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BASIC RESEARCH STUDIES

Hemodynamic coupling of a pair of venous valves

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Background: **In vivo studies have shown that valves in veins are paired in an orthogonal configuration. The aim of this study is to characterize the flow interaction of paired valves under controlled in vitro bench conditions.**

Methods: **A bench top in vitro experiment was set up at physiological flow conditions to simulate the flow inside a venous valve. Two bicuspid bioprosthetic valves paired in 0° and 90° orientations were tested in a 12-mm-diameter tube, and the two-dimensional velocity fields around the valve were measured by particle image velocimetry. The distance between the two valves was varied from 3 to 5 cm, and the corresponding velocities and vorticities were determined.**

Results: **Velocity field shows the flow exit from the orthogonal valve-pairing configurations forced the main jet stream to turn to the outer region of the tube. Flow patterns between the valves show significantly less stagnation region from the 90° valve pairing over a 0° valve pairing case. The variation in valves distance shows that the coupling effect of the two valves extends to a range beyond four times of the tube diameter, albeit the ability to alter the flow decreases at larger distances.**

Conclusions: **The findings suggest that the 90° valve pairing configuration regulates the flow between the valves, and the separation distance affects the hemodynamic efficiency of the two valves by reducing the total reverse flow volume. (J Vasc Surg: Venous and Lym Dis 2014;2:303-14.)**

Clinical Relevance: **This experimental work investigates the functions and performance of bioprosthetic venous valves coupled in orthogonal configurations. The effect of coupled venous valves was shown to be a determining factor in creating a more natural, helical flow pattern, which helps to optimize venous return. The results of this study provide valuable information that will improve not only the current understanding of blood flow patterns around native venous valves, but also the design of future prosthetic valves. Better prosthetic valve designs based on this work will provide a more effective alternative treatment for chronic venous insufficiency.**

Venous valves play a central role in the blood circulation of the lower extremities. Dysfunction of venous valves is the main cause of chronic venous inefficiency. Valve incompetence results in venous reflux and distal venous hypertension, which can lead to venous remodeling, inflammation, and prothrombotic changes of the endothelium.[1,2] Although the basic function of valves has been realized for many years, it is not until recently that advances in imaging have revealed interesting details about the venous valve. Animal and human studies show that the valve does not fully open[3,4] but forms a pocket region with the sinus wall to create a vortex structure behind the valve leaflets. A study by Lurie et al[5] showed that four phases can be identified in a complete valve cycle. Complex fluid mechanics phenomenon, such as flow separation and reattachment, and vortical flow in the sinus are likely to play important roles in the operation of the valves. The valve is also a modulator of the venous flow in addition to preventing retrograde flow in the vein. Nam et al[6] applied the velocimetry technique to veins with a high-frequency ultrasound image system to image the flow around the perivalvular area in a human superficial vein. Using echo speckles of red blood cells as flow tracers, the motions of valve cusps were simultaneously visualized, and large-scale vortices were observed behind the sinus pocket while the main bloodstream was directed proximally.

Although the functionality of a single venous valve has been studied, less attention has focused on the coupling effect of multiple valves. Anatomy of the lower extremity veins shows that the distribution of the valves is not uniformly spaced in the venous system. For example, in the great saphenous vein, there are more valves located below than above the knee. Similarly, there are more valves

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Author conflict of interest: The prosthetic valves used in this study are designed and manufactured by Cook Medical Inc. G.S.K. is the founder of 3DT. S.C. and J.K. are employees of Cook Medical Inc.

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in the tibial veins than popliteal veins and femoral.[7] Studies show that despite individual variability at the saphenofemoral junctions, multiple valves are present and the distance between two valves is approximately 3 to 5 cm.[1,8-10] These observations suggest that where and how the valves are spaced is important for the performance of the venous system.

Recently, Lurie and Kistner[11] studied 15 healthy volunteers and 13 unaffected limbs of patients with unilateral primary chronic venous disease. The distance and relative position between the two most proximal valves of the great saphenous vein and femoral vein were identified. The mean distance was found to be 3.8 to 4.6 cm, and the mean angle between the valve orientations was 84° to 88°. They hypothesized that this valve configuration increases the efficiency of venous return by creating a helical three-dimensional (3D) flow pattern. This was confirmed by a more recent study[12] using color and spectral Doppler imaging to calculate the velocity vectors at five cross-sectional planes of femoral and common femoral veins. Helical flow was present in close proximity and downstream from a valve and at valve junction, and was more prevalent when the calf muscle pump was active. When the valve was incompetent, the helical flow pattern disappeared and was replaced by disorganized flow. Helical flow patterns have been studied extensively in the heart and arterial systems,[13-15] and it was found that the helical flow limits flow instability[16,17] and increases the efficiency of the flow system.[18] These findings suggest that the venous valves may play a similar role to improve the efficiency and stabilize the blood flow in the venous system.

