

Long-term implantable left ventricular assist devices: out-of-hospital program

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In recent years the development of left ventricular assist devices (LVADs) has focused on implantable devices intended to be used as an alternative to heart transplantation. The results so far have been very encouraging with a reduction in infection complications and an almost normal quality of life for the patients. The following discussion describes the authors' experience with five implantable devices: the Novacor LVAS, the pneumatic and vented electric TCI HeartMate, the Arrow LionHeart LVD 2000 LVAD, and the Thoratec IVAD. The Novacor (N 100 LVAD, World Heart, Ottawa, Canada), as well as, the pneumatic and vented electric HeartMate (Heartmate 1205 VE device, formerly Thermo-cardiosystems, Woburn, MA, now Thoratec Inc., Pleasanton, CA) (Fig. 1) LVADs are well-established devices in the field of mechanical circulatory support and a detailed description of their function is found in numerous previous reports (see Chapter 1 this issue) [1–8]. The Novacor and the Heartmate LVADs are implanted through a median sternotomy access. The inflow cannula is inserted into the apex of the left ventricle, and the outflow cannula is connected to the ascending aorta about 3 to 4 cm distal to the aortic valve. Blood returns from the lungs to the left heart and exits via the left ventricular apex and across the inflow valve to the blood pump unit, which is placed within the abdominal wall. From here the

blood is actively pumped through an outflow valve into the ascending aorta. A transcutaneous line (electrical cable and air vent) is connected to a paracorporeal (external) battery pack and electronic controls, which can be worn usually on a belt or a shoulder holster. The portability of these two LVAD systems allowed the patients to leave the hospital. The rechargeable batteries provide power for 4 to 6 hours. Both systems can provide a cardiac output of up to 8 L/min, and both devices can be run in either a fixed-rate or an automatic mode. The auto mode mimics physiologic conditions, according to the patient's activity level. Because the electronic control units are located outside of the body, they can easily be checked in case of problems.

The traditional Thoratec VAD (Fig. 2), although intended as an intermediate term device, does play a role as a bridge to transplant system in patients with smaller body frames or patients requiring biventricular support. A newer implantable version has been developed by the company.

The recently developed Thoratec IVAD System (Thoratec Implantable Ventricular Assist Device, Thoratec Corp, Pleasanton, CA), can be used in several configurations to provide the circulation of blood in either or both the pulmonary and systemic vascular beds at physiologic pressures and flows (Fig. 3). It is also the first implantable system that can be used as a biventricular assist device (BiVAD), if necessary. The system has three major components: a blood pump, cannulae, and a driver.

The central part of the system is the blood pump, which can be used as an LVAD, right ventricular assist device (RVAD), or BiVAD. It has a titanium alloy case containing an elastomeric

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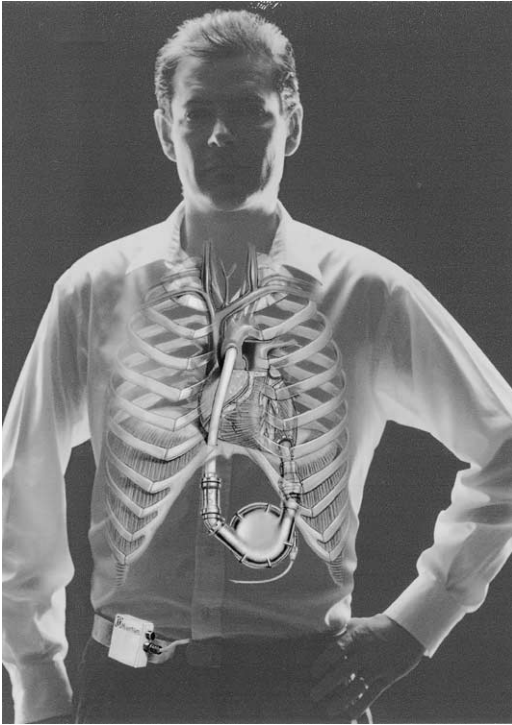


Fig. 1. HeartMate LVAD. (Courtesy of Thoratec Corp.)

blood-pumping sac composed of Thoralon, Thoratec's proprietary polyurethane multipolymer. The blood sac is compressed by air from a pneumatic drive console to eject blood from the sac. Mechanical valves, mounted in the inflow and outflow ports of the blood pump, control the direction of blood flow. The blood pump has an effective stroke volume of 65 mL and, depending on various conditions, will pump 6.5 L/min at a rate of 100 bpm.

