1%) had a third angioplasty procedure at one or more different sites, because of disease progression a mean of 36 months (range 2 to 73) after the second angioplasty procedure. Fifty-five patients (11.8%) required coronary bypass surgery a mean of 17 months (range 1.5 to 64) after the second angioplasty procedure. Overall, revascularization was performed for a second restenosis in 84 patients (18.1%).

During the follow-up period, 21 patients (4.5%) died. 13 (2.8%) of cardiac death. Twelve patients (2.6%) sustained a nonfatal myocardial infarction (Q wave in 8 and non-Q wave in 4): 3 of these 12 patients had crossed over to coronary bypass surgery. Figures 2 and 3 show results of Kaplan-Meier 5-year actuarial cardiac survival analysis and data on freedom from myocardial infarction, coronary bypass surgery, a third angioplasty procedure at the same site and an additional angioplasty procedure at a different site.

At last follow-up of 442 living patients, 388 (88%) had sustained functional improvement and 344 (78%) were free of angina. Of the 385 patients who underwent angioplasty as the only means of revascularization, 334 (87%) reported functional improvement and 301 (78%) were free of angina.

Angioplasty results and follow-up of the patients with a third angioplasty procedure for a second restenosis. Angioplasty was successful in 46 (93.9%) of 49 patients. One patient (2%) sustained a non-Q wave myocardial infarction. Two patients with uncomplicated, unsuccessful dilation underwent elective coronary bypass surgery as a later hospitalization. There were no procedural deaths. The patients were followed up for a mean of 30.5 months (range 1 to 70). During follow-up, 2 patients (4.1%) had a myocardial infarction and 3 (6.1%) died (1 of cardiac death). Eleven (22.4%) underwent coronary bypass surgery. 3 (6.1%) had a fourth angioplasty procedure at the same site and 4 (8.2%) a procedure at a different site. In one patient, the third angioplasty procedure was performed after crossover to coronary bypass surgery. At last follow-up, 41 (89%) of the 47 living patients reported sustained functional improvement and of whom 30 (65.2%) had angioplasty as the only means of revascularization. Thirty-five patients (76%) were free of angina; 26 (56.5%) of these had undergone angioplasty only.

Twenty-eight (61%) of the 46 living patients had angiographic follow-up: recurrence of stenosis was demonstrated.
in 16 of the 28 (57%). The six patients without angiographic follow-up who experienced recurrent angina after a period of symptomatic relief after angioplasty were also considered to have restenosis. Thus, a combined angiographic and clinical restenosis rate of 48% was calculated.

Factors predisposing to a second restenosis. Patients who had a third angioplasty procedure for a second restenosis did not differ significantly with regard to age, gender, hypercholesterolemia, diabetes mellitus, continued smoking, stenosis before and after angioplasty or vessel dilated from the other study patients. However, the mean time interval from the first to the second angioplasty procedure was 3.6 ± 2.4 months for patients who had a second restenosis versus 6.1 ± 4.9 months for those who did not require a third revascularization procedure for a second restenosis (p < 0.0001).

Discussion

This series represents the largest reported experience of repeat angioplasty for treatment of restenosis with 463 patients followed up for a mean of 40.5 months. Although previous studies (13–15) have shown the safety of repeat angioplasty for a first restenosis, because of the short duration of follow-up (mean follow-up times ranged from 8 to 16 months), no solid conclusions could be drawn regarding the long-term impact of such a strategy.

Coronary restenosis. That restenosis remains the major limitation of angioplasty needs no emphasis. Several clinical and anatomic characteristics predisposing to restenosis have been identified (16). These include male gender, diabetes mellitus (10), hypercholesterolemia (17), recent or unstable angina (10,11), previous myocardial infarction (10), continued smoking (17), severity of stenosis before angioplasty, residual stenosis and gradient (9,10), absence of intimal tear (11,18), increased lesion length (19), calcified lesion, eccentricity (9) and left anterior descending artery dilation (11). Efforts to combat restenosis with a variety of drugs, including aspirin, other platelet inhibitors, coumadin (2.20), calcium channel blockers (3.4) and prednisone (21), have been disappointing. Even the much anticipated impact of mechanical devices such as atherectomy and laser catheters, aimed at removing atherosclerotic material from the diseased arterial segment, has been at best limited, with initial reports (22,23) showing recurrent rates of stenosis similar to those of angioplasty. Until biologic modulators with proved effectiveness become part of clinical practice, repeat balloon angioplasty will remain the cornerstone of the nonsurgical approach to restenosis. Use of such an approach requires careful assessment of several factors: safety, immediate success and efficacy as judged by impact on functional status and major events such as death, myocardial infarction, coronary artery bypass surgery and repeat angioplasty.

