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Mechanical circulatory support: devices, outcomes and complications

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Abstract Systolic heart failure is a problem of substantial magnitude worldwide. Over the last 25 years great progress has been made in the medical management of heart failure with the recognition of the benefits of beta-adrenergic blockade, modulation of the renin-angiotensin and mineralocorticoid axes and judicious diuretic therapy. In addition, cardiac resynchronization therapy and prophylactic implantation of cardiac defibrillators have been responsible for measurable benefits in terms of functional status and dysrhythmia-related mortality, respectively. Unfortunately, progressive cardiac dysfunction often results in activity limitation, symptoms at rest, hospital admission, end-organ dysfunction and death despite maximal implementation of standard therapies. Heart transplantation has been a dramatic and effective therapy for end-stage heart failure, but it remains limited by a shortage of donor organs, strict criteria defining acceptable recipients and often unsatisfactory long-term success. Mechanical alternatives to support the failing circulation have been sought for the last 50 years. The history of device development has been marked in general by the slow progress achieved by a few dedicated and persevering pioneers. In the past decade, however, evolving technology has dramatically changed the field and broadened the options for the treatment of advanced heart failure. This review will detail the important milestones and the current state of the art, with an emphasis on implantable devices for intermediate to long term support.

Keywords Heart failure · Circulatory support · LVAD · Complications

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Historical context

Early efforts in the field of mechanical circulatory support were focused on both cardiac replacement and ventricular assistance. Once cardiopulmonary bypass systems were reliable enough to permit complex cardiac operations, post-cardiotomy shock became a problem in need of a solution. The first reported clinical use of a left ventricular assist device (LVAD) was by Liotta and Crawford in 1963. The pump, an intracorporeal pneumatically driven device, was implanted via a left thoracotomy using left atrial inflow and descending thoracic aortic outflow. Pulmonary edema cleared and systemic perfusion improved but the patient, who had sustained an anoxic injury prior to pump implantation, died [1]. DeBakey in 1966 utilized a paracorporeal pneumatic LVAD to support the left ventricle of a woman who had undergone aortic and mitral valve replacement for severe rheumatic disease. Left atrial inflow and right axillary arterial outflow were used. The device was weaned over 9 days post-surgery and the patient completely recovered [2]. The first clinical use of a total artificial heart (TAH) was reported in 1969 by Cooley. The Dacron and Silastic pneumatic device was placed as a bridge to transplant in a patient who could not be weaned from cardiopulmonary bypass after the aggressive resection of a left ventricular aneurysm. The patient awoke and was extubated early after surgery, with excellent hemodynamics provided by the TAH for 64 h. A donor organ became

available and functioned well for 32 h but the patient died from a fulminant necrotizing pseudomonas pneumonia [3]. Over the subsequent 20 years results after cardiac transplantation improved to modern standards, but donor organ availability remained stagnant. TAH heart development was pursued by two major groups, with two very different designs. The Jarvik/CardioWest device, which would ultimately become today's SynCardia TAH, generated tremendous publicity but clinical utility was still limited. Liotta at the Texas Heart Institute, in collaboration with engineers from Abiomed (Danvers, MA) and the University of Louisville continued quiet work on the device which would ultimately become the AbioCor [4].

Fig. 1 Thoratec PVAD and IVAD. Image courtesy of Thoratec, Inc

Extracorporeal and paracorporeal devices

In contrast, ventricular assist device (VAD) development and deployment was much more active. Initial clinical implementation was most commonly as either bridge to recovery (BTR) or bridge to transplantation (BTT) in patients with cardiogenic shock refractory to inotropes and intraaortic balloon counter pulsation (IABP) [5, 6]. In the United States the most important early design would become known as the Thoratec VAD, which was based on the work of Pierce and Donachy at Penn State University. This pneumatically-driven pulsatile device has undergone many modifications since it was developed in the 1970's but retains its essential characteristics to this day. Initially approved for short term use as a bridge to recovery, it was approved as a BTT device in 1994. McBride, in 1999 published results of a series of BTT and BTR patients supported on the Thoratec device. Major complications included bleeding (31–45%), thromboembolism (8.1%) and device-related infection (18%). Twelve of 44 patients recovered and 39 of 67 were bridged to successful orthotopic heart transplantation (OHT), with a 5 years post-transplant survival of 85% [7]. The Thoratec Paracorporeal VAD (PVAD) is the direct descendant of this device, and is currently approved as a BTT or BTR in either a univentricular or biventricular (BIVAD) configuration (Fig. 1).

It is most useful when an intermediate duration of support is anticipated. Korfer and colleagues supported 114 patients for a mean of 45 days between 1992 and 1998 with the PVAD. Forty-three required biventricular support, 84 were BTT and 17 were supported for post-cardiotomy shock. Sixty-eight percent of the BTT underwent OHT, with an 88% 1 year survival. Forty-seven of those bridged to recovery survived. Nineteen percent of those supported suffered a neurologic complication [8]. The more contemporary Levitronix Centrimag is an extracorporeal device approved for up to 6 h of support for patients in cardiogenic shock as a bridge to decision (BTD; Fig. 2).

It is also approved for use as a right ventricular assist device (RVAD) for up to 30 days of support. A Pivotal Trial in patients with post-cardiotomy cardiogenic shock (PCCS) who are unable to separate from cardiopulmonary bypass is accruing patients. As a bridge to decision, the Centrimag will allow transition to recovery, transplant or a long-term VAD. The Centrimag, a continuous flow centrifugal pump with a magnetically levitated rotor, is preload-dependent and afterload sensitive and can deliver flows of nearly 10 l per minute. Anticoagulation, with an activated clotting time of 160 s or activated partial thromboplastin time of 60–80 s is required. Magnetic levitation technology has been developed in blood pumps in order to capitalize on decreased component wear and

Fig. 2 Centrimag pump with motor. Image courtesy of Thoratec, Inc

heat generation, which are believed to translate into improved durability and minimal risk of hematologic damage [9]. The Centrimag is simple, portable and versatile and as a result has been used and reported in a variety of settings. The Utah Artificial Heart Program reported on 83 patients (2004–2009), 30 RVAD, 8 LVAD, 25 BiVAD and 30 patients supported with Centrimag-driven veno-arterial extracorporeal membrane oxygenation (V-A ECMO). Survival ranged from 63% in the LVAD group to 30% in the V-A ECMO group. There were no device failures, and bleeding related to anticoagulation was the most common complication [10]. A total of 18 patients at Harefield, 12 BTR and 6 BTD were supported for a mean of 14 days with a 50% survival in each group. Bleeding occurred in 44% and there was one stroke. No device failures were encountered [11]. John et al. [12] at Minnesota had 10 survivors from a group of 12 patients with BiVAD support as BTD. Eight were transitioned to long-term LVAD support and 2 were bridged to recovery. Twenty-seven patients failing medical management at Columbia, 89% with an IABP and 56% on more than one inotrope were bridged with the Centrimag for a mean of 16 days. Twenty of 27 survived to discharge, with 6 transitioning to an LVAD, 8 to OHT and 10 recovering. There were six strokes and no device failures [13]. Right ventricular support with the Centrimag in patients with implanted LVADs, either as a planned or rescue procedure is becoming common and is showing promising results [14–16].

Implantable left ventricular assist devices (LVAD)

The current Food and Drug Administration (FDA) approved devices in this category have a driveline which connects the intracorporeal device to either an external electrical power supply or a pneumatic driver. The HeartMate XVE and Heartmate II devices are electrically powered, while the Thoratec iVAD is powered pneumatically. Other electrically powered devices in varying stages of investigation include the Micromed DeBakey/HeartAssist 5, Jarvik 2000 FlowMaker, HeartWare, DuraHeart and BerlinHeart INCOR. Totally implantable devices with transcutaneous energy transfer (TET) technology are in early stages of development. Long-term implantable LVADs have customarily been studied and approved for bridge to transplant and destination therapy (DT) indications. Bridge to transplant criteria requires that a patient undergo a formal transplant evaluation and be considered a reasonable candidate for heart transplantation. If cardiac function deteriorates while awaiting the availability of a suitable donor then the LVAD is placed in order to improve heart failure-related organ dysfunction and reduce risk of waitlist mortality. Devices have been required to prove benefit in the BTT role prior to undergoing evaluation for the DT indication. DT LVADs are indicated for patients with end-stage heart failure who do not meet criteria for heart transplantation [17] (Table 1).

Table 1 Contraindications to cardiac transplantation

Pulmonary hypertension	Tobacco use, last 6 months
Immunologic sensitization	Psychosocial difficulties
Active malignancy	Documented medical non-compliance
Advanced age	Diabetes with end-organ damage
Obesity, BMI >30	Severe vascular disease
Kidney disease, GFR <40	
Severe lung, liver disease	
Substance dependence	

Device development has progressed in a relatively orderly fashion in terms of both strategy for use and pump mechanism. Initially, pumps were conceived as a method of rescue and support to recovery. As experience grew and reliability improved implementation in a BTT scheme became common. Naturally, as data accrued in support of longer-term assistance and the devices themselves grew more durable DT implantation accelerated. Because pulsatility was felt to be critical for organ recovery, initial LVAD designs featured pulsatile flow with a pump "systole", pump "diastole" and pump "stroke volume". The initial pulsatile devices were pneumatically driven and later electrically drive. In addition to numerous mechanical moving parts and bearings, the "first generation" devices required valves in order to create unidirectional flow. The multitude of complex mechanical components proved to be subject to wear and failure, and as duration of support increased the problem of finite device lifespan arose [18–20]. Progress in the design and testing of newer continuous flow pumps was relatively rapid. Studies confirmed that pulsatile aortic flow was not required to resuscitate and maintain organ function in patients with end-stage heart failure [21–24]. In addition, continuous flow LVADs were shown to provide significant benefits in objective quality of life and functional capacity [23, 25–29].

Clinically important devices

The Thoratec HeartMate XVE is the final iteration in the "HeartMate I" line (Table 2; Fig. 3).

It is an electrically driven pulsatile displacement pump of the pusher plate variety and is capable of up to 10 l of flow per minute. The inflow and outflow conduits contain porcine valves to maintain unidirectional flow. The inflow cannula is most commonly implanted in the apex of the left ventricle, and the outflow graft is sewn to the ascending aorta. The

Table 2 Current approved and investigational surgically implanted devices for circulatory support

Device	Mechanism	Type	United States (FDA)	Europe (CE mark)	Anticoagulation
Thoratec PVAD	Pneumatic, pulsatile	Paracorporeal	Approved BTT	Approved BTT	Required
Thoratec IVAD	Pneumatic, pulsatile	Intracorporeal	Approved BTT	Approved BTT	Required
Thoratec HeartMate XVE	Electric, pulsatile	Intracorporeal	Approved BTT, DT	Approved BTT, DT	Not required
BerlinHeart EXCOR	Pneumatic, pulsatile	Paracorporeal	Investigational	Approved BTT	Required
Thoratec HeartMate II	Electric, axial continuous flow	Intracorporeal	Approved BTT, DT	Approved BTT, DT	Required
HeartWare LVAS	Electric, centrifugal continuous flow	Intracorporeal	Investigational	Approved BTT, DT	Required
Levitronix/Thoratec Centrimag	Electric, centrifugal continuous flow	Extracorporeal	Approved BTD (6 h), temporary RVAD (30 days), ongoing investigation	Approved BTD, BTT	Required
Jarvik FlowMaker	Electric, axial continuous flow	Intracorporeal	Investigational	Approved BTT, DT	Required
Micromed DeBakey HeartAssist 5	Electric, axial continuous flow	Intracorporeal	Approved Pediatric BTT, ongoing Investigation	Approved BTT, DT	Required
Terumo DuraHeart	Electric, centrifugal continuous flow	Intracorporeal	Investigational	Approved BTT, DT	Required
BerlinHeart INCOR	Electric, axial continuous flow	Intracorporeal	Investigational	Approved BTT, DT	Required
SynCardia TAH	Pneumatic, pulsatile	Intracorporeal	Approved BTT	Approved BTT	Required
Abiomed Abiocor TAH	Electrohydraulic, pulsatile	Intracorporeal	Humanitarian IDE DT	Investigational	Required

