Evaluation of Transluminal Angioplasty of Chronic Coronary Artery Stenosis

Value and Limitations Assessed in Fresh Human Cadaver Hearts

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SUMMARY The possibility of increasing reduced blood flow in atherosclerotic coronary obstruction by catheter balloon dilatation offers a nonsurgical approach to relieve clinical coronary stenosis. To assess the ability of effectively dilating such diseased vessels by transluminal angioplasty, we used the Grünzig balloon-tipped catheter in 12 fresh human cadaver hearts in which the intervention was performed in 21 noncalcified stenotic areas, including each of the three major coronary arteries. Quantitative coronary arteriography documented decreased obstruction of each lesion; luminal diameter increased 58% (1.9 ± 0.2 mm to 2.8 ± 0.3; p < 0.001) and luminal diameter relative to the most proximal normal coronary segment diminished 61% (46 ± 4% to 18 ± 3%; p < 0.001). Angioplasty was most successfully applied in proximal, discrete, noncalcified lesions of the right and left anterior descending coronaries; calcified, tortuous, middle and distal lesions and the left circumflex coronary were entered with difficulty or unapproachable. Histologic examination revealed microanatomic changes, most often endothelial disruption and atheroma compression, but no serious vascular tears. Dilatation beyond normal coronary diameter caused vessel rupture. This study extends elucidation of the value and limitations of percutaneous transluminal angioplasty in the clinical use of this technique in selected patients for relieving coronary obstruction without surgery.

THE DESCRIPTION of a practical, nonsurgical technique for improving blood flow through peripheral atherosclerotic lesions by compression of atheroma by balloon catheter dilatation has caused considerable interest in extending this approach to patients with coronary artery disease. To further elucidate the value and limitations of percutaneous transluminal coronary angioplasty, we report our experience using a balloon-tipped catheter to dilate coronary stenotic lesions in human cadaver hearts. We investigated the potential for this technique to 1) increase the diameter of coronary artery segments narrowed by atherosclerotic obstruction, 2) assess the location and types of lesions that can be dilated, 3) determine the maximum dilating capacity of the coronary arteries, and 4) evaluate the dilated areas histologically.

Methods

Twelve intact postmortem human hearts were obtained within 24 hours after death from patients who died of complications of coronary heart disease (10 sudden death and two myocardial infarction). After removal from the body, each heart was mounted by needles on a paraffin block and placed under a fluorescent camera equipped with cineangiographic capabilities. An end-hole catheter was positioned in each of the coronary ostia. Coronary arteriography was done by injecting meglumine diatrizoate (Renografin-76) into each of the coronary arteries in the fixed right anterior oblique and/or left anterior oblique views. Stenotic lesions were identified and quantitative measurements were made on enlarged 8" × 10" roentgenograms with correction for magnification by known diameters of the angiography and balloon catheters. All hearts had at least one coronary artery with atherosclerotic luminal narrowing. There were 41 atherosclerotic coronary arteries with reduction in luminal diameter of 26–96% before angioplasty intervention. Dilatation of all diseased coronary arteries was attempted. We used a balloon-tipped catheter (Schneider Co., Zurich, Switzerland) specially designed for intraoperative use for this purpose clinically. The catheter was inserted with the balloon deflated (fig. 1A) into each coronary artery and positioned with the balloon at the site of the stenosis. The type (calcified or noncalcified), location and severity of each lesion, as well as the ease of catheter placement, were assessed in each of the three major coronary arteries of each heart.

To simulate the clinical procedure, four or five balloon inflation-deflation cycles were applied using five times atmospheric pressure during inflation (fig. 1B). Each cycle was 5–8 seconds in duration and inflation diameter was extended to approximate the diameter of the most proximal, angiographically normal segment. To determine the capacity of the
A. Lm 3mm
B. w-itd 3MM

FIGURE 1. Intraoperative Gruntzig balloon-tipped catheter for clinical dilatation of coronary atheromatous obstruction used A) before and B) after balloon inflation.

stenotic lesions to dilate, repeat coronary angiography and quantitative measurements were performed after balloon dilatation.

In addition, each of the dilated segments was sectioned and examined histologically. Preparation before microanatomic examination included rinsing the unfixed cadaver heart with water, flushing the coronaries with normal saline, injecting a warm gelatin-barium mixture into each coronary artery and cooling the heart rapidly in ice water. After solidification of the gelatin-barium mixture, each heart was fixed in 10% formalin. Histologic preparation did not disturb predilated microanatomy, as ascertained by examination of normal coronary segments and undilated atherosclerotic coronary segments not subjected to catheter intervention. Radiographs of the coronaries were then repeated of the formalin-fixed heart, so that magnification of these cineangiograms provided precise identification of the site of previously dilated coronary vessels selected for microscopic study. The entire coronary arteries for analysis were then dissected from the heart, carefully labeled as to site of balloon dilatation, and multiple series of cutblocks were obtained. These labeled blocks of coronary arteries were then embedded in paraffin and sectioned for staining with hematoxylin and eosin and trichrome and elastic stains. Approximately 15 blocks from each coronary artery analyzed were so prepared for histologic examination.

