

Surgical Innovation

An Implantable Bioprosthetic Venous Valve to Establish Deep Vein Competence for Post-Thrombotic Syndrome

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What Is the Innovation?

VenoValve is a bioprosthetic device designed to improve valvular competence in the deep venous system of the lower extremities and treat deep venous insufficiency (DVI). First-in-human studies have focused on use in patients with DVI stemming from post-thrombotic syndrome, although design features portend utility in those with primary disease as well. The innovation consists of a porcine aortic valve leaflet dissected and structured in a nonexpandable 10-mm stainless-steel frame forming a monocusp, unidirectional valve (Figure, A). The device is preserved with glutaraldehyde, which maintains the tissue's anatomic integrity, strength, and flexibility properties,¹ packaged in normal saline and sterilized by gamma radiation. VenoValve is implanted in the femoral vein through a thigh incision and secured with monofilament sutures (Figure, B). Early studies have required a vein of at least 8-mm diameter and, in some cases, a limited focal endovenectomy or bovine pericardial patch to close the venotomy. Proximal venous obstruction should be ruled out or treated prior to use of the device, and Duplex should be used to ensure adequate unidirectional flow after implantation.

VenoValve is the product of experimentation and refinement of a broadly studied concept: the surgical repair of deep venous valves. Initial attempts^{2,3} provided knowledge and promising results warranting further research on a prosthetic valve to restore function in patients with post-thrombotic syndrome. Experience in valve transplant, repair, and autologous neo valve creation^{2,3} combined with recent developments in tissue processing and endovascular device construct¹ provided the additional know-how that propelled this innovation. VenoValve has reached the clinical trial stage with satisfactory results in first-in-human studies.^{4,5}

What Are the Key Advantages Over Existing Approaches?

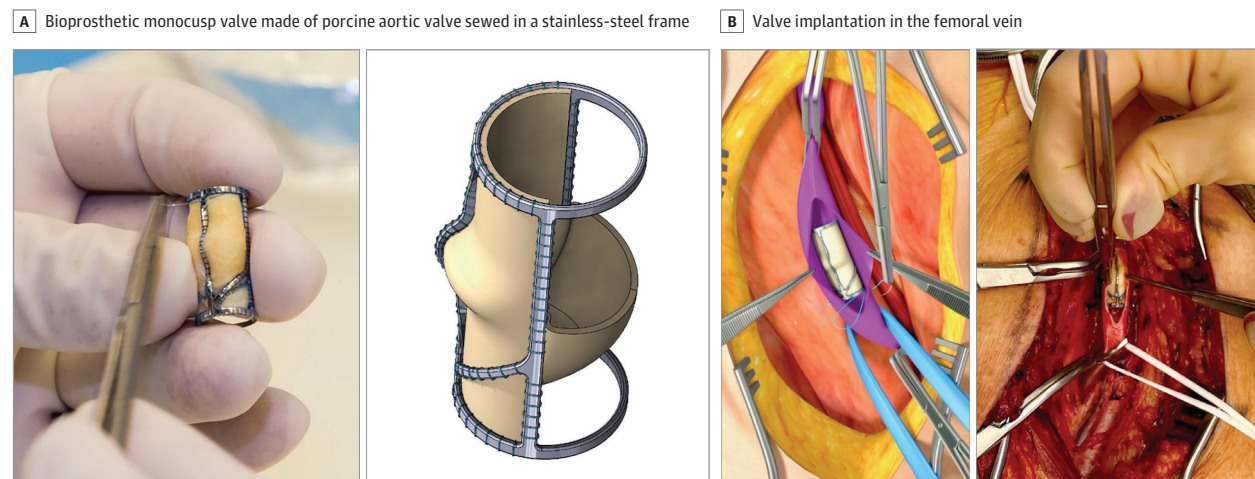
The mainstay of treatment for DVI is nonoperative with compression therapy, leg elevation, and wound care. Patients with post-thrombotic syndrome have a difficult disease course, with high ulceration rates and impaired quality of life.⁶ When conservative treatment fails, there are no commercially available device options, and direct open valve repair is rarely performed.⁷ VenoValve is the only bioprosthetic with evidence of improvement in venous reflux, clinical severity (Venous Clinical Severity Score), quality of life (VEINES QoL), and ulcer healing.