BTT bridge to transplant, *DT* destination therapy, *IDE* investigational device exemption, *RVAD* right ventricular assist device

Fig. 3 Thoratec HeartMate XVE. Image courtesy of Thoratec, Inc

device is rather large and is implanted either posterior to the rectus sheath in the left subcostal area or intraperitoneally. The dimensions limit implantation to adults. It was designed to deliver an 80 ml stroke volume, creating a normal, palpable pulse. Because of the textured blood contacting surfaces, safe operation does not require anticoagulation. The device receives power through a textured driveline which commonly exits the skin on the right side of the abdomen. The HeartMate XVE is approved for both BTT and DT. The DT indication was granted after the publication of a landmark trial published in the New England Journal of Medicine (NEJM) in 2001. The "Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure" (REMATCH) randomized 129 patients with end-stage heart failure who were not candidates for cardiac transplantation to receive either optimal medical management (OMM) or implantation of the Heartmate VE LVAD. The primary endpoint was death from any cause. Sixty-eight patients in the LVAD group were compared to 61 patients in the OMM group. Survival at 1 year was 52% with the LVAD versus 25% with OMM. Two year survival was 23% in the LVAD cohort versus 8% in the OMM cohort. In those under the age of 60 the 1 year survival was 74% with the LVAD versus 33% with OMM. The most common causes of death in the LVAD group were infection (41%) and device failure (17%). Ischemic stroke occurred in 10% of the LVAD patients. Quality of life and functional capacity were improved in the LVAD cohort compared to the patients

surviving with medical management [18]. The 48% reduction in the risk of death seen in the LVAD group stimulated enthusiasm for the concept of long-term mechanical circulatory support, with the caveat that improved devices were obviously going to be required in the future. An important follow up to the original HeartMate XVE DT study showed that the probability of fatal device failure or need for device exchange at 2 years was nearly 73% [30].

The Thoratec HeartMate II (HMII) is the most successful of the second generation LVAD cohort, with over 7,000 patients supported worldwide (Figs. 4, 5).

It is an electrically powered rotary continuous axial flow device with a left ventricular apical inflow cannula and an outflow graft anastomosed to the ascending aorta. The pump is preload dependent and afterload sensitive, runs in a fixed speed mode and is capable of up to 10 l per minute flow at a mean aortic pressure of 100 mm mercury (Hg). The only moving part is the axial rotor, which spins on ruby ball and cup bearings which are continuously washed by the flow stream. It is smaller and lighter than the XVE and therefore can be used in smaller adults. It is typically implanted in a small preperitoneal pocket in the left subcostal region, and utilizes a driveline which generally exits on the upper right side of the abdomen. Because it is a continuous flow pump patients generally do not have a palpable pulse, and pulse pressure measured by Doppler is 10–15 mm Hg depending on preload, afterload and residual left ventricular contractility. The HeartMate II is FDA approved for both BTT and DT and has proved to be safe and effective at relatively low levels of systemic anticoagulation [international normalized ratio (INR) of 1.5–2; 31].

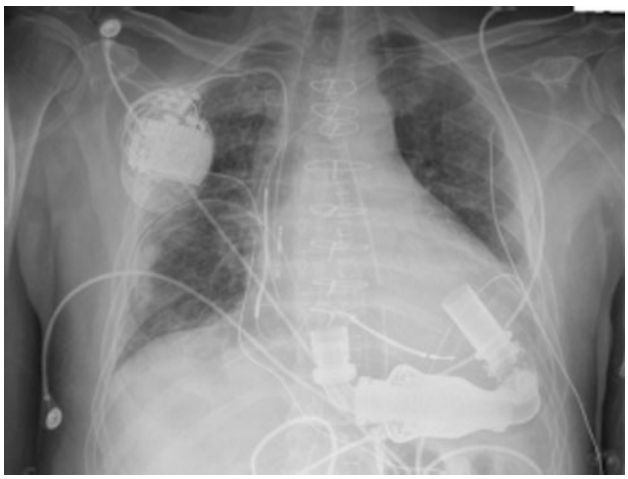

Fig. 5 Chest radiograph showing HeartMate II LVAD

The HMII bridge to transplant pivotal trial enrolled 133 patients at 26 centers in the US between March 2005 and May 2006 [32]. Patients were listed for transplantation as either United Network for Organ Sharing (UNOS) status IA or IB, and all had New York Heart Association (NYHA) class IV symptoms. Twenty-five percent were receiving more than one inotrope and 41% were supported by an IABP. The primary endpoints were the number of patients at 6 months who had either survived to transplant, recovered and survived explant of the device or who were still alive on device support and still eligible for transplant. Functional capacity and quality of life were also evaluated. Seventy-five percent of patients reached the primary endpoint at 180 days. Fifty-six patients were transplanted, with

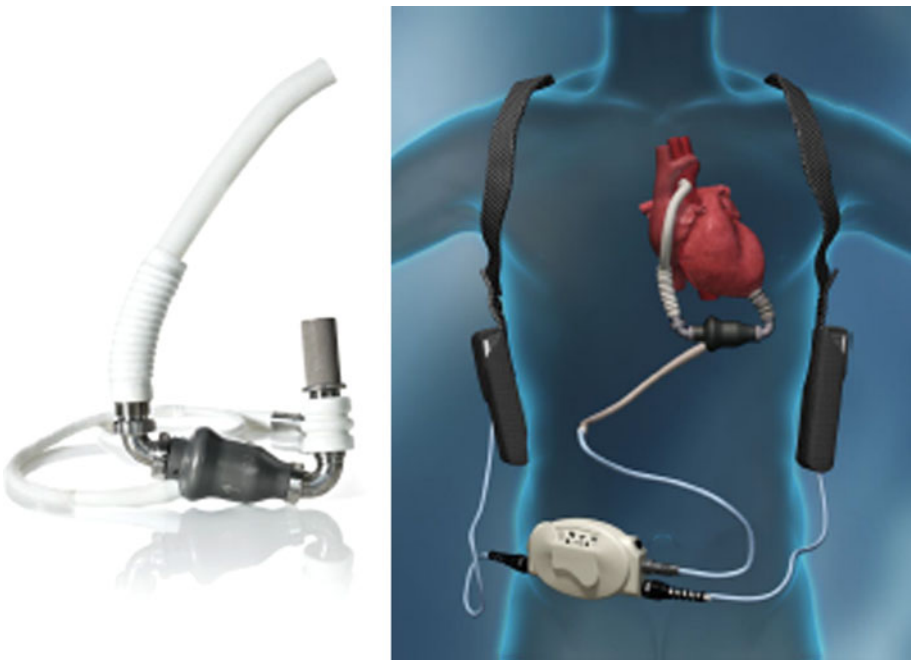

Fig. 4 Thoratec HeartMate II LVAD. Image courtesy of Thoratec, Inc

an 80% 1 year survival. One patient recovered and had the device explanted. Twenty-five patients died before 180 days (19%). Seventy-five percent of patients were discharged after LVAD implant; the median length of stay was 25 days. Adverse events included stroke in 11 patients (8%), 5 of which occurred within the first 48 h, device-related infection (14%), bleeding requiring surgery (31%) and pump thrombosis in 2 patients. There were no device failures, and improvements in quality of life as well as functional capacity were significant.

Additional follow up on the initial 133 patients as well as results for 148 additional patients implanted under a continued access protocol (CAP) showed that 222 (79%) achieved the primary endpoint at 18 months [33]. Of the 157 patients transplanted 86% were alive at 1 year post-transplant. Survival of patients remaining on LVAD support was 72% at 18 months. Adverse events included bleeding requiring surgery in 26%, driveline or pump infections in 16%, prolonged RV dysfunction in 13% and RV failure requiring an RVAD in 6%. Five percent had ischemic stroke and 3% hemorrhagic stroke. There were 4 pumps removed because of thrombus and no device failures. As in the initial study, quality of life and functional capacity were significantly improved.

The HMII was approved for BTT on the basis of the results reported above. Post-approval analysis was required by the FDA and was published in May of 2011 [34]. This study evaluated outcomes in the first 169 patients who received the HMII once it had become commercially available in order to give regulators feedback on the real world performance of the device outside of a clinical trial. Implantation of the now commercially available HMII allowed the data to be registered by the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), and the comparison group for this study was an INTERMACS cohort of 169 patients receiving another commercially available LVAD for BTT. The comparison group contained 135 patients with the Thoratec Heartmate XVE and 34 patients with the Thoratec IVAD, both pulsatile pumps. The baseline characteristics differed between the groups in renal function as well as the distribution by INTERMACS profile. The primary endpoint was survival; adverse events and quality of life were also evaluated. Ninety percent of the HMII group versus 80% of the comparison group achieved survival to transplant, survival on support or survival after device explant at 6 months. Overall 12 months survival was 85% in the HMII group versus 70% in the comp group. In hospital survival in the HMII group was significantly better at 94% compared to the comp group at 85%. Ninety-two percent of the HMII patients were discharged versus 75% of the comp group. Adverse events in the HMII included bleeding (21%), device infection (20.2%), stroke (6.5%), RV failure (15%) and device replacement (1.2%). The important aspects of this trial were that it confirmed the good results seen in previous studies, even in an uncontrolled setting, and it suggested that the morbidity and mortality associated with HMII implantation and support are decreasing with time. An additional analysis of 1,496 patients implanted post-approval was presented at the Society for Thoracic Surgery annual meeting in 2011 and confirmed the trend of improved survival and decreased adverse events. Survival at 12 months was 85%, bleeding 7%, device-related infection 15%, RV failure 1%, stroke 8% and need for device replacement 1% [35].

The encouraging device performance in the BTT pivotal trial resulted in pursuit of FDA approval for the DT indication [36]. In a separate DT trial, 38 centers in the US randomized patients 2:1 to receive either the HeartMate II or the Heartmate XVE. Patients had advanced heart failure and were not eligible for cardiac transplantation. Inclusion criteria were as follows: left ventricular ejection fraction less than 25%, peak oxygen consumption less than 14 ml per kg per minute and NYHA functional class IIIb or IV, *or* IABP-dependence for at least 7 days *or* inotrope-dependence for at least 14 days. Of the 200 patients enrolled, 80% were dependent on inotropes and 20% had an IABP. One hundred thirty-three patients received the HMII and 59 received the XVE. The primary endpoint was survival free from disabling stroke and reoperation to replace or repair the device at 2 years. The primary endpoint was reached by 46% of the HMII patients versus 11% of the XVE patients. Thirty-three percent of the HMII versus 41% of the XVE patients died within 2 years. In the HMII group stroke occurred in 11% and pump replacement in 10% compared to 36 and 12%, respectively in the XVE group. The XVE replacements were required for bearing wear, valve deterioration or infection, while broken percutaneous leads were the cause of the majority of the HMII replacements. Actuarial survival rates at 1 and 2 years for the HMII patients were 68 and 58% compared to 55 and 24% in the XVE patients. Quality of life and functional status were significantly improved in both groups. This trial showed improved survival and complication rates in advanced heart failure patients supported with the HMII continuous flow LVAD compared to those supported with the pulsatile HeartMate XVE. In addition, the improved durability of the HMII was demonstrated. In an abstract presented at the American Heart Association meeting in 2010 an additional cohort of DT patients (252 patients implanted between May 2007 and March 2009) was presented. There was a trend towards improved 1 year survival in the late group (74%) compared to the initial group (68%). In addition, device-related infections and hemorrhagic stroke occurred with significantly lower frequency in the late group compared to the initial cohort. The authors attributed these

improvements to better patient care rather than enhanced patient selection [37].

Several other "second generation" continuous flow LVADS have been developed and are either undergoing clinical trials or are approved for limited indications in the United States. A version of the Micromed DeBakey pump known as the HeartAssist 5 is a small, lightweight axial continuous flow device that is designed to be implanted within the pericardial space (Fig. 6).

