The role of mechanical circulatory device therapy has progressed rapidly over the last 2 decades, from supporting the failing heart in hospitalized patients awaiting heart transplantation to permanent or “destination” outpatient therapy in individuals with end-stage systolic heart failure (HF) for whom transplantation is not an option. Over this period, devices themselves have evolved through several generations. First-generation pulsatile devices have given way to second- and third-generation continuous flow ventricular assist devices (VADs), on the basis of axial and centrifugal flow, respectively. In this issue of the Journal, Stueber et al. (1) report their experience with the HeartWare Ventricular Assist System (HeartWare, Inc., Framingham, Massachusetts) as a bridge to cardiac transplantation in a multicenter prospective nonrandomized single-arm clinical trial. In this cohort of 50 patients, survival to heart transplantation, myocardial recovery and explant, or ongoing support at 6, 12, and 24 months was 90%, 84%, and 79%, respectively.

Device size. Earlier iterations of fully implantable VADs, such as the HeartMate XVE (Thoratec Corporation, Pleasanton, California), were large and required the patients to have the anatomical space to accept the pump, generally a body surface area of >1.5 m². With the advent of the axial flow HeartMate II (Thoratec Corporation), much smaller patients could physically accommodate the pump, which itself weighs only 290 g. The HeartWare device, weighing 140 g with a diameter of 53 mm, has the advantage of an integrated inflow cannula situated directly in the left ventricle with the pump placement in the pericardium, eliminating the need for entry into the abdominal space. Now a wide range of patients of varying sizes, including larger children and smaller adults, can benefit from VAD therapy. Durability. A major limitation of first-generation devices was durability. Incidence of device failure of HeartMate XVE (Thoratec Corporation) was on the order of 31% to 35% at 24 months, largely due to internal bearing wear and degradation of the valved inflow cannula (2,3). This issue has essentially been resolved with newer-generation devices. Longer-term experience with the HeartMate II (Thoratec Corporation) in a bridge-to-transplant cohort demonstrated no instances of primary mechanical pump failure in patients still receiving support at 18 months (4). In a comparison of the continuous flow HeartMate II with the pulsatile HeartMate XVE (Thoratec Corporation) in a destination therapy cohort, the need for device repair or replacement strongly favored the continuous-flow device: 10% versus 36% (p < 0.001) at 2 years (5). In the early experience with the HeartWare device presented by Stueber et al. (1), only 7 patients (14%) underwent device replacement, 2 for a manufacturing issue that was resolved without sequel.

Survival. The role of VAD therapy as a bridge to cardiac transplantation has been well-established since the early 1990s. Recently published studies have shown the benefit of newer VAD designs for this indication (6). It was the landmark REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial, published in 2001, that first established VADs as a permanent therapy for patients not suitable for heart transplantation. This study randomized 129 New York Heart Association functional class IV patients with end-stage HF who were ineligible for heart transplant to therapy with the HeartMate VE (Thoratec Corporation) left ventricular assist device (LVAD) versus ongoing “optimal medical management.” At the end of 12 months, survival was 52% in the LVAD-treated group versus 25% in the medically treated arm. At 2 years, survival was 23% versus 8%, respectively (3). The results of this study led to U.S. Food and Drug Administration approval of the HeartMate VE (and subsequently the HeartMate XVE) (Thoratec Corporation) for destination therapy. Although this was a great leap forward in the treatment of end-stage HF patients, many clinicians outside the VAD community were unconvinced of the long-term benefits of this therapy, given poor 2-year outcomes, despite further published data showing survival improvements in the post-REMATCH era (7,8). It was not until publication in 2009 of the results of the HeartMate II (Thoratec Corporation) destination therapy trial that a wider audience came to see the improvements in survival with second-generation axial flow devices (5). Further “real-world” experience from the INTERMACS (Inter-Agency Registry for Mechanically Assisted Circulatory Support) registry has shown that 1-year
survival in patients receiving continuous flow devices exceeds 80% (9). One can now confidently say that overall survival is improved with VAD therapy, compared with the estimated survival of HF patients.

