Alan Dardik, MD, PhD, **SECTION EDITOR**

Hemodynamics of venous valve pairing and implications on helical flow

Henry Y. Chen, PhD,[a] Jose A. Diaz, MD,[b] Fedor Lurie, MD,[c] Sean D. Chambers, PhD,[d] *and* Ghassan S. Kassab, PhD,[a] *San Diego, Calif; Ann Arbor, Mich; Toledo, Ohio; and Bloomington, Ind*

ABSTRACT

Background: It has been shown that venous valves have pairing arrangements with specific relative orientation and spacing that contribute to helical flows. The studies to date have not quantified the hemodynamic impact of helical flow formation. A computational model allows various valve orientations and spacings to be studied to better understand the hemodynamic effect of valve pairing.

Methods: Simulations were performed for paired valves at physiologically relevant spacing and orientations to study the flow features and hemodynamics associated with valve pairing configurations. The wall shear stress (WSS), residence time, and pressure drop were evaluated for the various valve pairing cases.

Results: It was found that the WSS on the lumen flow side (front) of the leaflet is several times higher than on the valve pocket side (back). With orthogonal paired valves, the WSS at the critical back side is increased. Helical flow was clearly observed only with orthogonal valve pairing. The residence time was reduced to less than half (0.47 vs 1.16 seconds) in the orthogonal valve case compared with the parallel valve cases. The farther spaced valves (6 cm) had the highest residence time.

Conclusions: This simulation study shows that helical flow in the veins of lower extremities is strongly dependent on the relative orientation and spacing of the valves. For optimal orientation (~90 degrees) and spacing (~4 cm), strong helical flow is seen, which enhances WSS and reduces the flow resistance and residence time. These findings demonstrate a structure-function relation that optimizes flow patterns in normal physiology, which can be compromised in venous valve disease. The results of this study provide valuable insights that improve the current understanding of blood flow patterns around venous valves and the design of future multiple paired prosthetic valves. (J Vasc Surg: Venous and Lym Dis 2018;6:517-22.)

Clinical Relevance: Clinical guidance for implantation of novel prosthetic valves during valve reconstructions requires knowledge of proper orientation and position of venous valves and basic understanding of native venous valve structure and function. The results of this study provide insights that may improve the current understanding of blood flow patterns around native venous valves and the design of future multiple paired prosthetic valves. Better prosthetic valve designs may lead to more effective treatment of chronic venous insufficiency.

Keywords: Wall shear stress; Residence time; Fluid-structure interaction; Valve pairing

Valve insufficiency is the key pathologic feature of chronic venous disease that contributes to its severity and progression by inefficient vein blood flow (reflux) and increases risk for deep venous thrombosis.[1,2] Surgical correction of valvular insufficiency is technically challenging and is reserved for a few selected cases.[3] A possible solution to address a larger need for treatment of venous insufficiency is the development of a valve prosthesis to revert the inefficient vein blood flow. Appropriate guidance for implanting novel valve replacement devices and for interventional decisions during valve reconstructions requires knowledge of proper orientation and position of venous valves and basic understanding of native venous valve structure and function.

Helical flow, a common pattern of flow in the circulatory system, is characterized by a spiral rotation of blood along a central axis. Helical flow patterns have been observed in the heart and aorta.[4,5] It was found that the helical flow limits flow instability and provides a natural optimization of fluid transport in the cardiovascular system.[5,6] In the venous system, the formation of helical flow between paired, functioning valves has been observed by Lurie and Kistner[3,7] in the femoral vein, where venous valve pairs are observed with a mean distance of 3.8 to 4.6 cm between valves and a mean angle between the valve orientations of 88 degrees. In addition, Tien et al[8] reported that paired prosthetic venous valves

---

From the California Medical Innovations Institute, San Diego[a]; the Vascular Surgery, Department of Surgery, University of Michigan, Ann Arbor[b]; the Jobst Vascular Institute, Toledo[c]; and the Cook Medical, Bloomington.[d]

Author conflict of interest: none.

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

Correspondence: Ghassan S. Kassab, PhD, California Medical Innovations Institute, 11107 Roselle St, Rm 211, San Diego, CA, 92121 (e-mail: gkassab@calmi2.org).