In contrast to the other continuous flow devices that calculate flows based on power consumption, the HeartAssist 5 contains an in line flow probe for direct measurement. This device is FDA approved for the pediatric BTT indication. Additional evaluation is ongoing. The original DeBakey pump trials were remarkable for a higher than expected incidence of thromboembolic events (22%) and pump thrombosis (11–36%) and higher mortality in the BTT role (45%) [38–40]. Modifications of the bearings and impeller as well as heparin bonding of the blood contacting surfaces may have improved the pump's performance [41].

The Jarvik 2000 FlowMaker is another axial continuous flow device approved for both BTT and DT in Europe (Fig. 7).

It too is completely intrapericardial, fitting directly into the LV apex, with an option for outflow to either the ascending or descending aorta. It is unique in several ways. First, it is intended to provide partial support, averaging 3–4 l per minute. Second, it allows patients some degree of freedom to adjust pump speed based on conditions and activity levels. Finally, in its DT configuration it features an innovative driveline strategy with a pedestal anchored to the retro auricular skull for driveline connection. Clinical trials in the United States are still ongoing [42].

The HeartWare left ventricular assist system (LVAS) is an advanced continuous flow device which is approved in Europe and undergoing trials in the United States (Figs. 8, 9).

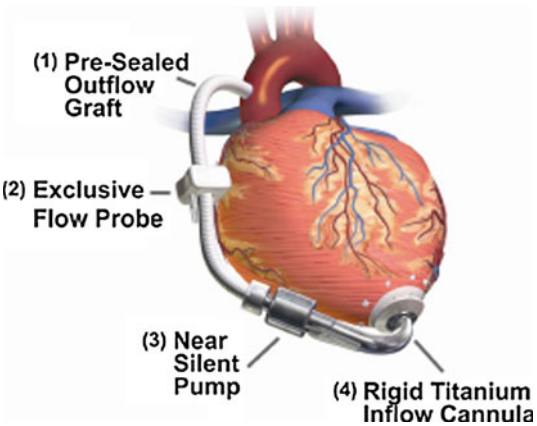

Fig. 6 Micromed DeBakey HeartAssist 5 LVAD. Image courtesy of Micromed, Inc

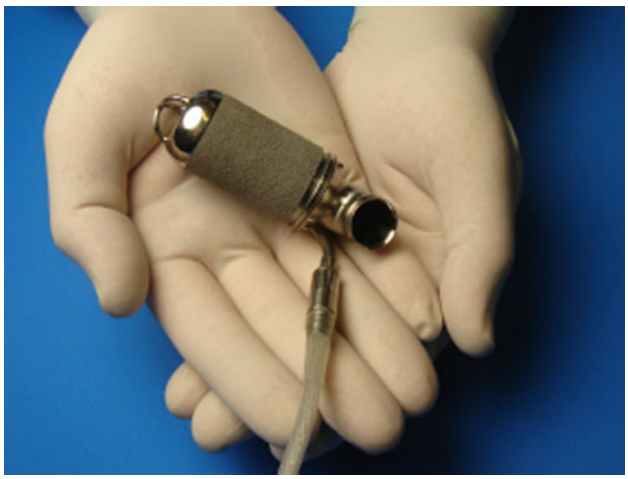

Fig. 7 Jarvik 2000 FlowMaker LVAD. Image courtesy of Robert Jarvik, M.D

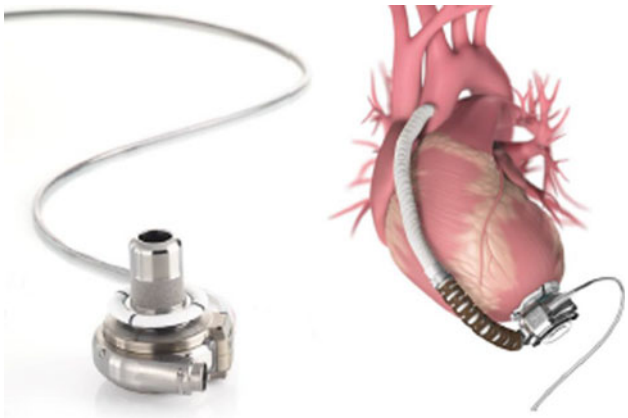

Fig. 8 HeartWare LVAD. Image courtesy of HeartWare, Inc

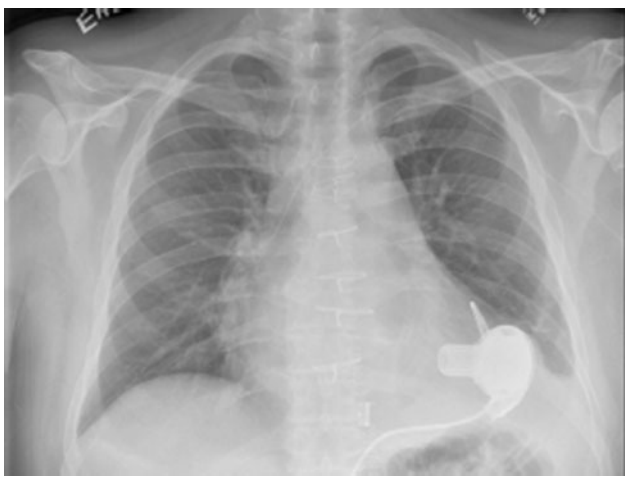

Fig. 9 Chest radiograph showing HeartWare LVAD

This centrifugal pump utilizes an innovative combination of passive magnetic levitation and hydrodynamic suspension to eliminate any contact between the impeller and pump housing. There are no mechanical bearings. The HeartWare is small and designed for completely intrapericardial implantation, with inflow from the LV apex and outflow via a graft to the ascending aorta (HeartWare International, Inc. Framingham, MA). Like other continuous flow pumps it is preload dependent and afterload sensitive, operates at in a fixed speed mode and is capable of delivering up to 10 l per minute. Results of HeartWare trials have been encouraging. In a BTT evaluation in 50 European patients 6 and 24 months survival to OHT, recovery or ongoing LVAD support was 90 and 79%, respectively. Nine deaths were from sepsis (3), multiple organ failure (3) and hemorrhagic stroke (3). Right ventricular (RV) failure was seen in 6 patients, 3 of whom required RVAD support. There was an 18% incidence of device-related infection, the majority of which was related to the driveline. Seven devices were replaced, 2 for complications related to the hydrodynamic suspension mechanism and 4 for pump thrombus. Anticoagulation was adjusted for an INR of 2.5–3.5 [29]. ADVANCE is a BTT trial performed at 30 American centers from 2008 to 2010 and includes 140 patients in the treatment group with end stage heart failure listed for cardiac transplant. Results in these patients were compared to 499 patient controls from INTERMACS, who had received an LVAD as BTT during the same time period. The primary outcome was survival on the original device, survival to OHT or recovery to explant at 180 days. Success was achieved in 92% of the HeartWare group versus 90.1% of the controls. Survival at 180 days and 1 year in the HeartWare group was 94 and 90.6% versus 90.2 and 85.7% in the controls. Adverse events included bleeding requiring surgery (15%), driveline infection (10.7%), stroke (10%), RV failure (22%) and pump thrombus requiring replacement (3%) [43]. Follow-up data was presented at the 2011 meeting of the International Society for Heart and Lung Transplantation (ISHLT) and included 110 additional patients approved by the FDA on a CAP. The same inclusion criteria were used but the CAP patients, based on INTERMACS classification, had more advanced heart failure. Adverse events among the total 250 patient study group were as follows: bleeding requiring surgery 9.2%, gastrointestinal bleeding 15.6%, ischemic stroke 7.2%, hemorrhagic stroke 3.2%, driveline infections 11.6%, RV failure 19.6% and death by 180 days 5%. Sixteen pumps developed thrombus (6.4%), 11 were exchanged and 5 were treated with intracavitary tissue plasminogen activator (tPA). Seventy-eight patients were transplanted with a 93% 180 day post-transplant survival [44]. A HeartWare DT trial, "ENDURANCE", is currently accruing patients in the United States.

Fig. 10 Terumo DuraHeart LVAD. Image courtesy of Terumo, Inc

True members of the "third generation" class of VADs include the Terumo DuraHeart and the Thoratec HeartMate III. The third generation tag refers to bearingless continuous flow devices with *active* magnetic levitation (MagLev) systems for impeller support.

The Terumo DuraHeart is currently undergoing clinical trials in the US, and is approved for use in the European Union (Fig. 10).

It is a centrifugal continuous flow pump implanted in a preperitoneal pocket with inflow from the LV apex and outflow through a graft sewn to the ascending aorta. The driveline generally exits the skin on the right side of the abdominal wall. Flow capability is 8 l per minute, and as the impeller is actively magnetically levitated there is no component on component contact. The system includes hydrodynamic levitation in the event of MagLev failure. Approximately 100 patients have undergone DuraHeart implantation worldwide. Survival in 68 patients in a European trial was 81% at 6 months and 77% at 1 year. Adverse event data from 33 patients was included in that report. No device failures or pump thrombus was seen. Other events included driveline infection in 15%, RV dysfunction in 27%, RVAD requirement in 1 patient, stroke 15% and bleeding requiring surgery in 12%. Three of the strokes were massive hemorrhagic events that resulted in deaths and occurred early in the trial. As a result anticoagulation intensity was decreased to a goal INR of 2–2.5 from the initial INR goal of 2.5–3.5 [45].

The HeartMate III is another third generation continuous flow VAD being developed by Thoratec. This centrifugal pump with active magnetic impeller levitation has shown promise in pre-clinical trials [9, 46].

Functional improvement and quality of life with LVADs

While the survival benefit achieved with mechanical circulatory support is profound, improved quality of life and

functional capacity must accompany the increased duration of life in order for the therapy to be considered a success. In certain situations quality of life may not be an important consideration, for example cardiogenic shock bridged to early transplantation. A period of time as an in-patient, tethered to a device or limited to bed rest, can be tolerable if it permits survival to a definitive and effective therapy. Long-term bridging, which is often necessary when the recipient is large, has blood type O or has significant immunologic sensitization is similar to DT in its requirement for quality survival. The HeartMate II (the only FDA approved BTT and DT continuous flow device) BTT and DT trials included assessments of quality of life and functional improvement [25]. Quality of life was measured with the Minnesota Living with Heart Failure Questionnaire (MLWHF) and the Kansas City Cardiomyopathy Questionnaire (KCCQ). NYHA functional class was estimated and exercise tolerance measured by 6 min walk distance. Evaluations occurred at baseline, 1, 3 and 6 months in the BTT patients and at baseline, 1, 3, 6, 12, 18 and 24 months in the DT patients. After LVAD implantation there were significant improvements in both quality of life and functional capacity that were sustained over the course of the studies. Mean 6 min walk increased from less than 50 m to almost 350 m, and 80% of patients showed a NYHA functional class improvement of $\geq$2. Quality of life improvements measured by both the KCCQ and MLWHF are displayed in Figs. 9 and 10. Additional analysis of the BTT and DT results revealed an interesting finding related to quality of life measures. The DT patients had a greater improvement in KCCQ and MLWHF scores than the BTT patients [26]. It is encouraging that the patient group obligated to spend the greatest amount of time with the device perceived its benefits more positively (Figs. 11, 12, 13).