Each IVAD blood pump is connected to the patient's heart and great vessels with cannulae. Cannulae can be inserted in the left or right atrium or placed in the left ventricular apex to provide inflow to the VAD blood pump. Blood is returned to the patient with an arterial graft in the aorta or the pulmonary artery, depending on whether the left or right ventricle is being assisted.

The driver, commonly referred to as TLC-II driver, supplies pulses of pneumatic pressure to the blood pump to eject blood into the body. Each injection period alternates with a filling period when blood, assisted by a slight vacuum, fills the IVAD. Air pulses provided by the pneumatic driver can be controlled in two different modes: a fixed-rate mode, when a particular rate and ejec-



Fig. 2. Thoratec VAS extracorporeal pneumatic blood pump. (From Pagani FD, Aaronson KD. Mechanical circulatory support. In: Greenfield LJ, editor. Surgery: scientific principles and practice. 3rd edition. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 1515; with permission.)

tion duration are set by the user and the driver maintains those conditions indefinitely (fixed rate); and an auto mode, when ejection begins the instant complete filling occurs (variable rate). The auto mode is used in most patients because the IVAD flow responds automatically to changes in physiologic conditions.

The LionHeart LVD 2000 is the first system designed for destination support. So far it has been tested in a clinical trial (Clinical Utility Baseline Study, LionHeart ventricular assist system, Arrow, Reading, PA) and was only applied in patients ineligible for heart transplantation. It consists of the following implanted components as illustrated in Fig. 4: pump/energy converter, implanted electronics and battery package, energy transmission secondary coil, and volume compensation (compliance) chamber.

The sac-type blood pump uses a smooth, segmented, polyurethane surface and careful design of transitions to valves and connectors to discourage thrombus formation. The pump is coupled to a rollerscrew energy converter. Implanted electronics with a back-up battery, thoracic compliance chamber, and inductive energy transmission enable the system to operate without percutaneous lines. External subsystems provide the recipient with multiple options for maintaining power to the system and carrying the necessary

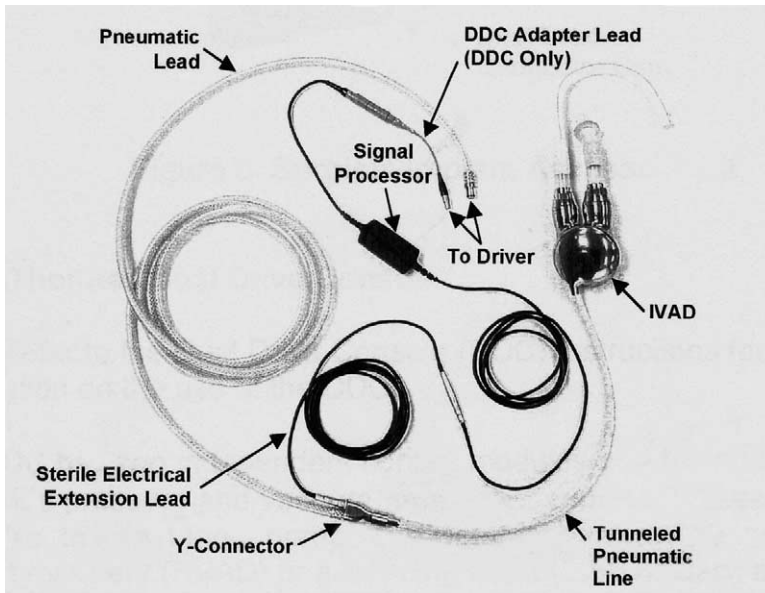


Fig. 3. IVAD: pneumatic and electrical lead connections.

equipment. The clinician is provided with a simple interface to determine the status of the system and make limited adjustments through a radio frequency telemetry link. A detailed description of the device had already been published by the Hershey group [9] and the authors' group [10].

