

**Proof of Concept: Hemodynamic Response to Long-Term Partial Ventricular Support With the Synergy Pocket Micro-Pump**

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*J. Am. Coll. Cardiol.* 2009;54:79-86; originally published online May 20, 2009;  
doi:10.1016/j.jacc.2009.04.023

**This information is current as of November 21, 2010**

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## Proof of Concept

### Hemodynamic Response to Long-Term Partial Ventricular Support With the Synergy Pocket Micro-Pump

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- Objectives** The purpose of this study was to test the hemodynamic effects of partial ventricular support in patients with advanced heart failure.
- Background** The use of current left ventricular assist devices (VADs) that provide full circulatory support is restricted to critically ill patients because of associated risks. Smaller, less-invasive devices could expand VAD use to a larger pool of less-sick patients but would pump less blood, providing only partial support.
- Methods** The Synergy Pocket Micro-pump device (CircuLite, Inc., Saddle Brook, New Jersey) pumps ~3.0 l/min, is implanted (off pump) via a mini-thoracotomy, and is positioned in a right subclavicular subcutaneous pocket (like a pacemaker). The inflow cannula inserts into the left atrium; the outflow graft connects to the right subclavian artery.
- Results** A total of 17 patients (14 men), age  $53 \pm 9$  years with ejection fraction  $21 \pm 6\%$ , mean arterial pressure  $73 \pm 7$  mm Hg, pulmonary capillary wedge pressure  $29 \pm 6$  mm Hg, and cardiac index  $1.9 \pm 0.4$  l/min/m<sup>2</sup> received an implant. Duration of support ranged from 6 to 213 (median 81) days. In addition to demonstration of significant acute hemodynamic improvements in the first day of support, 9 patients underwent follow-up right heart catheterization at  $10.6 \pm 6$  weeks. These patients showed significant increases in arterial pressure ( $67 \pm 8$  mm Hg vs.  $80 \pm 9$  mm Hg,  $p = 0.01$ ) and cardiac index ( $2.0 \pm 0.4$  l/min/m<sup>2</sup> vs.  $2.8 \pm 0.6$  l/min/m<sup>2</sup>,  $p = 0.01$ ) with large reductions in pulmonary capillary wedge pressure ( $30 \pm 5$  mm Hg vs.  $18 \pm 5$  mm Hg,  $p = 0.001$ ).
- Conclusions** Partial support appears to interrupt the progressive hemodynamic deterioration typical of late-stage heart failure. If proven safe and durable, this device could be used in a relatively large population of patients with severe heart failure who are not sick enough to justify use of currently available full support VADs. (Safety and Performance Evaluation of CircuLite Synergy; NCT00878527). (J Am Coll Cardiol 2009;54:79-86) © 2009 by the American College of Cardiology Foundation

Commonly used left ventricular assist devices (LVADs) are designed to provide full hemodynamic support for the end-stage failing heart (1). With flow rate capacities ranging from 5 to 10 l/min, these LVADs also provide profound left ventricular pressure and volume unloading, which, during prolonged use, results in structural and functional reverse

remodeling (1,2). However, even modern LVADs are relatively large, require a major surgical procedure with a sternotomy, and require extracorporeal circulation for their insertion. Such devices are associated with significant rates of morbidity and mortality.

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Manuscript received March 2, 2009; revised manuscript received April 3, 2009, accepted April 6, 2009.

We have recently introduced a smaller device that pumps 2.5 to 3.0 l/min (Synergy Pocket Micro-pump, CircuLite, Inc., Saddle Brook, New Jersey) and suggested that such a device could be used to provide hemodynamic benefit to patients with medically refractory, severe symptomatic heart failure but who do not yet meet current hemodynamic and clinical criteria to justify the risks associated with implan-

**Abbreviations  
and Acronyms****CT** = computed  
tomography**INR** = international  
normalized ratio**LVAD** = left ventricular  
assist device

tation of a contemporary full support LVAD (3,4). Patient selection and expectations concerning hemodynamic improvements initially were guided by results of previous short-term partial support devices (5–8) and a computer simulation that predicted hemodynamic responses in various degrees of heart failure

(9). We then embarked on a feasibility study to test, for the first time, the hypothesis that chronic partial ventricular support can interrupt the progressive hemodynamic deterioration typical of end-stage heart failure and result in benefits beyond what is achieved in the acute setting.