VenoValve implantation is accompanied by continued external compression therapy and treatment with oral anticoagulation medication. Thus far, the device's safety profile is favorable, with excellent freedom from life- and limb-threatening events such as thrombosis or device embolization. VenoValve is not intended to be curative as post-thrombotic syndrome has varied presentations conditioned by genetic, environmental, inflammatory, and mechanical factors; complete regression of the disease is rare.

How Will This Affect Clinical Care?

Chronic venous disease associated with DVI affects patients' health and quality of life. More than 2 million people in the US develop venous ulcers yearly, representing \$14.9 billion in health care costs.⁷ VenoValve has the potential to expand treatment options for severe, post-thrombotic syndrome resistant to current treatment strategies. Restoration of valvular function using this device may decrease venous hypertension, hydrostatic pressure, chronic inflammation, lower limb edema, ulceration, and pain. Given the functional burden of post-thrombotic syndrome on patients and the

Figure. Implantable Valve for Deep Venous Insufficiency, VenoValve



health care system's cost, this innovation's potential benefits could be significant. Additionally, experience gained with VenoValve may also lead to other innovations and approaches to restore valvular function, which could advance treatment options in the years to come.

Is There Evidence Supporting the Benefits of the Innovation?

VenoValve was developed after analyzing previous innovative efforts to restore deep venous valvular competence, most of which had poor results and did not progress to human studies. The main limitations of other approaches were thrombosis, intimal hyperplasia, leaflet stiffness, device collapse, and embolization.^{2,3} Informed by these previous experiences, VenoValve underwent extensive preclinical testing to optimize safety and hemodynamic performance, including flow dynamics to ensure undisturbed flow, accelerated wage test for durability, and hydrodynamic evaluation. The development of this innovation was also propelled by the established biocompatibility and durability features of porcine tissue¹ and Hancock Jaffe Laboratories' experience with cardiac valves.

As of August 2022, VenoValve has been implanted in 31 patients (11 in Colombia, 20 in the United States) with approximately 440 patient-months of follow-up. The first human trial included 11 patients with 6-month⁴ and 1-year⁵ results. This study showed a 54% reduction in deep venous reflux time, a 56% improvement in Venous Clinical Severity Score, and a 76% reduction in mean visual analog scale pain score, which confirmed the transition from severe to mild disease. Thirty-month results were presented at the 2022 American Venous Forum, reporting sustained improvement and patency without thrombotic events, ulcer recurrence, or serious ad-

verse events. In this trial, the device was safe, and surgeons optimized the technique such that implantation required less than 1 hour. Subsequently, a pivotal phase 2 trial called the Surgical Anti-reflux Venous Valve Endoprosthesis (SAVVE) study was initiated in conjunction with the US Food and Drug Administration (FDA) and is ongoing at more than 20 sites in the US.

What Are the Barriers to Implementing This Innovation More Broadly?

Placed into the femoral vein through an open incision, the implantation of the VenoValve is limited to those trained or experienced in vascular surgery. The device also requires patients to receive anticoagulation therapy, limiting its use in those with contraindications to anticoagulants. Although the FDA has approved the phase 2 Investigational Device Exemption study in the US, VenoValve is not commercially available. Findings from the Investigational Device Exemption and future clinical studies will generate data and increase familiarity such that regulatory approval and clinical adoption of the innovation can proceed.

In What Time Frame Will This Innovation Likely Be Applied Routinely?

The severity of the clinical condition, lack of alternative treatments, and promising results from initial studies portend the device will be in use in 2 to 5 years. Clinical experience will also provide a better understanding of the ideal number of valves to implant and the optimal location within the deep venous system in which to place them. Future device development and clinical study will focus on modifying this technology such that it or one of its derivatives can be delivered using less invasive endovascular techniques.

ARTICLE INFORMATION

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