

Improving Outcomes in Patients With Ventricular Assist Devices Transferred From Outlying to Tertiary Care Hospitals

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Abstract: In this retrospective study, the implant course and outcome of patients with ventricular assist devices (VADs) transferred from outlying “spoke” hospitals and converted nonsurgically to a device designed for ambulation at tertiary care “hub” hospitals are evaluated. Factors affecting the crucial decision to transfer and to convert devices have not previously been characterized. Data from 50 patients at 26 US hub institutions were voluntarily submitted to a VAD data registry at ABIOMED, between December 2003 and December 2005. The patients were transferred from 40 spokes on the BVS 5000 Blood Pump and converted to the AB5000 Ventricle (both ABIOMED) at hubs. Comparisons were made on implant indications, time-course, and end-organ function at the time of conversion between surviving patients and patients that had died. Patients who were transferred and converted had a survival to recovery or to next therapy rate of 42%. Eighteen of the surviving patients were still alive 30 days after the explant: 61% were weaned, 33% were transplanted, and 5.6% received a destination device. Average implant-to-transfer time was 1.5 vs. 2.0 days for 30-day survivors

and expired patients, respectively, whereas support time from transfer to conversion was 4.8 vs. 4 days, respectively. At the time of device conversion, a total bilirubin below a threshold level of 3.5 mg/dL was predictive of 30-day survival ($n = 26$, $p = .03$, odds ratio = 2.73, 95% confidence interval: 1.22–6.16). Patients who survived 30 days were supported longer than those who died (35 vs. 21.1 days, $p = .026$). At least 18 patients recovered sufficiently on the AB5000 Ventricle to tolerate extubation and 11 patients were able to ambulate. Liver function after implant both at the spoke and before conversion at the hub may be a good indicator of patient survivability. Patients transferred from the BVS 5000 Blood Pump benefited from easy, safe conversion to the AB5000 Ventricle, which provided them with additional support time and afforded the opportunity to recover native heart function. **Keywords:** ventricular assist device, regional referral network, tertiary care hospital, spoke, hub, bridge-to-transplant, bridge-to-recovery, ambulatory device. *JECT 2007;39:43–48*

Regional referral networks, where multiple community hospitals feed patients with complications to single tertiary care facilities, have become an essential element of efforts to improve patient outcomes and optimize health care resources. This “hub-and-spoke” model has functioned well to advance the care of patients needing cardiac assist device support at community heart surgery programs (1–3). Typically, seriously ill patients can be transferred to hub institutions on inotropic and/or intra-aortic balloon pump (IABP) support for advanced care. However, such support may not be sufficient or prudent for critically ill patients, such as postcardiotomy or post-acute myocardial

infarction (AMI) patients who are experiencing cardiogenic shock. For patients refractory to medical management, placement of short-term mechanical support devices, such as extracorporeal membrane oxygenation (ECMO) or ventricular assist devices (VADs) provides spoke caregivers with more therapeutic options. Patients who do not show timely native heart recovery can be safely transferred to hubs, which are typically heart transplant centers. Conventionally, these transferred patients with VADs are often prepared for transplantation as definitive therapy (3,4).

Often, conversion from a short-term VAD, such as the BVS 5000 Blood Pump (ABIOMED, Danvers, MA), to a longer-term bridge-to-transplant–approved VAD is necessary because of long waiting times (4). These conversions require major reoperations, therefore representing a risk factor in survival outcomes. With the advent of the AB5000 Ventricle (ABIOMED) in October 2003, caregivers at hubs now have an option to convert patients trans-

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ferred on the BVS 5000 Blood Pump without subjecting them to an open chest surgical procedure. This is primarily because the cannulae used are designed to be compatible with both the AB5000 Ventricle and the BVS 5000 Blood Pump. Patients can benefit from additional support time on a system designed for ambulation, giving them more time to recover their native heart functions. When recovery is deemed unlikely, other therapeutic options such as transplantation or conversion to destination devices may be considered. In this study, the outcome of patients who experienced a specific clinical course of events (i.e., BVS 5000 Blood Pump implant at spoke institutions and conversion to AB5000 Ventricle at hubs) are reported for the first time.

