IMPLANTABLE DEVICES: A BRIDGE TO HEART TRANSPLANTATION

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Terminal stage heart failure represents a substantial worldwide problem for the healthcare system. Despite significant improvements (medical heart failure treatment, implantable cardioverters, cardiac resynchronization devices), long-term survival and quality of life of these patients remain poor. Heart transplantation has been an effective therapy for terminal heart failure, but it remains limited by an increasing shortage of available donor organs along with strict criteria defining acceptable recipients.

Key words: heart transplantation, LVAD, bridge to transplantation.

ИМПЛАНТИРУЕМЫЕ УСТРОЙСТВА: МОСТ К ТРАНСПЛАНТАЦИИ СЕРДЦА

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Терминальная стадия сердечной недостаточности представляет существенную проблему для системы здравоохранения во всем мире. Несмотря на значительные усовершенствования (медикаментозное лечение сердечной недостаточности, имплантируемые кардиовертеры, устройства ресинхронизации), длительная выживаемость и качество жизни таких больных остаются неудовлетворительными. Трансплантация сердца является эффективным методом лечения терминальной сердечной недостаточности, однако ее применение ограничено увеличивающимся дефицитом доступных донорских органов одновременно с жесткими критериями отбора реципиентов.

Ключевые слова: трансплантация сердца, устройство левожелудочкового обхода, мост к трансплантации.

Ventricular assist devices (VADs) were initially primarily used as a bridge to recovery (BTR) for patients unable to wean from cardiopulmonary bypass despite inotropic support and intra-aortic Balloon pump (IABP) [1, 2] and then as a bridge to transplantation (BTT). Heart transplantation is still the gold standard for the treatment of end-stage heart failure patients, but lack of donor organs on one hand as well as increasing numbers of end-stage HF patients lead to a growing number of LVAD implantations (Fig. 1) [3].

In contrast to heart transplantation, left ventricular assist devices are available as «off-the-shelf product»; therefore, not only they can be implanted as a bridge to transplant or in acute settings for patients deteriorating on the waiting list, but also as destination therapy (DT) for patients too old for transplantation or with contraindications (Fig. 2).

FIRST-GENERATION LVADS

The first generation LVADs were designed as a BTT only. The first successful transplantation after LVAD implantation was performed in 1984 [4]. Over the years, miniaturization of the devices created new possibilities: more patients could be discharged on VAD, while still being listed and awaiting transplantation. However, the first generation VADs had several disadvantages: large size, noise emission, infections of cannulas and malfunction induced by tears in the membrane or degradation of valves which made everyday life difficult and sometimes caused fatal complications [5].

First-generation LVADs were membrane pumps either pneumatically or electrically driven, generating pulsatile flow with artificial heart valves as inlet and outlet. Examples are BerlinHeart EXCOR, Thoratec pVAD (Fig. 3) and VE/XVE. Connected to the heart via can-

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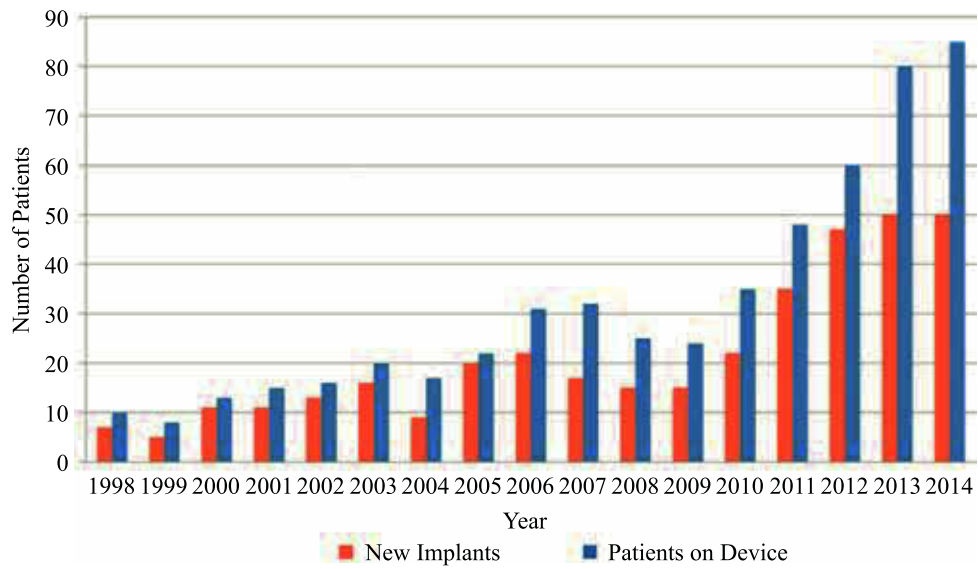
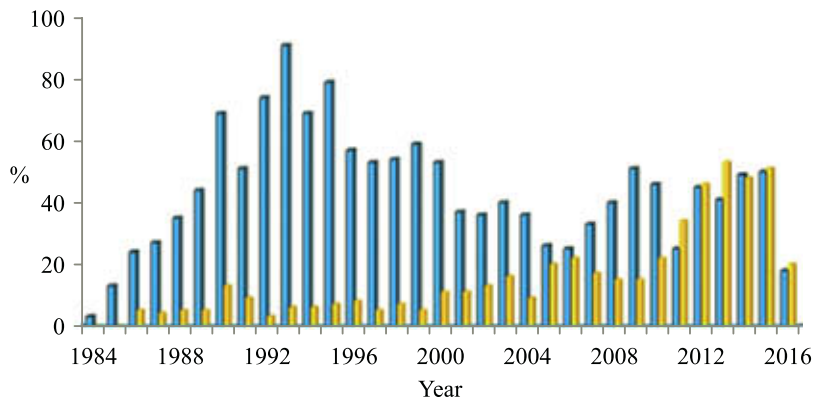Fig. 1. Permanent VAD Implantations in Medical University of Vienna

