Venous Valve Station Changes in "Primary" and Postthrombotic Reflux: An Analysis of 149 Cases

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The purpose of this study was to analyze valve station changes noted during venous valve reconstruction and the associated outcome. One hundred and forty-nine valve reconstructions were available for analysis at the time of surgical exploration; the venous valve was graded according to valve station changes (VS grades) from zero through six. Ascending venography was analyzed by a similar grading system and the two methods were compared. The results of this analysis showed that valve station wall changes are frequently present in patients with deep venous reflux and pose technical challenges during valve reconstruction; the outcome, however, appears unaffected. Grade 0 to 1 valve station changes are predominantly due to "primary" reflux, with an occasional instance of postthrombotic etiology. Grade 2 or 3 valve station changes are roughly evenly divided between phlebosclerosis of primary reflux and postthrombotic etiologies. The mechanism of onset of reflux with preservation of valve cusps in the latter group of postthrombotic cases is probably different from currently accepted theories of evolution of postthrombotic changes. Postthrombotic valve damage is variable, and the valve station anatomy may be sufficiently preserved in some patients to allow direct valve repair. (Ann Vasc Surg 2000;14:193-199.)
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INTRODUCTION

Venous valve reconstruction is effective in healing stasis ulceration and relieving symptoms of severe, chronic deep venous insufficiency.[1] The results are durable,[2] extending 10 years and beyond[3,4] after valve reconstruction. Although internal valvuloplasty is the original technique used for valve reconstruction, several other techniques for repairing the existing valve apparatus ("direct" repair) have since come into vogue.[5] If the valve apparatus has been damaged beyond repair by postthrombotic changes, however, a direct repair technique will not be feasible. An "indirect" technique, such as axillary vein valve transfer, is the preferred alternative under such circumstances.[5] In the course of our experience with venous valve reconstruction, we have noted that approximately 40% of patients undergoing valve repairs exhibited significant valve station wall changes. These changes consisted primarily of adventitial and muscular thickening and fibrosis, rendering the repaired valve segment opaque and obscuring the normally visible valve attachment lines on external inspection. Wall thickening was sometimes associated with periphlebitic inflammation. In some patients, these changes were confined to the venous wall without gross intimal changes; in others, endothelial changes on the valvular tissue and adjacent intima were also grossly visible. When associated with intraluminal trabeculae, such endothelial changes are obviously postthrombotic. Valve station wall changes with or without intimal and valvular involvement pose

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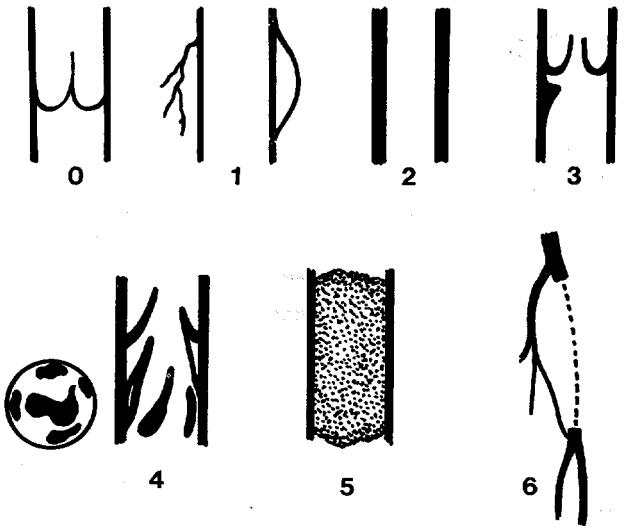

Fig. 1. Surgical grading of valve station changes grades 0 through 6 (see text for details).

etiological questions and obviously have an impact on the choice of techniques at the time of surgery. In this report, we provide an analysis of radiological and surgical findings with particular reference to valve station changes in 149 patients undergoing valve reconstruction surgery.

MATERIALS AND METHODS

A total of 149 superficial femoral valve explorations/reconstructions with intraoperative valve station data were available for analysis.

