Insertion of a left ventricular assist device in patients without thorough transplant evaluations: A worthwhile risk?

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Objectives: Patients in acute cardiogenic shock may require placement of left ventricular assist devices before undergoing standard pretransplant evaluations. This practice raises ethical and logistic concerns and has led us to investigate the short- and long-term outcomes for this patient population.

Methods and Results: We examined our adult bridge-to-transplant left ventricular assist device population over a 6-year period to characterize those patients with acute cardiogenic shock who received left ventricular assist devices on an emergency basis (ie, placement of a device within 24 hours of being listed for cardiac transplantation). Outcomes before and after transplant were compared with those of candidates with nonemergency evaluations by Kaplan-Meier survival curves and the Fisher exact test where appropriate. Of the 115 patients who required left ventricular assist device support, 73 (63%) patients required emergency placement; 70% of these patients survived to transplant compared with 83% of those with nonurgent device implantation (not statistically significant). Posttransplant survival curves were similar for patients with emergency device placement and those with nonurgent placement (not statistically significant). Twenty-two patients having emergency device placement did not undergo heart transplantation because of multisystem organ failure (14), device support withdrawal from irreversible neurologic injury (4), device or technical problems (2), and left ventricular assist device explant due to myocardial recovery (2).

Conclusions: At our institution, the majority of left ventricular assist devices are placed on an emergency basis. Few of these patients require discontinuation of device support due to undetected conditions during abbreviated preoperative evaluation. Survival before and after transplant is comparable with those of patients who undergo nonurgent left ventricular assist device placement or medical therapy.

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Patients with severe heart failure referred for cardiac transplantation undergo a comprehensive evaluation to assess the need for transplant as well as to identify significant comorbidities that could shorten posttransplant survival. All patients accepted for transplant are potential candidates for left ventricular assist device (LVAD) insertion as a bridge to transplantation. If a waitlist patient should require an LVAD bridge, this extensive evaluation is completed before LVAD support is begun.¹⁻⁴ At this point, only issues related to device placement have to be addressed.⁵⁻¹⁰ However, patients with acute cardiac shock syndromes frequently do not undergo

comprehensive evaluations before device placement due to time and logistic constraints, which do not permit a thorough examination before surgical intervention. Whether undetected problems due to the brevity of these emergency preevaluations decrease survival before and after cardiac transplantation compared with those candidates with non-urgent evaluations is unknown. Patients who receive LVADs on an emergency basis are generally sicker and less stable than those who receive the devices electively. These patients may therefore experience longer stays in the intensive care unit (ICU) with multisystem organ failure. Whether the extraordinary medical efforts devoted to these patients translate into any clinical benefit is unknown. Accordingly, we performed a retrospective analysis of LVAD recipients at a single large transplant center to investigate whether emergency LVAD placement was an expensive exercise in medical futility or beneficial therapy.

Methods

Study Design

Retrospective analysis of our adult bridge-to-transplant LVAD (HeartMate; Thermo Cardiosystems, Inc, Woburn, Mass) population and the medically managed patient population from May 1993 through September 1999 was performed. Recipients were separated into 2 groups, emergency and nonemergency. Patients were classified as nonemergency if they had undergone complete transplant evaluations and were listed for cardiac transplantation for more than 24 hours. Patients were classified as emergency if the device was placed within 24 hours of being listed for cardiac transplantation. Such patients were generally transferred to our center in acute cardiogenic shock resulting from myocarditis or acute myocardial ischemia, in postcardiotomy cardiogenic shock, or with rapidly worsening heart failure. None of these patients underwent a full transplant evaluation.

For the emergency patients, an abbreviated transplant evaluation was performed before device implantation. This included a review of available medical records, a history taken from the patient when possible, information from the family and/or the local physician, a physical examination, and a review of available laboratory data. Clearly, many elements of the routine transplant evaluation were not available (ie, assessment of vasculature [carotid, noninvasive flow studies]), including thorough psychosocial evaluation to assess future compliance, serologies, abdominal ultrasound, 24-hour creatinine clearance, and pulmonary function tests. Frequently patients were accepted despite the inability to fully assess neurologic status due to sedation. Patients were also accepted if renal failure was presumed to be acute and reversible. This process carried a potential risk of accepting patients with severe brain damage or other significant medical problems who are not transplant eligible. We accepted this risk for such emergency cases.