MATERIALS AND METHODS

Between December 2003 and December 2005, 50 patients implanted with the BVS 5000 Blood Pump at 40 US spoke hospitals were transferred to 26 US hub hospitals and converted to the AB5000 Ventricle. Data pertaining to these patients were voluntarily submitted to a VAD Data Registry at ABIOMED in accordance with Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule 45 CFR 164.512(b). Demographic data, implant indications, 30-day survival outcomes, and laboratory measures of end-organ function were compared for patients that survived vs. those who died. Where appropriate, the Student *t* test or Mood median test was used in the analysis. A two-tailed $p < .05$ was considered significant. Statistical analysis was performed using Minitab v14 (Minitab, Inc., State College, PA) and Microsoft Excel v2003 (Microsoft Inc., Redmond, WA).

RESULTS

The patients were predominantly men and ranged in age from 21 to 74 years. The indications for VAD implant at spokes are presented in Figure 1. One half of the patients were either unable to wean off cardiopulmonary bypass or experienced cardiogenic shock after cardiac surgery.

After conversion to the AB5000 Ventricle, 42% of the patients were successfully weaned, transplanted, or converted to third devices (either bridge-to-transplant or destination therapy devices). The three patients converted to third devices died within 30 days. Overall, postexplant 30-day survival was 36%. Sixteen of the eighteen 30-day survivors were confirmed to have been discharged from the hospital, either to return home or to a transitional rehabilitation facility. Of those who were not discharged, one was placed on a destination therapy device, whereas the other's discharge status could not be verified, although this native heart recovery patient was reported to have

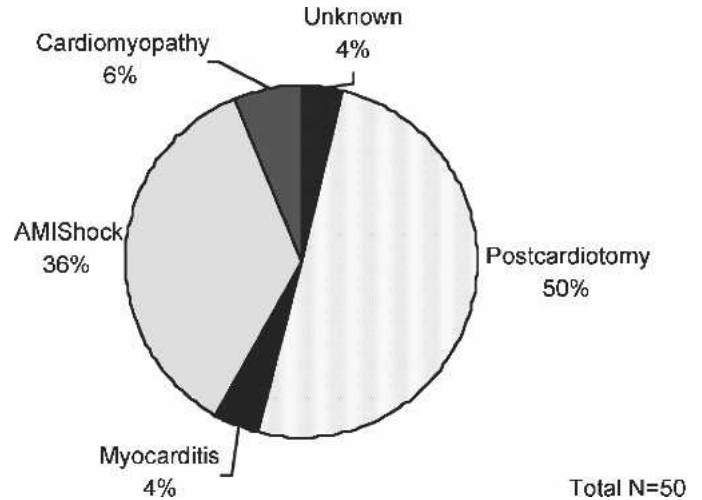


Figure 1. Indications for implantation of BVS 5000 Blood Pump at spoke hospitals.

died 5 months after explant because of pulmonary complications.

In this study, 61% of the 30-day survivors recovered native heart function and were successfully explanted from AB5000 Ventricle support. Patients' etiology for cardiogenic shock did not influence treatment outcomes because similar proportions of postcardiotomy and AMI shock patients were distributed in both the weaned and transplanted groups (Figure 2).