**Methods**

This was a prospective, treatment-only feasibility study. Patients were eligible for inclusion if they were between 18 and 70 years of age; had New York Heart Association functional class IIIb or IV symptoms despite appropriate treatment with diuretics, angiotensin-converting enzyme inhibitor or angiotensin receptor blockade, and beta-blocker (unless intolerant); or were listed for heart transplantation and were ambulatory, but whose condition was becoming clinically unstable (e.g., frequent hospitalizations for heart failure or increasingly symptomatic). The main exclusion criteria included the requirement for continuous inotropic support; isolated right heart failure; previous surgery in the right chest that could impede access to the left atrium from Waterson's groove for implantation of the inflow cannula; >2+ aortic regurgitation; mechanical mitral valve prosthesis; left atrial thrombus on echocardiogram; cerebrovascular accident within the previous 6 months; creatinine  $\geq 2.5$  mg/dl; aspartate aminotransferase, alanine aminotransferase, or total bilirubin  $\geq 2$  times the upper limit of normal; or contraindication to anticoagulation.

After informed consent, patients underwent a right heart catheterization, a cardiopulmonary stress test, and thoracic computed tomography (CT) scan with contrast (to exclude right subclavian artery stenosis), serum b-type natriuretic peptide level and routine blood chemistries and hematologic evaluation. An INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) heart failure severity score was also assigned (10). In brief, INTERMACS class 1 patients are patients with critical cardiogenic shock, class 2 patients are progressively declining on inotropic support, class 3 patients are stable but inotrope dependent, and class 4 patients exhibit recurrent decompensations requiring repeated hospitalizations.

After baseline information was obtained, the results were presented by the site principal investigator to a clinical review committee, which was composed of 2 heart failure surgeons (B.G. and R.D.) and 1 heart failure cardiologist (M.J.Z.). The purpose of the clinical review committee was

to ensure that the baseline data were complete, that the patient was not "too sick" to potentially derive clinical benefit from  $\sim 3.0$  l/min pump flow, and that there were no unforeseen contraindications for implantation.

**Surgical implantation procedure.** A 4-cm subclavicular incision was made to isolate the right subclavian artery. A small subcutaneous pocket was formed for the pump anterior to the right pectoralis major muscle, similar to a pacemaker pocket. An incision was then made in the right fourth intercostal space to gain access through Waterson's groove to the left atrium. A nitinol reinforced silicone inflow cannula with a titanium tip and Dacron cuff was inserted on a trocar over a guidewire into the left atrium between the insertions of the right upper and lower pulmonary veins and secured with 2 purse string sutures. The proximal end of inflow cannula was tunneled through the second intercostal space to exit the thorax in the area of the subcutaneous pocket. An 8-mm polytetrafluoroethylene outflow graft was anastomosed to the subclavian artery. The driveline of the pump was then tunneled to exit the body over the right upper quadrant of the abdomen. After completing the initial implant, the pump was turned on and speed was generally increased slowly from 20,000 to  $\sim 26,000$  rpm while cardiac output, pulmonary artery pressure, and arterial pressure were measured. The final speed was generally set at the level at which no further increase in cardiac output was observed, which generally was either 22,000 or 24,000 rpm, resulting in a pump flow of  $\sim 3.0$  l/min. After confirming proper pump functioning, the surgical wounds were closed.

After surgery, the patients were taken to the intensive care unit and, in clinically appropriate stages, were extubated, weaned from any inotropic support, brought to the regular medical ward, and ambulated, and physical therapy was initiated. The surgical procedures generally took from 90 to 120 min. Patients were extubated within 12 h of completing surgery (with some extubated in the operating room). Stays in the intensive care unit generally ranged from 1 to 4 days. Patients and family members were trained in the use of the controller, battery charger, and how to change batteries. After appropriate training, patients were discharged home. Hospital stays lasted a median of 17 days. Patients were anticoagulated with aspirin (100 mg/day) and warfarin. The initial international normalized ratio (INR) target was 2.0 to 2.5 based on the pre-clinical animal experience in which pumps were implanted for 90 days without any anticoagulation. As will be detailed herein, pump thrombosis did become an issue and, in addition to a device modification, the target range for INR was increased to 2.5 to 3.0.

The protocol called for patients to return for a right heart catheterization between 1 and 3 months after implantation of the device. Some patients underwent transplantation before this point, and in other cases the patients or physicians were reluctant to undergo this invasive test. At the present time, such data are available from 9 of the patients.

**Statistics.** Descriptive statistics are used to summarize data with results expressed as means with SDs, unless otherwise noted. Comparison of data between time points was made with paired *t* tests.