Surgical and Radiological Grading of Valve Station Wall Changes

The following valve station (VS) grading system was used: grade 0, normal-appearing valve station without wall changes; grade 1, increased collaterals/tributaries; grade 2, venous wall thickening/fibrosis at the valve station; grade 3, thickening of valve cusps and/or intima; grade 4, intraluminal trabeculae; grade 5, thrombosis/occlusion; and grade 6, postthrombotic dissolution/disappearance. Periphlebitic inflammatory reaction was noted when present and designated with the letter *I* after the numerical grade. This grading system is depicted in Figure 1. Ascending and descending venography as well as a detailed spectrum of venous functional and duplex studies were carried out before surgery and during follow-up. Hemodynamic grading of venous obstruction when present per arm/foot venous differential technique has been previously described.[6] Indications and method of selection of patients for valve reconstruction have been described in detail elsewhere.[2,4,5]

A detailed analysis of ascending venography films with regard to valve station changes was carried out by an observer blinded to the surgical techniques employed in the individual case. The radiological grading system was the same as the surgical grading system except VS grade 6 and periphlebitic inflammation could not be identified radiologically (Fig. 2).

Descending Venography

The presence or absence of valve leaflets as determined by descending venography was correlated with intraoperative findings.

Surgical Technique

The first superficial vein valve was preferentially approached through an oblique groin incision. The uppermost superficial femoral vein valve and, less commonly, the second valve located 2 to 5 cm distally were repaired. The relevant valve station undergoing repair in the proximal femoral venous segment is the object of current analysis.

The surgical techniques employed could be classified as direct or indirect. The former involved repair of some type of existing valve structure and included internal valvuloplasty, external valvuloplasty, prosthetic sleeve in situ, or transcommissural valvuloplasty with optional angioscopy. Indirect valve reconstruction techniques consisted mostly of axillary vein transfer or occasionally de novo valve reconstruction[5] and were undertaken when postthrombotic damage to the valve apparatus was so extensive as to preclude direct repair. In 71 cases one or more valves (profunda, posterior tibial) in addition to the proximal femoral valve were repaired. In such multiple repairs, only the femoral valve segment was included in the analysis for the sake of anatomic and radiologic uniformity in analyzing valve station wall changes.

Valve Station Pathology

Valve station biopsies (2 to 3 mm biopsy of venous wall at valve station; entire valve station in cases of indirect repairs) were available for examination in a series of 32 recent cases (separate from the main series of 149 cases).

Statistics

Multivariate analysis was carried out on actuarial data using Cox's technique.