Success rate of repeat angioplasty. In the present series, the success rate was high for repeat angioplasty performed for a first restenosis (96.8%) and for a third procedure performed for a second restenosis (93.9%). Similar success rates have been reported by other groups (13,15,21) and represent a significant improvement over the success rate of approximately 85% in the earlier (1984) National Heart, Lung, and Blood Institute experience (14).

Safety. The incidence of myocardial infarction for a second angioplasty was 0.86% in this series, and the rate of in-hospital coronary bypass surgery was 1.5% (0.6% for emergency bypass surgery). In patients requiring a third angioplasty procedure for a second restenosis, there was a 2% myocardial infarction rate (one non-Q wave infarction) and no in-hospital bypass surgery was needed. There were no procedural deaths. Similarly low complication rates have been reported by Meier et al. (13) and the National Heart, Lung, and Blood Institute Registry (14).

Efficacy. Efficacy can be viewed as the modification exerted by a procedure on the natural history of a disease. In the patient group studied with a 53% incidence of multivessel coronary artery disease, the actuarial 5-year cardiac survival rate was 96%. This high rate reflects the contribution not only of angioplasty in modifying the natural history of coronary artery disease, but also of coronary bypass surgery, which was needed in 60 patients (12.9%). Nevertheless, a strong case can be made for a prudent revascularization strategy that allows effective application of angioplasty as the initial revascularization procedure and recognizes an important and complementary role for coronary artery bypass surgery when multiple restenoses or progression to more complex forms of disease prevail.

Freedom from major events and restenosis are interrelated. If additional angioplasty at any site is excluded from analysis with the associated angioplasty-related complications included, 77% of patients were free of myocardial infarction, coronary bypass surgery and cardiac death at 5 years. After adding a third or fourth angioplasty procedure at the same site, 71% remained event-free at 5 years. Including angioplasty at any site, 64% of patients remained event-free at 5 years.

These figures could be amenable to a variety of interpretations depending on one's point of view. However, when dealing with the treatment of a debilitating and often progressive disease, incapacitating symptoms (functional status) and morbidity events (myocardial infarction and death) are the focus of attention. The need for coronary artery bypass surgery is an important event that nonetheless should not be ascribed the negative connotation it has been traditionally associated with when it is viewed as a failure of angioplasty strategy. The concept of bypass surgery and angioplasty as being two complementary revascularization procedures in the management of patients with coronary artery disease is not only appropriate, but is being applied in a rapidly increasing number of patients. In this regard, at a mean follow-up of 40.5 months, 88% of patients had experienced sustained functional improvement,
whereas the 5-year actuarial morbid event-free survival rate was 92%.

Third angioplasty for restenosis. The 49 patients who required a third angioplasty procedure for a second restenosis were followed up for a mean of 30.5 months. Three patients (6%) required repeat angioplasty at the same site. 11 (22.5%) required coronary bypass surgery and 30 (65.2%) experienced sustained functional improvement with angioplasty as the only means of revascularization. The combined angiographic and clinical restenosis rate was calculated as 47.8%.

Teirstein et al. (15) have reported the most extensive experience with a third angioplasty procedure for a second restenosis. At a mean follow-up interval of 16 months, 64% of their 74 patients were free of angina after either a third, fourth or fifth angioplasty procedure: 27% required coronary bypass surgery. The restenosis rate after a third or fourth dilation was approximately 50% and factors associated with a third restenosis included a shorter time interval between previous angioplasty procedures and dilation of the left anterior descending coronary artery. In the current study, the only predictor of a second restenosis was a shorter time interval between the first and second angioplasty procedures in those patients who subsequently required a third angioplasty procedure.

The patients who require a third or fourth angioplasty procedure test the limitations of the procedure as a viable alternative in the setting of repeat restenosis, as well as the ability of the interventional cardiologist to rein his emotions and let judgment consistently prevail. There are mixed feelings among the patients of which disappointment and frustration are the most prominent. So, multiple restenoses can be an emotion-laden issue. It is the physician's responsibility to draw the line between a technically feasible versus an effective procedure integrating available information, expectation of sustained results and weighing the risks and benefits of alternate procedures.

Limitations of the present study. Complete angiographic follow-up after a second or third angioplasty procedure would be desirable. However, from a strictly clinical viewpoint, the length of the follow-up period in this study (mean 40.5 months) temporizes the lack of such information. The value of diagnostic catheterization procedures for precise anatomic definition notwithstanding, it is the clinical events and the patient's functional status that define the efficacy of any revascularization procedure.

Conclusions. The current series consists of a large number of patients followed up over a long period of time and treated according to the prevailing and ever changing trend of angioplasty practice by various physicians. When applied judiciously as treatment for restenosis, angioplasty is an effective approach, associated with a high success rate and a low incidence of procedural complications, that provides sustained functional improvement in combination with an acceptable rate of crossover to coronary artery bypass surgery. There is a trend for diminished efficacy after a second restenosis. Therefore, decisions for further revascularization should be made after careful review of available options.

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References