**Results**

**Patient characteristics.** Baseline demographics and treatments of the 17 patients treated are summarized in Table 1. Surgeries were performed in Leuven, Belgium (n = 10), and Münster (n = 3) and Hannover (n = 4), Germany. Patients were between 34 and 63 years of age, were mainly men, and heart failure was mainly on the basis of ischemic cardiomyopathy. Most patients were INTERMACS class 4, but there was 1 class 2 and 1 class 3 patient. These latter 2 patients (both deviations from the protocol) were admitted to the protocol early in the study after several, initial successful outcomes (see the “Overall clinical outcomes and adverse events” section for more details). Almost one-half of the patients had atrial fibrillation. Sixty percent of patients had an internal cardiac defibrillator, and most patients were on optimal medical therapy with diuretics, angiotensin-converting enzyme inhibitor or angiotensin receptor blockade, beta-blocker, and aldosterone inhibitor.

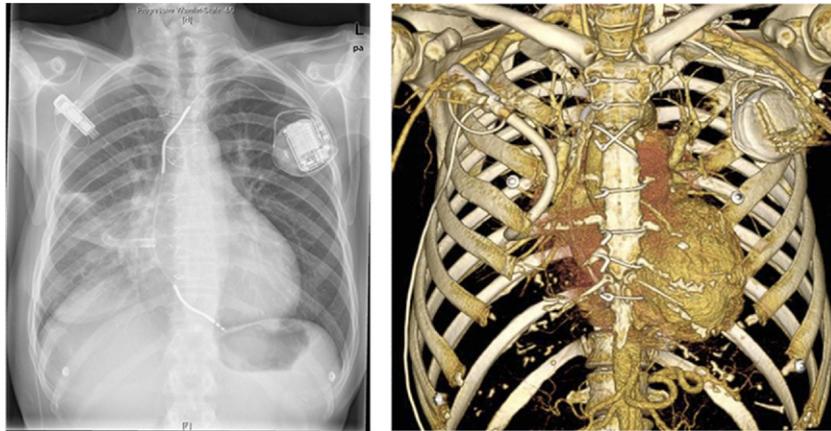
	Mean	SD	Minimum	Maximum
Age (yrs)	52.6	8.7	34	63
Body surface area (m <sup>2</sup> )	2.0	0.2	1.7	2.3
Body mass index (kg/m <sup>2</sup> )	26.0	3.5	21.2	34.0
	n	%		
<b>Sex</b>				
Male	14	82.4		
Female	3	17.6		
<b>Congestive heart failure etiology</b>				
Ischemic cardiomyopathy	14	82.4		
Dilated cardiomyopathy	3	17.6		
<b>Interagency Registry for Mechanically Assisted Circulatory Support</b>				
Class 2	1	5.9		
Class 3	1	5.9		
Class 4	15	88.2		
Diabetes mellitus	4	24		
Atrial fibrillation	7	41		
<b>Treatments</b>				
Implantable cardioverter-defibrillator	10	59		
Diuretic	17	100		
Beta-blocker	12	71		
Angiotensin-converting enzyme inhibitor	11	65		
Angiotensin receptor blockade	3	18		
Aldactone	13	76		
Aspirin	8	47		
Warfarin	3	18		
Statin drug	8	47		
Inotrope(s)	2	12		

	Mean	SD	Minimum	Maximum
<b>Hemodynamics</b>				
Heart rate (beats/min)	79.4	17.4	50	112
Systolic blood pressure (mm Hg)	96.2	13.2	80	122
Diastolic blood pressure (mm Hg)	63.0	7.1	52	80
Mean arterial pressure (mm Hg)	73.2	7.4	61	91
Central venous pressure (mm Hg)	13.4	3.9	7	22
Systolic PAP (mm Hg)	57.4	14.3	36	90
Diastolic PAP (mm Hg)	28.8	7.1	20	45
Mean PAP (mm Hg)	38.9	7.5	28	56
PCWP (mm Hg)	29.4	6.0	21	43
Cardiac output (l/min)	3.8	0.8	2.5	5
Cardiac index (l/min/m <sup>2</sup> )	1.9	0.4	1.3	2.6
Systemic vascular resistance (Wood units)	14.8	2.8	11.1	20.4
Pulmonary vascular resistance (Wood units)	2.5	1.1	1.3	5.2
<b>Echocardiography</b>				
Ejection fraction (%)	20.9	6.2	10.0	32.0
Left ventricular end-diastolic and -systolic dimension (cm)	6.9	0.9	5.4	9.2
Mitral regurgitation (grade)	1.6	0.7	0.0	3.0
Aortic regurgitation (grade)	0.3	0.5	0.0	1.0
Peak VO <sub>2</sub> (ml/kg/min)	9.7	2.0	6.3	12.9
<b>Laboratory findings</b>				
Brain natriuretic peptide (pg/ml)	7,251	5,758	1,011	21,359
Creatinine (mg/dl)	1.4	0.5	0.7	2.6
Total bilirubin (mg/dl)	1.0	0.6	0.5	2.8
Aspartate aminotransferase (U/l)	28	14	14	62
Alanine aminotransferase (U/l)	39	26	12	128

