Laboratory Investigation

Temporary Support with TandemHeart® pVAD during Percutaneous Aortic Valve Replacement in an Animal Model

Rationale and Methodology

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Surgical aortic valve replacement is the preferred treatment for aortic stenosis.[1] However, hemodynamic instability, heart failure, or comorbid conditions can leave patients at too high a risk of surgical complications. When surgery is not an option, aortic balloon valvuloplasty may be used to produce temporary clinical improvement.[2] One disadvantage of balloon valvuloplasty is that the rate of restenosis within months after the procedure remains unacceptably high.[3]

Replacement heart valves that can be percutaneously implanted to treat aortic valvular disease are being developed in order to minimize complications in high-risk patients. These percutaneous heart valves (PHVs) have been studied preclinically[4-6] but have only recently been used in human beings. In 2000, Bonhoeffer and colleagues[7] reported the 1st clinical implantation of a PHV of any type. They deployed a bioprosthetic pulmonary valve made from a bovine jugular vein. The patient was a 12-year-old boy who had stenosis and insufficiency of a right ventricle-to-pulmonary artery graft conduit.[7] In 2002, Cribier and associates[8] reported the 1st antegrade percutaneous replacement of an aortic valve in a human being. The valve was made of bovine pericardium mounted within a stainless-steel balloon-expandable stent.[8] More recently, this same group reported 5 implantations of a similar valve made of equine pericardium (Percutaneous Valve Technologies Inc.; Fort Lee, NJ), in patients for whom surgery was not an option.[9] The authors successfully and accurately deployed the PHV in 5 out of 6 patients. The lone exception had a torn aortic valve leaflet resulting from a previous balloon valvuloplasty, which reportedly prohibited secure valve placement. The remaining 5 patients demonstrated immediate clinical improvement. Three of them survived for 18, 4, and 2 weeks, before dying of noncardiac complications; the other 2 were clinically stable when the paper was written.[9] Human clinical trials of the Cribier aortic prosthesis are expected to begin soon in the United States.[10] Paniagua and coworkers,[11] in the current issue of this journal, report the 1st case of percutaneous retrograde implantation of their aortic valve in a human being, performed in April 2003. Earlier this year, Hanzel and colleagues[12] reported a similar case of percutaneous implantation of an aortic valve in a human patient, which took place in August 2003.

Notwithstanding the successful deployment seen in this small series of patients, percutaneous aortic valve replacement still poses a significant risk. Implanting the valve within the aortic orifice requires that the systemic circulation be transiently disrupted for as long as it takes to deploy the device. The danger of this was illustrated in October 2004 when, during a live telecast from a European center, a patient undergoing the procedure died. In addition, interrupting coronary blood flow in patients who are already hemodynamically compromised greatly increases the risk of arrhythmia and acute hemodynamic decompensation.[13]

Because the time of circulatory interruption must be minimized, valve deployment must be done very quickly. This time limitation may, however, compromise the operator's ability to properly place the valve. Improper placement introduces a

number of potential complications. Because the coronary ostia are nearby, imprecise orthotopic placement may obstruct coronary blood flow.[14] A valve that is incompletely secured within the aortic orifice may become dislodged, or the seal between the valve-stent and the aortic annulus may become incompetent and result in paravalvular regurgitation.[5]

In addition, blood being ejected from the left ventricle through the aortic valve may dislodge the PHV. To avoid this, some have used a transseptal antegrade approach to allow delivery of the valve in the same direction as the blood flow.[8,9] However, this approach requires accessing the left atrium through a transseptal puncture, which is considerably more difficult than approaching the aortic valve in retrograde fashion. The transseptal approach raises the possibility of left atrial rupture and residual atrial septal defect after implantation. Moreover, a wire must be passed through the mitral valve and the left ventricle before the aortic valve can be reached. Traction on this wire could interfere with the movement of the anterior leaflet of the mitral valve, resulting in severe mitral regurgitation and hemodynamic collapse.[9] Displacement of the PHV within the left ventricular outflow tract might also interfere with the movement of the anterior leaflet.[14]

Mechanical circulatory support may reduce the risk of these complications and facilitate percutaneous aortic heart valve placement. For instance, unloading the left ventricle with a ventricular assist device would allow ample time to properly deploy the valve by maintaining the systemic circulation, including the coronary arteries, throughout the procedure. Ventricular unloading would also make aortic valve placement via the retrograde approach easier, since it would presumably lower to a minimum the pressure gradient across the aortic valve.

TandemHeart® Percutaneous Ventricular Assist Device

Short-term circulatory support has been achieved in patients undergoing high-risk percutaneous coronary interventions (PCI) and in patients in cardiogenic shock by using a recently developed percutaneous ventricular assist device (pVAD) called the TandemHeart® pVAD™ (CardiacAssist, Inc., Pittsburgh, Pa).[4,15] The TandemHeart pVAD is a continuous-flow centrifugal pump designed to provide up to 4.0 L/min of systemic blood flow. The pump requires a priming volume of 10 mL. The device can be rapidly inserted in the catheterization laboratory via a standard transseptal approach. The inflow cannula is inserted into the femoral vein and is advanced across the interatrial septum into the left atrium; the outflow cannula returns oxygenated blood to the femoral artery (Fig. 1). Continuous infusion of a heparinized saline solution (900 U/h) provides a hydrodynamic bearing for the pump, while cooling the pump motor and providing local anticoagulation. The inflow and outflow cannulas are connected to the pump with standard 3/8-inch polyvinyl chloride tubing.

