MORPHOLOGIC STUDIES

Morphologic Observations After Percutaneous Transluminal Balloon Angioplasty of Early and Late Aortocoronary Saphenous Vein Bypass Grafts

BRUCE F. WALLER, MD, FACC,∗† DONALD A. ROTHBAUM, MD, FACC,‡
H. JOEL GORFINKEL, MD, FACC,§ THOMAS M. ULBRIGHT, MD,*
THOMAS J. LINNEMEIER, MD,‡ STEPHEN M. BERGER, MD, FACC§

Indianapolis, Indiana and Columbus, Ohio

Clinical and morphologic observations from two patients undergoing percutaneous transluminal angioplasty of stenotic aortocoronary saphenous vein bypass grafts early (3 months) and late (56 months) after graft insertion are described. Each patient had one or more clinically successful graft dilations resulting in an angiographic increase in luminal diameter and a decrease in mean transstenotic gradient, and each had restenosis of the graft at the site of previous angioplasty within 2 months of dilation. Both operatively excised grafts had diffuse but variable amounts of intimal fibrous thickening and severe narrowing at the previous angioplasty site. The early graft had no evidence of dilation injury, and the intimal thickening consisted solely of fibrocollagenous tissue free of calcific deposits. In contrast, the late graft had a healing intimal dissection at the angioplasty site, and the intimal thickening consisted of atherosclerotic plaque with calcific deposits.

Angiographic and morphologic correlations suggest that the mechanism of saphenous vein angioplasty early (<1 year) after insertion is by graft "stretching," while late (>1 year) after insertion it is by atherosclerotic plaque "fracture" similar to that observed in atherosclerotic coronary arteries subjected to angioplasty procedures.

Several reports (1,2) of percutaneous transluminal angioplasty have demonstrated its clinical usefulness as a nonoperative treatment for atherosclerotic coronary disease. Recently, application of this technique has been extended to obstructed aortocoronary saphenous vein bypass grafts (3–6). Although early and late morphologic changes in human coronary arteries subjected to percutaneous transluminal angioplasty have been reported (7,8), only acute morphologic changes in a single saphenous vein bypass graft undergoing angioplasty have been described (9). The present report describes clinical and morphologic observations from two patients undergoing percutaneous transluminal angioplasty of saphenous vein bypass grafts early and late after graft insertion and suggests possible therapeutic implications resulting from morphologic analysis of bypass grafts.

Case Reports

Case 1: Angioplasty of Saphenous Vein Graft Early (<1 year) After Bypass Surgery

Clinical features. A 63 year old man (Table I, Fig. 1 to 3) with angina pectoris underwent percutaneous transluminal angioplasty of the left anterior descending coronary artery on March 11, 1983. Despite an initially successful dilation, this artery suddenly closed. Multiple balloon inflations did not keep the artery from reclosing and the patient underwent aortocoronary saphenous vein bypass grafting to this artery. Seven weeks after bypass surgery, the patient had recurrent angina pectoris, and angiography disclosed 95% symmetric diameter reduction of the saphenous vein bypass graft at the proximal (aortic) anastomotic site. The vein graft was dilated during angioplasty, resulting in a
Table 1. Clinical and Morphologic Data From Two Patients Undergoing Percutaneous Transluminal Balloon Angioplasty of Stenotic Saphenous Vein Bypass Grafts Early (≤ 1 year) and Late (>1 year) After Aortocoronary Bypass Operation

<table>
<thead>
<tr>
<th>Observation</th>
<th>Case 1: Early Graft (63 yr/male)</th>
<th>Case 2: Late Graft (42 yr/male)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mo) of SV graft</td>
<td>3</td>
<td>56</td>
</tr>
<tr>
<td>Interval (mo) from bypass operation to PTA</td>
<td>2</td>
<td>52</td>
</tr>
<tr>
<td>Interval (mo) from PTA to SV graft excision</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Angiography-angioplasty data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal SV graft narrowing (% DR) (location) before PTA</td>
<td>95 (proximal)</td>
<td>95 (mid)</td>
</tr>
<tr>
<td>Maximal SV graft narrowing (% DR) after PTA (total ↓)</td>
<td>10 (50%)</td>
<td>25 (70%)</td>
</tr>
<tr>
<td>Mean intra-graft pressure (mm Hg) before → after PTA (total ↓)</td>
<td>37 → 4 (33)</td>
<td>60 → 15 (45)</td>
</tr>
<tr>
<td>Number of balloon inflations</td>
<td>Multiple</td>
<td>4</td>
</tr>
<tr>
<td>Maximal balloon inflation pressure (atm)</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Duration (seconds) of balloon inflation</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>Dilating catheter(s)</td>
<td>S25-30</td>
<td>G20-30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiographic ’dissection’ or ’split’ before SV excision</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Maximal SV graft narrowing (% DR)</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Morphologic data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal SV graft narrowing (% XSA)</td>
<td>76 to 100</td>
<td>76 to 100</td>
</tr>
<tr>
<td>Graft narrowing (% XSA) at site of PTA</td>
<td>76 to 100</td>
<td>76 to 100</td>
</tr>
<tr>
<td>Cause of graft narrowing</td>
<td>IFT</td>
<td>IFT + AP</td>
</tr>
<tr>
<td>Calcific deposits</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Evidence of PTA</td>
<td>Yes*</td>
<td></td>
</tr>
</tbody>
</table>