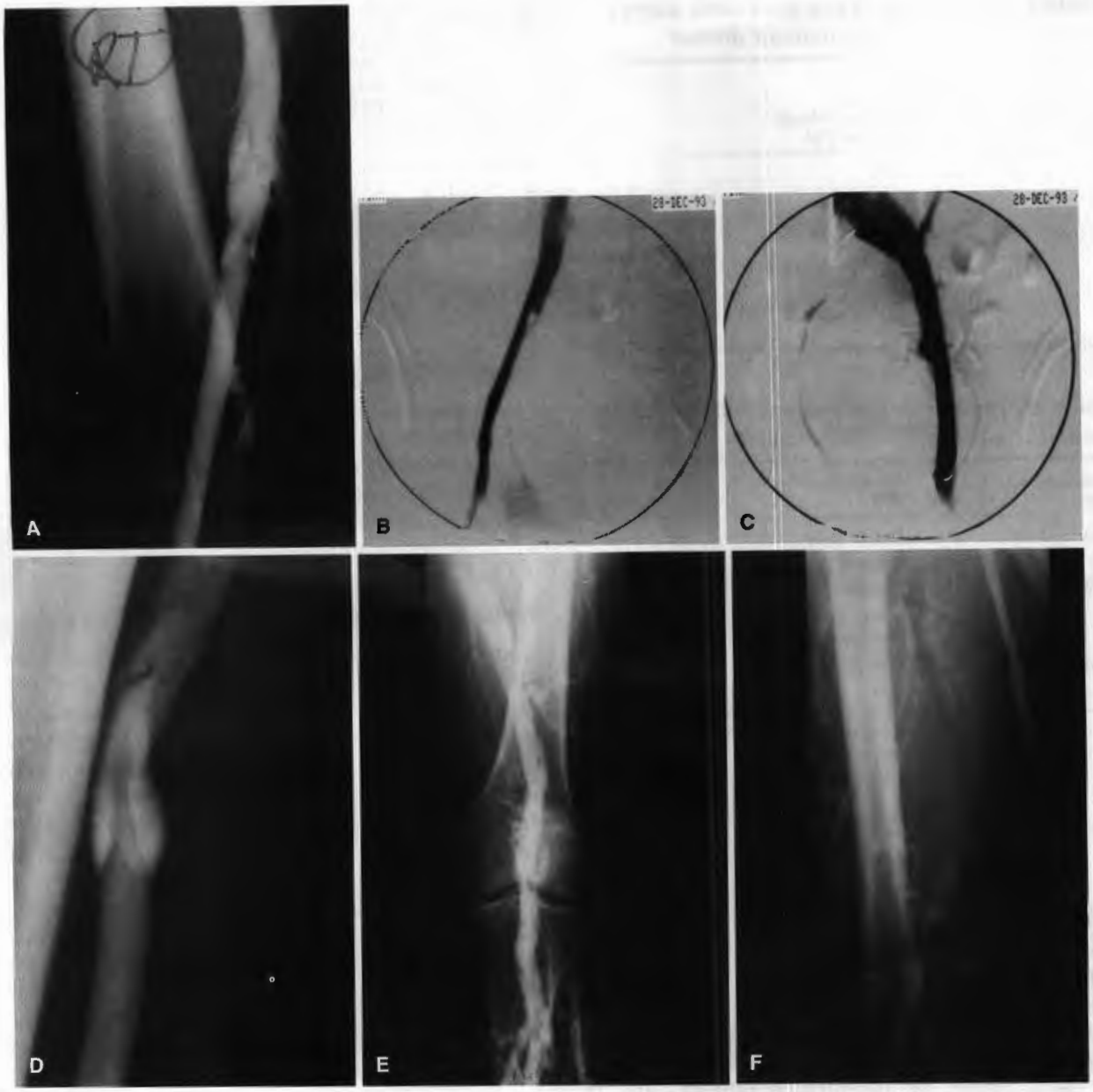

Fig. 2. Examples of valve station grading by ascending venography. A grading system similar to that for surgical grading (see Fig. 1) was employed. **A** Grade 1: note collateral tributary. **B** Grade 2: note smaller caliber iliac vein compared to the opposite **C** normal side. **D** Grade 3 with thickened valve cusp. **E** Grade 4 with trabeculae. **F** Grade 5: the femoral vein is occluded.

RESULTS

Periphlebitic inflammation was noted in 7% of cases VS grades 2 and higher. Postthrombotic changes distal to the repaired femoral valve station were present in 66% of cases on ascending venography; the incidence of distal disease, however, was higher, corresponding to the VS grade of the proximal femoral valve (Table I). In 37% of cases, distal thrombotic changes were present in association with significant valve station changes of VS grade 2 or higher; in 29%, distal thrombotic changes were present without valve station changes (VS grade 0 to 1). In 34% of cases, the distal venous tree was normal looking without postthrombotic changes; in 23%, the valve station was normal (VS grade 0 to 1) in appearance as well, but in 11% of cases, significant valve station changes of VS grade 2 or higher were present. There was a 41% incidence of venous obstruction as determined by arm/venous pressure

Table I. Relationship of proximal valve station changes and distal postthrombotic disease

Valve station grade	Cases [*n* (%)]	Incidence of distal postthrombotic disease (%)
0	67 (47)	49
1	9 (6)	0
2	12 (8)	50
3	33 (23)	58
4	14 (10)	86
5	3 (2)	100
6	5 (3)	80

Table II. Comparison of venographic and surgical grading of proximal femoral segment