Fig. 2. Heart Transplants and Permanent Assist Devices in Medical University of Vienna. Cardiac Transplants (1984–2015), n = 1453; Mechanical Assist Devices (1985–2015), n = 511

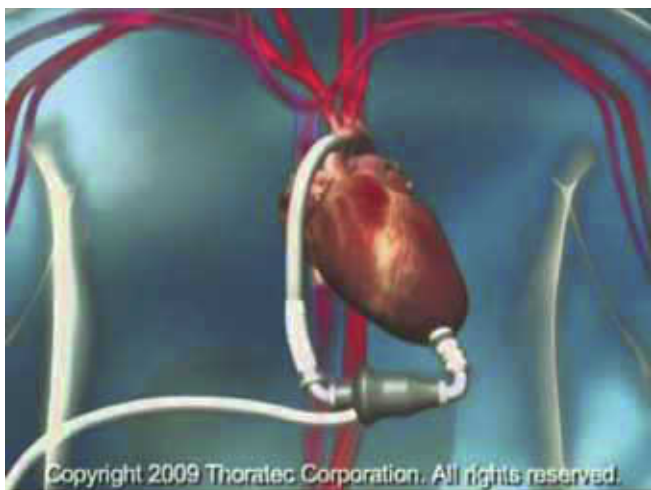Fig. 3. The Thoratec pVAD (Thoratec, Pleasanton, CA, USA)

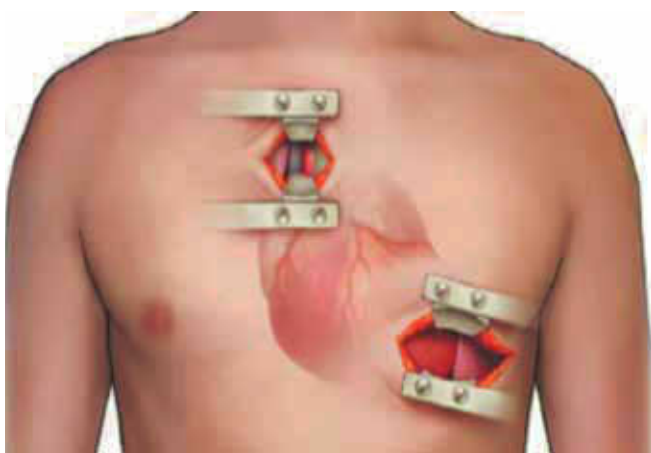Fig. 4. Thoratec HeartMate II (Thoratec, Pleasanton, CA, USA)

Fig. 5. Left mini-thoracotomy and upper hemisternotomy (3rd or 4th ICR)

nulas, these pumps can be used either as isolated left-, right- or biventricular VAD (LVAD, RVAD, BiVAD). If used for biventricular support, pump chambers have to be positioned extracorporeally due to size. For simple left ventricular support, intracorporeal placement is possible, depending on the type of VAD.