PAP = pulmonary arterial pressure; PCWP = pulmonary capillary wedge pressure; VO<sub>2</sub> = rate of oxygen uptake.

Baseline hemodynamic and functional parameters are summarized in Table 2. As seen, patients were significantly compromised, with increased heart rates, low blood pressures, increased central venous, pulmonary and capillary wedge pressures, low cardiac indexes, increased pulmonary vascular resistances, dilated poorly contracting left ventricles (frequently with significant mitral regurgitation), and very compromised exercise tolerances. Twelve of the patients had no detectible aortic regurgitation, and 5 patients had 1+ aortic regurgitation. Brain natriuretic peptide levels were significantly increased. Renal and hepatic functions were generally well preserved.

Figure 1 shows an X-ray image and a 3-dimensional reconstructed CT scan after a Synergy Pocket Micro-pump implant in a patient with previous cardiac surgery and an implantable cardioverter-defibrillator. The CT scan shows the inflow cannula exiting the left atrium in a direct lateral direction, taking a serpentine course anteriorly and superi-



**Figure 1** Patient With Synergy Pump

Chest X-ray (left) and corresponding 3-dimensional reconstruction (right) of a patient with a Synergy Micro-pump.

only to exit the thorax in the second intercostal space to reach the pump. The outflow graft is shown anastomosed to the subclavian artery. The driveline is also seen coursing inferiorly on the exterior of the thoracic cage.

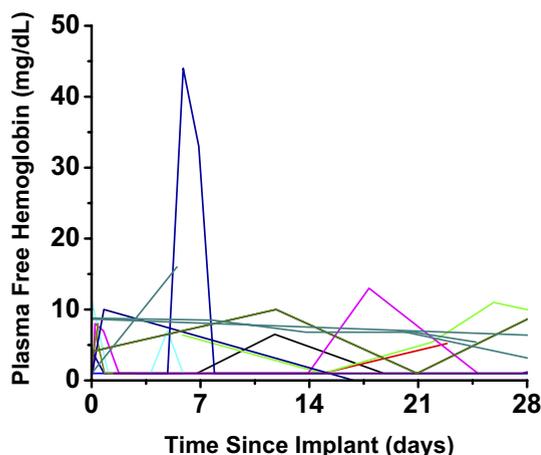
**Plasma-free hemoglobin.** Plasma-free hemoglobin measurements that were taken during the first month of support were obtained from 14 of the patients. Results, summarized in Figure 2, show that with the exception of 1 patient in which plasma-free hemoglobin reached 44 mg/dl, the measurements were typically undetectable and rarely exceeded 10 mg/dl. Measurements made at longer time points (available in some of the patients) showed no late events of hemolysis.

**Acute hemodynamic effects.** Pump speed the day after surgery ranged between 20,000 and 25,000 rpm and esti-

mated pump flow was  $3.0 \pm 0.4$  l/min. Hemodynamics measured the day after surgery showed that compared with baseline results, mean blood pressure was maintained ( $71 \pm 8$  mm Hg vs.  $71 \pm 9$  mm Hg,  $p = 0.79$ ) and that diastolic pulmonary artery pressure decreased from  $27 \pm 3$  mm Hg to  $21 \pm 7$  mm Hg ( $p = 0.01$ ), cardiac output increased from  $3.8 \pm 0.8$  l/min to  $6.3 \pm 1.7$  l/min ( $p < 0.0001$ ), and cardiac index increased from  $2.0 \pm 0.4$  l/min/m<sup>2</sup> to  $3.3 \pm 1.0$  l/min/m<sup>2</sup> ( $p < 0.0001$ ). When patients were grouped according to minimal (0 or 1+,  $n = 6$ ) or moderate (2+ or 3+,  $n = 11$ ) mitral regurgitation, no significant differences in hemodynamic effects were identified ( $p$  values by unpaired  $t$  test  $>0.34$  for all hemodynamic variables tested).

