



Keeping Off the Wrong Track on the Right Side

Planning for Transcatheter Caval Valve Implantation

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Presence of severe tricuspid regurgitation (TR) is associated with increasing mortality and morbidity in patients with heart failure (1). Severe TR leads to reversal of blood flow into the inferior vena cava (IVC), resulting in wasted myocardial work and worsening of right heart function, congestive hepatopathy, and ascites. In a previous Editor's Page, we highlighted the peculiarities of blood flow in the right ventricle (RV) and the complexities of right and left ventricular structure-function interactions that were difficult to overcome in a failing RV (2). As an alternate approach, investigators have suggested the use of inferior vena caval valve implantation (CAVI) as a solution for reducing the deleterious flow reversals in the portal and mesenteric circulation developing from the presence of severe TR and a failing RV (3-8). In this issue of *iJACC*, O'Neill et al. (9) illustrate a precise approach using 3-dimensional printing of computed tomography images for modeling optimal device fitting for successful CAVI (9). In this Editor's Page, we have extended these novel insights by revisiting the physiology of venous circulation, the factors that contribute to venous return, the hemodynamic effects of valvulation of IVC, and the potential benefits and pitfalls for heart failure patients with severe TR.

NORMAL PHYSIOLOGY OF IVC FLOW

The blood flow in the aorta is pulsatile due to intermittent ejection of blood from the left ventricle, with transient reversal seen in diastole due to aortic valve closure. By the time the blood reaches the capillary

network and the venous system the bloodstream is unidirectional, with minimal reversal seen in the IVC at end-systole and end-diastole. Although the competence of venous valves are pivotal for 1-way circulation of the blood, these are only adapted for preventing gravitational venous pooling and do not require reversal of flow for valve closure (10). The ballooning of the sinus aids local pressure that is built up to effect venous valve closure and prevent flow reversal. Valves are, however, not present in the central venous system. The milking and suctioning effects of abdominal and thoracic pressure variations during the respiratory cycle result in a unidirectional continuous flow in the IVC and prevent blood pooling in the central venous system.

The forces that help establish continuous flow in the veins are, however, multifactorial and include cardiac chamber function, respiratory cycle, venous anatomy, resistance, subject position, and activity level. There are also peculiarities of vascular anatomy; whereas the abdominal aorta tapers in size inferiorly, the IVC tapers in size superiorly toward the heart (11), which creates a siphon-like effect in modulating the forward velocity of flowing venous blood.

The existence of multiple mechanisms for effecting continuous flow in the veins, however, does not protect from abnormal blood pooling from other possible scenarios, such as the large reverse flow seen in patients with tricuspid regurgitation. A minute reversal of flow in IVC may be encountered at end-systole and end-diastole. However, in patients with severe TR, the reversal of flow is seen not only in the IVC, but also in the portal circulation, where the continuous flow is interrupted and reversed in systole. The presence of systolic reversal and added

volume in IVC and mesenteric venous circulation leads to visceral congestion and increased hydrostatic pressure, which causes hepatic, renal, and intestinal congestion as well as ascites.

HEMODYNAMIC ROLE OF ARTIFICIAL VALVES IN IVC

The approach to implant 2 valves in the superior and inferior vena cava (IVC) for palliating the effects of right heart failure in patients with severe TR was first proposed by Davidson et al. (3). However, the major challenges to valve implantation in IVC include the complex anatomy and large diameter of the IVC. It has been suggested that, for overcoming congestion in the IVC, valves are useful in patients within the failing Fontan circulation (12,13) and, more recently, within the IVC in patients with severe tricuspid regurgitation and right heart failure (3-8). Although in both strategies, valvulation has been targeted for reducing the mesenteric congestion, there are unique hemodynamic differences. The Fontan physiology is distinct; the cardiac output in this setting is almost exclusively pre-load dependent and varies with gravity and respiration. During expiration, part of the IVC blood flows back into the abdominal compartment. Valvulation of the Fontan pathway was therefore suggested to reduce respiratory variations, decrease the backward congestion, and increase pre-load and cardiac output. However, actual chronic studies in humans have been disappointing (13). Over a period of time, the valve leaflets appear to become nonfunctional and completely embedded in the vascular wall, leaving a canalized, nonvalved conduit. It has been hypothesized that, in the absence of a beat-to-beat cyclical closure (in the absence of a functioning RV), the valve becomes nonfunctional over a period of time. Similar findings have been reported in the clinical setting when the Melody valve (Medtronic, Minneapolis, Minnesota) was inserted in the tricuspid position in patients with unfavorable RV function. Interestingly, respiratory rates of over 30 breaths/min can keep the valve-in-valves in the Fontan circuit operational (13).

Preliminary data suggests that, contrary to the Fontan circuit, valvulation of the short segment of IVC between the right atrial-IVC junction could lead to sustainable benefits in patients with severe TR (4). The use of CAVI in all previous reports has demonstrated hemodynamic improvement via a decreased venous regurgitation as well as diminished symptoms of right heart failure (3-8). This was also seen in other reports, such as a patient presented in this issue of

iJACC by O'Neill et al. (9), in whom the right heart failure and right-sided recurrent pleural effusion was seen to subside over a period of time. Moreover, a recent experimental chronic animal model of severe TR confirmed the functional value of heterotopically-implanted valves showing hemodynamic improvement for up to 6 months after implantation. A post-mortem evaluation was recently performed 3 months after the implantation in a patient who received the first-in-man CAVI but died due to intracranial hemorrhage (14). The valve was well anchored within the upper part of IVC while leaving the hepatic veins unobstructed. The stent struts were well covered by fibrous tissue, and the leaflets were mobile with sufficient coaptation and without evidence of degeneration. This initial promising use of CAVI in patients with severe TR, however, required prospective evaluation.

There may be several technical and clinical challenges associated with CAVI. First, CAVI only addresses the regurgitation of TR into the IVC and not into the superior vena cava. It has been suggested that this may work as a safety valve to prevent unnecessary increase of hemodynamic afterload over a failing RV. However, at the same time, the potential of collateral flow through the azygous veins (similar to superior vena cava obstruction syndrome) may potentially limit the clinical benefits. Furthermore, the effects of chronic congestion in the neck and central nervous system veins remain unknown. Second, the CAVI leaflets may become nonfunctional in the event there is not significant cyclical hemodynamic load, as seen in the Fontan circuit. Third, CAVI may not alter the performance of a failing RV because the increase in afterload by exclusion of backward regurgitation may lead to further decompensation of RV function. The exact threshold for RV function where this strategy would lead to improvement of cardiac function remains speculative. Finally, the use of 3-dimensional printing to understand the complex geometry of the IVC and to test the valve size for the given anatomy of the IVC highlights the burgeoning interest in direct modeling and testing for device selection. The exact incremental value and cost-effectiveness of 3-dimensional printing for such scenarios, however, need to be prospectively evaluated.

To summarize, CAVI appears to be an intriguing strategy for patients with severe TR given the challenges associated with percutaneous treatment of the tricuspid valve. There are newer percutaneous techniques, such as bicuspidization of the tricuspid valve, implanting an Impella (Abiomed, Danvers,

Massachusetts) on the right side, or catheter-deployed percutaneous right-sided ventricular assist devices, and the relative merits, pitfalls, and applications of these techniques will be defined over the next few years. Although technological innovations promise new solutions, techniques in 3-dimensional printing and advanced pre-procedural computational modeling will be pivotal for designing personalized

approaches for operative planning and reducing operating time, the number of repeat interventions, and the overall cost of the procedures.

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