Statistical significance was determined by the t test for paired data. Quantitative data are expressed as mean ± SEM.

Results

Effect of Dilatation on Stenotic Lesions

Dilatation was accomplished in 21 noncalcified stenotic areas in the 12 fresh human cadaver hearts. Each of these stenotic areas was examined angiographically before and after the procedure. The predilatation stenotic luminal diameter was significantly increased after balloon dilatation from 1.9 ± 0.2 mm to 2.8 ± 0.3 mm (p < 0.001) (fig. 2). This increase in luminal diameter after dilatation of these 21 non-calcified, obstructive lesions was 13–200% (average 58%). Comparison of the percent obstruction in luminal diameter relative to the most proximal angiographically normal coronary artery segment

FIGURE 2. Extent of luminal diameter widening of the 21 diseased coronary arteries dilated by the Gruntzig balloon-tipped catheter.
before and after dilatation revealed a significant decrease from 46 ± 4% predilatation to 18 ± 3% postdilatation (−61%, p < 0.001) (fig. 3). Further, there was a decrease in luminal stenosis after dilatation in each of these 21 noncalcified lesions.

**Efficacy of Procedure Relative to Location and Type of Coronary Lesion**

The right coronary arteries were entered (14 noncalcified, dilatable lesions) more readily (figs. 4 and 5) than the left coronary arteries (seven noncalcified, dilatable lesions). In the left coronary artery system, the left anterior descending coronary arteries were entered more easily than the left circumflex arteries. The proximal third of all three major arteries was more accessible to balloon dilatation (11 of 11 noncalcified lesions) (fig. 4) than the middle third (10 of 15 noncalcified lesions). The balloon catheter could not be passed into the distal third of any of the left coronary arteries (four with distal stenosis), and in only three of the 12 hearts could this be achieved in the right coronary artery (five with distal stenosis). Tortuous vessels were also difficult to enter. The balloon catheter could not be passed through three of six heavily calcified stenotic lesions. Of the three other heavily calcified lesions in which the balloon-tipped catheter could be positioned at the stenosis site, no improvement in luminal diameter was produced.

**Dilating Capacity of Coronary Arteries**

Neither coronary rupture nor gross evidence of trauma was observed when balloon inflation was expanded to the extent of angiographically normal coronary diameter (figs. 4 and 5). However, coronary rupture did occur in the diseased area of three of the four arteries in which balloon inflation was produced.

**Figure 3.** Comparison of the percent luminal diameter obstruction relative to the most proximal angiographically normal coronary artery segment before and after the balloon dilatation procedure.

**Figure 4.** Representative example of the efficacy of balloon angioplasty in the successful dilatation of discrete obstructive lesions of the right coronary artery. Two areas of proximal (upper two arrows) and one area of middle (lower arrow) vessel stenoses are shown angiographically before (left) and after (right) balloon inflation.
Pre-Dilation

Post-Dilation

Figure 5. Representative example of effective balloon dilatation of an isolated area of mid-right coronary artery obstruction (arrows) shown by angiography before (left) and after (right) dilatation.

Figure 6. Representative example of diseased vessel rupture (arrows) of the distal portion of the right coronary artery produced by excessive expansion of the balloon-tipped catheter, shown angiographically before (left) and after (right) intervention. Intramyocardial extravasation of contrast dye is evident after dilatation (right arrow).

to a diameter approximately twice that of the non-diseased proximal normal coronary segment (fig. 6). The ruptures involved the middle (two vessels) and distal (one vessel) (fig. 6) thirds of the coronary arteries in which the procedure was performed.

Microanatomic Examination of Dilated Coronary Areas

One or more of six different types of alterations were observed on histologic examination of dilated segments from coronary arterial walls after balloon dilatation.
Transluminal coronary angioplasty (fig. 7). These changes included: 1) endothelial disruption of the intimal lining, 2) derangement of collagenous and elastic fibers within the tunica intima, 3) disturbance of smooth muscle and connective tissue in the tunica media, 4) separation of collagen comprising fibrous areas of scar formation, 5) stretching of the tunica adventitia surrounding the vessels, and 6) compression of atheroma with calcified plaques remaining intact. While these changes were randomly distributed among the dilated coronary arteries, disruption of the endothelium and atherosomatous compression were the most common findings (fig. 7). There were neither ruptures of the entire wall nor severe intimal tears in any of the blood vessels expanded according to the therapeutic procedure. Usually the types of wall layer disruptions delineated above were minute, requiring microscopic detection, without gross evidence of vessel damage.