To evaluate ICU outcomes, an analysis was performed to gauge the efficacy of each emergency LVAD placement in a subset of LVAD recipients from January 1, 1997, to December 31, 1998. Patients were again divided into emergency and nonemergency groups. These patients were characterized by length of stay in the

ICU into 3 categories. Those with an ICU length of stay of 14 days or more were considered "prolonged ICU stays," whereas others were either "standard ICU stays" or "death in the ICU" if they had not survived 14 days after LVAD insertion.

Statistical Analysis

Patient status was determined to October 2000 and each person's outcome was characterized as transplantation, ongoing device support, device explantation, or death. Survival data was compared by Kaplan-Meier survival curves and Fisher exact tests where appropriate.

Results

Between August 1993 and September 1999, a total of 115 LVADs were placed; 73 (63%) were considered emergency LVAD placements. Clinical characteristics of these groups are shown in Table 1. Age, sex, and baseline left ventricular ejection fractions were similar between the 2 groups although more patients in the emergency group had coronary artery disease and more in the nonurgent group had chronic dilated cardiomyopathy. Table 2 displays the indications for each emergency insertion. Fifty-one patients who received emergency LVADs were transferred directly from outside institutions, and 16 of them arrived with temporary assist devices in place. All patients were transferred within 48 hours of acute decompensation. Among the devices they had in place were intra-aortic balloon pumps, biventricular assist devices, extracorporeal membrane oxygenators, BioMedicus devices (Medtronic BioMedicus, Eden Prairie, Minn), and Abiomed BVS devices (Abiomed, Inc, Danvers, Mass). Fewer than 5% of patients required support with a biventricular device, and of these roughly 70% could be subsequently weaned off the right ventricular assist device.

Survival Before and After Transplant

Fifty-one of the 73 (70%) patients in the emergency group ultimately received transplants, which was slightly lower but not statistically different from the 35 of 42 (83%) patients in the nonemergency LVAD population ($P = .109$). The emergency LVAD patients not receiving a transplant had a broad range of outcomes. Fourteen (19%) of these patients died of progression of multisystem organ failure, 4 (5%) had device support withdrawn because of irreversible neurologic dysfunction, 2 (3%) died of device or other technical difficulties, and 2 (3%) patients underwent LVAD explantation due to myocardial recovery. Kaplan-Meier survival curves for all LVAD recipients are shown in Figure 1. "Survival" is defined in terms of actuarial life or death (irrespective of receiving a transplant) and "day 0" is the day when an LVAD was placed. Survivals for both the emergency and nonemergency LVAD groups were comparable, with both groups exhibiting greater than 50% cumulative survival at a point 1000 days after LVAD placement. The highest mortality occurs within the first few months

TABLE 1. Clinical characteristics

	All LVADs	Emergency	Nonemergency	<i>P</i> value emergency versus nonemergency
Age (years)	52.1 ± 11.1	52.3 ± 11.2	51.8 ± 11.1	NS
Gender				
Male (n)	91	57	34	NS
Female (n)	24	16	8	NS
Etiology of CHF				
CAD	65	50	15	.0009
Dilated cardiomyopathy	42	19	23	.003
Acute cardiomyopathy (Presumed myocarditis, Postpartum CM, etc.)	3	3	0	NS
Postcardiotomy	5	1	4	NS
LVEF	20% ± 7%	20% ± 8%	20% ± 7%	NS

LVAD, Left ventricular assist device; CHF, congestive heart failure; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; NS, not significant; CM, cardiomyopathy.

