Neovalve construction in postthrombotic syndrome

Oscar Maleti, MD, and **Marzia Lugli, MD,** *Modena, Italy*

Objective: **The purpose of this study was to evaluate a new neovalve construction technique in postthrombotic syndrome. The surgical procedure is described, and preliminary results of the first case series are given.**
Methods: **From December 2000 to June 2004, neovalve construction in 18 limbs was performed on 16 patients (8 male and 8 female; median age, 55.5 years; range, 34-79 years) to treat severe chronic venous insufficiency in cases of postthrombotic syndrome. Surgical treatment was recommended in cases of nonhealing or recurrent ulcers (CEAP classification class C6). Preoperative duplex scanning, ascending/descending venography, and air plethysmography were routinely performed. Valvular cusps were created by dissecting the thickened venous wall to obtain material with which to fashion a new monocuspid or bicuspid valve. Mean follow-up was 22 months (range, 1-42 months). Postoperative duplex scanning and air plethysmography were performed in all patients. Descending venography was performed after surgery in 15 limbs.**
Results: **In 16 lower extremities (89%), the ulcer healed within 4 to 25 weeks (median, 12 weeks), and no recurrences occurred. Neovalve competence was confirmed in 17 cases (95%). Postoperative duplex scan and air plethysmography showed a significant improvement in hemodynamic parameters ($P < .001$), especially in younger patients with good muscle pump function. In 17 limbs (95%), the treated segments remained primarily patent at median follow-up of 22 months. Early thrombosis below the neovalve site occurred in two patients (12%). No perioperative pulmonary embolism was observed. A late occlusion occurred in one patient (6%), 8 months after surgery. Minor postoperative complications occurred in three patients (17%).**
Conclusions: **Neovalve construction seems to be effective in restoring femoral competence in postthrombotic reflux. Although these preliminary results are encouraging, long-term follow-up and a larger series are required to validate the technique. (J Vasc Surg 2006;43:794-9.)**

Deep venous incompetence is the main cause of severe chronic venous insufficiency. Significant symptoms and trophic lesions occur as a consequence of persistent deep venous reflux. The most common etiology of deep venous reflux is postthrombotic syndrome,[1] whereas primary congenital reflux is less frequent and congenital aplasia is very rare.[2]

However, primary and secondary deep venous reflux are sometimes found in combination.[1] Medical treatments and compression therapy are commonly used to control symptoms, whereas deep venous reconstructive surgery is reserved for cases that do not respond to conservative therapies.

Primary valve incompetence can be treated with direct valvuloplasty, first proposed by Kistner,[3] with subsequent variations in the technique,[4,5] or with a closed procedure,[6,7] angioscopy assisted where required.[8-11] In contrast, femoral vein transposition[12] and venous segment transplantation[13-15] may be the only available treatment in postthrombotic syndrome. However, transposition and transplantation are not always feasible, above all where adverse anatomical and functional conditions prevent their use. In such cases, venous reflux correction with a cryopreserved vein valve[16,17] or other technical solutions[18] might be attempted. Additionally, in isolated reports an autogenous valve has been created by inverting a saphenous vein segment.[19,20]

We propose a further technique that involves the construction of a neovalve by using vein wall dissection.[21] This article describes the first case series in which this surgical procedure was performed on the femoral segment of 16 patients affected by postthrombotic syndrome.

MATERIALS AND METHODS

From December 2000 to June 2004, 18 lower extremities of 16 patients affected by severe chronic venous insufficiency underwent operation to construct a neovalve. The group comprised eight male patients and eight female patients, with an age range from 34 to 79 years (median, 55.5 years). All patients had a postthrombotic deep venous reflux assessed at Kistner grade IV by using descending venography.[22] In all cases, the thrombosis episode had occurred more than 10 years before surgery and was of known origin: the thrombotic events were due to trauma in 9 limbs and childbirth in 3 limbs and were a complication of nonvascular surgery in 6 limbs. No patient had thrombophylia: protein C and S deficiency, antithrombin III deficiency, and Leiden factor testing yielded negative results. The CEAP classification, in accordance with Reporting Standards of the International Society for Cardiovascular Surgery, was $C_{6,S}E_SA_{P,D}P_R$ in all patients. General clinical

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Reprint requests: Oscar Maleti, MD, Department of Cardiovascular Surgery, Hesperia Hospital, Via Arquà 80/A, 41100, Modena, Italy (e-mail: chir.vasc@hesperia.it).
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Table. Hemodynamic parameters: preoperative and postoperative (at 1 month) values