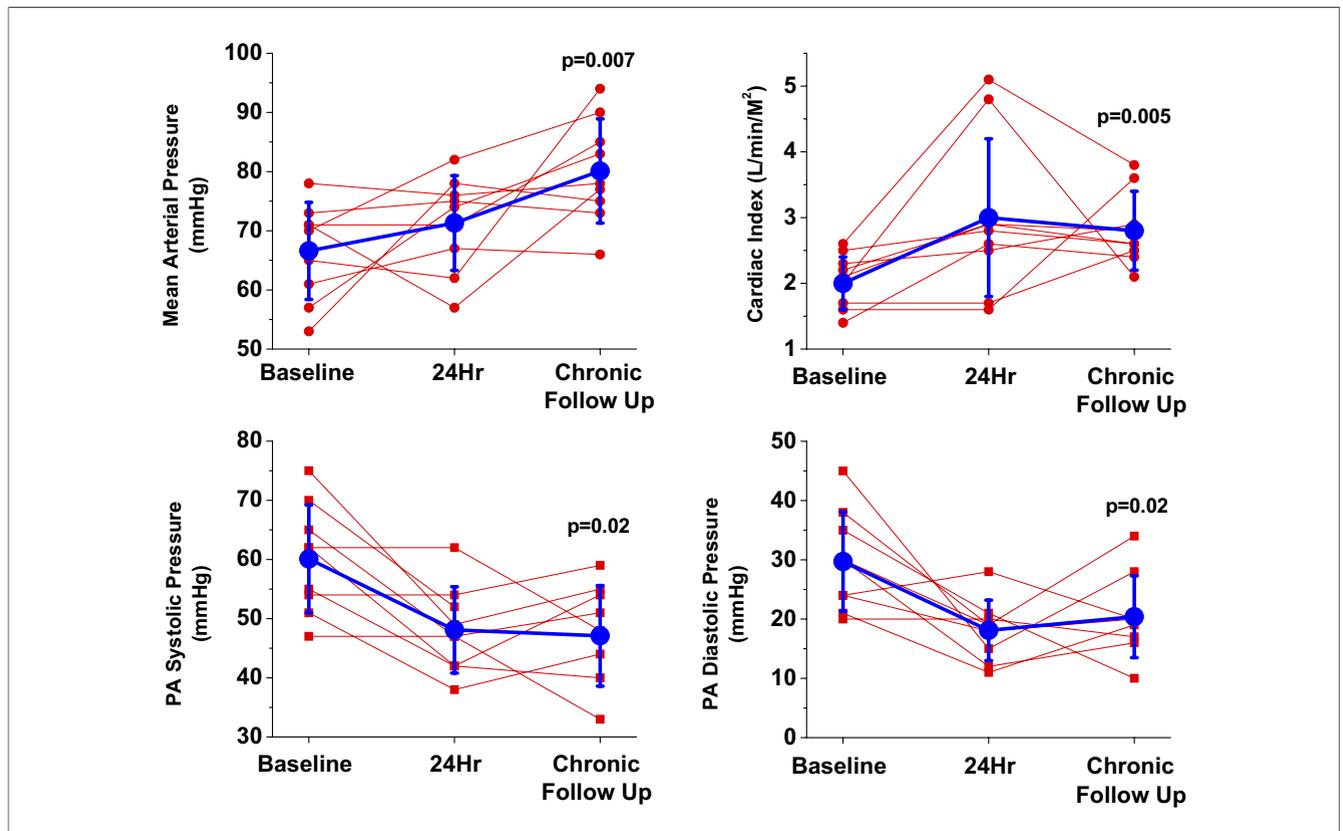
**Chronic effects.** Nine of the patients returned for the protocol-specified right heart catheterization 4 to 19 (mean 10) weeks after implant. Results are summarized in Figure 3. As reviewed previously for the entire cohort, significant hemodynamic improvements were realized within the first 24 h of support, with estimated pump flows of  $2.8 \pm 0.4$  l/min. In the chronic setting, with estimated pump flow also averaging  $2.8 \pm 0.4$  l/min, increases in blood pressure, reductions in pulmonary artery systolic pressure, and maintenance of improved cardiac indexes and pulmonary artery diastolic pressures are observed. Pulmonary capillary wedge pressures (not generally available at the 24-h time point) decreased from a baseline of  $29.7 \pm 5.0$  mm Hg to  $17.8 \pm 5.3$  mm Hg ( $p = 0.001$ ). Serum creatinine was maintained or decreased over this follow-up period, averaging  $1.5 \pm 0.6$  mg/dl at baseline to  $1.3 \pm 0.6$  mg/dl at follow-up. A comparison of medication use before implant and at the time of the follow-up showed a slightly greater use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone inhibitors, with a slight reduction in diuretic use in the follow-up period.