Venographic grade	*n*	Surgical grade (%)
Grade 0 or 1	91	Same (64)
		Higher (36)
Grade 2 or 3	26	Lower (46)
		Same (42)
		Higher (12)
Grades 4 to 6	27	Lower (48)
		Same (52)

Overall specificity of venographic grading = 65%; overall sensitivity of venographic grading = 66%.

differential technique (79/133 cases), suggesting postthrombotic etiology in slightly more than half the cases. Seventy-one percent were compensated obstructions, 22% were partially compensated, and 7% were severe obstructions. Comparison of the surgical and radiological grades of the repaired proximal femoral venous segment yielded poor sensitivity and specificity for ascending venography (Table II), owing primarily to lack of a reliable radiological marker for intermediate (grades 2 and 3) wall changes. Both overestimations (false positives) and underestimations (false negatives) occurred frequently in venographic interpretation. Thirty percent of the films that were read as grade 0 or 1 and 26% of the films that were read as grades 4 through 6 actually had grade 2 or 3 changes at surgery. Forty-six percent of the films that were read as grade 2 or 3 were actually found to be free of wall changes (grade 0 or 1) at surgery.

Descending Venography

Descending venography was not totally reliable in predicting the presence or absence of a repairable valve at the valve station. In 24 cases a repairable valve was thought to be absent on descending venography. Six of 24 (25%) of these cases proved to have a repairable valve at surgery, the valve structure having presumably been obscured by massive reflux of contrast. A valve was thought to be present on descending venography in 118 cases, but none was found at surgery in 13 of these (11%), despite a careful search. In each of these instances, intraluminal trabeculation (grade 4) was present, giving the spurious appearance of a valve on descending venography.

Table III. Valve reconstruction technique according to valve station wall changes

Valve station grade[a]	Total (*n*)	Direct repair [*n* (%)]	Indirect technique [*n* (%)]
0 or 1	78	72 (92)	6 (8)
2 or 3	38	33 (87)	5 (13)
4 through 6	12	3 (25)	9 (75)

[a]Surgical grading.

Surgical Technique

Identification of valve attachment lines is an essential preliminary step in employing most of the specific valve reconstruction techniques described.[5] When valve station wall thickening is absent (grades 0 and 1), the attachment lines are often clearly visible through the glistening vein wall. Any degree of wall thickening associated with grades 2 and higher requires adventitial dissection of varying degrees to expose the valve attachment lines. At times such an exposure can be tedious and extensive. Without exception, absence of valve attachment lines despite adequate adventitial dissection denotes absence of valve cusps.[5] Further time and effort should not be wasted in trying to locate nonexistent valve cusps by doing a venotomy for an open search. Under these circumstances, one should proceed immediately with an axillary exploration for valve transfer.

The type of valve repair (direct/indirect) carried out and the corresponding surgical grading at the repaired valve site are shown in Table III. A direct repair technique (internal/external valvuloplasty, transcommissural repair, or prosthetic sleeve in situ) was possible in 92% of cases with VS grade 0 or 1; an indirect repair was required in a small number in this group, mainly because of technical failure of the initially attempted direct valve repair. It is noteworthy that a direct type of valve repair was also feasible in 87% of cases with VS grade 2 or 3 despite significant valve station wall thickening and intimal changes. As expected, an indirect technique (axillary vein transfer or de novo valve reconstruc-