Hemodynamic parameters	*n*	*Preoperative values, median (range)*	*Postoperative values, median (range)*	P *value*
Reflux time (s)	18	6 (5-9)	1 (1-4)	<.001
Venous filling index (mL/s)	18	12.2 (8.6-18.4)	2.5 (1.2-4.2)	<.001
Ejection fraction (%)	18	33 (18-41)	53 (36-69)	<.001

assessment revealed the presence of significant comorbidities: hypertension was detected in seven patients, and diabetes type 2 (insulin dependent) was detected in two patients. Idiopathic thrombocitemia (platelets >600,000/mmc), hepatitis C virus–related cirrhosis, chronic renal insufficiency (creatinine serum level >1.6 mg/dL), and inflammatory bowel disease (colitis ulcerosa) were present in one patient each.

All patients underwent preoperative duplex scanning[23] with standardized compression, air plethysmography[24] (Angioflow Microlab, Padova, Italy), and ascending/descending venography. Preoperative hemodynamic parameters (venous filling index [VFI], reflux time [RT], and ejection fraction [EF]) are shown in the Table. All patients were screened carefully for superficial vein reflux. All identified superficial refluxes were treated at least 1 year before assessment for deep venous surgery.

Deep reconstructive surgery was recommended for patients presenting with ulcers resistant to common conservative therapies for more than 5 years and in cases of frequent ulcer recurrence (within a year) associated with slow healing. Exclusion criteria were contraindications to anticoagulant therapy, severely limited ambulation, and thrombophylic syndromes. The feasibility of standard alternative surgical procedures was also examined in all cases, and only when these alternatives proved impracticable was recourse to neovalve construction considered. In all cases, ultrasound scanning and ascending/descending venography were used to assess profunda femoris competence, axillary and femoral vein diameter, morphology, and anatomic features. Neovalve construction was thus proposed only when transposition and transfer were assessed as being unavailable options. All patients were briefed about the innovative nature of this technique and gave their informed consent.

Four operations were performed under general and 14 under epidural anesthesia. The American Society of Anesthesiologists classification was class III for six patients, class II for five patients, and class I for five patients. Short-term antibiotic prophylaxis (cefuroxime according to weight) was routinely administered. The position of the patient on the operating table was supine with the leg rotated externally and the knee slightly flexed. A longitudinal incision was made approximately 10 cm in length running along the outside edge of the sartorius muscle. The incision extended between 10 and 15 cm below the inguinal ligament and was deepened to expose and isolate the femoral vein vertically. Extreme care is required during exposure to avoid damage to lymphatic vessels. Once the reconstruction site has been identified, complete control of the area is achieved. Before surgery, the reconstruction site was defined by using ultrasound and venogram evaluation, and the most suitable vein segment was located. However, intraoperative examination proved to be the crucial factor in determining the site.

Systemic anticoagulation with intravenous heparin (150 UI/kg) was performed, and activated clotting time was tested. Clamping was performed with light, coated clamps. A longitudinal or T-shaped venotomy was performed, usually 2 to 3 cm long. Careful parietal dissection was performed to obtain an intimal flap. Microsurgical instruments and optical magnification are required. The intimal dissection was performed with an ophthalmic blade or microscissors. The depth of dissection depends on the thickness of the vein wall. Care must be taken to avoid damage to the residual vein wall and leaflets. Once the flap was obtained, it was shaped to mimic a natural valve. When postthrombotic parietal thickening affects the entire vein circumference, a bicuspid valve can be constructed. If damage to the vein wall is partial, it may be possible to fashion only a single flap, and in this case a monocuspid valve is created. To obtain a monocuspid valve, the crosswise dissection must be slightly longer than half the vein's circumference. The lengthwise dissection should be three quarters the size of the crosswise dissection. To obtain a bicuspid valve, the crosswise dissection should be equal to the entire circumference of the vein. The lengthwise dissection must be equal to half the circumference. The size of the flaps must be accurately gauged because excessive width may lead to valve prolapse. Creating a correctly dimensioned valve is thus critical in preventing reflux. To this end, ultrasonography was used to evaluate the femoral vein's diameter in the standing position before the procedure. A millimeter rule used during valve creation facilitates the task of construction. The free edge of the flap was fixed with a 6-0 or 7-0 Prolene suture (Ethicon, Inc, Somerville, NJ), and after flushing, the closing suture was performed. Valve function was assessed directly by using a strip test (Figs 1 and 2). In three patients, parietal dissection led to excessive vein wall thinness, and a bovine pericardium cuff was applied to avoid aneurysmal enlargement. In all 18 cases, the surgical procedure lasted from 75 to 145 minutes, with a mean duration of 116 minutes.