*Loss of endothelial lining in area of balloon dilation but no tears, breaks or cracks; †healing intimal separation (intimal flap); AP = atherosclerotic plaque; DR = diameter reduction; IFT = intimal fibrous thickening; mo = months; PTA = percutaneous transluminal angioplasty; SV = saphenous vein; total ↓ = total decrease; XSA = cross-sectional area.

marked increase in luminal diameter. Four weeks after successful bypass graft angioplasty (3 months after graft insertion), the patient had recurrent angina. On June 15, 1983, angiography again disclosed severe graft narrowing (restenosis) at the previous dilation site. This time, however, the stenotic segment was not smooth and symmetric, but irregular and asymmetric. Because of the angiographic appearance of the stenotic segment and the rapid recurrence of stenosis, the patient underwent repeat bypass grafting. The proximal portion of the graft was excised at operation.

Morphologic features. The operatively excised portion of the saphenous vein graft (Fig. 1) was 40 mm long and free of calcific deposits. The excised segment included the site of maximal balloon inflation and a short distal portion in which the dilating catheter and guide wire had passed, but in which balloon inflation had not occurred. The external diameter of the proximal 30 mm of graft (dilated segment) was slightly wider compared with the external diameter of the distal 10 mm (nondilated segment). The entire specimen was cut transversely into 5 mm segments labeled 1 to 8. Segments 1 to 6 were from areas of previous balloon dilation, and segments 7 and 8 were from nondilated areas. The lumen of each of the eight 5 mm saphenous vein segments was narrowed more than 75% in cross-sectional area by intimal thickening (Fig. 2).

Histologically, the diffuse intimal thickening of both dilated and nondilated segments consisted of cellular fibrocollagenous tissue without foam cells or cholesterol clefts (intimal "fibrous hyperplasia," "fibrous proliferation"). Segments 1 to 8 were serially sectioned at 10 μm intervals and searched for sites of "splits," "tears," "cracks" or other morphologic evidence of previous angioplasty. Histologic assessment by light microscopy did not disclose any distinctive morphologic lesions in the intimal, medial or adventitial layers of dilated or nondilated segments of the saphenous vein graft.
Figure 1. Case 1. Operatively excised portion of a 3 month old saphenous vein graft. Top, The diameter of the proximal portion (aortic anastomotic end [AI]) subjected to percutaneous transluminal angioplasty (PTA) is slightly wider than the diameter of the distal nondilated segment. The numbers represent sites of transverse sections appearing in Figure 2. Bottom, Radiograph of specimen discloses no calcific deposits.

Ultrastructural evaluation of segments 2 (dilated) and 8 (nondilated) (Fig. 3) disclosed the absence of endothelial luminal cells in the dilated segment compared with their presence in the nondilated segment. No distinctive differences in myofibroblasts or collagen fibrils were noted between segments 2 and 8.

Case 2. Angioplasty of Saphenous Vein Graft Late (>1 year) After Bypass Surgery

Clinical features. A 42 year old man (Table 1, Fig. 4 and 5) was hospitalized with acute myocardial infarction in February 1978. Continued chest pain prompted coronary angiography and subsequent double aortocoronary saphenous vein bypass grafting to the left circumflex coronary artery (marginal branch and distal left circumflex artery). Repeat angiography for recurrent chest pain 3 years later (1981) disclosed total occlusion of the graft to the distal left circumflex artery and 50% diameter reduction in the mid portion of the graft to the left circumflex marginal branch. The patient underwent repeat aortocoronary bypass operation with insertion of new grafts to the left anterior descending and right coronary systems. In June 1983, angina pectoris recurred and repeat angiography showed that the graft to the right coronary artery was open, the graft to the left anterior descending system was closed and the graft to the left circumflex marginal branch was narrowed 95% in diameter. The patient underwent percutaneous transluminal angioplasty of the left circumflex graft (52 months after graft insertion), resulting in decreased graft luminal narrowing and decreased transstenotic mean pressure gradient (Table 1). Two months later, he had recurrent angina and angiography disclosed 95% diameter narrowing of the left circumflex graft at the site of previous angioplasty dilation.