Evolution of out-of-hospital program

Since we started our mechanical circulatory program in 1987, pulsatile VADs were implanted in 165 patients (152 men, 13 women, aged 15–71 years, mean 53.7 ± 13 years). Ninety-five patients received a Novacor device, 12 patients the pneumatic HeartMate, 46 patients the vented electric HeartMate system, nine patients the Arrow LionHeart, and three patients the Thoratec IVAD. The pneumatic version of the HeartMate system was implanted at the authors' center until 1993, when it was replaced by the electrically driven device. A detailed description of demographics, as well as other preoperative data with regard to the system applied, is listed in Table 1. All patients suffered from end-stage cardiac failure, were in NYHA class IV, and were dependent on inotropes. Intention for treatment was bridging to transplantation in 137 patients (82 Novacor, 53 HeartMate, and two Thoratec IVAD), bridging to recovery in six patients (all of them Novacor), and alternative to transplantation in

22 patients (seven Novacor, five HeartMate VE, nine LionHeart, and one Thoratec IVAD). The LionHeart was exclusively applied as an alternative to transplantation. In five patients (four HeartMate, one Novacor), device implantation was accompanied by aortic valve replacement—in one of these patients because of mechanical valve replacement and in the remaining four because of significant aortic insufficiency.

Out of all of the patients, 29.5% received their device on an emergency basis (39.7% of Novacor, 15.1% of HeartMate, none of the LionHeart patients, and all patients with a Thoratec IVAD).

The system selection guidelines were based mainly on the intention to treat and the duration of support, as shown in Table 2. Body surface area also influenced the choice of system; patients with a body surface area $<1.5 \text{ m}^2$ receive an IVAD system. Moreover, it is essential to determine whether the patient needs an LVAD or a BiVAD. A BiVAD is used for patients with severe biventricular heart failure, patients showing signs of beginning multiple organ failure, or patients with a pulmonary resistance of $>500 \text{ dyn}\cdot\text{sec}\cdot\text{m}^5$. Patients requiring a BiVAD will also receive an IVAD system.

Feasibility of out-of-hospital program

The authors started their out-of-hospital (OOH) program in May 1994. Careful patient selection is crucial not only for the success of the

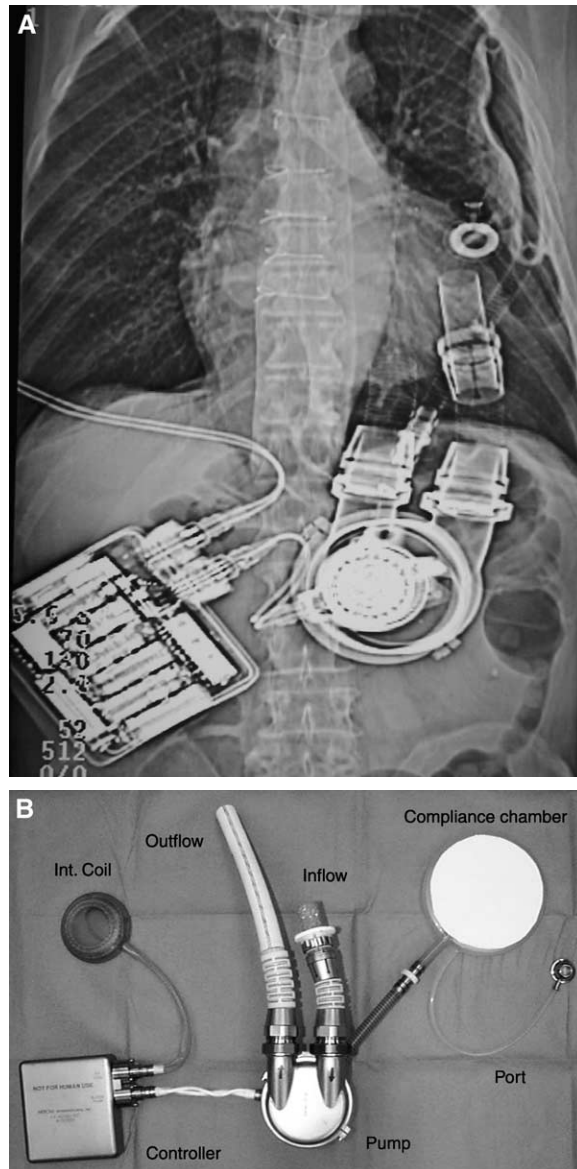


Fig. 4. LionHeart. (A) CT scan. (B) Implantables.

mechanical circulatory support but also for the OOH management. The authors' experience with OOH patients allowed them to establish protocols for the selection of patients to be discharged home, for their home management, and also for their long-term follow-up. For OOH management, patient should:

- have fully recovered and be ambulatory
- not have end-stage organ failure
- be in NYHA class I or II

- have partial recovery of left ventricle
- have adequate family/social support
- be able to operate the assist device

In the authors' center, patient selection and management are the responsibility of a VAD team, which consists of a cardiac surgeon, a cardiologist, and three VAD coordinators. Patients and their family members can reach a member of the team 24 hours a day because someone is always designated to be on call.