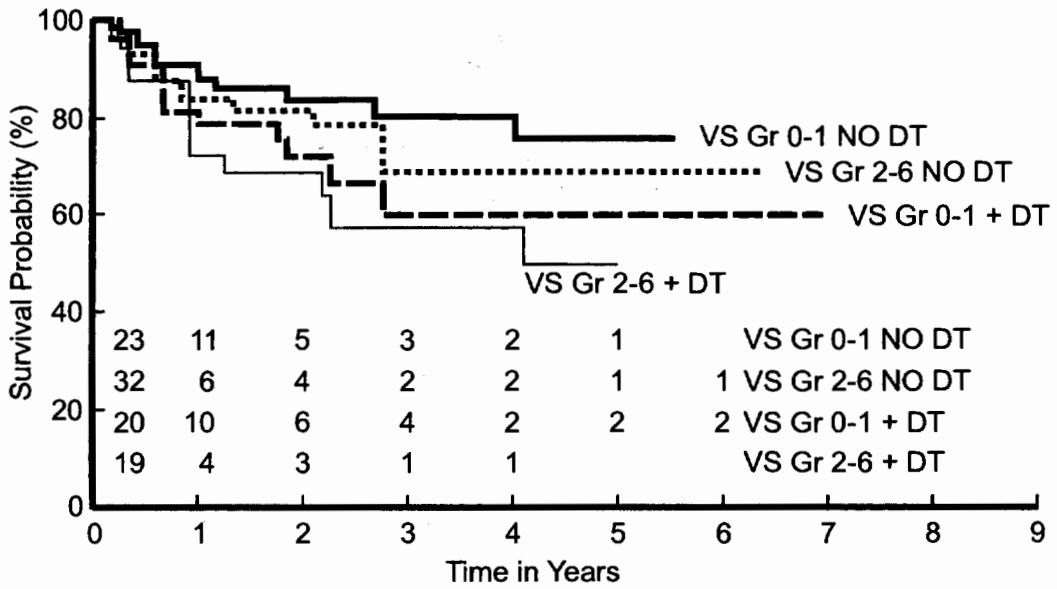

Fig. 3. Actuarial ulcer-free survival after valve repair in the various VS grades with and without distal thrombotic changes. Cases at risk at various time intervals are also shown. VS Gr, VS grade; DT, distal thrombotic changes.

tion) was required in an overwhelming majority of cases VS grades 4 or higher, but a direct valve reconstruction was still possible in 3 of 12 cases in this group. In these three cases, valve structure was preserved despite the presence of luminal trabeculae and extensive postthrombotic scarring. In one of the three cases, direct repair was possible after freeing a valve cusp adherent to the sinus wall by sharp dissection.

Valve station changes had no bearing on clinical results following valve reconstruction. Actuarial ulcer recurrence was the same in the various VS grades. The presence or absence of postthrombotic changes in the distal venous tree also had no bearing on the clinical outcome following valve reconstruction. Actuarial ulcer-free survival for various VS grades with and without distal thrombosis was similar (Fig. 3). Cox analysis of ulcer recurrence showed no difference between direct and indirect valve repair techniques (Fig. 4).

Venous Valve Station Wall Biopsy

In a recent series of 32 cases, 2- to 3-mm vein wall biopsies at or near the valve station were available for microscopy. Among the 32 biopsies studied, 4 were from surgical grade 0 or 1, 11 were from intermediate grades (grades 2 and 3), and the remaining 17 from clearly postthrombotic valves, i.e., grades 4 and higher (entire valve stations available for pathology in these). There was good correlation between pathologic microscopic findings and surgical grading in the first and last groups. Only one of four grade 0 to 1 specimens was postthrombotic on biopsy. Sixteen of 17 specimens of VS grades 4 and higher were read as postthrombotic on biopsy. Microscopy was indicative of a postthrombotic etiology in 6 of 11 VS grade 2 and 3 biopsies. These showed neocollagen deposition at the biopsy site with characteristic neovascularization seen in postthrombotic valve stations. The other five showed excessive collagen bundles that were fragmented without capillary invasion or neovascularization. Presumably, the wall thickening noted in the latter group was due to phlebosclerosis of nonthrombotic origin and resulted from neocollagenization associated with primary reflux. Based on microscopy it appears that the grade 2 or 3 valve station changes were roughly equally split between postthrombotic and phlebosclerotic etiologies.