First-generation LVADs available on the market were bulky and far too big for any kind of minimally invasive surgical approach. Along with the evolution of these devices and especially the development of continuous flow pumps began the clinical success of VAD surgery.

SECOND-GENERATION LVADS

In the 1990s the development of continuous flow centrifugal pump devices improved patient outcome by reducing size of pump and susceptibility for infections. In addition, significant noise reduction enhanced the quality of life. Designed exclusively for intrathoracic implantation, their utilization was possible only as LVAD, as the devices were too large to be used as BiVAD.

The Thoratec HeartMate II (HMII) is the most successful of the second generation LVAD cohort, with over 20,000 [6] patients supported worldwide (Fig. 4). It is a rotary continuous axial flow pump with an external electrical power source. Inflow cannula is inserted apically and an outflow graft anastomosed to the ascending aorta (in most of the cases) or alternatively to the subclavian artery as bailout strategy. The pump is preload dependent and afterload sensitive, runs in a fixed speed mode and is capable of up to 10 litres 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 HeartMate VE (HMI), offering the possibility of fully intrathoracic implantation as well as implantations even in small adults. The HMII is typically implanted into a properly sized preperitoneal pocket in the left subcostal region and utilizes a driveline, which generally exits on the upper abdomen.

Nevertheless, a minimally invasive implantation of this pump is also feasible; however, the surgical approach has to be modified slightly. Instead of a left-sided thoracotomy, a subcostal incision is used running along the left-sided ribcage (Fig. 5, 6). After division of the abdominal muscles, preparation is performed anteriorly to the diaphragm. Through this access, the pericardium can be divided and the left ventricular apex is easily identified. We are proponents of the running suture technique when securing HM II inflow cannula towards the left ventricle; however, single stitches may be also used.

Aiming for the subclavian artery as the target vessel for outflow graft anastomosis is also feasible in HMII; however, due to the design of the device, one has to use the right-sided subclavian artery instead of the left
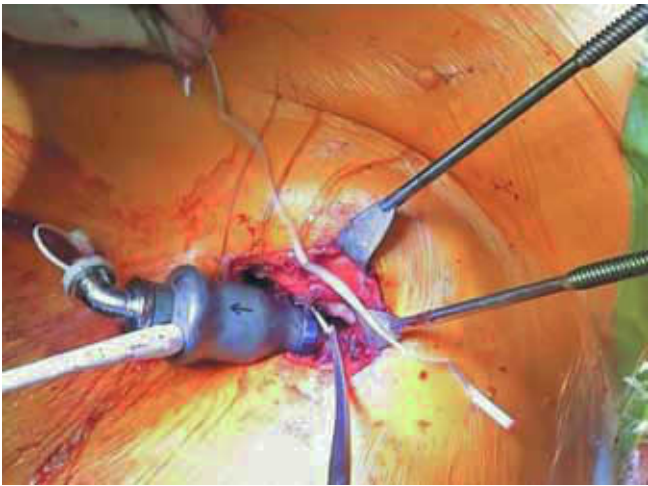
Fig. 6. Thoratec HeartMate II insertion throught subcostal incision

Fig. 7. CT scan reconstruction of outflow graft to the right subclavian artery

(Fig. 7). Exchange of the HeartMate II in case of pump thrombosis can also be performed through this access if needed [7]. Levin AP et al. described a series of 232 HeartMate II patients of which 28 required 36 pump exchanges. They found 100% survival in their subcostal (minimally invasive) exchanges whereas only 63% survived the exchange when performed via sternotomy approach, while both groups had the same (high) risk of thrombus recurrence (31%).

THIRD-GENERATION LVADS

The era of intracorporeal continuous flow pumps has initiated significant success of LVAD surgery. However, median sternotomy has been the only surgical approach for implantation over many years. During the last decade, the less invasive ways of access gained popularity.

The HeartWare VAD (HVAD) is the centrifugal pump which utilizes an innovative combination of passive magnetic levitation and hydrodynamic suspension to eliminate any contact between the impeller and pump housing (Fig. 8). There are no mechanical bearings. The Heart-Ware is small and designed for completely intrapericardial implantation, with inflow from the left ventricular apex and outflow via a graft to the ascending aorta. Like other continuous flow pumps it is preload dependent and afterload sensitive, operates at a fixed speed mode and is capable of delivering up to 10 litres per minute.

