ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ORIGINAL CLINICAL SCIENCE

The first-in-human experience with a minimally invasive, ambulatory, counterpulsation heart assist system for advanced congestive heart failure

Valluvan Jeevanandam, MD,[a] Tae Song, MD,[a] David Onsager, MD,[a] Takeyoshi Ota, MD,[a] Colleen Juricek LaBuhn, RN, MSN,[a] Thomas Lammy, BS,[a] Gabriel Sayer, MD,[a,c] Gene Kim, MD,[a,c] Sonna Patel-Raman, PhD,[a,b] and Nir Uriel, MD[a,c]

From the [a]Department of Surgery, University of Chicago Medical Center, Chicago, Illinois, USA; [b]NuPulseCV, Raleigh, NC, USA; and the [c]Department of Medicine, University of Chicago Medical Center, Chicago, Illinois, USA.

KEYWORDS:
congestive heart failure;
counterpulsation;
mechanical assist device;
cardiogenic shock;
transplantation

BACKGROUND: The intravascular ventricular assist system (iVAS) is a new, minimally invasive, ambulatory counterpulsation heart assist system delivered via the subclavian artery and powered by a portable driver. It is designed for recovery, bridge to transplantation (BTT) or for prolonging medical therapy. We report the first-in-human (FIH) experience with iVAS.

METHODS: This is a prospective, non-randomized single arm, U.S. Food and Drug Administration (FDA)-approved early feasibility trial in patients listed for cardiac transplantation. The primary endpoint was survival to transplant or stroke-free survival at 30 days.

RESULTS: Fourteen patients were enrolled and 13 (92.8%) were treated with iVAS. At time of implant, the average age was 58 ± 6.7 years; 85% were male; 28% had ischemic cardiomyopathy; and 3 were Interagency Registry for Mechanically Assisted Devices (INTERMACS) Level 2, 9 were Level 3, and 1 was Level 4. The mean left ventricular ejection fraction was 22%, left ventricular internal diameter diastole was 7.13 mm, and 69% had moderate or severe mitral regurgitation. There were no intra-operative complications. Intensive care unit stay after implant was 6 ± 6 days. All patients were transplanted after 32 ± 21 days. There were no deaths or thromboembolic events: 1 patient required escalation of mechanical support, and post-implant complications included pleuritis/pericarditis ($n = 1$) and neuropathy ($n = 2$). No intra-operative blood transfusions were required.

CONCLUSIONS: This study demonstrates a high rate of successful outcomes with an excellent risk-to-benefit profile. This FIH experience reveals that the iVAS can be successfully inserted in a standardized approach, provide hemodynamic support, can be interrupted for short periods, and allows for ambulation. A multicenter trial to investigate effectiveness and safety is warranted.

J Heart Lung Transplant ■■■;■:■■■–■■■

Each year, there are over 100,000 new patients with advanced congestive heart failure (aCHF) who could receive a heart transplant.[1] However, heart transplantation is limited by the shortage of donor organs. Worldwide, there were only 4,300 heart transplants reported in 2015, with 2,800 in the United States.[2,3] As a result, over 4,000 continuous-flow LVADs (cfLVADs) are implanted per year and have become the mainstay therapy. These devices have improved survival and quality of life in aCHF patients[4]; however,

Reprint requests: Valluvan Jeevanandam, MD, Cardiovascular Surgery Section, Department of Surgery, University of Chicago Medical Center, 5841 South Maryland Avenue, Chicago, IL 60637. Telephone: +773 702 2500. Fax: +773 702 4187.
E-mail address: jeevan@uchicago.edu

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2017.10.011

according to the Interagency Registry for Mechanically Assisted Devices (INTERMACS), there is a 70% incidence of a major complication (death, thrombosis, hemolysis, bleeding, stroke) within the first year.[4] Newer devices, like the HeartMate 3 (Thoratec Abbott, Pleasanton, CA), have lower thrombosis rates, but other complications remain unabated.[5] For non–inotrope-dependent patients, considered "less critically ill," the medical community is reluctant to implant cfLVADs due to the need for an invasive procedure (sternotomy or thoracotomy) and the complication profile.