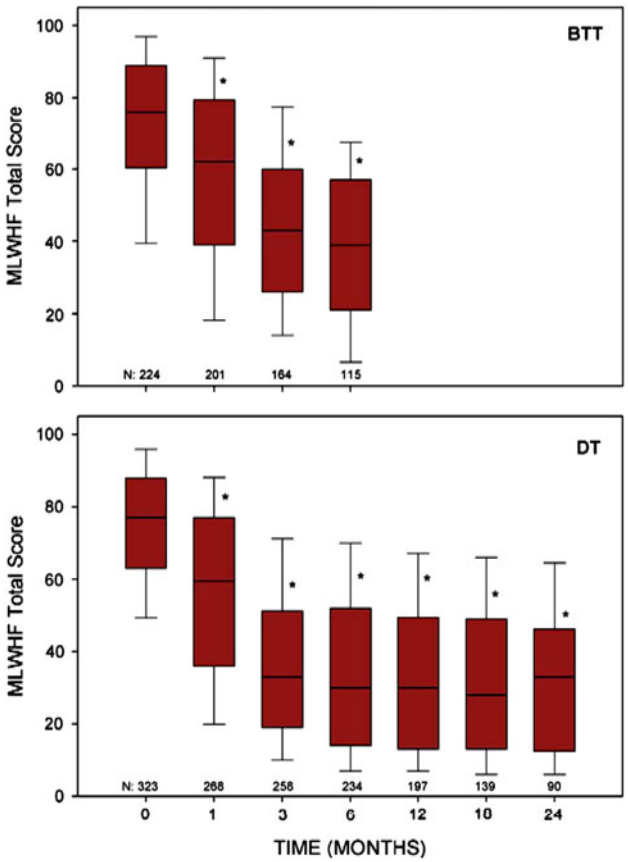

Fig. 11 Improvement in Minnesota Living with Heart Failure Score with LVAD therapy

Total artificial heart (TAH)

Despite over 50 years of interest and effort by multiple investigators there is currently only one TAH which has received FDA approval as a bridge to transplant. The SynCardia TAH is a pneumatically driven dual ventricle system that replaces both ventricles and all 4 native valves (Fig. 14).

It features two percutaneous drivelines and 4 prosthetic tilting disk valves, and is capable of pumping up to 9.5 l per minute in a pulsatile manner. Until recently patients supported with this device were obligated to remain hospitalized. A smaller mobile drive unit has permitted hospital discharge, and an even more portable (wearable) Freedom Driver is undergoing trials [47]. With two 70 cc pumping chambers and a displacement volume of 750 cc the SynCardia device requires a minimum of 10.5 cm antero-posterior dimension and a recommended minimal body surface area of at least 1.7 square meters [4, 48]. A modified version for smaller patients with 50 cc pumping chambers is being developed. There have been over 950 implants worldwide, and since FDA BTT approval was granted in 2004 the number of implants and certified centers in the US has been increasing. The BTT trial consisted of 81 patients implanted between 1993 and 2002, all critically ill with mean central venous pressure (CVP) of 20 and mean pulmonary capillary wedge pressure (PCWP) of 30. Forty-two percent were mechanically ventilated, 37% had suffered cardiac arrest within the preceding 24 h. Survival to OHT was 79%. Post-transplant survival was 86% at one and 64% at 5 years. Hepatic and renal function by laboratory analysis normalized within 3 weeks post-implant. Significant bleeding occurred in 28%, there were 6 strokes with persistent neurologic deficit, 17 driveline infections and one device malfunction [49]. The post-approval use has yielded similar results [50]. Since the BTT trial an increasing number of centers have begun to utilize the SynCardia TAH for advanced heart failure patients eligible for transplant. The Virginia Commonwealth program began SynCardia

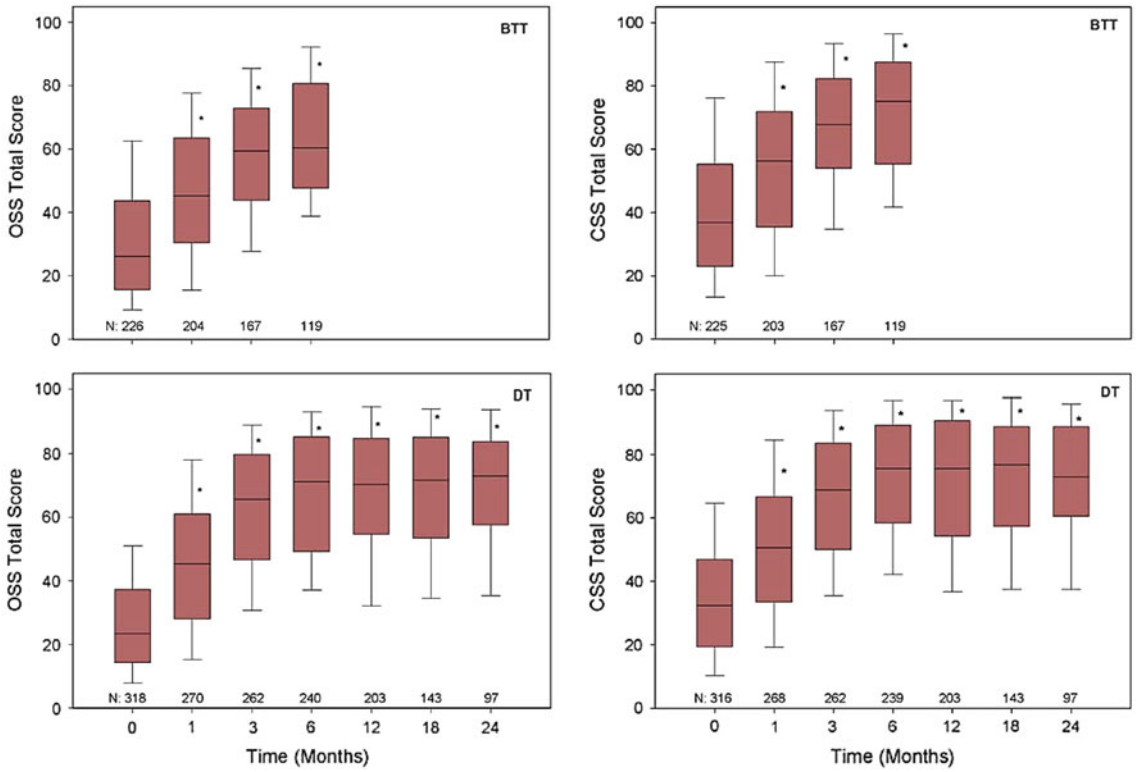

Fig. 12 Improvement in Kansas City Cardiomyopathy Questionnaire with LVAD therapy

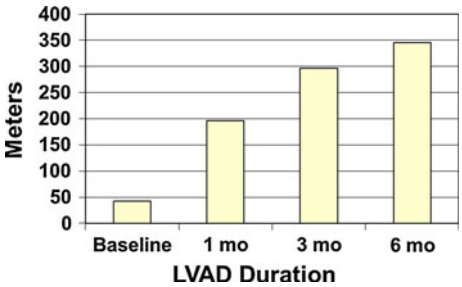

Fig. 13 Improvement in 6 min walk distance with LVAD therapy

Fig. 14 SynCardia TAH. Image courtesy of SynCardia, Inc

TAH implants in 2006. Since its inception over 50 patients have received this TAH with exceptional results [48].

The Abiocor is a TAH developed by Abiomed, Inc. as a destination device. It is a completely implantable titanium and plastic dual chamber pump that utilizes an electrohydraulic mechanism to alternate ejection between chambers. Four trileaflet polyurethane valves maintain forward flow. The pump, internal battery, controller and TET coil are all implanted components. There is no percutaneous driveline. The initial series of implants began in 2001 under an FDA investigational device exemption (IDE). Patients had end stage heart failure, were not candidates for heart transplant or any other device therapy and were predicted to have a 30 days mortality of greater than or equal to 70% in order to be considered for the trial. A total of 14 patients were implanted. Results were published on the first 7 patients in 2004 after a total of 759 patient days of support. Two patients were alive at the time and had achieved hospital discharge. Of the other 5 patients one died from

intraoperative bleeding, 3 from embolic stroke. One of these patients was unable to tolerate anticoagulation. One patient died from a presumed aprotinin reaction. There were no pump-related infections. The stroke mortalities prompted modification of the interior surface of the atrial cuffs [51]. Since that publication all patients have died. The longest duration of support was 512 days. In 2006 the FDA granted a humanitarian device exemption (HDE) for additional implants, and three US institutions have been certified.

The TAH offers the ability to completely replace the failing heart and eliminates the need for inotropes and balloon pumps post-implantation. Patients in cardiogenic shock who would most benefit from prompt restoration of cardiac output and perfusion pressure and normalization of elevated venous pressure obtain immediate benefit after implantation. Right ventricular dysfunction, always a concern in patients treated with an LVAD is eliminated by the TAH. The overall necessity of the TAH has always been difficult to assess. While the majority of patients with advanced heart failure and severe left ventricular dysfunction have some degree of right ventricular dysfunction many of these patients can be managed with an LVAD alone. Accepted indications for the TAH as a bridge to transplant are shown in Table 3 below.

LVAD complications

Review of the results of LVAD clinical trials over time shows an improvement in survival rates and device durability coupled with a trend towards a declining incidence of adverse events. It is apparent that LVAD support, when provided at the appropriate time to the appropriate patient is the most effective therapy available short of transplant. Like transplant, however, success with LVAD therapy is still limited by a significant list of potential complications such as driveline infections, bleeding, thrombotic and thromboembolic events, aortic valve pathology related to LVAD physiology and arrhythmias. The assessment and management of the unsupported right ventricle remains a challenge in many LVAD patients. Related to RV dysfunction is functional tricuspid valve regurgitation (TR) which may need to be surgically addressed in LVAD patients.

Table 3 Indications for total artificial heart

Severe bi-ventricular failure
Myocardial rupture/ventricular septal defect
Post-transplant rejection
Infiltrative or restrictive cardiomyopathy
Refractory ventricular dysrhythmia
Left ventricular thrombus

Infection remains one of the Achilles heels of driveline-equipped implantable LVADs. Compared to the pulsatile HeartMate XVE the incidence of driveline infection in trials of continuous flow pumps is lower [18, 35, 44, 52]. While this is a positive trend these infections remain a significant problem as the lowest incidence is still about 11%, as seen in the HeartWare BTT trial [43]. A more accurate estimate is probably 15–20% although some reports cite an even higher incidence [53]. Most of these are superficial and are caused by skin flora but gram negative rods are cultured from a surprising number. Prolonged antibiotic treatment, debridement, local wound care and negative pressure wound therapy with driveline repositioning are the most commonly utilized measures [54]. Prevention is critically important and meticulous exit site care along with avoidance of driveline traction is believed to help. Driveline infections have been shown to negatively impact survival compared to patients without these infections [53]. Device-related infection involving the body of the pump or the blood-contacting elements is less common but generally catastrophic as long-term eradication is nearly impossible. HeartMate II patients with bacteremia were found to have a risk of hemorrhagic stroke 5.9 times greater than those without bacteremia [55]. Device exchange along with lifetime suppressive antibiotic therapy is indicated. Rescue transplantation for LVAD failure is probably the best option if the clinical scenario permits. The importance of infections in the VAD patient population prompted the creation of a comprehensive set of guidelines and definitions regarding this critical issue [56].

Bleeding complicates LVAD therapy in multiple ways. Perioperative bleeding, particularly in patients with previous cardiac operations and/or coagulopathy related to hepatic dysfunction, occurs with much greater frequency than after other types of cardiac surgery. A single center review of its HM II BTT enrollees reported that 5 of 32 (15.6%) required re-exploration for bleeding [57]. The HM II BTT trial as a whole reported that 30% of patients experienced perioperative bleeding which required re-operation [32]. The post-approval HM II study reported an overall incidence of 44% but it is not clear how much of that was perioperative [34]. Meticulous surgical technique and aggressive correction of coagulopathy and platelet dysfunction are necessary to minimize the risk; it is often necessary to leave the chest open temporarily as part of a planned mediastinal washout with delayed closure.