There is some evidence that the rate of pump thrombosis in HVAD patients could be slightly higher in comparison to other contemporary devices. Therefore, some centres including our own, started to change the anticoagulation regimen. At our department we give HeartWare patients two doses of 100 mg aspirin daily in addition to the standard treatment with phenprocoumon with a target INR of 2.5.

The HVAD currently is the smallest CE (Conformité Européenne) marked and FDA (US Food and Drug Administration) approved pump on the market. Therefore, it offers a lot of versatility and possibilities for minimally invasive access surgery. In the scientific literature, the
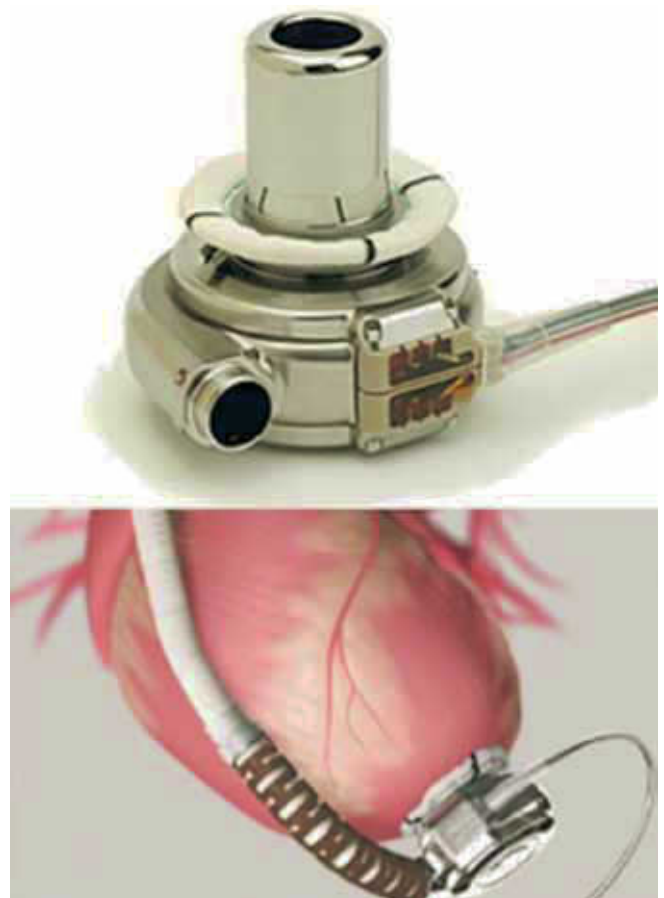

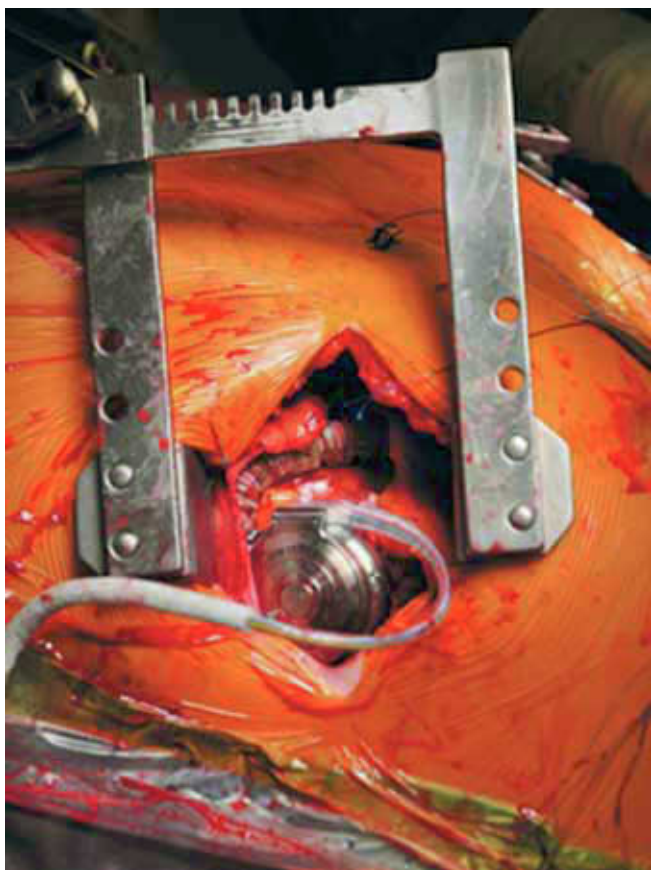Fig. 8. HeartWare VAD (HeartWare International Inc, Framingham, MA, US)

Fig. 9. Minimally invasive HVAD pump exchange

Fig. 10. Outflow graft anastomosis to the ascending aorta

HVAD system is the device with the most minimally invasive implantation experience.