Patients were generally transferred to the hubs within 2 days of the BVS 5000 Blood Pump implants (Figure 3A). After transfer, patients were converted to the AB5000 Ventricle, generally within 4 days. There were no significant differences between the 30-day survivor group and the group that died regarding transfer and conversion times, given the resolution of the timing data reported. The range of support duration for the entire study population was between 2 and 81 days. Thirty-day survivors tended to be supported longer in total than patients that

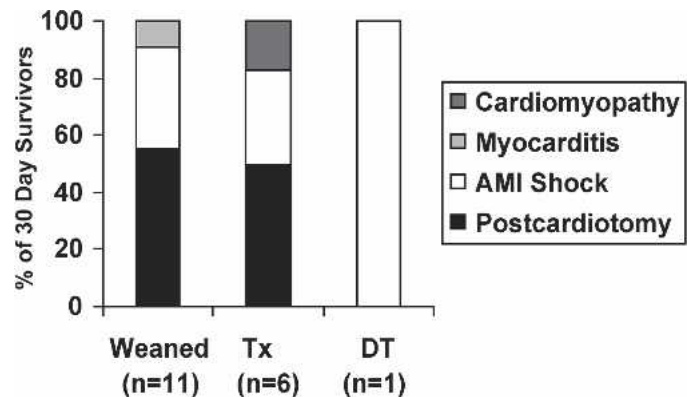


Figure 2. Distribution of pre-implant indicators for each survival outcome group.

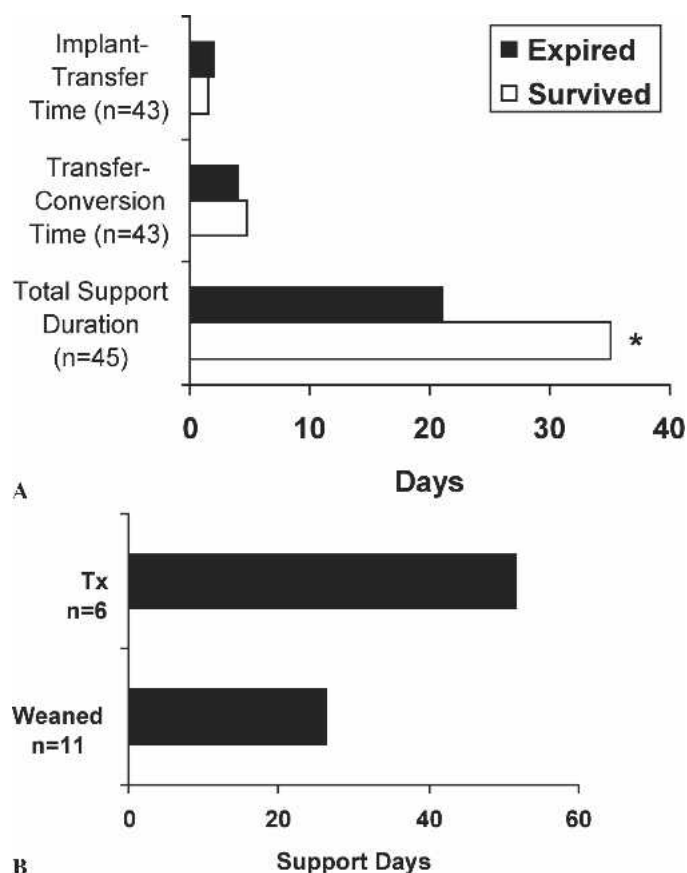


Figure 3. A, Comparison of time durations between major events and total support duration. * $p = .026$. B, Comparison of support duration between transplanted and weaned patients.

died (Figure 3A). As shown in Figure 3B, for 30-day post-explant survivors, average support duration of transplanted patients was substantially longer than for weaned patients. Patients who were transplanted were supported for durations ranging from 28 to 81 days, whereas weaned patients who survived 30 days after explant were supported over a range of 9–44 days. With the longer support duration and mobile capabilities provided by the AB5000 Ventricle, among all patients, 18 were extubated and 11 recovered sufficiently well to ambulate.

To study whether the status of end-organ function at the time of VAD conversion was predictive for patient outcomes, serum chemistry values for kidney and liver function were examined. Data used were from tests performed

Table 1.