TABLE 2. Emergency LVADs, August 1993 to September 1999

Etiology	Number of patients
Failed coronary artery bypass grafts/ percutaneous transluminal coronary angioplasty	26
Acute decompensation of congestive heart failure	26
Acute myocardial infarction	13
Acute myocarditis	7
Failed coarctation repair	1
Total	73

LVAD, Left ventricular assist device.

after LVAD insertion. Posttransplant survivals for the emergency LVAD, nonemergency LVAD, and medically treated populations are shown in Figure 2. Survival after transplant was similar in all groups.

From January 1, 1997 to December 31, 1998, 54 patients underwent LVAD placement. Twenty-eight patients received their LVADs on an emergency basis; 6 of the 28 emergency LVAD recipients died in the ICU after a stay of less than 14 days. Six of these 54 recipients had ICU stays of 14 days or longer. This "prolonged ICU stay" subgroup consisted of 10 emergency LVAD recipients and 6 non-emergency LVAD recipients. Six of the 10 emergency LVAD recipients in the prolonged ICU stay group survived, while 4 died. Two other emergency LVAD recipients who survived their initial ICU stay died later in their course. Overall, 16 of 28 emergency LVAD recipients in 1997 and 1998 survived until transplantation.

Discussion

As a major tertiary referral center, our institution accepts patients from outside institutions who are in acute cardiogenic shock due to a variety of causes. Our retrospective analysis reveals that the majority of LVADs are placed on an emergency basis in patients having complications of coronary artery disease. Although this group receives an abbreviated transplant evaluation relative to the non-emergency recipients, the majority of these patients survive to transplant. Furthermore, our analysis indicates that few inappropriate devices are placed due to limited preevaluation time. Our conclusions offer a different perspective from the existing literature, which focuses more on the tailoring of transplant evaluations to improve bridge-to-transplantation programs.¹¹⁻¹³ Our conclusions also differ from the existing literature, which suggests that thorough transplant evaluation before LVAD insertion is crucial to the success of bridge-to-transplantation programs.¹⁴ Deng and colleagues¹⁴ performed a similar retrospective analysis of all LVAD recipients at the Muenster University hospital between 1990 and 1996. Using criteria comparable with that employed in our analysis, the authors divided the LVAD recipients into 3 subgroups: elective bridging, urgent bridging, and emergency bridging. Overall survival, including the posttransplantation period, in their study was superior in the elective group compared with either the urgent or emergency group and the combined urgent/emergency group. Perioperative mortality rate in the Muenster study, defined as death within 30 days after LVAD operation, was 33% in the emergency LVAD group compared with 11% in the urgent and 5% in the elective LVAD groups. Only 33% of the patients in the emergency bridging group survived until transplantation. Deng and colleagues¹⁴ assert that the he-

Figure 1. Kaplan-Meier survival curves for the nonemergency and emergency LVAD recipients between August 1993 and September 1999. In this figure, day 0 is defined as the day on which an LVAD was initially inserted in a patient. Survival is defined in terms of actuarial life or death. The individual *circles* shown in the figure represent points at which cumulative survival dropped due to patient death(s). This figure highlights the remarkable similarities in survival between the 2 groups of LVAD recipients.

Figure 2. Kaplan-Meier actuarial survival curves comparing patients receiving a transplant after LVAD support (*thick line*) to transplant patients who did require LVAD support (*dashed line*) ($P = NS$).

modynamic deterioration experienced by patients in the urgent and emergency LVAD groups often leads to multiorgan dysfunction. This multiorgan dysfunction entails immunologic sequelae that are exacerbated by the trauma of ventricular assist device implantation. The authors suggest that these alterations make favorable outcomes unlikely. The authors specifically refer to continual activation of inflammatory cascades and suppression of the T-cell-mediated immune response as mechanisms that lead to increased

susceptibility to systemic infection.¹⁵⁻¹⁸ The authors also postulate that in the context of multiorgan dysfunction, LVAD insertion may lead to activation and dysfunction of the coagulation cascade with subsequent disabling neurologic sequelae.¹⁹⁻²¹ On the basis of the Muenster survival data, they conclude that surgeons should be restrictive in their use of ventricular assist devices in emergency cases and should attempt to place these devices sooner, before rapid deterioration occurs.