At the end of the operation, a 35 mm Hg foot/thigh stocking or a short stretch bandage was applied. The choice between the two methods of compression was dictated by the precise medication requirements of the ulcer. Kinesitherapy and distal bed elevation (30°) commenced the day of the operation, whereas active mobilization commenced on the second postoperative day. Drainage was maintained for a minimum of 3 days. Full anticoagulation with intravenous heparin was administered until the second postoperative day, followed by oral anticoagulant therapy to obtain an international normalized ratio of 2.5 to 3 for a 6-month

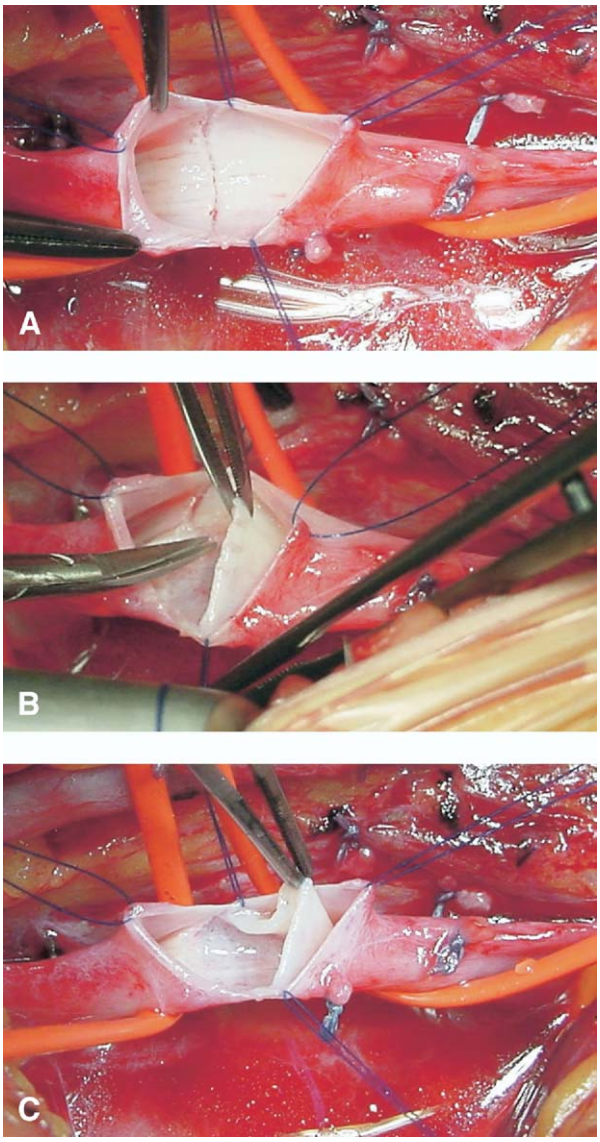

Fig 1. Monocuspid valve. **A,** Parietal incision. **B,** Proceeding on parietal dissection. **C,** Complete dissection.

period. Daily use of a class I elastic stocking or short stretch bandage was recommended for at least 1 month or until complete ulcer healing was achieved.

RESULTS

During follow-up, venous patency and neovalve competence were assessed by both clinical examination and ultrasound scanning. All lower extremities were screened with duplex scanning 6 hours after the operation and daily thereafter until discharge. Neovalve competence was assumed to have been achieved when reflux immediately below the reconstruction site was less than 1 second. Air plethysmography was performed 1 month after surgery to assess VFI, RT, and EF variations. Descending venography was performed on 15 limbs before patient discharge. Duplex scanning was scheduled at 1 and 6 months after the operation and thereafter at 1-year intervals. Air plethysmography assessment was also performed annually (the median follow-up was 22 months; range, 1-42 months).

The median hospital stay was 4.5 days (range, 3-8 days). The operative and postoperative mortality rate was 0%. Minor postoperative complications occurred in three patients (17%): one (6%) wound hematoma and two (12%) seromas necessitating no further surgical correction. A subcutaneous hardening of lymphatic origin was observed in more than half of the cases, but it was of only slight significance and transitory in all situations. No wound infection was observed.