**Overall clinical outcomes and adverse events.** The duration of support has ranged from 6 to 213 (median 81)



**Figure 2** Plasma-Free Hemoglobin Over Time

Plasma-free hemoglobin values obtained during the first 4 weeks of support show that there is minimal hemolysis during use of the Synergy Micro-pump.



**Figure 3 Hemodynamics Over Time**

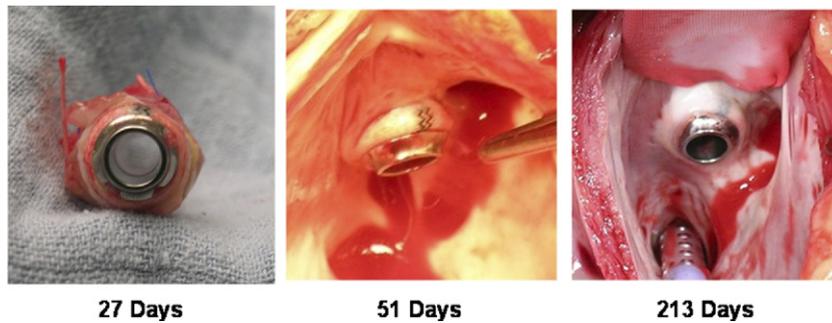
Hemodynamic parameters from 9 patients (with mean and SD) who returned for follow-up right heart catheterization a mean of  $10 \pm 6$  weeks after implantation. The p values are for comparison between baseline and chronic follow-up. **Red lines** are individual patients; **blue lines** are group averages. PA = pulmonary artery.

days. At the time of this writing, 4 of the 17 patients are currently on continued support and doing well (at post-operative days 176, 121, 46, and 29). Nine patients have undergone transplantation successfully. Among these are the INTERMACS class 2 and 3 patients; these patients avoided the need for implantation of a full support LVAD, although they remained hospitalized for the duration of support until heart transplant.

Thirteen of the 17 patients were discharged to home with a mean time to discharge of 18 (range 12 to 26) days. At one site (Hannover), the patients were initially discharged to a cardiac rehabilitation center, which is standard post-cardiac surgical care; all of these patients eventually went home. By report, all of these patients markedly increased their level of activity. Follow-up B-type natriuretic protein values, available from 9 of these ambulatory patients between 1 and 3 months after device implant, showed a mean ( $\pm$ SEE) reduction of  $4,475 \pm 1,389$  pg/ml (from  $6,856 \pm 1,952$  pg/ml to  $2,381 \pm 675$  pg/ml,  $p = 0.02$ ). Formal stress testing was performed in only 5 of the ambulatory patients at both baseline and between 1 and 3 months after discharge; peak  $VO_2$  increased by a mean value ( $\pm$ SD) of  $4.5 \pm 2.0$  ml/kg/min (from  $9.6 \pm 2.0$  ml/kg/min to  $14.1 \pm 1.6$  ml/kg/min,  $p = 0.01$ ).

One patient required conversion to a biventricular support device on post-operative day 7; in this case, the Synergy pump was removed, and the patient was implanted with an Excor (Berlin Heart, Berlin, Germany) full biventricular support device.

There were 3 deaths. One was the consequence of sepsis from an unrecognized renal abscess (post-operative day 7). The second patient, who was clinically stable and doing very well at home, returned to the hospital for the protocol-specified outpatient right heart catheterization (post-operative day 70). The patient developed a fever that evening but did not notify the investigator. He was brought to the hospital urgently 2 days later with hypotension, altered mental status, and renal failure; blood cultures were positive for *Staphylococcus aureus*. Despite aggressive resuscitation, intubation, and antibiotic therapy, the patient succumbed to multiorgan failure. The third death occurred in a patient who was successfully supported for 167 days who self-discontinued his anticoagulation; after  $\sim 6$  days without anticoagulants, the patient returned to the hospital, at which time extensive pump thrombosis and an INR of 1.0 were noted. The patient was stable, and an elective procedure to replace the pump was performed, which resulted in an intraoperative embolic event.