In contrast, our analysis suggests that emergency LVAD placement does, in fact, result in a significant net benefit to patients. In our study, the majority of patients who received LVADs on an emergency basis survived until donor hearts became available for transplantation. Moreover, the survival of patients in the emergency LVAD group was comparable with that of the nonemergency LVAD recipients. Finally, despite the fact that medical comorbidities and psychosocial problems were inadequately addressed in the emergency context, our outcome was acceptable. Nonetheless, the tremendous importance and impact of such factors should not, by any means, be discounted.

There are several plausible explanations for the difference between our results and those of the Muenster study. The time frames of our studies are slightly different, with our group including patients with devices implanted beyond 1996. As surgeons become more experienced in the operative placement of LVADs and the clinical management of LVAD patients, survival to transplant is expected to improve. Also, the quality of the devices being used is also expected to improve with time, resulting in increased survival. Moreover, we participate in a multihospital network that provides our surgeons with rapid access to patients from other institutions.²² Thus, many patients who lapse into cardiogenic shock are rapidly offered LVADs before extensive multiorgan damage has occurred. In this manner, Columbia's relationship with other area hospitals may play a significant role in improving patient outcomes.

Our analysis of the LVAD population in 1997 and 1998 further supports the use of emergency LVAD insertion. Emergency LVAD patients who remain in the ICU for 14 days or longer can undergo successful bridging to transplantation. Typically these patients experience more difficult recoveries than the elective LVAD recipients but the majority of emergency LVAD recipients do recover. In 1997 to 1998, 6 of the 10 emergency LVAD recipients with prolonged ICU stays survived until transplant. This is a significant survival figure, and it indicates that the extensive efforts and resources devoted to these patients are worthwhile. However, the desire to place these devices in increasingly ill and unstable patients must be balanced by economic realism if ventricular assist programs are to remain viable in the long run.

The notion that LVADs should be placed sooner rather than later has been widely advocated and in general we agree with this principle. Unfortunately, it is difficult to predict which patients are likely to undergo hemodynamic deterioration necessitating mechanical support while waiting for a donor heart. Because LVAD insertion entails a significant amount of perioperative risk, surgeons cannot ethically insert these devices in all patients on heart transplant lists. However, for patients who are in acute cardiogenic shock, LVAD placement often represents the lone

hope of survival. Our analysis suggests that these patients do experience a net benefit from "eleventh hour" LVAD placement. Therefore, lack of thorough evaluation of patients in cardiogenic shock should not preclude LVAD insertion. In our cohort only 4 patients with irreversible neurologic dysfunction required withdrawal of device support, and in those patients who survived to transplant, no significant premorbid conditions that would have precluded transplant were identified. Nevertheless, the possibility of device withdrawal is discussed with patient families at the time of device insertion regarding the development of irreversible medical conditions that preclude transplant. This emergency implantation is further justified by our demonstration that once transplanted, these patients do just as well as the medically treated recipients.

On the other hand, the practice of emergency LVAD placement with regard to transplant listing creates a potential ethical quandary because these patients may end up diverting hearts away from other patients who have been waiting on transplant lists for longer time periods. One could argue that the relatively "stable" patients waiting on transplant lists should not be "leap-frogged" by patients who are listed on an emergency basis, especially in light of the current scarcity of donor hearts. However, one could also argue that patients requiring urgent LVAD placement are in the gravest danger of dying and thus should receive priority on transplant lists. These are difficult issues for which no simple resolutions exist. The current system presents the best efforts of transplant programs to balance the needs of all patients involved in this admittedly imperfect process. As the medical community gains more experience in placing LVADs, clinically managing LVAD recipients, and accurately identifying individuals who can benefit from LVAD support, the utility of this device as a bridge to transplantation will continue to improve.

In conclusion, the majority of devices at our institution are placed for emergency indications. Although the short-term survival appears to be less than that for patients receiving devices for nonemergency indications, a comparable number ultimately receive transplants. Additionally, the long-term survival is similar for both of these populations, especially with transplantation. Therefore, the use of devices for acute catastrophic situations appears warranted despite the abbreviated transplant evaluations.

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