2213-333X

https://doi.org/10.1016/j.jvsv.2018.02.005

showed helical flow when their orientations were orthogonal, mimicking what was seen in vivo in a pulse duplicator. In venous insufficiency, the valve pairing, distances, and orientations are compromised, and the features of helical flow are absent.[3,7]

It is known that the back side of the valve leaflet, especially the base region, is prone to accumulation of inflammatory and thrombotic cells, leading to adhesion of the valve leaflets and stenosis.[9] This rarely occurs on the front side of the leaflets, where the flow is not blocked by the leaflets. It has also been reported that the back side of valve leaflets has elevated expression of inflammatory genes, such as vascular cell adhesion molecule 1 and intracellular adhesion molecule 1.[10] Low wall shear stress (WSS) reduces the endothelium nitric oxide production and endothelial nitric oxide synthase, which are atheroprotective and anti-inflammatory.[11] The phenotype of endothelium is also found to be influenced by fluid shear stress, in which disturbed flow leads to unfavorable endothelial phenotype. Low shear stress is related to higher residence time, which enhances low-density lipoprotein invasion and platelet deposition, important contributors to thrombus initiation and progression to vessel disease.

Although clinical studies have demonstrated a preferred orientation and spacing of venous valves for helical flow formation, computational studies on venous valve pairing and associated hemodynamics are lacking. These studies are valuable to better understand the flow's impact, such as WSS on endothelial biology (nitric oxide, endothelial nitric oxide synthase) to assist in treating valvular dysfunction. To address this gap, fluid-structure interaction simulations were performed in this study for variously spaced valves and orientations to study the flow features associated with valve pairing configurations. Hemodynamic parameters such as WSS, pressure drop, and residence time were also evaluated under different venous valve arrangements.

METHODS

The flow was modeled as incompressible pulsatile flow at 20 cycles/min, mimicking respiration rate. The density and viscosity were 1050 kg/m^3 and 0.004 kg/m·s, respectively, based on the average values for human blood.[12,13] The diameter of the vessel lumen and valve was set to 10 mm, representative of a typical femoral vein and valve. For the wall interface, there is no slip between fluid and the wall and no permeability of the vessel wall as is commonly assumed.[14] Valve spacings of 2, 4, and 6 cm were simulated (4 cm is approximately the physiologic spacing), as well as parallel (0 degrees) relative orientation and perpendicular (90 degrees) relative valve orientation as shown in Fig 1.

The arbitrary Lagrangian-Eulerian method (a numerical method to solve the physical equations) was used, which allows the fluid mesh to deform around the moving leaflets, enabling the model to track the blood flow patterns as the flow encounters the leaflets.[12,13] The detailed formulations of the methods and parameters are summarized in the Appendix (online only). A Dell Quad-core workstation (Dell, Round Rock, Tex) was used for the simulations. Both the fluid and structural components were modeled with a finite number of elements, connected at a discrete number of points known as nodes. The positions of the structural nodes and fluid nodes were coupled on the fluid-structure interaction interfaces, which are determined by the kinematic conditions.[12,15] The Navier-Stokes equations for the fluid and the momentum and equilibrium equations for the solid (leaflets and vessel wall) were coupled on the fluid-solid interface through the kinematic and dynamic conditions. The arbitrary Lagrangian-Eulerian modified governing equations for fluid flow were then solved. The fluid stresses were integrated along the fluid-solid interface and applied on the corresponding solid nodes. The solution process continued until solutions for solid and fluid nodes converged on the fluid-structure interface and steady solution was achieved.

ARTICLE HIGHLIGHTS

- **Type of Research:** Flow simulation model using multiple venous valves
- **Take Home Message:** This simulation study, performed for paired valves, showed that helical flow in veins is dependent on relative orientation and spacing of the valves. For optimal orientation (~90 degrees) and spacing (~4 cm), strong helical flow was seen, which enhances wall shear stress and reduces resistance and residence time.
- **Recommendation:** The study provides insights into designs of multiple paired prosthetic valves.

RESULTS

The WSS at the lumen flow (front) side of the leaflet is several times higher than at the valve pocket (back) side. The parallel paired valves decreased the WSS at the back side to only approximately one-sixth (0.13 vs 0.90 Pa) of the WSS at the front side (Fig 2). With orthogonal paired valves, the WSS at the back side was increased (0.24 vs 0.13 Pa). This figure also shows that in the case of orthogonal valves, the WSSs at the front and back sides are more similar. WSS at the front side is slightly lower, whereas WSS at the critical back side is increased.

The effects of valve spacing were evaluated first, and the optimal spacing was found to be 4 cm, consistent with physiologic measurements of 3.8 to 4.6 cm (2 cm and 6 cm are outside of physiologic range). Thereafter, the effect of perpendicular orientation was evaluated, and the physiologic 4-cm spacing was the focus. It was found that the 4-cm, 90-degree configuration resulted