**Figure 4** Cannula Tips at Time of Heart Transplant

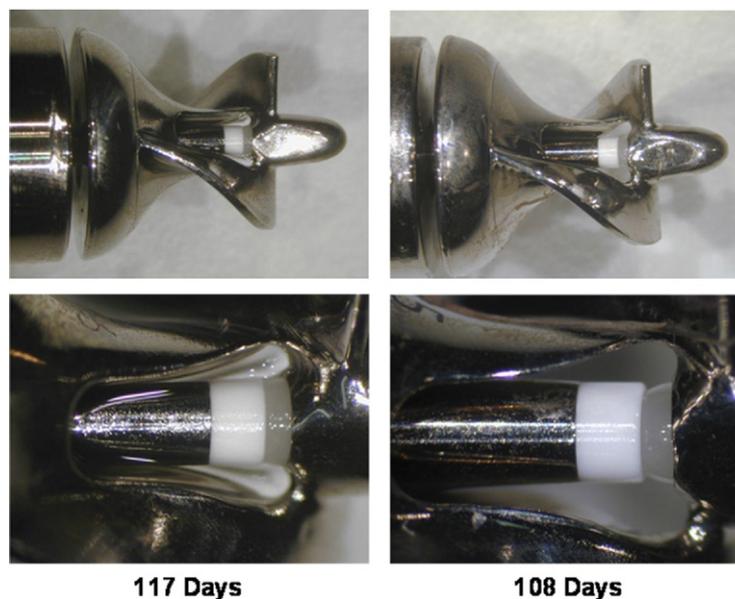
Pictures of the tip of the inflow cannula taken from the left atrium of 3 patients obtained at the time of heart transplant. The cannula is well healed.

In addition to the aforementioned deaths and conversion to biventricular support, notable major adverse events observed included 3 pocket hematomas in the perioperative period that required surgical drainage (although no specific bleeding was noted), a large serous pleural effusion that required thoracentesis, 1 pump pocket infection that cleared with the administration of antibiotics, 1 gastrointestinal bleed that necessitated the discontinuation of warfarin, and 1 transient renal failure (in the patient who was INTERMACS class 2 at baseline).

In addition, 8 of the first 12 patients required pump exchanges because of thrombus formation and pump stoppage. To address this, the study was temporarily halted, the dimensions of a washout channel within the pump rotor were increased to enhance washing within the rotor, and the

target range for INR was increased from 2.0–2.5 to 2.5–3.0. Nine of the modified rotors have been used with no episodes of thrombosis during long-term use (discussed in the “Device explants at transplant” section). Bench testing showed that the pressure–flow characteristics of the pump was not changed detectably by this minor design change, which justifies pooling of the previous hemodynamic data. Device exchanges were performed within 24 h of pump stoppage in a procedure that lasted 30 to 60 min.

**Device explants at transplant.** Examples of inflow cannula tip appearances at the time of heart transplantation (after 27, 51, and 213 days of support) are shown in Figure 4. These examples, typical of all explants, show well-healed tissue covering the Dacron cuff and no tissue on the titanium tip. Examples of rotors (with the increased dimen-



**Figure 5** Rotor Images at Time of Explant

Pictures of the rotor after the specified number of days of support showing that the rotor is free of thrombus and remnants of cellular debris.

sions of the washout channel) and the pivot bearings on which they rotate, explanted after 117 and 108 days of use, are shown in Figure 5. The rotors and bearings are completely free of thrombus and cellular debris.

## Discussion

Aside from acute applications in cardiogenic shock (5–8), most previous studies of long-term use of LVADs have been with devices that completely replace the functioning of the heart. The present study is the first to evaluate the long-term hemodynamic impact of partial ventricular support in patients with chronic heart failure. The estimated flow of the Synergy pump in both the acute setting and during longer-term use was ~3 l/min. The acute hemodynamic effects were similar to those observed previously with partial support devices (such as the TandemHeart [CardiacAssist, Inc., Pittsburgh, Pennsylvania] and Impella [Abiomed, Danvers, Massachusetts] devices), with a ~1.5 to 2 l/min increase in net cardiac output (i.e., the sum of flow through the device and native cardiac output) and ~7 mm Hg reduction in pulmonary artery diastolic pressure (a surrogate of pulmonary capillary wedge pressure), with relatively little impact on arterial blood pressure (6,7).