Bleeding unrelated to the implantation procedure also contributes substantially to morbidity after the perioperative period. The incidence of non-surgical mucosal bleeding such as gastrointestinal, gingival and nasal bleeding has been reported to occur at rates significantly higher than

would be expected in patients simply anticoagulated to an INR of between 1.5 and 2.5. Reviews of HM II patients have cited an incidence of gastrointestinal bleeding (GIB) of 25–55%, and the incidence of GIB and epistaxis combined has been reported to be as high as 65% per year [58–61]. The incidence seen after pulsatile pump implantation is significantly lower [62], and data on other continuous flow devices is scant but suggests that GIB rates are similarly higher than expected [63]. The absence of multimeric von Willebrand Factor (vWF) identified during a comprehensive hematologic evaluation in a German LVAD patient after an unexplained hemorrhagic stroke stimulated investigation into the possibility that an acquired form of von Willebrand's disease was present in CF LVAD patients. Several studies have since confirmed that patients supported with the HM II have low to absent levels of high molecular weight vWF multimers [58, 59, 61, 62, 64]. Patients in these studies were re-analyzed after device explantation for heart transplant and were found to have normalized their vWF multimer levels [61, 64]. The mechanism responsible for the development of acquired VW syndrome is thought to be similar to the presumed cause of Heyde's Syndrome, the acquired VW syndrome that exists in patients with degenerative aortic stenosis. Shear stress related to the rotating impeller is believed to be similar to the turbulent flow across a stenotic aortic valve. Other than the morbidity of recurrent GIB and transfusion, particularly in a population such as BTT patients in whom transfusion can have such an adverse immunologic effect, the existence of an acquired coagulation defect at the time of VAD explant and OHT can increase bleeding and result in increased transfusion requirement [61]. An additional potential contribution to continuous flow LVAD-related bleeding is the likelihood that the decreased pulse pressure is associated with an increased density of gastrointestinal arteriovenous malformations [65, 66]. Hemorrhagic stroke is a bleeding complication that has been reported in all continuous flow LVAD trials. The DuraHeart BTT trial reported a 9% incidence, the HM II DT trial 11%, the HM II BTT trial 2%, a mid-term Jarvik trial 18% and the HeartWare BTT 2.9% [32, 36, 42, 43, 45]. The HM II post-approval study reported a decreased incidence of 1.1% [34]. The anticoagulation strategies for these devices have been dynamic in response to early and accruing clinical data. The HeartMate II has been found to be more resistant to thromboembolic and thrombotic events than had been anticipated [31]. Most centers have decreased their INR goal to a range of 1.5–2.0, likely accounting for a decrease in intracranial hemorrhage. As mentioned earlier infection, specifically bacteremia seems to be associated with an increased risk of hemorrhagic stroke by a mechanism unrelated to the degree of anticoagulation [55].

Thrombotic complications such as ischemic stroke and pump thrombosis have also been important causes of morbidity and mortality in CF LVAD trials. The ischemic stroke rate was 8% in the HM II DT trial and 6% in the HM II BTT trial [32, 36]. The most contemporary results in the ongoing evaluation of the HM II reported an incidence of ischemic stroke of 4% [35]. The HeartWare BTT trial has shown a 7.2% incidence, with 4% in the European trial [29, 44]. HeartWare pump thrombus occurred in 4.4% of the US and 8% of the European BTT implants [29, 44]. HeartMate II pump thrombus was noted in 4% of the DT implants and 1.4% of the HeartMate II BTT plus CAP implants [33, 36]. The DeBakey device was prone early in its development to the development of pump thrombus (8 of 22 Patients in one report) but modifications have been made which to address the problem [40, 41]. It has generally not been possible to determine in many of these cases whether the thrombus formed de novo on internal device components or was ingested from other locations such as the left atrial appendage or the left ventricle. Pump thrombus is often heralded by hemolysis, with increasing lactate dehydrogenase, bilirubin and plasma free hemoglobin along with decreasing haptoglobin. Hemolysis has been associated with an increase in the risk of death and thrombotic events in HeartMate II recipients [67]. Clinically, there is evidence of inadequate cardiac output and impaired ventricular decompression. Renal and hepatic dysfunction usually results. Patients often report fluid retention, dyspnea and generally feeling poorly. Thrombus accumulation directly involving the impeller causes increased power consumption, decreased pulsatility index and increased estimated flows. Large thrombus deposits obstructing flow without directly involving the impeller cause decreased power consumption, decreased estimated flow and decreased pulsatility index [68, 69]. It is important to note that LVAD display values should not be viewed in isolation. Trends in display parameters in the context of the clinical scenario can help with diagnostic dilemmas. Additional tools helpful in diagnosis include echocardiography, right heart catheterization and non-contrast cardiac-gated computerized tomography (CT) [68–70]. Treatment of pump thrombosis consists of aggressive anticoagulation with heparin or direct thrombin inhibitors. Intraventricular thrombolytic therapy and intravenous glycoprotein IIb IIIa inhibitors have been effective in many cases, but pump replacement may ultimately be required [40, 69, 71, 72].

Hemolysis in the absence of pump thrombus is rare with the currently available axial and centrifugal continuous flow pumps. Conditions that result in increased flow velocities or turbulence can certainly predispose towards red cell destruction. Outflow graft stenosis or kinking, inflow cannula malposition and excessively high pump

speeds are potential causes of hemolysis but there is little data available characterizing their incidence.

Right ventricular failure (RVF)

Adequate right ventricular function is necessary for proper LVAD function. RVF results in persistently elevated venous pressure and insufficient LVAD preload. RVF has been reported in from 6 to 35% LVAD recipients [73, 74]. In the US HeartMate II BTT and DT trials, RVF was identified in 13 and 24% of patients post implant [32, 36], and in the US HeartWare BTT trial a 20% incidence was reported [44]. The European HeartWare trial reported an incidence of 12% [29]. The US trials defined RVF as either need for mechanical RV assistance or need for greater than 14 days of inotropic support post-implantation. Institution of inotropic support at any point after 14 days also constituted RVF. RVF is a complex problem because it can be caused by intrinsic RV myocardial failure, increased RV afterload or abnormal patterns of ventricular interdependence [75, 76]. To the extent that inadequate trans pulmonary flow is related to the factors that are normalized by a well-functioning LVAD, RV dysfunction could be expected to resolve with time [75]. Unfortunately, RVF remains a considerable problem at most centers. Survival, incidence of adverse events, length of stay, cost and even post-transplant survival are all significantly negatively impacted by RVF [74, 77–79]. A clinically useful RVF risk assessment tool is needed, and several risk scores utilizing pre-operative characteristics have been proposed. Ochiai and colleagues reviewed a 245 patient cohort for risk factors present in the 9% who required an RVAD. Univariate analysis showed that female sex, pre-op circulatory support, low BSA, non-ischemic etiology (NICM), pre-LVAD ventilator support, low pulmonary artery pressure and low right ventricular stroke work index (RVSWI) were associated with RVF. Multivariable logistic regression showed that only female sex, pre-op circulatory support and NICM were significant [80]. In a review of 197 LVAD implants Matthews and colleagues evaluated the 68 patients with RVF in order to create an RVF Risk Score [74]. Only 14% of these devices were continuous flow pumps. Vasopressor requirement, aspartate aminotransferase (AST) >80, total bilirubin >2 and creatinine >2.3 were combined to create an estimate of risk. An RVF risk score of >55 was highly specific, but 20% of patients with a low risk score still had RVF [74]. Thirty-three LVAD patients, 11 of whom had RVF were evaluated with echocardiography by Puwanant et al. Tricuspid valve annular motion, also known as tricuspid annular plane systolic excursion (TAPSE) less than 7.5 mm was found to be predictive of RVF, with a specificity of 91% and sensitivity of 46% [81]. However, another recent report utilizing echocardiographic characteristics did not find TAPSE to be predictive of RVF. This study did show that an RV to LV end-diastolic diameter ratio of >0.72 was associated with an increased risk of RVF [76]. Undoubtedly the investigators' protocol of using BIVAD or TAH support rather than LVAD support in all patients manifesting grade III or IV tricuspid regurgitation influenced the findings. Kormos and colleagues in 2010 evaluated the 98 patients with RVF from the HeartMate II BTT plus CAP study, which totaled 484 total implants. Thirty required an RVAD, 35 needed extended inotropic support and 33 required inotropes after 14 days. A central venous pressure to pulmonary capillary wedge pressure ratio (CVP: PCW) of >0.63, pre-operative ventilator support and a BUN >39 were predictive of RVF [77]. In summary, RVF is a significant problem in LVAD supported patients. Patient selection is difficult when attempting to predict RV response to LVAD implantation. Thoughtful integration of the clinical scenario along with hemodynamic and echocardiographic characteristics can potentially improve results. Table 4 lists variables which have been associated with post-LVAD RVF. When RVF does occur after LVAD implantation, early recognition, optimization of RV function, management of pulmonary vasoconstriction and if necessary early rather than delayed RVAD support are the cornerstones of treatment [15, 82]. If RVF persists and long-term RV support is required then the TAH is an option for those patients who are eligible for transplant. In DT settings, BIVAD support with two implantable continuous flow devices has been reported [83–86].

Tricuspid regurgitation

Closely related to the issues surrounding RV function is the management of tricuspid regurgitation (TR). Significant TR caused by valvular pathology such as tethering and

Table 4 Predictors of right ventricular failure

Echocardiographic	Clinical
TAPSE <7.5 mm	CVP:PCW >0.63
RVEDV:LVEDV >0.72	RVSWI <600
Moderate to severe TR (uncorrected)	Elevated CVP with low PA pressure
	Pre-LVAD mechanical ventilation
	Female
	Non-ischemic etiology
	BUN >39, Cr > T Bili >2, AST >80
	Pre-LVAD circulatory support

fibrosis from transvalvular leads should be addressed by repair or replacement. Functional TR (from annular dilatation secondary to RV pressure/volume overload) is a controversial topic. Many groups routinely perform annuloplasty for TR graded as moderate or greater at the time of LVAD implantation. Because improvements in pulmonary vascular resistance and RV geometry do not occur immediately (if they occur at all) after LVAD implantation, concomitant TV repair offers the benefit of an immediate reduction in CVP compared to those with persistent TR after LVAD. In the immediate postoperative period a lower CVP results in decreased visceral venous pressure and improved visceral perfusion pressure. While this approach is theoretically sound the question of TR correction at the time of LVAD placement has not been studied prospectively. Stulak and colleagues evaluated 149 patients with >mild RV dysfunction at the time of LVAD implantation by echocardiography at a median of 7.4 months and found that almost half had developed some progression of TR. Thirty-five percent had worsened by 1 grade, 13% by more than 2 grades. They found that while TR did progress it did not adversely impact survival or need for re-admission [87]. Piacentino and colleagues found that patients with significant TR pre-LVAD had a longer length of stay, longer inotrope requirement, greater tendency towards RVAD requirement and a trend towards decreased post-operative survival when compared to a contemporary group with insignificant TR. On post-operative echocardiography significant TR persisted in 41% [88]. A limited retrospective report comparing 8 patients with moderate to severe TR who had TV repair to 24 patients with moderate to severe TR who did not have TV repair showed that the repair group had more postoperative bleeding and transfusion and longer operative times. There was no difference in post-operative mortality, RVF or hepatic dysfunction. Azotemia was worse in the TVR group, and the TVR group had a lower mean arterial pressure in the early post-operative period. Pump flow data, other hemodynamic data and postoperative echocardiographic findings were not reported [89]. Results of a more recent retrospective comparison of LVAD plus TV repair or replacement versus LVAD alone in 115 patients with moderate to severe TR were presented at the annual meeting of the STS in 2011 [90]. Thirty-one patients had tricuspid repair or replacement; this group had evidence of worse RV function based on the CVP:PCW ratio and also had a higher percentage of pre-operative severe TR (62 vs. 33%) compared to the LVAD alone group. Post-operatively the group without tricuspid repair/replacement required RVAD support more frequently (10 vs. 2.9%), had a prolonged need for inotropic support, had a higher incidence of renal dysfunction and a longer hospital stay. There was a trend towards decreased survival in the isolated LVAD group as well.