No early thrombosis at the operative site occurred. Early thrombosis below the neovalve site was detected in two limbs, although neither case was complicated by clinical pulmonary embolism. One patient discontinued anticoagulant therapy of his own volition, but no demonstrable causes were identified for these recurrences of thrombosis. Both patients had complete recanalization at follow-up assessment 1 year after the operation. A late occlusion at the repair site occurred in one patient 8 months after surgery and in concomitance with a course of oral contraceptives. Thus, all repair sites except one have remained patent with no thrombosis to date (95% patency). Furthermore, the overall patency was equal to 83.3%, which includes early and late events either involving or not the site of the neovalve construction. Valve competence was assessed in 17 cases, and no deterioration was detected at the follow-up examination.

Ulcer healing was observed in 16 (88.8%) of the 18 operated limbs within 4 and 25 weeks after surgery (median, 12 weeks) with no ulcer recurrence to date. Two patients did not achieve ulcer healing, despite attempts at skin grafting. The first of these patients (77 years old) presented with deep parallel reflux,[25] which was underestimated in the preoperative assessment. The second patient (79 years old) presented an unexpectedly grave tibiotarsic anchylosis that led to severely impaired ambulation.[23] However, both ulcers decreased in size, and both patients reported relief of symptoms.

Postoperative evaluation at 1 month showed a statistically significant improvement ($P < .001$) in all parameters examined by air plethysmography (VFI, EF, and RT), as presented in the Table. Additionally, this improvement in parameter values (VFI, EF, and RT) was maintained during the follow-up phase with no signs of deterioration. Younger patients (38, 38, 42, and 46 years) with a preoperative EF of more than 35% seem to present a better hemodynamic performance (the postoperative VFI showed a decrease of more than 10 mL/s). In the two patients whose ulcers failed to heal, only a slight improvement in RT and EF was observed.

DISCUSSION

The objective of deep venous surgery is to re-establish correct venous back-flow. Restoring normal venous hemodynamics helps to reduce or abolish most serious symptoms