	BUN ($n = 33$)	Creatinine ($n = 34$)	SGOT ($n = 26$)	Total Bilirubin ($n = 30$)
Survived	37.6 ± 22.3	1.64 ± 1.25	115 ± 80	3.03 ± 2.11
Died	40.4 ± 18.2	1.95 ± 0.91	237 ± 557	8.56 ± 8.98
p value	0.37	0.15	0.85	0.03

within 48 hours before conversion. As shown in Table 1, 30-day post-explant survivors tended to have better end-organ functions immediately before or at conversion compared with patients that died. Only total serum bilirubin, however, was found to be significantly lower for 30-day survivors. Statistical analysis revealed a significant difference ($p = .03$) with an odds ratio of 2.74 (95% confidence interval: 1.22–6.16) for 30-day post-explant survival, with a total bilirubin level of ≤ 3.5 mg/dL at the time of or before conversion.

The main causes of death were multisystem organ failure, responsible for deaths in 22% (11 of 50) of all patients, and major neurologic injury. Of patients whose support were selectively terminated because of major neurologic injury, five (10%) never fully woke up from their original implant surgery, whereas another five patients (10%) died from neurologic events occurring after conversion to AB5000 support. Two of these latter five patients suffered hemorrhagic strokes: one was coagulopathic caused by heparin-induced thrombocytopenia and another had a cerebrovascular accident history. Another two patients (4%) suffered neurologic events after conversion to a third device from different manufacturers. Other causes of death were sepsis (6%; 3 of 50) and miscellaneous (12%; 6 of 50).

DISCUSSION

Cardiogenic shock, whether postcardiotomy or post-AMI, is associated with poor prognosis (5–7). When medical therapy, including IABP support, proves inadequate to support such patients at spokes, affordable short-term VADs can be used to support them. Ventilated postcardiotomy patients with deteriorating end-organ functions and on temporary support devices can have dismal mortality rates (8–10). Participation in a “hub-and-spoke” model can improve outcomes because patients with short-term VADs are transferred to centers where more aggressive therapeutic options are offered.

A similar spoke-to-hub study at The University of Pennsylvania (UPenn) (3) provides a perspective for comparison to this study. One cohort of 28 patients in that study were similarly implanted with VADs at spokes (18 patients had BVS 5000 Blood Pumps) and transferred to hubs. Six of the transferred patients were converted to longer-term devices other than the AB5000 Ventricle, which was not yet commercially available. The 1-year survival rate was of 32% (9 of 28). A major difference between the two studies can be observed when comparing the treatment outcomes (Figure 4A). All of the surviving patients in the UPenn report were transplanted, whereas almost two thirds of 30-day survivors in this study recovered native heart functions. Figure 4B shows the similar-