DISCUSSION

Since many of the valve station changes appear to be postthrombotic in etiology, it is not surprising that the relative distribution of valve station wall thickening and distal postthrombotic changes is strikingly similar to the segmental incidence in acute venous thrombosis.[7] An interesting observation not previously reported is an incidence of six cases of postthrombotic dissolution of the femoral vein in which no trace of this anatomical structure was found on surgical exploration in our hands. In four of these cases, a prior exploration of the femo-

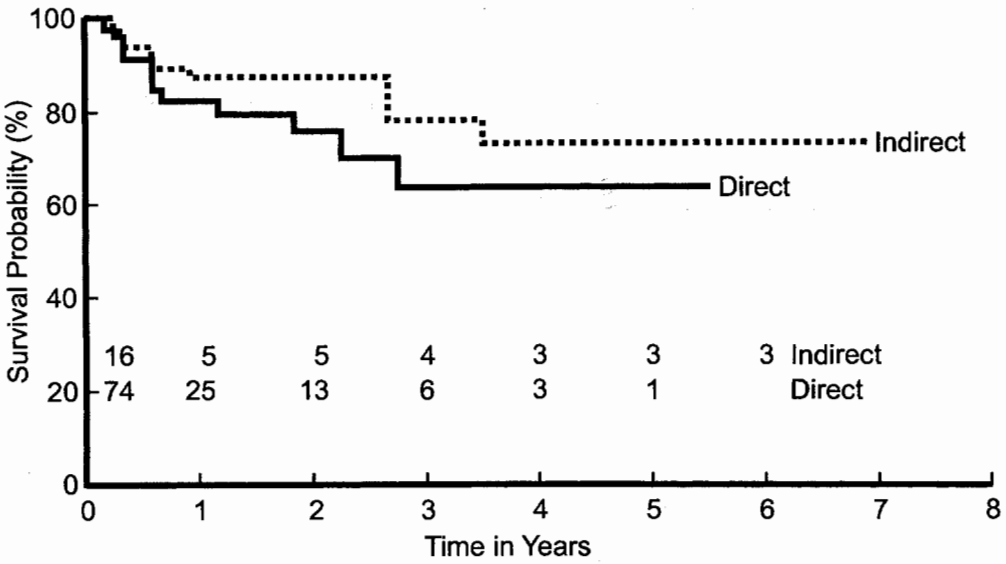

Fig. 4. Ulcer-free survival curves: direct versus indirect valve reconstruction techniques. There was no difference between direct and indirect valve repairs. Cases at risk at various time intervals are also shown.

ral venous segment had been undertaken elsewhere. In all six cases the previous presence of the dissolved venous segment had been documented venographically or surgically. It appears that in extreme instances, postthrombotic organization can lead to complete dissolution or conversion of the venous segment into a fibrous cord beyond recognition. Perivenous fibrosis induced by prior surgical intervention appears to result in this process. This phenomenon appears to be unique to the venous system in the vascular tree. We have not encountered similar dissolution of femoral arteries even after long-standing thrombosis.

Increased collateral/tributaries noted in grade 1 may be the result of reflux collateralization of primary reflux or postthrombotic tributaries persisting after the offending thrombus has disappeared, dissolved or organized. Occasionally, a grossly normal-appearing valve station may present postthrombotic evidence on microscopy due to near-perfect resolution of previous limited thrombus. While advanced valve station changes (grades 4 and 5) are undoubtedly postthrombotic, intermediate degrees of wall thickening (grades 2 and 3) could be the result of phlebosclerosis of primary reflux or of previous thrombosis. Histological examination of wall biopsies suggests that either pathological mechanism may be responsible in the individual case.

The gross appearance during surgical inspection of VS grade 2 and 3 valve leaflets was similar to that of VS grade 0 to 1 "primary" refluxive valves with some differences: the valve cusps were redundant and refluxive, but the valve annulus was smaller because of wall thickening and fibrosis. Distensibility of the valve station during angioscopic irrigation was excellent in "primary" valves (grades 0 or 1), with doubling of lumen size frequently observed. In contrast, this distensibility was distinctly and visibly limited in valves with valve station fibrosis. During angioscopy, intimal thickening, surface irregularities, and focal patches of fibrosis in the intima adjacent to the valve cusps and on the valve cusps themselves could be seen in several cases. "Violin string" trabeculae were observed in a few cases. Externally, the adventitia was densely adherent and thickened with localized inflammatory reaction over these focal intimal fibrotic lesions. These focal lesions may represent the end stage of localized sinus thrombi described by Sevitt.[8] The presumption of thrombotic etiology for these types of valve station changes, whether focal or generalized, is quite strong, based on gross appearance and histology. If phlebosclerosis of "primary" reflux is the pathological mechanism in valve station fibrosis, preservation of valve cusps and the presence of valve reflux are easily explained. However, a postthrombotic etiology that would seem to be the case in many instances raises many questions: how did these valves escape thrombotic destruction and how did they develop reflux? Although thrombotic changes could have been superimposed on a "primary" refluxive valve in a few cases, it is likely that most of the valves were normal nonrefluxive valves before the onset of thrombosis. We speculate that the redundancy and reflux of the valve cusps in the postthrombotic subset are "secondary" to the observed