Table 1
Preoperative data

	Novacor (n = 95)	HeartMate (n = 58)	LionHeart (n = 9)	Thoratec IVAD (n = 3)
Age (y)	57 ± 9	55 ± 11	64 ± 5	59 ± 7
Male/female	84/11	56/2	9/0	3/0
Ischemic etiology (%)	42	40	56	66
Risk factors				
IABP (%)	38	42	11	33
Ventilation (%)	11	18	11	—
CVVH (%)	15	30	11	33
Redo	16	17	11	67
Echocardiography				
LVESD (mm)	66 ± 10	64 ± 13	63 ± 9	63 ± 7
LVEDD (mm)	72 ± 15	73 ± 12	74 ± 4	70 ± 8
EF (%)	25 ± 5	27 ± 13	25 ± 4	25 ± 3
Hemodynamics				
CVP (mmHg)	12.5 ± 5.3	12.2 ± 6.7	10.9 ± 5.6	22.3 ± 9.3
PAP (mmHg)	35.5 ± 7.0	36.1 ± 8.0	30.4 ± 7.0	39.0 ± 8.2
PVR (dyn/sec/m ⁵)	261.9 ± 126.8	220.6 ± 91.9	290.0 ± 131.4	259.3 ± 12.0
SVR (dyn/sec/m ⁵)	1227.1 ± 398.2	1194.1 ± 406.9	1394.7 ± 575.2	817.7 ± 141.4
CI (L/min/m ²)	2.1 ± 0.4	2.1 ± 0.5	1.9 ± 0.5	2.3 ± 0.3
PCWP (mmHg)	24.4 ± 5.3	24.0 ± 7.5	20.4 ± 6.5	23.0 ± 9.5

Abbreviations: IABP, intraaortic balloon pump; CVVH, continuous veno-venous hemofiltration.

Patient and family training

As soon as possible after transfer of the patient from the ICU to the VAD ward, an intensive training program is started. Its main objective is to enable the patients to operate the assist device on their own. Patients and family members are instructed about the operation of their support device until they feel fully competent to operate it under any circumstance. They are also taught to take care of their exit site themselves. Before discharging the patient, one of the VAD coordinators visits the patient's home to check the facilities.

Table 2
System selection guidelines

Intention and duration of support	Novacor	HeartMate	LionHeart	IVAD
BTT < 1 y	+	++	—	++
BTT > 1 y	++	+	—	+
BTR	++	+	—	+
ATT	+	—	++	—

Symbols: ++, Best. +, Acceptable. —, Not acceptable.

Abbreviations: ATT, alternative to transplantation; BTR, bridge to recovery; BTT, bridge to transplantation.

Follow-up protocol of OOH patients

Once patients are discharged, they have to come back for an ambulatory visit to the outpatient department every 6 to 8 weeks. The clinical check-up consists of an electrocardiogram, echocardiogram, blood tests, clinical examination, wound inspection, and a quality-of-life questionnaire.

At home, patients have to perform daily tests, such as recording their blood pressure, body temperature, and VAD-flow. They are also instructed to measure their international normalized ratio (INR) themselves and take their anticoagulation drugs accordingly. Moreover, the VAD team establishes and relies on a good relationship with the family doctors of the patient. For the LionHeart patients, who require regular puncture of the access port pressure chamber, their family doctors are instructed how to perform the procedure.

OOH medication

In addition to their anticoagulation medicine, patients receive standard heart failure medication (β -blockers, angiotensin-converting enzyme inhibitors, and diuretics) to maintain a mean arterial pressure of 80 to 100 mm Hg and to keep the heart rate at a level of 90 bpm \pm 10. If patients were

taking Amiodarone previously, this was continued in the outpatient management.