These observations are also in complete alignment with original theoretical predictions of the impact of 3 l/min partial support in chronic heart failure (9). The important findings of the present study are that they confirm expectations that under longer-term use, partial support would lead to further improvements, which were evidenced by significant further increases in arterial pressure and significant reductions in pulmonary systolic pressures with maintained improvements in cardiac output and pulmonary diastolic pressures. In the backdrop of this improved, stable, and more optimal hemodynamic profile, renal function was maintained or even improved during the period of support.

The study targeted ambulatory patients on the transplant waiting list with severe symptomatic heart failure but preserved end-organ function who were not inotropic dependent. Not uncommonly, this group of patients deteriorates over a relatively short period of time to the point at which they exhibit renal dysfunction, increasing fatigability, and dyspnea. Such patients are hospitalized more frequently and may require either inotropic support or a full-support LVAD. Examination of the baseline demographics and hemodynamics shows that the patients included in the present study were severely compromised and only slightly better than those enrolled in studies of full support assist devices (11,12). For example, the clinical, hemodynamic and laboratory characteristics of the present cohort is not that different than that described for the recent HeartMate II bridge-to-transplant study (12).

Two of the patients with more advanced disease (INTERMACS class 2 and 3) did not reach the treatment goals of being free of inotropic support and out of the hospital. These patients were accepted into the study after

earlier successes and the hope that sicker patients (more typical of the normal LVAD population) could also benefit. Although treatment goals were not met, these patients were considered clinical successes by the treating physicians because the patients were successfully supported to transplant without the need for implantation of a full support device.

The original version of the rotor used in the first 12 patients had a propensity for thrombus formation, resulting in pump stoppages and the need for several pump exchanges. Although this situation was problematic and required interruption of the study and relatively minor modification of the rotor, several important points were demonstrated. First, the major advantages of having a subcutaneously placed pump were demonstrated; specifically, the pump could be changed without entering the thorax in a procedure that was as short as 30 min. Second, if the patients are appropriately anticoagulated and the pump is exchanged within a day of stoppage, the procedure is relatively easy, and no embolic events were noted. However, if the device is allowed to thrombose extensively, there is a significant risk of major thromboembolism during the exchange procedure. Fortunately, after rotor modifications, pump thrombosis has not been observed (9 implants with durations of support almost reaching 4 months). Nevertheless, it is reassuring to know that should a pump malfunction, an exchange procedure can be performed relatively simply and that patients are adequately supported by their native cardiac output.

The present study represents the initial clinical experience with the Synergy system, with the longest duration of support being just >7 months. The main findings of sustained improvements in patients' hemodynamic profiles, although very consistent, were obtained in a relatively small number of patients. Assessment of clinical benefits will ultimately need to be made by comparing outcomes in patients receiving the Synergy system versus those continued on medical therapy. Comparisons would include the nature and severity of adverse events, the time spent in the hospital and the ability to prevent heart failure deteriorations as indexed by progressive end organ dysfunction, the need for long-term inotropic support, transplantation from a high urgency status, or insertion of a full-support ventricular assist device.

The ultimate use of the Synergy system is as a permanent implant in patients who do not qualify for heart transplant, who have a very long expected wait time for a donor organ, or in whom another sternotomy would be too difficult because of previous cardiac operations. The results of the present study provide initial proof of concept that the heart failure state can be improved and stabilized by a device as small as Synergy pumping ~3 l/min. The elective off-pump implantation procedure performed through a mini-thoracotomy was well tolerated and not itself associated with any significant adverse events. Infections related to the device or driveline also were limited to one incidence that

was resolved with the administration of antibiotics. With many of the patients returning home after relatively short hospitalizations and resumption of physical therapy and many activities, the present results provide important proof of concept that a small, partial support pump implanted via a less invasive procedure can provide substantial clinical benefits. Collectively, these findings set the stage for expanding study of this device in longer-term applications, including nontransplant candidates.

#### Acknowledgments

The authors are grateful to Elizabeth Kaufman and Carol Krieger for critical assistance with database management and analysis.

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**Key Words:** left ventricular device ■ hemodynamics ■ heart failure ■ partial support.

**Proof of Concept: Hemodynamic Response to Long-Term Partial Ventricular Support With the Synergy Pocket Micro-Pump**

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*J. Am. Coll. Cardiol.* 2009;54:79-86; originally published online May 20, 2009;  
doi:10.1016/j.jacc.2009.04.023

**This information is current as of November 21, 2010**

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