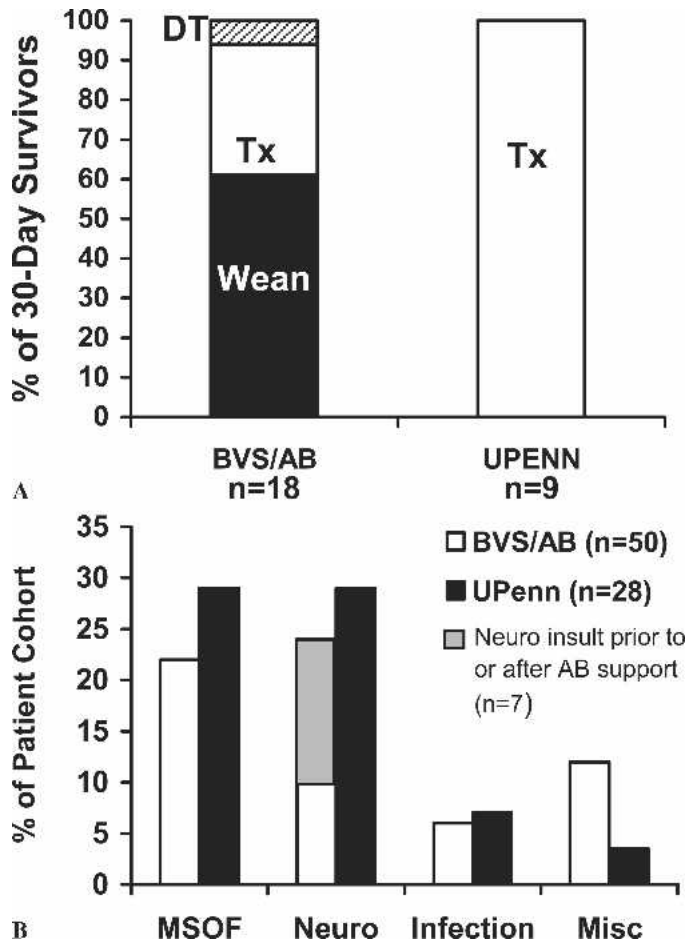


Figure 4. Comparison of survival outcomes (A) and causes of death (B) between patients implanted with BVS 5000 Blood Pump at spokes and converted to AB5000 Ventricle at hubs vs. comparable group from UPenn study (3). DT, destination therapy; Tx, heart transplantation; MSOF, multisystem organ failure; Neuro, neurologic injury.

ties in causes of death between the two studies. Multiorgan failure and all-cause neurologic injuries with no evidence of improvement would eliminate any patient from consideration for heart transplantation and were indeed the most frequent causes of death in both groups of this profoundly ill patient population. In this study, five patients who ultimately died from neurologic causes either never woke up after the initial implant or suffered neurologic events while on BVS 5000 support. Adequate neurologic evaluation before conversion at the hub is thus still an essential element for optimizing future outcomes.

At hubs, all transferred patients should be evaluated for potential myocardial recovery. If recovery is unlikely, patients are usually evaluated for heart transplantation. Unfortunately, many patients may need more time than a short-term VAD can safely provide to show either myocardial recovery or end-organ recovery sufficient to qualify for transplantation (and thus, for conversion surgery).

The Columbia-Presbyterian group recommends making a decision on the potential for myocardial recovery within 24 hours of receiving a transferred patient with a short-term VAD (1). The patients in this study received additional time to recover when they were nonsurgically converted to the AB5000 Ventricle from the BVS 5000 Blood Pump. Successfully weaned patients averaged a total support duration of 26.3 days, whereas that of transplanted patients was 51.7 days, both well beyond the reported average support duration (4.9 ± 4.1 days) of the BVS 5000 Blood Pump (11). All of the transplanted patients survived to discharge, again indicating adequate systemic recovery time on support to become good transplant candidates.

Before the introduction of the AB5000 Ventricle, conversion to a longer-term device meant setting patients with a BVS 5000 Blood Pump back with an invasive explant-reimplant surgical procedure. In contrast, conversion from the BVS 5000 Blood Pump to the AB5000 Ventricle can be conducted at the bedside with minimal support disruption and limited risks of bleeding and infection. Although unproven, eliminating invasive surgical conversion procedures likely increases the odds that myocardial recovery would occur. For patients who do need transplantation, surgical conversion introduces risks that could hinder their recovery or completely disqualify them from receiving donor hearts. In this study, four patients were surgically converted from the AB5000 Ventricle to third devices. Three of these patients died within 30 days of conversion, one of whom had already successfully been supported for 80 days and was ambulating before surgery. Only six patients in the UPenn report were surgically converted (initial support device is unknown), four of whom survived to transplantation (3). Support durations were not reported in that study. More widespread adoption of the AB5000 Ventricle technology at spokes in the future could allow for smoother patient transfers and potentially eliminate the need for any device conversions.