**Drive-line related infections.** The incidence of LVAD pocket infections has improved with smaller continuous-flow VADs. The HeartWare VAD does not even require the creation of a pump pocket, because of its intrapericardial placement. However, the Achilles’ heel of VAD therapy might well be drive-line infection. The percutaneous driveline that connects the internal pump to the external system controller and power source is tunneled through the abdominal wall. The disruption of the skin at the exit site represents a portal for infection and poses a lifetime risk to the patient. Despite significant improvements in many aspects of the care of VAD patients, the incidence of drive-line infection remains high: 0.37 to 0.48 events/patient-year (5,6). Once a driveline infection develops, it might be difficult to cure even with prolonged antibiotic therapy and surgical intervention (10). Either complete eradication of the driveline by transcutaneous power transfer technology or improvements in current driveline design and/or materials will be necessary to eliminate this significant long-term risk to VAD patients.

**Bleeding and thrombotic complications.** Concerns for thromboembolic events, especially stroke, exist with VAD therapy. One advantage of the pulsatile HeartMate XVE (Thoratec Corporation) was the fact that it did not require systemic anticoagulation with warfarin. Stroke rates were on the order of 0.19 events/patient-year (11). Newer-generation continuous-flow pumps require anticoagulation therapy with warfarin, generally with an international normalized ratio of 2 to 3, although there are data suggesting that lower international normalized ratio targets are appropriate in patients with the HeartMate II (Thoratec Corporation) (12). Antiplatelet therapy with aspirin, dipyridamole, and/or clopidogrel is also used. Ischemic stroke rates with second-generation VADs are on the order of 0.06 to 0.13 events/patient-year (5,6). Although stroke rates are lower, new concerns about increased bleeding risk with continuous-flow circulation due to acquired von Willebrand factor are emerging (13). As the horizon of support with these devices increases on the order of years, further experience and data will emerge on the long-term consequences of pump–blood component interaction and nonpulsatile perfusion on bleeding and clotting risk.

**Acceptance and adoption of VAD therapy.** Approximately 5 million Americans have HF, with National Hospital Discharge Survey data from 1979 to 2004 indicating that the number of hospital stays with any mention of HF tripled from 1,274,000 in 1979 to 3,860,000 in 2004 (14,15). Heart transplantation rates have remained static, in part due to limited donor organ supply. In 2008, approximately 2,000 heart transplants were performed (16). It would seem that the chasm between the numbers in need of advanced HF therapy and the limited donor supply could be filled with the use of VAD therapy. Although numbers of VADs implanted/year are increasing, it is still a relatively rare treatment in the spectrum of HF therapy. From March 2006 to June 2010, 2,933 VAD implants were reported to INTERMACS, a national registry for patients who are receiving U.S. Food and Drug Administration–approved mechanical circulatory support device therapy to treat advanced HF. Patients participating in clinical trials are excluded from this registry; however, if it is estimated that this group comprised an additional 500 to 1,000 patients in the U.S., the total number of VAD implants is still small compared with the potential pool of patients who could benefit. There may be many reasons for this gap, but more than likely it includes a lack of awareness of the therapy itself in the greater medical community as opposed to poor acceptance of the concept of mechanical circulatory support by patients. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta-blockers—the benefits of which were well-established in HF trials—took years to be incorporated into the armamentarium of therapies of many physicians and are still not prescribed to all who might benefit (17). Ventricular assist device therapy, being an exponentially more specialized and dramatic intervention, will likely face substantial barriers to widespread adoption, compared with challenges of acceptance of pharmacological therapies.

With current VAD technology, including devices such as the HeartWare, hurdles 1, 2, and 3 have been overcome to a significant degree. However, the remaining 3 continue to present significant challenges to clinicians who manage patients with mechanical circulatory support device therapy. Hurdles 4 and 5 will likely be surmounted as technology and medical management evolves. The final hurdle might be the most difficult to conquer. Dissemination of scientific data showing benefits of VAD therapy is critical. However, the most powerful tool might be the patients themselves. As more patients receive VADs and return to their communities with improved quality of life, they will serve as ambassadors for this lifesaving therapy.

**References**


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