Aortic insufficiency (AI)

It is generally held that aortic regurgitation greater than mild at the time of LVAD implantation requires correction, either by aortic valve closure or aortic valve replacement with a bioprosthetic [91–93]. Aortic insufficiency results in recirculation of blood volume from the outflow graft and aortic root back into the left ventricle, which causes recurrence of heart failure symptoms related to inadequate systemic perfusion and increased LV pressure. In addition, AI increases the work performed by the device and can result in accelerated wear. Progression of AI and even the de novo development of AI in previously normal valves have been reported with increasing frequency after LVAD placement [94–97]. LVAD support results in hemodynamics much different from those that exist prior to the LVAD. Left ventricular diastolic and systolic pressures are substantially reduced with LVAD unloading. Continuous flow from the outflow graft into the ascending aorta results in a persistently increased aortic transvalvular pressure gradient. This is particularly problematic when pump speed and loading conditions do not permit even intermittent aortic valve opening. These factors expose the aortic valvular apparatus to unnatural stress. Aortic valves from patients after pulsatile and continuous flow LVAD support explanted at transplant and autopsy have demonstrated progressive commissural fusion [93, 95, 98]. Clinically relevant echocardiographic follow up in LVAD-supported patients has confirmed the development and progression of AI with increasing duration of LVAD support [92, 94, 97, 99]. Risk factors for the development and progression of de novo AI during LVAD support include female sex, small stature, larger aortic root diameter, pre-operative mitral regurgitation >2+, lower LV volumes on support and failure of the aortic valve to open while on support [97, 99]. The clinical significance is at this time unclear but the suggestion that AI progresses with time is not comforting. At least one report has demonstrated an association between de novo AI and increased risk of mortality and recurrent heart failure syndrome in a group supported by pulsatile devices [99]. It is possible that aortic valve degeneration on continuous flow LVAD support can be mitigated by careful speed adjustment to allow regular aortic valve opening [95].

Ventricular arrhythmias (VA)

The function of an LVAD is not directly affected by ventricular tachycardia (VT) or ventricular fibrillation (VF). These dysrhythmias do however have the potential to adversely impact the ability of the right ventricle to deliver blood across the pulmonary circulation. Theoretically in

the presence of normal pulmonary vascular resistance passive transpulmonary flow may be sufficient, but this set of circumstances is not likely to be seen in the vast majority of LVAD patients. VA after LVAD placement can occur because of ventricular substrate problems such as ischemia or infarction associated scar. Non-ischemic etiologies of ventricular dysfunction can also be associated with electrical instability. The LVAD itself can cause VA secondary to scar at the apical core border zone. Inflow cannula interaction with septal and lateral wall endocardium can also cause mechanical irritation and result in VA. Finally, inappropriately high LVAD speed settings can excessively decompress the LV and result in suction events. The incidence of post-LVAD VA ranges from 20 to 50% [100, 101]. VAs caused by suction events are generally easily managed by manipulation of the pump speed and preload [68]. Persistent VA despite echocardiography-confirmed speed and preload optimization are often less simple. Inflow cannula position can be studied by review of serial chest X-rays, dynamic echocardiography with patient position changes and CT scanning. Pump repositioning may be required and can be successful [102]. VAs related to myocardial substrate can be the most difficult to correct. Antiarrhythmic medications and clinical electrophysiology consultation are necessary. In at least one review the incidence of post-LVAD VA was associated with lack of beta blockade. In patients with previously placed implanted defibrillators (ICD), recurrent shocks are often poorly tolerated because with LVAD support VA often do not cause acute hemodynamic compromise and loss of consciousness. Thresholds should be adjusted to minimize sensed and treated events. Unfortunately, in these patients ICD shocks have been associated with an increased risk of mortality [100, 103]. Intractable ventricular arrhythmias in LVAD patients are difficult problems. Biventricular implantable VAD support in DT patients is a heroic but potentially lifesaving measure. In transplant eligible patients, intractable VA is an accepted indication for the TAH (Table 5).

Table 5 Etiology of ventricular arrhythmias in LVAD patients

Ischemic substrate
Infarction-related scar
Conduction abnormality in NICM
Apical cannulation site scar
Inflow cannula malposition
Excessive LVAD speed with suction

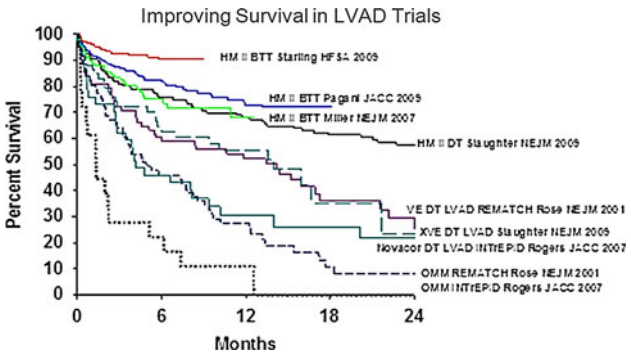

Fig. 15 Improved survival in LVAD trials over time

Conclusion

Since the results of REMATCH in 2001 the outcomes of mechanical circulatory support with implantable devices have dramatically improved (Fig. 15).

In contrast, there have been no significant improvements in the outcomes provided by the optimal medical management of this same group of patients. The most contemporary morbidity and mortality data on patients supported by continuous flow LVADs is approaching the results seen with cardiac transplantation. This trend has appropriately sparked interest in the evaluation of the potential benefits of implantable LVAD support in less critically ill patients. REVIVE-IT (Randomized Evaluation of VAD Intervention before Inotropic Therapy) will begin enrolling patients in 2011 and is designed to help clarify this question [104]. This trial will randomize 100 patients 1:1 to receive either optimal medical therapy or implantation of a HeartWare LVAD. The subjects will be adults, not transplant-eligible, who are ambulatory and have NYHA class III symptoms with a left ventricular ejection fraction (LVEF) of less than or equal to 35% on no inotropic support. Additional inclusion criteria will include a 6 min walk distance of between 200 and 350 m and a peak oxygen consumption of between 35 and 50% of predicted on cardiopulmonary exercise testing (CPX). Study endpoints will include survival, freedom from stroke, improvement in 6 min walk distance of greater than or equal to 75 m and improvement in peak oxygen consumption of at least 15% on CPX testing. Additional assessment of functional capacity and quality of life will be evaluated.

ROADMAP (risk assessment and comparative effectiveness of LVAD and medical management in ambulatory heart failure patients) will also begin enrolling patients with less advanced heart failure, comparing HeartMate II LVAD therapy with best medical therapy (personal communication, Dr. Joseph Rogers, Duke University). This will be a non-randomized observational study of ambulatory adults with NYHA class IIIb or IV symptoms and an LVEF less than or equal to 25% who are not inotrope-dependent and not candidates for cardiac transplantation. Fifty to 67%

of the planned enrollment of 200 patients will be treated with optimal medical management and 33–50% with LVAD implantation; assignment will be based on patient choice. Endpoints will include survival, freedom from stroke, improvement in 6 min walk distance and functional status as well as measures of quality of life. ROADMAP analysis will also focus on the accuracy of risk prediction models in an effort to define specific patient populations most likely to benefit from LVAD therapy.

Reliable and durable devices along with improved techniques and strategies for perioperative care have resulted in lower complication rates and shorter hospital stays. As a result, the cost-effectiveness of implantable LVAD therapy has also improved [105, 106]. It is hoped that new generations of devices will continue the positive trends established over the last decade. Advances to watch for include elimination of the driveline, miniaturization, improved biocompatibility and enhanced durability.

Conflicts of interest Dr. Alan Simeone has no conflicts of interest or financial ties to disclose. Dr. Carmelo Milano periodically directs and is an instructor at LVAD implantation courses at Duke University with support from Thoratec, Inc.

References

1. Liotta D, Hall CW, Henly WS, Cooley DA, Crawford ES, DeBakey ME (1963) Prolonged assisted circulation during and after cardiac or aortic surgery: prolonged partial left ventricular bypass by means of intracorporeal circulation. Am J Cardiol 12(3):399–405
2. DeBakey ME (1971) Left ventricular bypass pump for cardiac assistance. Clinical experience. Am J Cardiol 27(1):3–11
3. Cooley DA, Liotta D, Hallman GL, Bloodwell RD, Leachman RD, Milam JD (1969) Orthotopic cardiac prosthesis for two-staged cardiac replacement. Am J Cardiol 24(5):723–730
4. Gaitan BD, Thunberg CA, Stansbury LG, Jaroszewski DE, Arabia FA, Griffith BP, Grigore AM (2011) Development, current status, and anesthetic management of the implanted artificial heart. J Cardiothorac Vasc Anesth 25(6):1179–1192
5. Hill JD (1986) Use of a prosthetic ventricle as a bridge to cardiac transplantation for postinfarction cardiogenic shock. N Engl J Med 314(10):626–628
6. Pierce WS, Parr GVS, Myers JL, Pae WE, Bull AP, Waldhausen JA (1981) Ventricular-assist pumping in patients with cardiogenic shock after cardiac operations. N Engl J Med 305(27): 1606–1610
7. McBride LR, Naunheim KS, Fiore AC, Moroney DA, Swartz MT (1999) Clinical experience with 111 thoratec ventricular assist devices. Ann Thorac Surg 67(5):1233–1238
8. Korfer R, El-Banayosy A, Arusoglu L, Minami K, Korner MM, Kizner L, Fey O, Schutt U, Morshuis M, Posival H (2000) Single center experience with the thoratec ventricular assist device. J Thorac Cardiovasc Surg 119(3):596–600
9. Schoeb R (2000) A bearingless motor for a left ventricular assist device. Paper presented at the International Symposium on Magnetic Bearings, Zurich, Switzerland, August 23–25, 2000
10. McCormick AJ, Reid BB, Budge D, Clayson SE, Revenaugh JR, Stoker S, Raymond AL, Smith HK, Doty JR, Caine WT, Alharethi R, Kfoury AG (2010) 296: versatility and patient outcomes with the levitronix centrimag temporary ventricular assist device. J Heart Lung Transpl 29(2, Supplement 1):S100
11. De Robertis F, Birks EJ, Rogers P, Dreyfus G, Pepper JR, Khaghani A (2006) Clinical performance with the Levitronix Centrimag short-term ventricular assist device. J Heart Lung Transpl 25(2):181–186
12. John R, Liao K, Lietz K, Kamdar F, Colvin-Adams M, Boyle A, Miller L, Joyce L (2007) Experience with the Levitronix CentriMag circulatory support system as a bridge to decision in patients with refractory acute cardiogenic shock and multisystem organ failure. J Thorac Cardiovasc Surg 134(2):351–358
13. Worku B, Takayama H, Van Patten D, Pak P, Naka Y (2010) The Columbia experience with the Levitronix CentriMag as a rescue device in high risk patients. J Heart Lung Transpl 29(2, Supplement 1):S9
14. Bhama JK, Kormos RL, Toyoda Y, Teuteberg JJ, McCurry KR, Siegenthaler MP (2009) Clinical experience using the Levitronix Centrimag system for temporary right ventricular mechanical circulatory support. J Heart Lung Transpl 28(9):971–976
15. Loforte A, Montalto A, Lilla Della Monica P, Musumeci F (2010) Simultaneous temporary CentriMag right ventricular assist device placement in HeartMate II left ventricular assist system recipients at high risk of right ventricular failure. Interact CardioVasc Thorac Surg 10(6):847–850
16. Stepanenko A, Loforte A, Dranishnikov N, Potapov EV, Montalto A, Pasic M, Weng YG, Dandel M, Siniawski H, Kukucka M, Krabatsch T, Musumeci F, Hetzer R (2011) 468 temporary right ventricular support in left ventricular assist device recipients. J Heart Lung Transpl 30(4, Supplement 1):S159–S160
17. Mehra MR, Kobashigawa J, Starling R, Russell S, Uber PA, Parameshwar J, Mohacsi P, Augustine S, Aaronson K, Barr M (2006) Listing criteria for heart transplantation: International society for heart and lung transplantation guidelines for the care of cardiac transplant candidates–2006. J Heart Lung Transpl 25(9):1024–1042
18. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL, Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure Study G (2001) Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 345(20):1435–1443
19. Nativi JN, Drakos SG, Kucheryavaya AY, Edwards LB, Selzman CH, Taylor DO, Hertz MI, Kfoury AG, Stehlik J (2011) Changing outcomes in patients bridged to heart transplantation with continuous—versus pulsatile-flow ventricular assist devices: an analysis of the registry of the International Society for Heart and Lung Transplantation. J Heart Lung Transpl 30(8): 854–861
20. Long JW, Healy AH, Rasmusson BY, Cowley CG, Nelson KE, Kfoury AG, Clayson SE, Reid BB, Moore SA, Blank DU, Renlund DG (2008) Improving outcomes with long-term "destination" therapy using left ventricular assist devices. J Thorac Cardiovasc Surg 135(6):1353–1360; discussion 1360–1351
21. Kamdar F, Boyle A, Liao K, Colvin-adams M, Joyce L, John R (2009) Effects of centrifugal, axial, and pulsatile left ventricular assist device support on end-organ function in heart failure patients. J Heart Lung Transpl 28(4):352–359
22. Russell SD, Rogers JG, Milano CA, Dyke DB, Pagani FD, Aranda JM, Klodell CT Jr, Boyle AJ, John R, Chen L, Massey HT, Farrar DJ, Conte JV (2009) Renal and hepatic function improve in advanced heart failure patients during continuous-