**Discussion**

This study shows that coronary stenoses of clinically significant severity are amenable to considerable dilatation by balloon-tipped catheters. In noncalcified lesions, this technique produced a major increase (average 58%) in luminal diameter (fig. 2), shown by quantitative coronary angiographic measurements. In addition, there was a significant decrease (−61%) in luminal obstruction in relation to the patent, upstream, nondiseased coronary artery segment (fig. 3). However, the technique appears to be of limited applicability in calcified lesions and in tortuous coronary vessels, as we had considerable difficulty in passing the balloon catheter through heavily calcified lesions and there was no increase in luminal diameter of such segments after the dilatation procedure. The catheter either could not be passed through tortuous vessels or traversed them with
difficulty, and passage beyond the middle or distal third of the coronary arteries was problematic and not readily achieved in any of the three major vessels. In our experience, the right coronary artery was entered more easily by the balloon catheter (figs. 4 and 5) than the left coronary artery, and the left anterior descending coronary artery was generally more accessible to the balloon catheter than the left circumflex coronary artery. Coronary rupture occurred only when maximum balloon inflation greatly exceeded the diameter of the normal coronary segment (fig. 6). While the cadaver model is useful for evaluating the angioplasty technique, the isolated heart does not necessarily simulate certain important aspects of the intact, viable coronary artery system, such as vascular tonus, which may impede or render the dilatation procedure more difficult than in the passive, cadaver coronary vessels.

Microscopic examination of the dilated regions of the moderately and severely diseased coronaries revealed minimal disruption of the arterial wall substructure with compression of atheroma causing mild, stenotic and subtotal obstructions (fig. 7). Marked tears of the expanded vessels were not observed after balloon dilatation to the extent carried out clinically. In addition, to further simulate the procedure in patients, the dilatation catheter was not forced through tight lesions. Our findings show that the endothelial, medial or adventitial layers are not strictly intact, in contrast to postmortem studies by two other groups. Nevertheless, the histologic disturbances delineated herein were microscopic, unlike the major vascular dissections in cadaver hearts reported in a third investigation in which the dilatation catheter was forced into obstructing lesions. Moreover, our macroanatomic observations are consistent with the clinical results of transluminal angioplasty of atheromatous obstruction in which macroscopic damage of the dilated coronaries has not been produced.

The concept of transluminal dilatation of arteriosclerotic lesions was originated by Dotter and Judkins in 1962. They produced dilatation of peripheral arterial lesions by using progressively larger dilatation catheters. Luminal enlargement was shown to be secondary to compression of the obstructive atheromatous plaque and success rate was greater than 80%. More recently, Grünzig designed and used a single catheter with a distensible balloon segment at its tip, which was positioned in the lumen at the site of the stenotic peripheral arterial segment. Balloon inflation then resulted in compression of the atheromatous lesion, thereby increasing the diameter of the lumen. After balloon dilatation, immediate, objective improvement at the site of the lesion was documented by angiography. In initial trials, the procedure has been effective and is brief, relatively inexpensive and causes little discomfort. Furthermore, compared with reconstructive surgery, risks of mortality and morbidity are reduced because the technique requires neither general anesthesia nor surgical incisions. In over 225 patients who have undergone peripheral percutaneous transluminal angioplasty since 1971, there has been an 84% initial patency rate and a 73% patency rate after 2 years. Moreover, the great majority of patients had concomitant major symptomatic improvement.

Percutaneous transluminal angioplasty with smaller balloon-tipped catheters has been recently extended to the coronary vessels. Initially, the canine model was used to evaluate the balloon catheters and ancillary apparatus, and to assess the ability to dilate the coronary lesions and document the potential for complications. After assessment in experimental animals, the procedure was extended to the clinical setting by intraoperative coronary dilatation during the course of aortocoronary bypass graft surgery. This was carried out by advancing a balloon catheter (fig. 1) through an arteriotomy into a coronary artery and then to the lesion; after balloon dilatation, there was no evidence of embolic debris as evaluated by millipore filter collection distal to the lesion.

Initial results of coronary percutaneous angioplasty in patients with coronary artery disease indicate beneficial anatomic and clinical effects. Of 54 patients in whom the balloon catheter was successfully positioned at the site of the lesion, 49 (91%) had successful dilatation, as shown by a decrease in the degree of luminal obstruction and improvement in exercise stress testing and/or thallium scintigraphy at least 3 months later. In patients in whom coronary arteriography was repeated 6–9 months after coronary percutaneous transluminal angioplasty, a further improvement of vessel patency and internal wall smoothness after dilatation was noted. Although the potential for complications by this procedure is apparent, no deaths, major myocardial infarction or coronary rupture have been reported.

In conclusion, initial evaluation of percutaneous transluminal coronary angioplasty suggests its potential for beneficial applications in selected patients with coronary artery disease. Appropriate patients for this procedure will probably constitute a minority of patients with coronary artery disease suitable for operative revascularization. Nevertheless, the percutaneous angioplasty technique appears capable of obviating the need for coronary artery bypass surgery in certain coronary patients requiring relief of atheromatous obstruction. The results we report, as well as our clinical experience, indicate that patients in whom percutaneous angioplasty appears most promising are those with proximal, discrete, noncalcified obstructive lesions, particularly in the left main, left anterior descending and right coronary arteries. An additional potential of the catheter dilatation method is in patients with discrete stenosis of a bypass graft, a proportion of whom may be candidates for graft dilatation, thereby eliminating the necessity for repeat surgical intervention. However, early graft stenosis may be inflammatory or traumatic, and late graft stenosis is often a diffuse and extensive process; therefore, the results of graft dilatation may be less satisfactory than in native atheromatous disease.
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