Depending on the surgical requirements and the clinical presentation of the patient, the following minimally invasive approaches are feasible:

For isolated LVAD implantation, access to the left ventricular apex can be gained through a left-sided anterolateral mini-thoracotomy in the fifth intercostal space (Fig. 9); appropriate pump position is verified with TEE guidance, and the HVAD sewing ring is secured to the left ventricular apex with 4–0 prolene in a running suture technique.

Coring of the left ventricle and connection of the pump can be performed in the usual manner similar to open implantation technique. If the outflow graft is to be attached to the ascending aorta, our approach is a right-sided mini-thoracotomy in the second intercostal space. After passing the outflow graft from the left thoracotomy towards the right thoracotomy, a side-biting clamp is attached on the ascending aorta. After adequate incision of the aorta, the graft is anastomosed in the usual manner (Fig. 10). Finally, the driveline is tunneled into the right upper quadrant of the abdomen.

Our own group published the initial results of the first 27 patients implanted via a less invasive bilateral thoracotomy approach. This series showed rather promising results in a cohort of 85% male patients, 29% Intermacs I, and 22% redo surgeries, and there was a 30-day mortality of 7.5% with no postoperative RV failure, three patients (11%) underwent surgical revision for bleeding, and one (4%) pump thrombosis [8].

Alternatively to the right-sided thoracotomy, some centers prefer a hemi-sternotomy access for the outflow graft anastomosis. This technique was described by Schmitto et al. in 2012.

At our center, we use this approach if additional procedures are necessary: in case of an additional aortic valve replacement, we opt for a hemi-sternotomy in the third intercostal space, and in case of an additional tricuspid repair, we aim for the fourth intercostal space.

For anastomosis of the outflow graft, different target vessels beside the ascending aorta can be suitable. One promising target vessel might be the subclavian artery. In case of minimally invasive HVAD implantation, the previously described technique can be used in a similar way. However, there is no need for a second thoracotomy since a left-sided incision two centimeters below the left clavicle is used similar to an incision for a pacemaker implantation. After identification and preparation of the subclavian artery, the outflow graft is tunneled through the second intercostal space. It is recommended to enlarge the interspace and to cover the outflow graft with an additional Gore-Tex prosthesis at the area passing the ribcage in order to avoid the graft kinking.

Before anastomosing the outflow graft, a suitable position on the inferior side of the subclavian artery is identified. After performing the anastomosis and the establishment of the LVAD flow, a banding distal to the anastomosis is attached around the subclavian artery aiming for equal blood pressure levels in both arms [9].

The subclavian approach seems very appealing in cases of severe calcification of the ascending aorta; also, VAD implantation in redo scenarios can be facilitated thus avoiding re-sternotomy. However, there are concerns regarding hyperperfusion of the arm and issues

related to a mismatch between the diameter of the outflow graft and the size of the target vessel which might be predisposing for pump thrombosis.

HeartMate III (Fig. 11) is the latest CE marked continuous flow LVAD device on the market. It is especially appealing due to promising low rates of pump thrombosis in the CE mark trial.

Fig. 11. Thoratec HeartMate III (Thoratec, Pleasanton, CA, USA)

Fig. 12. View of Thoratec HeartMate III through a left-sided thoracotomy

While within the CE mark trial, the 30-day survival rate was excellent with 98% and the rate of adverse events (bleeding 30%, arrhythmia 28%, infections 20%, strokes 4%) was throughout comparable to other contemporary devices. Especially, the 0% pump-thrombosis rate appears promising [10].

The profile of the pump is a little higher than the profile of the HVAD and the sewing ring is different. However, in minimally invasive implantation, techniques similar to the described HVAD implantation can be used (Fig. 12).

To implant the pump through a left-sided thoracotomy, a slightly greater incision than for the HVAD implantation is recommended; however, there are also special instruments under development facilitating the implantation of this pump through this access. Due to the different designs of the sewing ring, we recommend 2–0 prolene in a running suture technique. For anastomosis of the outflow graft, the techniques and approaches previously described in less invasive HVAD implantation can be used here in same fashion.