flow support with the HeartMate II left ventricular assist device. Circulation 120(23):2352–2357
23. Drews T, Jurmann M, Michael D, Miralem P, Weng Y, Hetzer R (2008) Differences in pulsatile and non-pulsatile mechanical circulatory support in long-term use. J Heart Lung Transpl 27(10):1096–1101
24. Radovancevic B, Vrtovec B, de Kort E, Radovancevic R, Gregoric ID, Frazier OH (2007) End-organ function in patients on long-term circulatory support with continuous- or pulsatile-flow assist devices. J Heart Lung Transpl 26(8):815–818
25. Rogers JG, Aaronson KD, Boyle AJ, Russell SD, Milano CA, Pagani FD, Edwards BS, Park S, John R, Conte JV, Farrar DJ, Slaughter MS (2010) Continuous flow left ventricular assist device improves functional capacity and quality of life of advanced heart failure patients. J Am Coll Cardiol 55(17): 1826–1834
26. Aranda Jr JM, Rogers JG, Aronson KD, Boyle AJ, Russell SD, Edwards B, Zucker MJ, Klodell Jr CT, Sundareswaran KS, Farrar DJ, Slaughter MS, HeartMate IICI (2010) Quality of life improvements are greater in destination therapy than bridge to transplant patients with a continuous flow left ventricular assist device. J Am Coll Cardiol 55(10, Supplement 1):A22.E210–A222.E210
27. Fabienne D, Hilde B, Bart M (2011) To "pump up" quality of life and exercise performance studies in patients with left ventricular assist devices. J Heart Lung Transpl 30(2):141–143
28. Kugler C, Malehsa D, Tegtbur U, Guetzlaff E, Meyer AL, Bara C, Haverich A, Strueber M (2011) Health-related quality of life and exercise tolerance in recipients of heart transplants and left ventricular assist devices: a prospective, comparative study. J Heart Lung Transpl 30(2):204–210
29. Strueber M, O'Driscoll G, Jansz P, Khaghani A, Levy WC, Wieselthaler GM, Heart Ware Investigators (2011) Multicenter evaluation of an intrapericardial left ventricular assist system. J Am Coll Cardiol 57(12):1375–1382
30. Lietz K, Long JW, Kfoury AG, Slaughter MS, Silver MA, Milano CA, Rogers JG, Naka Y, Mancini D, Miller LW (2007) Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era. Circulation 116(5): 497–505
31. Boyle AJ, Russell SD, Teuteberg JJ, Slaughter MS, Moazami N, Pagani FD, Frazier OH, Heatley G, Farrar DJ, John R (2009) Low thromboembolism and pump thrombosis with the HeartMate II left ventricular assist device: analysis of outpatient anticoagulation. J Heart Lung Transpl 28(9):881–887
32. Miller LW, Pagani FD, Russell SD, John R, Boyle AJ, Aaronson KD, Conte JV, Naka Y, Mancini D, Delgado RM, MacGillivray TE, Farrar DJ, Frazier OH (2007) Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med 357(9):885–896
33. Pagani FD, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ, Conte JV, Bogaev RC, MacGillivray TE, Naka Y, Mancini D, Massey HT, Chen L, Klodell CT, Aranda JM, Moazami N, Ewald GA, Farrar DJ, Frazier OH (2009) Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol 54(4):312–321
34. Starling RC, Naka Y, Boyle AJ, Gonzalez-Stawinski G, John R, Jorde U, Russell SD, Conte JV, Aaronson KD, McGee EC Jr, Cotts WG, DeNofrio D, Pham DT, Farrar DJ, Pagani FD (2011) Results of the post-U.S. Food and Drug Administration-approval study with a continuous flow left ventricular assist device as a bridge to heart transplantation: a prospective study using the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). J Am Coll Cardiol 57(19):1890–1898
35. John R, Naka Y, Smedira N (2011) Outcomes with a continuous flow left ventricular assist device in over 1,000 patients in commercial use compared to clinical trial experience. Paper presented at the Society of Thoracic Surgeons, San Diego, CA
36. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatooles AJ, Delgado RM III, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH (2009) Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 361(23):2241–2251
37. Park SJ, Milano CA, Tatooles AJ, Rogers JG, Adamson RM, Steidley DE, Ewald GA, Farrar DJ, Slaughter MS, The HeartMate II Clinical Investigators (2010) Abstract 14430: outcomes in advanced heart failure with left ventricular assist devices for destination therapy. Circulation 122(21 Supplement):A14430
38. Goldstein DJ (2003) Worldwide experience with the MicroMed DeBakey Ventricular Assist Device® as a bridge to transplantation. Circulation 108(10 suppl 1):II-272–II-277
39. Goldstein DJ, Zucker M, Arroyo L, McCarthy P, Noon G (2003) The Micromed-Debakey VAD: initial American experience. J Heart Lung Transpl 22(1, Supplement 1):S218
40. Rothenburger M, Wilhelm MJ, Hammel D, Schmidt C, Tjan TDT, Böcker D, Scheld HH, Schmid C (2002) Treatment of thrombus formation associated with the MicroMed DeBakey VAD using recombinant tissue plasminogen activator. Circulation 106(12 suppl 1):I-189–I-192
41. Loebe M, Noon GP, Benkowski R, Gruber P, Richards T (2007) 103: Improved clinical results with the redesigned MicroMed DeBakey VAD. J Heart Lung Transpl 26(2, Supplement 1):S96–S97
42. Haj-Yahia S, Birks EJ, Rogers P, Bowles C, Hipkins M, George R, Amrani M, Petrou M, Pepper J, Dreyfus G, Khaghani A (2007) Midterm experience with the Jarvik 2000 axial flow left ventricular assist device. J Thorac Cardiovasc Surg 134(1):199–203
43. Aronson K, Slaughter M, McGee E (2010) Evaluation of the HeartWare HVAD left ventricular assist system for the treatment of advanced heart failure: results of the ADVANCE Bridge to transplant trial. Paper presented at the American Heart Association Scientific Sessions 2010, Chicago, Il, November 2010
44. Slaughter M, Aronson K, Boyce S, Miller L (2011) Evaluation of the HeartWare HVAD left ventricular assist system for the treatment of advanced heart failure: results of the ADVANCE bridge to transplant trial with continued access patients. Paper presented at the International Society of Heart and Lung Transplantation, San Diego, CA, April 2011
45. Morshuis M, El-Banayosy A, Arusoglu L, Koerfer R, Hetzer R, Wieselthaler G, Pavie A, Nojiri C (2009) European experience of DuraHeartTM magnetically levitated centrifugal left ventricular assist system. Eur J Cardiothorac Surg 35(6):1020–1028
46. Loree HM, Bourque K, Gernes DB, Richardson JS, Poirier VL, Barletta N, Fleischli A, Foiera G, Gempp TM, Schoeb R, Litwak KN, Akimoto T, Kameneva M, Watach MJ, Litwak P (2001) The HeartMate III: design and in vivo studies of a maglev centrifugal left ventricular assist device. Artif Organs 25(5): 386–391
47. Jaroszewski DE, Anderson EM, Pierce CN, Arabia FA (2011) The SynCardia freedom driver: a portable driver for discharge home with the total artificial heart. J Heart Lung Transplant 30(7):844–845
48. Slepian MJ (2011) The SynCardia temporary total artificial heart—evolving clinical role and future status. US Cardiol 8(1):39–46
49. Copeland JG, Smith RG, Arabia FA, Nolan PE, Sethi GK, Tsau PH, McClellan D, Slepian MJ (2004) Cardiac replacement with a total artificial heart as a bridge to transplantation. N Engl J Med 351(9):859–867