A second angioplasty of the left circumflex graft was performed with serial dilations using progressively larger balloons and variable inflation pressures and durations (Table 1). The dilations resulted in decreased graft luminal narrowing and decreased mean transstenotic gradient. Angiograms disclosed a localized dissection ("break," "crack," "fracture") at the angioplasty site (Fig. 5A). Recurrent angina 2 months later prompted a sixth coronary angiogram which disclosed restenosis (95% diameter reduction) of the graft to the left circumflex marginal branch. The patient underwent a third aortocoronary bypass operation and the mid portion of the left circumflex graft was excised.

Morphologic features. The operatively excised portion of saphenous graft was 42 mm long and had foci of calcific deposits in the area of dilation. The entire specimen was cut transversely into 5 mm long segments labeled 1 to 8 (Fig. 4). Segments 4 to 6 were from the site of maximal balloon inflation and the area of the angioplasty dissection noted angiographically was specifically localized on the excised saphenous vein specimen (Fig. 5). The lumen of each of the eight 5 mm saphenous vein segments had diffuse but variable degrees of intimal thickening (Fig. 5). The maximal cross-sectional area luminal reduction by intimal thickening occurred in segments 4, 5 and 6.

Histologically, the intimal thickening in segments 4 to 6 consisted of foam cells, cholesterol clefts, fibrocollagenous tissue, foci of myofibroblasts and calcific deposits characteristic of atherosclerotic plaque. Intimal thickening of segments 1 to 3 and 7 and 8 were predominantly fibrocollagenous in nature except for occasional foci of foam cells, cholesterol clefts and calcium. The site of angioplasty dissection (segments 4 to 6) (Fig. 4 and 5) had partial separation of the intima from the media. This "intimal flap" had begun to reattach to the wall of the graft (Fig. 5), representing healing of a localized plaque tear or fracture.

Discussion

Early versus late vein graft stenosis. Each of the two patients described in this report had one or more clinically successful percutaneous transluminal angioplasty dilations of a stenotic saphenous vein bypass graft early (2 months) or late (52 and 54 months) after graft insertion. Angiographic similarities between the early (Case 1) and late
Figure 2. Case 1. Morphologic and histologic photographs of the eight segments of the early saphenous vein graft corresponding to the sites labeled in Figure 1. Segments 1 to 6 are from the area of balloon inflation and dilation, and segments 7 and 8 are from nondilated portions of the graft ("controls"). Each of the eight segments has diffuse and severe cross-sectional area luminal narrowing by intimal thickening consisting of fibrocollagenous tissue. No segments contain atherosclerotic plaque or calcium deposits. No distinctive histologic changes are observed in the segments subjected to balloon angioplasty compared with control segments. (Elastic stains, magnification ×6, reduced by 9%.)

(Case 2) Saphenous vein grafts included an increase in luminal diameter associated with a decrease in mean transstenotic gradient after angioplasty, and restenosis of the bypass graft at the site of previous dilation 1 or 2 months later. Angiographic differences between the grafts included the absence of cracks, breaks or splits after dilation in the early graft, but the presence of an intimal split after the second angioplasty procedure in the late graft, and the proximal versus mid segment location of the graft stenosis in the early and late grafts, respectively.
Figure 3. Case 1. Light and electron micrographs of dilated (segment 2 [A, B and C]) and nondilated (segment 8 [D, E and F]) portions of the early saphenous vein graft. Light micrographs of dilated (A) and nondilated (D) segments show that both segments have marked intimal thickening (I) composed of smooth muscle cells and fibrocollagenous tissue (elastic stains, magnification × 40). Electron micrographs at the luminal border of dilated (B) and nondilated (E) segments show a loss of endothelial cells lining the saphenous vein lumen (L) in the dilated segment (magnification × 8,300). Electron micrographs from deeper portions of the intimal thickening of the dilated (C) and nondilated (F) segments show similar types of myofibroblastic cells (MF) and dense bundles of collagen fibrils (magnification × 8,300, reduced by 20%).
Morphologic similarities between the grafts included diffuse intimal thickening by fibrocollagenous tissue with fibrotic medial and adventitial layers. Morphologic differences were distinct: the early graft had a thickened intima without atherosclerotic plaque changes or calcific deposits and no morphologic evidence of previous dilations, whereas the late graft had a thickened intima typical of atherosclerotic plaque with focal calcific deposits and morphologic evidence of dilation injury.