Outcomes

Mean duration of support was 289 days (± 361) for LionHeart patients, 93 days (± 73) for IVAD patients, 162.7 days (± 188) for the HeartMate group, and 161 (± 183) days in the Novacor group. So far though, the number of patients included in the LionHeart and the IVAD group is too low to compare these data with the other two groups.

The overall number of survivors to discharge (including post Htx survivors) of the Novacor group was 57%, the HeartMate group 56%, the IVAD group 66%, and the LionHeart group 33%.

Of the 165 patients with pulsatile devices, a total of 88 patients fulfilled the criteria for being discharged home. The mean duration of OOH support was 178.7 days in the Novacor group, 225.2 days in the HeartMate group, and 549.7 days in the LionHeart group. The total OOH experience equaled a cumulative OOH time of 48 years (Table 3).

Patients could be discharged home after a mean duration of 75 days. The authors registered 71 readmissions for OOH patients on pulsatile devices in 48 patients between 1994 and 2002. The OOH status of the patients was in no case the reason for the development of complications. Major complications are presented in Table 4. The incidence of complications is presented in Table 5.

The growing need for alternative treatments for advanced cardiac failure has led to the development of different ventricular assist devices. As the patients and their needs are diverse, many technological advances have been made to adjust the assist devices to these needs. Recently, demand is increasing for these devices to fulfill permanent support needs, which means that the mechanical circulatory support devices have to guarantee not only optimal functioning, durability, and reliability but also an acceptable quality of life for the

patients. Intracorporeal devices with acceptable sizes have the potential to become a true alternative in the management of end-stage cardiac failure. Conventional therapy is associated with constant progression of the disease, high mortality rates, and high rates of hospital readmissions for the patients as shown, for instance, in the French EPICAL study [11,12]. The protocol developed by the authors allows patients to be discharged home, and their experience has demonstrated that, so far, this is a safe therapy option.

A further reduction of complications, particularly of bleeding and cerebrovascular accidents (CVAs), is desirable. CVAs, as well as bleeding and infections, are the most common complications associated with mechanical circulatory support. Patients supported with a Novacor system initially had a higher incidence of CVAs, but since the introduction of a new inflow and outflow cannula (before: 22 mm in cross-section, now: 18 mm in cross-section) plus the use of a new expanded polytetrafluoroethylene (PTFE) graft (World Heart Inc., Oakland, CA), the incidence of CVAs was reduced from 30% to 15% within the Novacor cohort.

Patients supported with a LionHeart also had a high incidence of CVAs (44.4%). This was most probably caused by problems with fill-to-empty mode, which is in the process of being fixed.

Bleeding occurs either as an early complication resulting from the operating technique or as a late complication at connector sites. An important factor in the management of bleeding is meticulous hemostasis during the operation. Aprotinin is given to patients with nonsurgical causes of bleeding, heparin is replaced by protamine, and fresh-frozen-plasma and platelets are given when required. According to our anticoagulation protocol, patients do not receive heparin within the first 24 hours postoperatively. The heart-lung machine blood is washed before being returned.

Table 3
Out-of-hospital (OOH) data

	Novacor (n = 95)	HeartMate (n = 58)	LionHeart (n = 9)	Thoratec IVAD (n = 3)
OOH (n = patients)	51	27	3	1
Maximum OOH support (d)	1043	802	638	167
Mean duration of OOH support (d)	178.7	225.2	549.7	—
Cumulative experience (y)	24.96	16.65	4.52	2.41

Abbreviation: OOH, out of hospital.

Table 4
Definitions of major complications

Complication	Definition
Bleeding	Blood loss resulting in at least one of the following: <ol style="list-style-type: none"> 1. Transfusion of >6 units of RBC in 24 h 2. Reoperation 3. Death 4. Any other intervention for a hemorrhage
Cerebrovascular accident	Any central nervous deficit that is sudden in onset and persists for more than 24 h. Deficit must be confirmed as having an embolic origin by conventional diagnostic methods (eg, CT-scan) or can be demonstrated to result from an infarct (at autopsy)
Infection	Any confirmed infection All infections should be categorized as: exit site, pump pocket, systemic/septicaemia, other (eg, respiratory)
Right heart failure	Cardiac Index <2.2 L/min/m ² for >6 h in the absence of device failure, anatomic restrictions, left-sided dysfunction or hypovolemia (CVP >18 mmHg), requiring intervention
Liver failure	Bilirubin >5 mg/dL

For all the systems, the authors noticed a reduction in bleeding complications as their experience grew. For instance, they discovered that preoperative liver function influences postoperative bleeding. Thus, in the long-run, even more careful patient selection may reduce the incidence of bleeding complications.