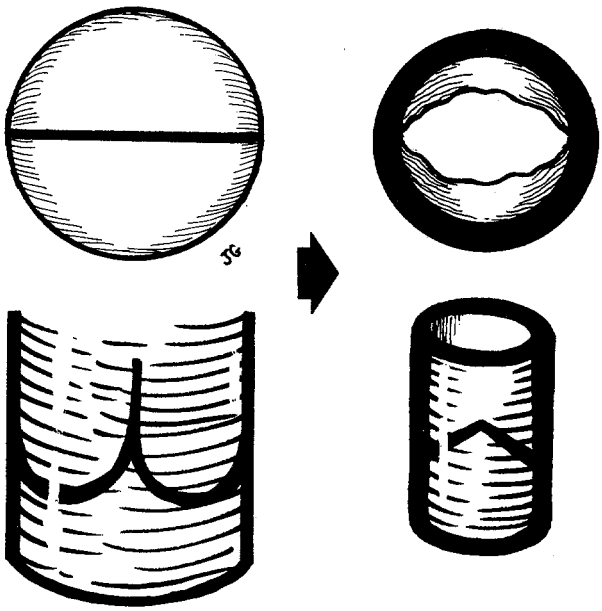

Fig. 5. A possible mechanism for the production of valve redundancy and reflux in postthrombotic valve stations. Valve station fibrosis may lead to luminal constriction resulting in "secondary" valve leaflet redundancy and reflux. Foreshortening of the valve station may lead to widening of the commissural valve angle, contributing further to development of reflux.

restrictive wall changes (Fig. 5), a mechanism that is probably different from "primary" reflux, where the redundancy results from elongation of the valve leaflets. It would appear that the restrictive wall changes extend far higher and more proximally beyond the site of gross venous thrombus seen on venography. Such a mechanism would explain not only the preservation of the valve cusps within the fibrotic valve station but also the development of reflux in them. Serial duplex observation by Killewich[9] and colleagues of patients developing deep venous thrombosis lends credence to this theory. These authors noted new development of reflux in proximal venous segments not involved in the original distal venous thrombosis. This interesting observation has now been confirmed by others.[10,11] Killewich et al. also noted rapid dissolution of thrombus in 14% of cases within a week after onset. It is possible that such rapid dissolution with modern anticoagulation therapy may spare the valve structure intact. We have recently witnessed preservation of valve cusps and function up to a year after catheter-directed urokinase thrombolysis of clot involving the valve apparatus and the adjoining venous segment. Pathological studies of experimental venous thrombosis have clearly demonstrated that when the thrombus organizes without rapid resolution, the valve structure is invariably involved and is destroyed in the organizing process.[12] As a result of such studies, the belief that postthrombotic evolution invariably leads to valve destruction has become firmly established. The presence of repairable, intact, refluxive valve cusps with surrounding fibrotic wall changes of postthrombotic etiology, as noted in VS grade 2 and 3 cases in the present study, is therefore a unique observation and should prompt a reexamination of the preceding concept.

Valve station changes (VS grade differences) did not affect clinical outcome within the reported follow-up time (80 months), but these pathological wall changes could be expected to affect the choice of reconstruction technique that can be used in an individual case. Nevertheless, in a surprising 33 of 38 cases with grade 2 or 3 valve station changes, a direct valve repair technique was feasible.

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