An alternative to continuous-flow pumps is counterpulsation, which consists of supplying energy to the circulation at the beginning of diastole. This decreases the workload of the heart and increases myocardial perfusion. Intra-aortic balloon pumps (IABPs) are implanted more than 200,000 times/year worldwide, and are often the first-line therapy for patients presenting with circulatory insufficiency.[6] Due to insertion in the femoral artery, and size/complexity of the drive mechanism, patients are forced to stay in an intensive care unit (ICU). This limits support duration and patient mobility. Recently, in small studies, the IABP has demonstrated safe and effective prolonged support by using the subclavian artery for access (subIABP), allowing for ambulation while bridging to LVAD, transplant or recovery.[7,8]

The NuPulseCV (NuPulseCV, Inc., Raleigh, NC) intravascular ventricular assist system (iVAS) combines the benefits of IABP and cfLVADs by providing counterpulsation, while allowing ambulation in and out of the hospital. The iVAS is minimally invasive and requires no access to the heart. It has been tested on the bench for over 2.5 years. Should an iVAS fail, it can be easily exchanged. If a patient's condition deteriorates, support can easily be escalated, as the iVAS is "forward compatible" (i.e., surgical planes and access for transplant or cfLVADs are not disturbed). Although we review the results of a first-in-human (FIH) early feasibility trial of the iVAS as a bridge to transplant device, longer term clinical studies are planned to evaluate extended duration of support in patients with New York Heart Association (NYHA) Class III/IV aCHF.

Methods

Between April 2016 and April 2017, 14 patients were enrolled in our study at the University of Chicago Medicine (UCMC). Informed consent was obtained from all patients according to the requirements of an FDA-approved clinical study, along with approval of the UCMC institutional review board.

Trial design

This trial was designed to assess a device with no previous human experience in a patient population presumably in need of a short, finite period of support. The trial was conducted to demonstrate a measurable benefit by evaluating safety and performance, including adverse events, device malfunctions and failures, functional assessments, procedural success and hemodynamics. The primary end-point was either survival to transplant or stroke-free survival at 30 days.

The main criterion for inclusion was for patients to be listed for cardiac transplant United Network for Organ Sharing (UNOS) Status 1A or 1B. Key exclusion criteria included: aortic diameter <20 mm; subclavian diameter <7 mm; abnormalities of the aorta including heavy calcification or aneurysms; and/or uncontrollable atrial or ventricular arrhythmias that prevent proper electrocardiogram (ECG) tracking.

Investigational device

The iVAS is an external heart assist device that has several components (Figure 1). The intravascular component is a 50-cc displacement pump (similar to an intra-aortic balloon) placed in the descending aorta. The skin interface device (SID) is an electromechanical and pneumatic conduit with a chimney that allows for shuttling of air between the pump and external driver and communication of the captured ECG signals that are transmitted to the driver from 3 subcutaneous electrodes. The SID is placed onto the lower chest cage and connects a driver to an external drive-line. An external and wearable drive unit provides compressed ambient air to inflate and deflate the pump. Similar to an IABP, the pump can be operated in 1:1, 1:2 and 1:3 modes, and the amount of augmentation is adjustable.

Procedure

A small incision is made below the right or left clavicle to access the subclavian artery. An anastomosis is performed between a custom-designed Dacron graft and the artery. A guide-wire is directed using fluoroscopy to the descending aorta. An Atrieve vascular snare (Argon Medical Devices, Plano, TX) is inserted via the femoral artery. The snare is used to engage the guide-wire and is exteriorized through the subclavian graft. The iVAS is placed within the loops of the snare and is guided into the descending aorta. A hemostatic plug is placed around the pump drive-line and is secured with sutures to the inside of the graft. A subcutaneous pocket is made for the SID along the anterior axillary line, above the ipsilateral costal margin. Using a trephine, a skin button is created and the chimney of the SID exteriorized. Three 52-cm bipolar electrodes (Capsure Novus, Medtronic, Minneapolis, MN) are tunneled subcutaneously and connected to the SID. The pump

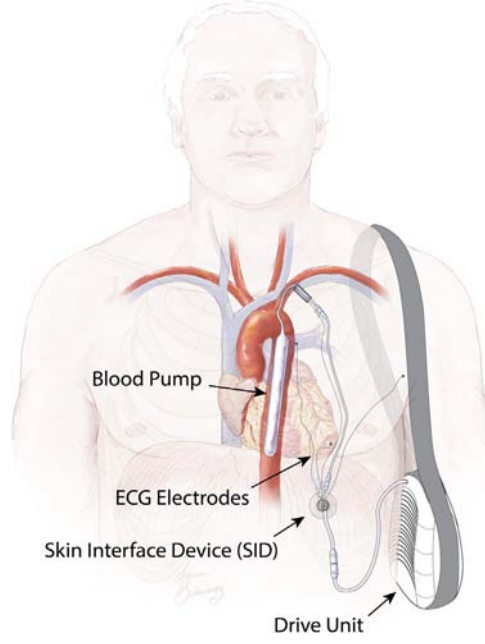

Figure 1