The previous studies were done in vivo and provide qualitative observations on flow patterns around a pair of valves. Due to the technological limitations, however, quantitative analysis of the flow field was limited to the bulk velocity, and the detailed velocity distribution was unattainable. Since all of the valve pairs observed in the previous in vivo studies were misaligned by at least 60°, no control group (0° alignment) was investigated in vivo to study the coupling effect between the valves. The objective of this study is to overcome some of these limitations by the use of a high-resolution particle imaging velocimetry (PIV) technique to study the flow around a pair of prosthetic venous valves (at various angles and separation distances) in an in vitro setup. The PIV technique provides higher-resolution velocity distribution around the valve and the temporal evolution of the flow pattern of each valve phase as compared to in vivo ultrasound. A control group with a valve pair of 0° apart was tested, and distance between the valve pair was varied to investigate the coupling effect of valves. The results provide a more detailed understanding of the flow pattern around the venous valve and complement the in vivo observations.

METHODS

A pulse duplicator (PD) was utilized (BDC Laboratories, Wheat Ridge, Colo) to generate pulsatile flow through a venous valve with a bench top flow loop. Physiologic pressures and flow were duplicated and recorded for subsequent analysis. The flow system provided flow directional control and mean pressure control.

The test section consisted of a square container made of Plexiglas and a round glass tube (12 mm ID) to mimic the geometry of the vein. Two pressure transducers were used to measure the upstream and downstream pressure of the test section to evaluate the valve performance. An ultrasound flow probe (ME13PXN; Transonic System Inc, Ithaca, NY) was mounted upstream to provide flow rate measurement of the system. For experiments in the present study, the mean flow rate was set at 0.35 L/min at 15 beats per minutes rate, and the peak pressure difference under diastolic phase was adjusted to 2 mm Hg. The pressure and flow rate data were recorded at a 5-kHz data rate for 15 seconds, and the data were phase-averaged after processing.

The bioprosthetic valves used for the present study were provided by Cook Biotech Inc (West Lafayette, Ind). The bicuspid valves were the third-generation bioprosthetic venous valve frame with a 12-mm nominal diameter; detailed information of the valve can be found in Pavcnik et al.[19] The proximal side and distal side refer to the leaflet surfaces that were facing the venous flow proximal or distal to the heart.

To mimic the viscosity of blood and reduce the image distortion because of refraction, the working fluid was a solution of glycerol and water at a volume ratio of 2:3 with a resultant viscosity of 3.6 cP (25°C) with a 1.4 refraction index. At the current testing conditions, the Reynolds and Womersley numbers were 358 and 4.5, respectively.

PIV setup was used in conjunction with the PD flow loop platform to perform the velocity measurements. A double-pulsed Nd:YAG laser (Solo 120XT; New Wave Research, Fremont, Calif) was used to illuminate the flow tracers. The PD flow loop was seeded with polystyrene fluorescent particles (Nile Red 10-14 μm; Spherotech, Lake Forest, Ill). The fluorescent lights emitted from the particles were excited by the 532-nm wavelength illuminating laser light. Lens optics was used to shape the laser beam into a thin laser sheet (∼1 mm) to illuminate the area of interest. A 10-bit monochrome CCD camera (UP-1830-10; Uniq Vision, Santa Clara, Calif) was used to capture tracer motions within this area. The resolution of the camera was 1024 × 1030 pixels to provide a 15.4-μm/pixel spatial resolution, corresponding to an imaging area of 15.8 × 15.9 mm.

The PIV images were first preprocessed to remove the valve area and reflections from the glass wall. The interrogation window used in the PIV processing algorithm was set with a 50% overlap and iteratively refined to 48 × 48 pixels with the window deformation technique.[20] Vector outliers were identified using the universal outlier detection method[21] and then replaced by interpolating the neighboring vectors.

Fig 1 shows the coordinate system used in the experiments and the PIV measurement locations. The valve orientation was defined as the angle Θ to the horizontal plane (X-Z plane) in Fig 1. The angle between the two valves, Θ_2-Θ_1, was set to 0° and 90°. To investigate the coupling effect of the two valves, three different separation