Percutaneous Venous Valve Bioprosthesis: Initial Observations

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Chronic deep venous insufficiency remains a major health problem in the United States and worldwide. Selected patients benefit from direct deep vein valve repair or valve transplantation; however, most are not candidates for these procedures. Experience with the bovine monocusp venous valve surgically inserted into the common femoral vein (CFV) demonstrates potential benefit and good long-term patency. A venous valve placed distal to the CFV via percutaneous access has great appeal and potential for further improving venous hemodynamics, as well as reducing ambulatory venous hypertension and ulceration. Two patients were treated with a percutaneous venous valve bioprosthesis as part of a Phase I trial. The primary objective was to evaluate the safety, patency, and efficacy of the percutaneous venous valve bioprosthesis to restore competency to the deep venous system.

Introduction

Chronic deep venous insufficiency (CVI) remains a major health problem in the United States and worldwide. Selected patients benefit from direct deep vein valve repair or valve transplantation; however, most are not candidates for these procedures. Experience with the bovine monocusp venous valve surgically inserted into the common femoral vein (CFV) demonstrates potential benefit and good long-term patency.[1] A venous valve placed distal to the CFV via percutaneous access has great appeal and potential for further improving venous hemodynamics, as well as reducing ambulatory venous hypertension and ulceration.

We report results of 2 patients treated with a percutaneous venous valve bioprosthesis (PVVB) as part of a Phase I trial. The primary objective of the trial was to evaluate the safety, patency, and efficacy of the PVVB (VenPro Corporation, Irvine, CA) to restore competency to the deep venous system.

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Materials and Methods

Between December 2001 and February 2002, 2 patients with CEAP C_5–C_6 CVI, primary valvular

insufficiency, and no contraindication to long-term anticoagulation were enrolled in the PVVB trial. Patients were identified for the trial through a vascular surgery clinical practice serving a tertiary care hospital in a midsize metropolitan area.

Patient inclusion criteria for the trial included male or female subjects 21 years of age or older; primary CVI; CVI CEAP Clinical Classification grade 5 or 6 without clinically significant venous outflow obstruction; subjects who had not had a deep vein thrombosis (DVT) within the last 6 months as determined by venous duplex; subjects who had failed conservative therapy lasting more than 3 months before study enrollment; subjects whose CVI might be mitigated by implantation of a single PVVB into the femoral vein; and subjects who had been adequately informed of their participation in the clinical study, what would be required of them, and had provided written informed consent.

Patient #1 was a 44-year-old woman with a 14-year history of chronic venous insufficiency of the left leg with a non-healing venous stasis ulcer measuring 17.3 × 6.5 cm. A biopsy of the ulcer was consistent with venous stasis. The patient had no history of diabetes, arterial insufficiency or deep vein thrombosis (DVT). The patient's history included saphenous vein stripping 10 years before, numerous ulcer debridements, multiple episodes of cellulitis treated with antibiotics, unsuccessful use of growth factor therapy, and a failed skin graft. She had worn compression hose in the past without ulcer improvement and had used a compression pump.

Patient #2 was a 62-year-old man with a 30-year history of chronic venous insufficiency in both legs. The patient had no history of diabetes, arterial insufficiency, or DVT. The patient had bilateral saphenous vein stripping 29 years before and a large bulging varicose vein on the lower left leg with venous stasis skin changes and superficial ulcers that had healed with compression therapy. The patient wore compression knee-high stockings regularly.

Device Description

The PVVB is a glutaraldehyde-preserved, bovine venous bicuspid valve mounted on a Nitinol frame. It is implanted through a catheter inserted through the right internal jugular vein to the target site (Figure 1). The PVVB is available in 4 sizes based on outside diameter (OD) of the valve: 12 mm, 14 mm, 16 mm and 18 mm.

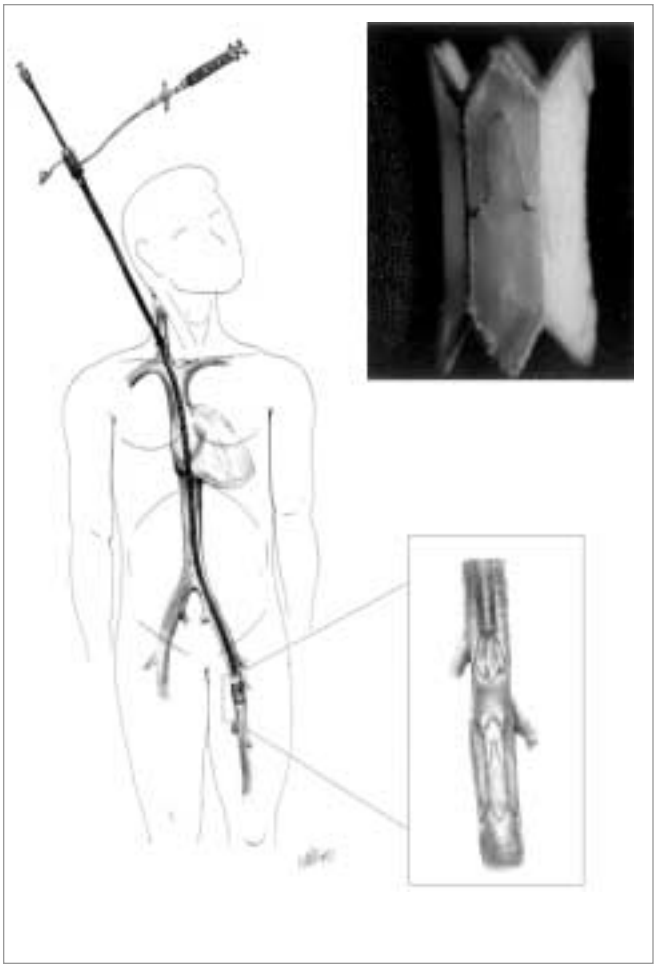

Figure 1.
Left: Percutaneous technique.
Right top: Glutaraldehyde-fixed PVVB.
Right bottom: Valve deployment.