Therapeutic implications for saphenous vein angioplasty derived from morphologic observations. Functionally significant saphenous vein bypass graft stenoses developing between 1 month and 1 year (early) after graft insertion usually are characterized by intimal thickening histologically composed of cellular or acellular fibrocollagenous tissue. The venous medial and adventitial layers become fibrotic and the graft resembles a thick fibrous tube. Focally stenotic lesions produced by this intimal thickening appear amenable to dilation by balloon angioplasty, as illustrated by Case 1. However, in view of the histologic composition of the intima, the dilating mechanism is probably not "intimal compression" (3) or "breaking" but rather graft "stretching" (Fig. 6). Depending on the degree of graft stretching, the dilating procedure may have limited...
therapeutic success (week to months) with graft restenosis representing gradual "restitution of tone" of an overstretched graft segment.

Saphenous vein graft stenoses occurring beyond 1 year (late) and generally after 3 years after graft insertion usually consist of atherosclerotic plaque and intimal fibrous thickening (10–16). The atherosclerotic plaque in a saphenous vein graft appears morphologically similar to that observed in native coronary arteries: foam cells, cholesterol clefts, blood product debris, fibrocollagenous tissue and calcific deposits (14,17). Focal stenoses produced by this type of lesion also appear amenable to dilation by balloon angioplasty, as illustrated in Case 2. The mechanism or mechanisms of graft dilation in this setting appear similar to that proposed for coronary artery angioplasty: plaque splitting, cracking or breaking with or without localized intimal-medial dissection (Fig. 6) (7,18,19). Therapeutic limitations in dilating saphenous vein grafts narrowed by atherosclerotic plaque should be similar to those observed in atherosclerotic coronary arteries subjected to transluminal angioplasty.

In addition to age of the bypass graft, at least two other anatomic factors appear to influence the therapeutic success of percutaneous transluminal angioplasty of saphenous vein bypass grafts: 1) length of stenosis, and 2) location of stenosis. Long stenotic segments (> 15 to 20 mm) of saphenous vein are frequently technically more difficult to dilate and are associated with a lower primary therapeutic success compared with short stenotic segments (≤ 5 mm) (3,6). Graft stenoses may be located at anastomotic sites (aorta-graft or coronary artery-graft) or within the body of the graft. Angiographic studies (3–6) have suggested that saphenous vein graft stenoses at the coronary artery-graft anastomotic site have the best therapeutic results, followed by lesions in the graft body and at the aorta-graft anastomotic site, respectively. An anatomic factor supporting the relatively high success rate of dilating stenotic coronary artery-graft anastomotic sites is the presence of atherosclerotic plaque in the coronary portion of the anastomosis (13). Stenoses in the graft body or aortic anastomotic site are less likely to have the potential angioplasty advantage of associated atherosclerotic plaque unless the graft is older than 3 years of age (12,14–16).

Previous reports. Although therapeutic implications derived from the morphologic evaluation of two patients with saphenous vein angioplasty are limited, early angiographic results of 112 saphenous vein grafts subjected to balloon angioplasty (4–6,8) support the preceding described clinical and morphologic claims. Of 62 grafts reported by Douglas et al. (5), 40 (65%) were dilated early (≤ 1 year)
Figure 6. Diagram illustrating possible mechanism of percutaneous transluminal balloon angioplasty in stenotic aorto-coronary saphenous vein (SV) bypass grafts. Two types of lesions characterize the saphenous vein stenoses depending on the interval from graft insertion to obstruction. In early (≤1 year) lesions, grafts (a, left) contain intimal thickening composed primarily of fibrocollagenous tissue without calcium, and dilation is probably accomplished by graft stretching. In late (>1 year) lesions, grafts (a, b and c, right) contain intimal thickening composed of atherosclerotic plaque and calcium, and dilation is accomplished by plaque compression (unlikely), graft stretching or plaque fracture or break (B) (most likely). Ao = aorta; LAD = left anterior descending coronary artery; LC = left circumflex coronary artery; LM = left main coronary artery.

and 22 (35%) were dilated late (>1 year) after insertion. Of the early grafts, primary success occurred in 37 grafts (93%) with restenosis 6 months or later in 9 (24%). Of the 22 late grafts, primary success occurred in 21 grafts (95%) with the same restenosis rate as for the early grafts (24%). Breakdown of the early and late grafts into stenosis location sites revealed the distal bypass graft stenoses (early and late) had a high initial dilation success and lower restenosis rate. Graft stenoses located in the body or proximal end had a slightly lower initial dilation success, but three times the restenosis frequency compared with those in distal sites (39 versus 13%).

Block et al. (6) recently reported results of saphenous vein angioplasty in 40 patients. Initial angioplasty success occurred in 31 grafts (78%) with restenosis within 8 months occurring in 38%. Although a detailed breakdown of all graft ages was not provided, six patients had bypass grafts inserted 60 months or longer before angioplasty. Four of the six late graft dilations were successful, with only one restenosis. Furthermore, of all graft restenoses, 59% occurred in proximal graft or aorta-anastomotic sites compared with only 15% restenosis in the mid to distal graft or coronary artery anastomotic sites.

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References