50. Roussel JC, Sénage T, Baron O, Périgaud C, Habash O, Rigal JC, Treilhaud M, Trochu JN, Despins P, Duveau D (2009) CardioWest (Jarvik) total artificial heart: a single-center experience with 42 patients. Ann Thorac Surg 87(1):124–130
51. Dowling RD, Gray LA, Etoch SW, Laks H, Marelli D, Samuels L, Entwistle J, Couper G, Vlahakes GJ, Frazier OH (2004) Initial experience with the AbioCor implantable replacement heart system. J Thorac Cardiovasc Surg 127(1):131–141
52. Topkara VK, Kondareddy S, Malik F, Wang IW, Mann DL, Ewald GA, Moazami N (2010) Infectious complications in patients with left ventricular assist device: etiology and outcomes in the continuous-flow era. Ann Thorac Surg 90(4):1270–1277
53. Goldstein DJ, Naftel DC, Holman WL, Bellumkonda L, Pamboukian SV, Pagani FD, Kirklin JK (2011) 7 Driveline Infections in LVADs: is it the pump or the patient? J Heart Lung Transpl 30(4, Supplement 1):S10
54. Bomholt T, Moser C, Sander K, Boesgaard S, Kober L, Olsen PS, Hansen PB, Mortensen SA, Gustafsson F (2011) Driveline infections in patients supported with a HeartMate II: incidence, aetiology and outcome. Scand Cardiovasc J 45(5):273–278
55. Baumblatt JA, Pauwaa S, Treitman A, Gallagher C, Blair C, Pappas P, Tatooles AJ, Bhat G (2011) 6 are blood stream infections associated with increased risk of stroke in patients with a continuous flow left ventricular assist device? J Heart Lung Transplant 30(4, Supplement 1):S9–S10
56. Hannan MM, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR, Schueler S, Holman WL, Lawler LP, Gordon SM, Mahon NG, Herre JM, Gould K, Montoya JG, Padera RF, Kormos RL, Conte JV, Mooney ML (2011) Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. J Heart Lung Transpl 30(4):375–384
57. John R, Kamdar F, Liao K, Colvin-Adams M, Boyle A, Joyce L (2008) Improved survival and decreasing incidence of adverse events with the HeartMate II left ventricular assist device as bridge-to-transplant therapy. Ann Thorac Surg 86(4):1227–1234; discussion 1234–1225
58. Geisen U, Heilmann C, Beyersdorf F, Benk C, Berchtold-Herz M, Schlensak C, Budde U, Zieger B (2008) Non-surgical bleeding in patients with ventricular assist devices could be explained by acquired von Willebrand disease. Eur J Cardiothorac Surg 33(4):679–684
59. Crow S, Chen D, Milano C, Thomas W, Joyce L, Piacentino V III, Sharma R, Wu J, Arepally G, Bowles D, Rogers J, Villamizar-Ortiz N (2010) Acquired von Willebrand syndrome in continuous-flow ventricular assist device recipients. Ann Thorac Surg 90(4):1263–1269; discussion 1269
60. Stern DR, Kazam J, Edwards P, Maybaum S, Bello RA, D'Alessandro DA, Goldstein DJ (2010) Increased incidence of gastrointestinal bleeding following implantation of the HeartMate II LVAD. J Card Surg 25(3):352–356
61. Uriel N, Pak S-W, Jorde UP, Jude B, Susen S, Vincentelli A, Ennezat P-V, Cappleman S, Naka Y, Mancini D (2010) Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. J Am Coll Cardiol 56(15):1207–1213
62. Crow S, John R, Boyle A, Shumway S, Liao K, Colvin-Adams M, Toninato C, Missov E, Pritzker M, Martin C, Garry D, Thomas W, Joyce L (2009) Gastrointestinal bleeding rates in recipients of nonpulsatile and pulsatile left ventricular assist devices. J Thorac Cardiovasc Surg 137(1):208–215
63. Strueber M, Malehsa D, Avsar M, Jahr N, Bara C, Haverich A (2011) 453 gastrointestinal bleeding after implantation of the HeartWare HVAD left ventricular assist device. J Heart Lung Transpl 30(4):S154
64. Meyer AL, Malehsa D, Bara C, Budde U, Slaughter MS, Haverich A, Strueber M (2010) Acquired von Willebrand syndrome in patients with an axial flow left ventricular assist device/clinical perspective. Circ Heart Fail 3(6):675–681
65. Azzouz M, Young SD, Meyer MM, Sun B, Firstenberg MS (2011) Gastrointestinal bleeding in patients with ventricular assist devices: a diagnostic and treatment algorithm. J Heart Lung Transpl 30(4):S154
66. Demirozu ZT, Radovancevic R, Hochman LF, Gregoric ID, Letsou GV, Kar B, Bogaev RC, Frazier OH (2011) Arteriovenous malformation and gastrointestinal bleeding in patients with the HeartMate II left ventricular assist device. J Heart Lung Transpl 30(8):849–853
67. Romano MA, Haft JW, Stulak JM, Aaronson KD, Pagani FD, Cowger J (2011) 9 hemolysis predicts poor outcome following LVAD implant. J Heart Lung Transpl 30(4, Supplement):S11
68. Slaughter MS, Pagani FD, Rogers JG, Miller LW, Sun B, Russell SD, Starling RC, Chen L, Boyle AJ, Chillcott S, Adamson RM, Blood MS, Camacho MT, Idrissi KA, Petty M, Sobieski M, Wright S, Myers TJ, Farrar DJ (2010) Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. J Heart Lung Transpl 29(4 Suppl): S1–S39
69. Kiernan MS, Pham DT, Denofrio D, Kapur NK (2011) Management of HeartWare left ventricular assist device thrombosis using intracavitary thrombolytics. J Thorac Cardiovasc Surg 142(3):712–714
70. Paluszkiewicz L, Gursoy D, Spiliopoulos S, Dogan G, Daliakopoulos S, Tenderich M, Korfer R, Tenderich G (2011) HeartMate II ventricular assist device thrombosis-an echocardiographic approach to diagnosis: can Doppler evaluation of flow be useful? J Am Soc Echocardiogr 24(3):350 e351–e354
71. Thomas MD, Wood C, Lovett M, Dembo L, O'Driscoll G (2008) Successful treatment of rotary pump thrombus with the glycoprotein IIb/IIIa inhibitor tirofiban. J Heart Lung Transpl 27(8):925–927
72. Delgado Iii R, Frazier OH, Myers TJ, Gregoric ID, Robertson K, Shah NA, Kar B (2005) Direct thrombolytic therapy for intraventricular thrombosis in patients with the Jarvik 2000 left ventricular assist device. J Heart Lung Transpl 24(2):231–233
73. Krabatsch T, Schweiger M, Stepanenko A, Kukucka M, Vierecke J, Lehmkuhl HB, Huebler M, Hennig E, Potapov E, Hetzer R (2011) Mechanical circulatory support-results, developments and trends. J Cardiovasc Transl Res 4(3):332–339
74. Matthews JC, Koelling TM, Pagani FD, Aaronson KD (2008) The right ventricular failure risk score a pre-operative tool for assessing the risk of right ventricular failure in left ventricular assist device candidates. J Am Coll Cardiol 51(22):2163–2172
75. Lee S, Kamdar F, Madlon-Kay R, Boyle A, Colvin-Adams M, Pritzker M, John R (2010) Effects of the HeartMate II continuous-flow left ventricular assist device on right ventricular function. J Heart Lung Transpl 29(2):209–215
76. Kukucka M, Stepanenko A, Potapov E, Krabatsch T, Redlin M, Mladenow A, Kuppe H, Hetzer R, Habazettl H (2011) Right-to-left ventricular end-diastolic diameter ratio and prediction of right ventricular failure with continuous-flow left ventricular assist devices. J Heart Lung Transpl 30(1):64–69
77. Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, Miller LW, Massey T, Milano CA, Moazami N, Sundareswaran KS, Farrar DJ (2010) Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. J Thorac Cardiovasc Surg 139(5):1316–1324

78. Baumwol J, Macdonald PS, Keogh AM, Kotlyar E, Spratt P, Jansz P, Hayward CS (2011) Right heart failure and "failure to thrive" after left ventricular assist device: clinical predictors and outcomes. J Heart Lung Transpl 30(8):888–895
79. Iribarne A, Pak S-W, Russo MJ, Easterwood R, Yang J, Takayama H, Mancini D, Naka Y (2011) Incremental cost of right ventricular failure after left ventricular assist device placement. J Am Coll Cardiol 57(14, Supplement 1):E313
80. Ochiai Y, McCarthy PM, Smedira NG, Banbury MK, Navia JL, Feng J, Hsu AP, Yeager ML, Buda T, Hoercher KJ, Howard MW, Takagaki M, Doi K, Fukamachi K (2002) Predictors of severe right ventricular failure after implantable left ventricular assist device insertion: analysis of 245 patients. Circulation 106(12 suppl 1):I-198–I-202
81. Puwanant S, Hamilton KK, Klodell CT, Hill JA, Schofield RS, Cleeton TS, Pauly DF, Aranda JM Jr (2008) Tricuspid annular motion as a predictor of severe right ventricular failure after left ventricular assist device implantation. J Heart Lung Transpl 27(10):1102–1107
82. Fitzpatrick JR III, Frederick JR, Hiesinger W, Hsu VM, McCormick RC, Kozin ED, Laporte CM, O'Hara ML, Howell E, Dougherty D, Cohen JE, Southerland KW, Howard JL, Paulson EC, Acker MA, Morris RJ, Woo YJ (2009) Early planned institution of biventricular mechanical circulatory support results in improved outcomes compared with delayed conversion of a left ventricular assist device to a biventricular assist device. J Thorac Cardiovasc Surg 137(4):971–977
83. Frazier OH, Myers TJ, Gregoric I (2004) Biventricular assistance with the Jarvik FlowMaker: a case report. J Thorac Cardiovasc Surg 128(4):625–626
84. Stulak JM, Griffith KE, Nicklas JM, Pagani FD (2011) The use of the HeartWare HVAD for long-term right ventricular support after implantation of the HeartMate II device. J Thorac Cardiovasc Surg 142(3):e140–e142
85. Strueber M, Meyer AL, Malehsa D, Haverich A (2010) Successful use of the HeartWare HVAD rotary blood pump for biventricular support. J Thorac Cardiovasc Surg 140(4):936–937
86. Saito S, Sakaguchi T, Miyagawa S, Yoshikawa Y, Yamauchi T, Ueno T, Kuratani T, Sawa Y (2011) Biventricular support using implantable continuous-flow ventricular assist devices. J Heart Lung Transpl 30(4):475–478
87. Stulak JM, Cowger J, Haft JW, Romano MA, Aaronson KD, Pagani FD (2011) 469 the natural history of tricuspid valve and right ventricular function following left ventricular assist device implantation. J Heart Lung Transpl 30(4, Supplement):S160
88. Piacentino V III, Williams ML, Depp T, Garcia-Huerta K, Blue L, Lodge AJ, Mackensen GB, Swaminathan M, Rogers JG, Milano CA (2011) Impact of tricuspid valve regurgitation in patients treated with implantable left ventricular assist devices. Ann Thorac Surg 91(5):1342–1346; discussion 1346–1347
89. Saeed D, Kidambi T, Shalli S, Lapin B, Malaisrie SC, Lee R, Cotts WG, McGee EC Jr (2011) Tricuspid valve repair with left ventricular assist device implantation: is it warranted? J Heart Lung Transpl 30(5):530–535
90. Piacentino V, Troupes C, Ganapathi A, Blue L, Mackensen GB, Swaminathan M, Felker GM, Stafford-Smith M, Lodge AJ, Rogers J, Milano C (2011) Clinical impact of concomitant tricuspid valve procedures during left ventricular assist device implantation. Paper presented at the Society of Thoracic Surgeons Annual Meeting, San Diego, CA
91. Park SJ, Liao KK, Segurola R, Madhu KP, Miller LW (2004) Management of aortic insufficiency in patients with left ventricular assist devices: a simple coaptation stitch method (Park's stitch). J Heart Lung Transpl 127(1):264–266
92. Adamson RM, Dembitsky WP, Baradarian S, Chammas J, May-Newman K, Chillcott S, Stahovich M, McCalmont V, Ortiz K, Hoagland P, Jaski B (2011) Aortic valve closure associated with HeartMate left ventricular device support: technical considerations and long-term results. J Heart Lung Transpl 30(5):576–582
93. Letsou GV, Connelly JH, Delgado RM III, Myers TJ, Gregoric ID, Smart FW, Frazier OH (2006) Is native aortic valve commissural fusion in patients with long-term left ventricular assist devices associated with clinically important aortic insufficiency? J Heart Lung Transpl 25(4):395–399
94. Matthews JC, Aaronson KD, Jain R, Pagani FD, Kolias TJ (2009) 692: aortic insufficiency—trends over time in LVAD supported patients. J Heart Lung Transpl 28(2, Supplement):S306
95. John R, Mantz K, Eckman P, Rose A, May-Newman K (2010) Aortic valve pathophysiology during left ventricular assist device support. J Heart Lung Transpl 29(12):1321–1329
96. Pak S-W, Uriel N, Takayama H, Cappleman S, Song R, Colombo PC, Charles S, Mancini D, Gillam L, Naka Y, Jorde UP (2010) Prevalence of de novo aortic insufficiency during long-term support with left ventricular assist devices. J Heart Lung Transpl 29(10):1172–1176
97. Cowger J, Pagani FD, Haft JW, Romano MA, Aaronson KD, Kolias TJ (2010) The development of aortic insufficiency in left ventricular assist device-supported patients/clinical perspective. Circ Heart Fail 3(6):668–674
98. Mudd JO, Cuda JD, Halushka M, Soderlund KA, Conte JV, Russell SD (2008) Fusion of aortic valve commissures in patients supported by a continuous axial flow left ventricular assist device. J Heart Lung Transpl 27(12):1269–1274
99. Toda K, Fujita T, Domae K, Shimahara Y, Kobayashi J, Nakatani T (2011) Late aortic insufficiency related to poor prognosis during left ventricular assist device support. Ann Thorac Surg 92(3):929–934
100. Bedi M, Kormos R, Winowich S, McNamara DM, Mathier MA, Murali S (2007) Ventricular arrhythmias during left ventricular assist device support. Am J Cardiol 99(8):1151–1153
101. Andersen M, Videbaek R, Boesgaard S, Sander K, Hartsen PB, Gustafsson F (2009) Incidence of ventricular arrhythmias in patients on long-term support with a continuous-flow assist device (HeartMate II). J Heart Lung Transpl 28(7):733–735
102. Milano CA, Simeone AA, Blue LJ, Rogers JG (2011) Presentation and management of left ventricular assist device inflow cannula malposition. J Heart Lung Transpl 30(7):838–840
103. Ambardekar AV, Allen LA, Lindenfeld J, Lowery CM, Cannon AP, Cleveland JC Jr, Brieke A, Sauer WH (2010) Implantable cardioverter-defibrillator shocks in patients with a left ventricular assist device. J Heart Lung Transpl 29(7):771–776
104. Miller LW (2011) Left ventricular assist devices are underutilized/response to miller. Circulation 123(14):1552–1558
105. Russo MJ, Gelijns A, Aaronson K, Miller L, Hong K, Oz M, Ascheim D, Pagani F, Naka Y, Rose E, Moskowitz A (2010) Changing cost-effectiveness of left ventricular assist devices as destination therapy. J Am Coll Cardiol 55(10, Supplement 1):A18.E169–A118.E169
106. Slaughter MS, Russo M, Bostic R, Rogers J (2010) Abstract 12375: cost effectiveness of continuous-flow left ventricular assist device as destination therapy in advanced heart failure. Circulation 122(21 Supplement):A12375