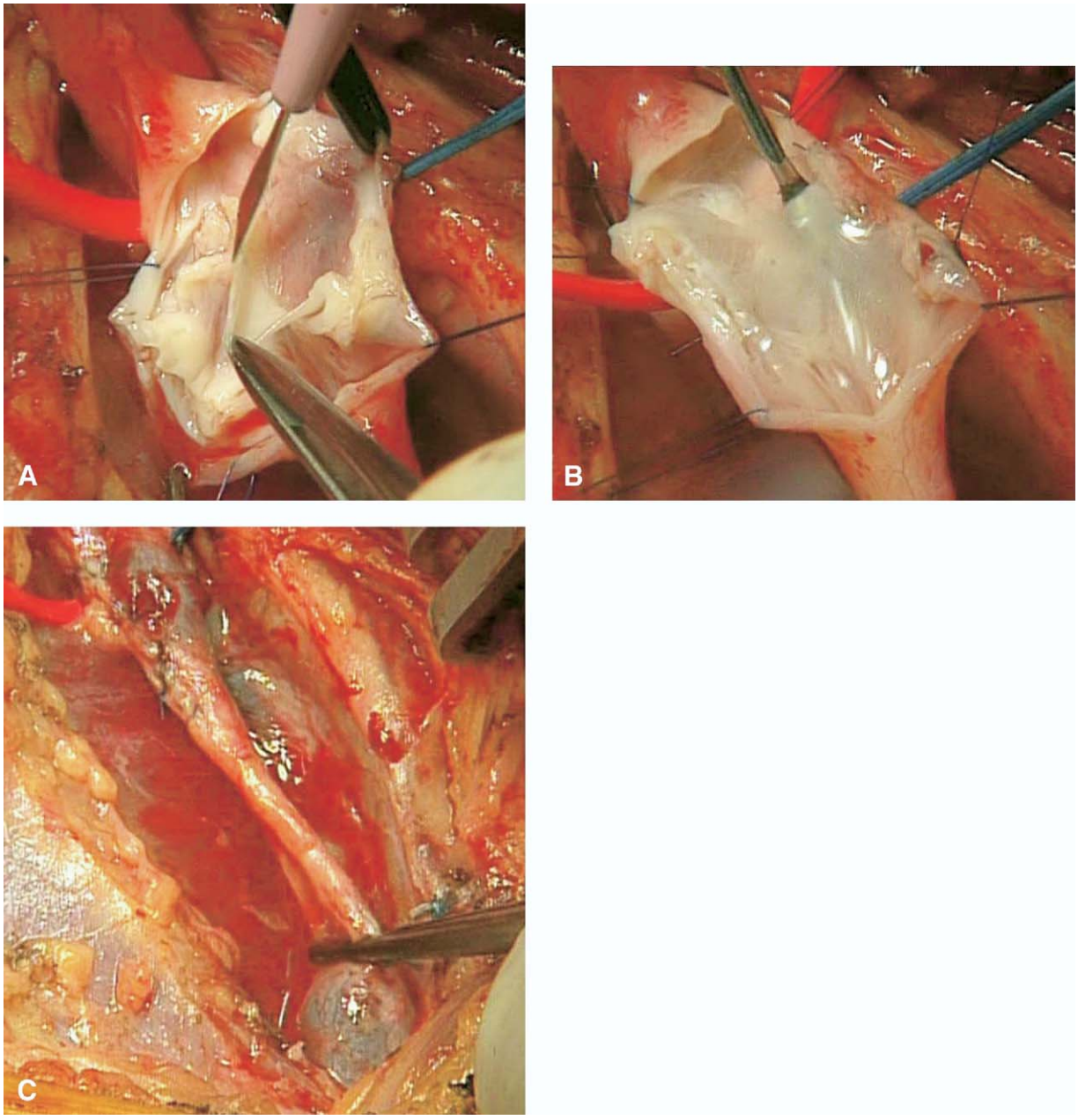

Fig 2. Bicuspid valve. **A,** Parietal dissection. **B,** Complete dissection. **C,** Milking test.

associated with chronic venous insufficiency.[13,26] Nevertheless, deep venous surgery is still rarely practiced, and most surgeons doubt its real efficacy.[27] Conservative treatments are widely favored, but in cases of inefficacy or intolerance, surgery may become necessary.

Research into new deep-reflux correction techniques has multiplied, and their success has led to standardized operations. However, this applies mostly to techniques for treatment of primary venous insufficiency[3,28]: deep venous surgery for postthrombotic syndrome treatment is still under discussion. As mentioned previously, transposition and transplantation are not technically feasible in all cases of postthrombotic syndrome necessitating surgery. Adverse anatomy and insufficiency of the first segment of the profunda femoris vein are common contraindications to transposition.[12] Conversely, the lack of an appropriate donor segment with a competent valve of appropriate diameter or patient refusal of vein harvest from distant sites frequently precludes transplantation techniques.[13,29] Other techniques such as cryopreserved, bioprosthetic, or stent-supported valves remain experimental and require further study to be validated.[17,30-32] Regardless, a variety of alter-

native techniques described as case reports or animal experimentation indicate growing interest in this field.[32-36]

The idea of creating a neovalve at the femoral site is clearly one of several directions in which research in deep venous surgery for correction of reflux in patients with postthrombotic syndrome is moving.[18,19] Parietal thickening of the venous wall in the recanalized femoral vein is commonly observed during transposition procedures, and it is this that led us to consider creating a new valve by means of parietal dissection.[21] Results from this initial report of the use of this technique have been encouraging. However, whereas the risk of postoperative thrombosis was lower than expected, lymphatic disorders and a troublesome subcutaneous hardening of the thigh were frequent. To avoid these complications, a more accurate dissection and ligation of all lymphatic vessels were performed when interruption was necessary.

The choice of the neovalve site is by no means simple, but it is a crucial element in this technique. The most suitable site for valve reconstruction seems to be the popliteal vein,[14] but in these preliminary attempts we preferred the femoral vein: a site where a thrombotic complication would be less risky thanks to the availability of better collateral veins. Additionally, on occasion synechie and parietal alterations are found during surgical exposure. These were not demonstrated by preliminary ultrasound and radiologic evaluation.[26] Therefore, in some cases endophlebectomia[37] was necessary before the neovalve construction.

In summary, in this preliminary report of neovalve construction to correct reflux in patients with postthrombotic syndrome, results were encouraging, with no mortality and morbidity. Additionally, even if complete abolition of reflux at the popliteal level was not achieved, an improvement in venous reflux led to a marked relief in symptoms. Deep venous reflux surgery has previously achieved good results, especially for venous valve repair in cases of primitive insufficiency (70% success rate), whereas the outcome in cases of postthrombotic disease was not as satisfactory.[38,39] Nevertheless, the results presented here compare favorably to other surgical techniques for the treatment of venous ulcers in patients with postthrombotic syndrome (eg, subfascial perforating ligation). All these features make deep venous reflux surgery in such patients an interesting field, in terms of both clinical practice and research.

Additional material for this article may be found online at www.jvascsurg.org.

AUTHOR CONTRIBUTIONS

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Analysis and interpretation: OM, ML
Data collection: ML
Writing the article: OM
Critical revision of the article: OM, ML
Final approval of the article: OM, ML
Statistical analysis: ML
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