Infections are another major complication of mechanical circulatory support. Patients may suffer non-system-related infections, affecting the respiratory or urinary tract or other organ systems. Some patients even may develop septicemia via an infected intravenous line. There are also system-related infections, which may develop at the exit site, the driveline, or the pocket and can lead to a conduit endocarditis. Prevention of infection includes careful patient selection and also operating room discipline, short-term antimicrobial prophylaxis or specific treatment, sterile dressing changes, and local care of exit sites. Intravenous lines should be removed as early as possible, and an early extubation as well as early mobilization might help in the prevention of infections.

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New methods of implantation techniques have also led to a reduction in infection complications, for instance, in the HeartMate group. The authors developed a modified implantation technique for the HeartMate VE by covering the upper surface of the pump with a patch of knitted graft material. This led to a reduction of the incidence in pocket infections for the HeartMate cohort from 33% to 11% [13].

The absence of infection complications in the LionHeart group proves that with totally implantable systems, pocket infections can be significantly reduced.

Table 5
Complications during mechanical circulatory support

	Novacor (n = 95)	HeartMate (n = 58)	LionHeart (n = 9)	Thoratec IVAD (n = 3)
Cerebrovascular accident	30.1%	9.3%	44.4%	—
Bleeding	24.7%	35.2%	66.7%	100%
Pocket infection	7.3%	10.2%	—	—
Driveline infection	20%	25.3%	—	—
Hemolysis	—	1.9%	22.2%	—
Liver failure	14.5%	11.1%	44.4%	1/3 ^a
Right heart failure	24.5%	25.9%	14.3%	—
Gastrointestinal complications	19.3%	9.3%	44.4%	—
Arrhythmias	3.15%	1.7%	—	—

^a Number too small to be expressed as a percentage.

Hemolysis is a rare complication and usually does not persist for a long time. One of the two LionHeart patients with hemolysis had a kinking of the outflow cannula; after surgical correction of the kinking, the hemolysis disappeared. In the other patient, hemolysis was also temporarily present, caused by a software problem.

Liver failure is a complication that has a particularly bad prognosis. No adequate replacement therapy has been established for severe liver failure. Recently, the authors started to use the Molecular Adsorbent Recirculating System (MARS) technique in patients with liver failure, with promising results. MARS is a modified dialysis method that combines the detoxification of the blood by removal of albumin-bound toxins with the removal of water-soluble toxins. This relatively new procedure may lead to improvement in the outcome of liver failure.

Right heart failure is another complication associated with LVADs. The diagnosis should be verified by transesophageal echocardiography. In the Novacor and the HeartMate groups, it occurred in about 25% of the patients. About 7% of the patients in each of these groups had to be supported by an additional right heart support device. Most patients could be managed through drug therapy. Right heart failure in the LionHeart patients was resolved in all cases by conventional drug therapy.

Fortunately, device failures were rare in the authors' experience, demonstrating the reliability of assist devices.

OOH treatment will improve not only the physical state but also the psychological and emotional well-being of the patients. Many of them can enjoy an even better quality of life than conventionally treated patients do. The RE-MATCH trial showed that of 129 patients with end-stage cardiac failure, those supported by a VAD had a better 2-year-survival rate with a better quality of life than did those treated with standard drug therapy [14]. In another study, Dew et al compared the quality of life of inpatients and outpatients under left ventricular support and found that the well-being of the outpatient cohort was greater [15]. OOH patients often had complaints related to anxiety about their device failing, but this can be avoided with a good training program that gives them complete confidence in handling their system [16]. The OOH option also reduces the high costs associated with the use of mechanical circulatory support devices.

Summary

The assist devices demonstrate the safety and reliability of these systems in the management of end-stage cardiac failure, not only in an in-hospital setting, but also in the cohort of OOH patients. The OOH option has led to a significant improvement in the quality of life of those patients. However, VADs are still associated with a considerable number of complications. The newly introduced fully implantable system (LionHeart) has reduced significantly the system-related infection complications. Further miniaturization of the systems might reduce the comorbidities and increase the acceptance of this therapeutic option in the management of end-stage cardiac failure.

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