Procedure

Both patients underwent preoperative duplex ultrasound and descending venography (Figure 2). A 12 mm PVVB was inserted via a right internal jugular vein puncture and deployed into the femoral vein in midthigh of both patients. The procedures were performed under fluoroscopic guidance.

Patients were anticoagulated postinsertion and followed up with venous duplex imaging for patency and valve function.

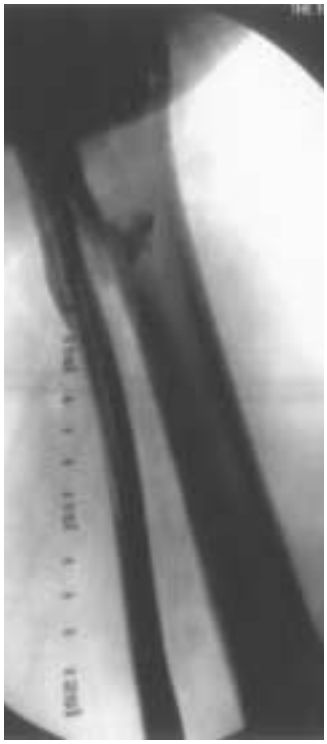

Figure 2.
Descending preoperative venogram, patient #1.

Figure 3. Left: Deployed valve. Right: Absence of reflux on retrograde venography.

Results

Percutaneous deployment was successful in both patients (Figure 3). Intraoperative completion venography showed competent valve function at the conclusion of the procedure in both patients.

Patient #1 has a patent and competent PVVB documented by serial postoperative duplex ultrasonography. The patient underwent ligation and stripping of an incompetent left short saphenous vein after 12 months to further reduce venous hypertension. More recently, after a 2-month course of nanocrystalline silver and firm compression dressings, the ulcer dramatically improved and a skin graft was placed. The skin graft appears to be a complete take and the patient is free of discomfort for the first time in 14 years.

Patient #2 suffered postinsertion thrombosis of the PVVB likely due to subtherapeutic anticoagulation. Catheter-directed thrombolysis and mechanical thrombus extraction restored valve patency and the patient was therapeutically anticoagulated. Follow-up duplex ultrasound showed a persistently patent but incompetent valve. The patient underwent radiofrequency ablation of an incompetent left short saphenous vein together with phlebectomy of calf varicose veins due to recurrence of a stasis ulcer. After 2 months, the ulcer remains healed.

Both patients are clinically improved. Postinsertion femoral vein diameters are reduced by 25% and 20%, respectively ($p < 0.05$). The international normalized ratio (INR) has been maintained between 2 and 2.5 in both patients since the time of the procedure.

Discussion

Percutaneous insertion of a glutaraldehyde-fixed bovine venous valve is feasible. Both patients had clinically successful outcomes, although a secondary procedure was required in the second patient to restore valve patency owing to subtherapeutic anticoagulation. Valve function in the first patient has been maintained for 16 months and healing of the chronic ulcer has been accomplished. In the second patient valve patency has been maintained for 14 months, although the valve is incompetent. This is likely due to leaflet rigidity caused by the postoperative thrombosis. In this patient, there was a 7-day delay between valve thrombosis and clot lysis. This raises the

question whether valve function could have been preserved with earlier thrombolysis. We believe that therapeutic anticoagulation is important, at least during the immediate postimplant period. In the second patient, the factor that could be attributable to the postoperative thrombosis was a subtherapeutic INR at the time of hospital discharge. Additional contributing factors were the lack of aggressive postoperative mobilization or utilization of EPC cuffs to accelerate venous flow through the valve.

Interestingly, femoral vein diameters were reduced after valve placement in both patients. The clinical significance of this observation is not clear but could reflect improved venous hemodynamics related to reduction in deep venous reflux.

Patient recruitment for this study was a problem owing to the stringent enrollment criteria. In our patient population it was difficult to find C5 and C6 patients with primary valvular insufficiency. We recognize the obvious need for a larger series to determine whether this procedure will have a future role in treatment of deep venous reflux. In this regard, opening the enrollment to select individuals with secondary valvular insufficiency may help with both enrollment issues and assessing the procedure's utility in the group of patients most commonly encountered in clinical practice. However, the risk of failure is likely to be higher.

Regarding the PVVB design, there was some concern that the amount of tissue and reduced midgraft radial strength could have adversely affected valve function. This first-generation device is no longer available. Design modifications in the next generation of the percutaneous valve include a shorter device with considerably less tissue, a 3-cusp valve constructed from porcine pericardium, and increased radial strength to reduce midstent compliance.

Conclusion

The percutaneous insertion of a glutaraldehyde-fixed bovine venous valve into the femoral vein is possible. Patency can be maintained; however, systemic anticoagulation appears to be important. In our small series, valve function is maintained up to 16 months thus far. Femoral vein diameter is reduced and is associated with clinical improvement. A new-generation valve design will be forthcoming to address some of the thrombotic issues associated with the first-generation PVVP.

REFERENCE

1. Garcia-Rinaldi R, Revuelta JM, Martinez MJ, et al: Femoral vein valve incompetence: Treatment with a xenograft monocusp patch. J Vasc Surg 3:932-935, 1986.