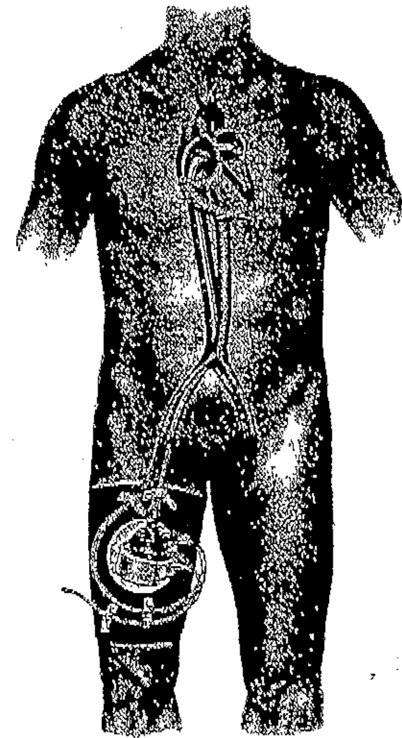

Fig. 1 TandemHeart® pVAD™ system. The inflow cannula is inserted into the femoral vein and advanced across the interatrial septum into the left atrium. (Courtesy of CardiacAssist, Inc., Pittsburgh, Pa)

At our institution, we have used the pVAD for protective circulatory support in 6 high-risk percutaneous coronary interventions (PCIs). Circulatory support and revascularization were successfully accomplished in all 6 cases, and the pVAD provided adequate support even during periods of ventricular standstill. On the basis of this experience with high-risk PCI, we hypothesize that the TandemHeart pVAD will adequately support the systemic and coronary circulation and avert serious procedural complications when used during percutaneous aortic valve placement. We also hypothesize that it will facilitate retrograde placement by decreasing aortic ejection and eliminating the hemodynamic forces that would normally—detrimentally—be applied to the valve and the deployment balloon.

Study Protocol

To test these hypotheses, we will evaluate the safety, feasibility, and efficacy of deploying a PHV in a sheep with a normal native aortic valve, during concomitant circulatory support with the TandemHeart pVAD.

The primary endpoints of the study will be 1) hemodynamic stability throughout PHV placement; 2) successful deployment of the PHV; 3) time required to properly place the valve within the aortic orifice; 4) end-organ and myocardial ischemia; 5) hemolysis; and 6) neurologic events.

The PHV to be used in this study will be an aortic valve prosthesis designed and created by Paniagua, Fish, and coworkers (Paniagua Heart Valve, Endoluminal Technology Research; Miami, Fla). The valve consists of biologic vascular tissue mounted in a metallic stent.

Six sheep will be used. They will be categorized into an experimental group (n=3) or a control group (n=3). Sheep in the experimental group will undergo placement of the PHV while being supported by the pVAD. Sheep in the control group will undergo PHV placement without circulatory support. All procedures will be conducted with the sheep under general anesthesia and with the use of fluoroscopic guidance. Before the initiation of any surgery-related procedures, a pulmonary artery catheter will be inserted for continuous hemodynamic monitoring. The PHV placement procedure will be identical for both groups. Hemodynamics will be monitored and recorded before, during, and after valve placement. Blood samples will be collected before and after PHV deployment and assessed for the presence of laboratory markers of end-organ function and hemolysis. Proper placement of the PHV will be verified by use of angiography and intravascular echocardiography. Circulatory support with the TandemHeart pVAD will be terminated shortly after placement of the PHV in the experimental group. All 6 sheep will be euthanized after valve placement, and postmortem examinations will be performed to confirm accurate placement of the PHVs.

Discussion

The current state of development of percutaneous aortic valve replacement is very limited. At present, the procedure is a high-risk endeavor, and there is no standardized method of implantation. We propose a new technique that will potentially solve these problems. We have completed a pilot study of 4 sheep using this implantation technique and have achieved the hemodynamic goals and procedural success predicted above in all 4 cases. After implantation in a larger number of animals, the overall results will be disseminated. We believe that this strategy will be superior to femoral cardiopulmonary bypass, which is more invasive and expensive, does not fully unload the left ventricle, and exposes the patient to the inflammatory syndrome associated with the bypass circuit. Although the TandemHeart is expensive for such short-term use, this cost may be comparable to the surgical alternative with its associated morbidity, mortality, and prolonged intensive care management. We hope that this technique will mitigate or even eliminate some of the drawbacks of the current techniques of percutaneous valve replacement and that the above-described protocol, with modifications made on the basis of experience, will advance the field of percutaneous aortic valve replacement.

Conclusion

Using the existing TandemHeart pVAD to support the circulation and unload the left ventricle during placement of a PHV may improve both the safety and the success of the procedure. If so, percutaneous aortic valve replacement may soon become a safe, feasible, and effective clinical option for high-risk patients who have no other treatment alternatives.

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