Although the survival outcomes of this study were satisfactory and consistent with reports in the literature, improvements are certainly possible. Best-practice protocols can contribute, especially because the frequency of VAD use and transfers are low. None of the spokes transferred more than two patients, and one half of the hubs only received one patient. The other half received two to five patients each. Owing to more extensive VAD programs, many hubs already have protocols, such as for patient screening and VAD conversion, early extubation and ambulation, anticoagulation, infection, and nutritional management, as well as for VAD weaning. Patient management algorithms, such as that proposed by the surgical group at Columbia-Presbyterian, could prove invaluable (1). This study showed that liver function before conver-

sion is predictive of mortality, which is in agreement with previous studies showing preoperative liver function as a predictor of VAD outcomes in bridge-to-transplant patients (10). More extensive studies will be needed to determine if other pre-implant factors are predictive of recovery and survival, therefore further facilitating screening by hubs.

Spoke hospitals also play a key role in determining outcomes. Factors such as timing to implant, timing to transfer, choice of device, and configuration used [Left VAD (LVAD) or Biventricular VAD (BiVAD)] are all crucial decisions. Communication with a hub center was encouraged within 12 hours of postcardiotomy failure by the Columbia-Presbyterian group (1). Issues reviewed should include cardiac, pulmonary, renal, hepatic, and neurologic function, cardiac enzymes, hemostasis, anticoagulation, and device-specific technical considerations. Early VAD implantation for failure to wean from cardiopulmonary bypass vs. repeated weaning attempts using maximal inotropes and an IABP has previously been recommended to avoid damaging the myocardium further (12,13). AMI patients in profound cardiogenic shock should also be implanted early because favorable outcomes (46% survival to discharge, of whom 58% recovered native heart function) have previously been shown with AB5000 Ventricle support (14). Right ventricular function should be carefully assessed with left-sided support patients (15). Technical issues, such as careful cannula placement with transesophageal echocardiography guidance, can avoid future inflow limitation problems. If long-term support is anticipated, left ventricular apical placement should be considered to minimize the risks of thrombosis. Conversion to AB5000 Ventricle support is also facilitated when the inflow cannula is positioned on the right side of the outflow cannula. Rapid transfer, within 72 hours of implantation, has been recommended, barring inadequate hemostasis and oxygenation (12).

This retrospective study is limited by the voluntary nature of registry databases. Two thirds of the patients in this study needed BiVAD support before transfer compared with only 2 of 28 patients (7%) in the UPenn group (3). While this may hint at a difference in severity of cardiac dysfunction, a proper comparison will require additional data. The number of patients in each comparison group for the end-organ dysfunction analysis in this study were similar, but did not include all 50 patients because of limitations in data availability. The registry also did not receive adequate data for comparisons to patients with the BVS 5000 Blood Pump who were not transferred or those who were transferred but not converted to the AB5000 Ventricle. To fully understand recovery outcomes vs. transplantation outcomes, prospective multi-hub studies are needed to adequately analyze preimplant conditions,

courses, and long-term outcomes. Such a study may be feasible if it is based off a national device registry such as the recently initiated Interagency Registry for Mechanical Circulatory Support (INTERMACS).

In conclusion, with donor heart availability not likely to increase, the most efficacious use of what is offered is necessary. Transfer of profoundly ill patients from spoke hospitals to transplant centers does not mean cardiac transplantation is inevitable. Cardiac transplantation and all its associated comorbidities can be avoided in some patients. Patient groups from both this study and one cohort of the UPenn study arrived at hub institutions under similar circumstances, but the clinical outcomes were different for many patients. Sixty-one percent of patients who survived 30 days after explant in this study benefited from the opportunity to recover their own native heart functions, whereas all the survivors from the UPenn study did not. Implementation of best-practice protocols, combined with safe, easy conversion to the AB5000 Ventricle, can provide transferred patients with the BVS 5000 Blood Pump with the best opportunity for myocardial recovery, which should always be the first goal. When such recovery is not possible, patients converted to the AB5000 Ventricle were shown in this study to be successfully supported and rehabilitated to transplantation.

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