HeartWare MVAD (Fig. 13) is a continuous axial flow pump, approximately one-third the size of the HVAD.
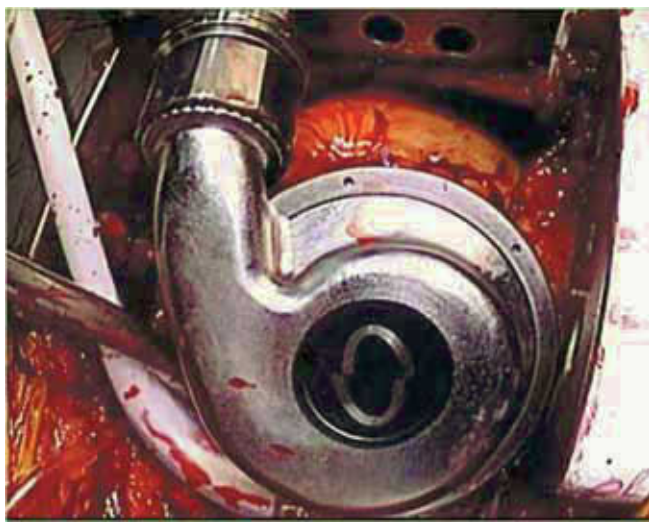

Fig. 13. HeartWare MVAD (HeartWare International Inc, Framingham, MA, US)

Table

Minimally invasive implantation techniques overview

|	HeartWare HVAD	HeartMate II	HeartMate III
LVAD only: Surgical access	Bilateral mini-thoracotomy or left thoracotomy + left A. subclavia	Subcostal incision + right thoracotomy or right A. subclavia	Bilateral mini-thoracotomy or left thoracotomy + left A. subclavia
Circulatory support	ECMO or off pump or CPB	CPB	CPB
LVAD + AVR: Surgical access	Left mini-thoracotomy + upper hemisternotomy (3rd ICR)	Subcostal incision + upper hemisternotomy (3rd ICR)	Left mini-thoracotomy + upper hemisternotomy (3rd ICR)
Circulatory support	CPB	CPB	CPB
+ LVAD + TK-repair ± AVR: Surgical access	Left mini-thoracotomy + upper hemisternotomy (4th ICR)	Subcostal incision + upper hemisternotomy (4th ICR)	Left mini-thoracotomy + upper hemisternotomy (4th ICR)
Circulatory support	CPB	CPB	CPB
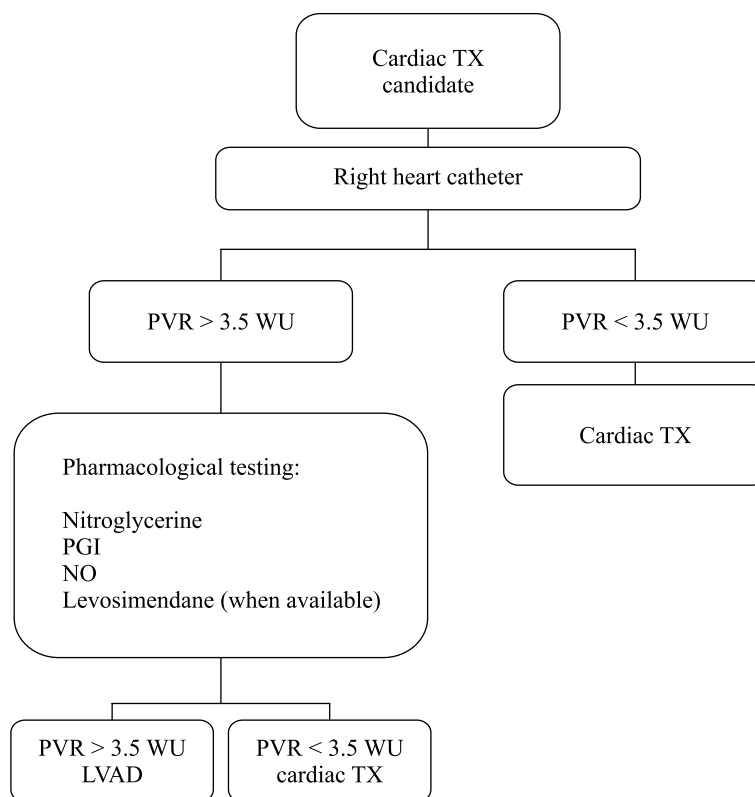
Fig. 14. Pharmacologic testing: decision-making tree. TX, Transplant; PVR, pulmonary vascular resistance; WU, Wood units; PG, prostaglandin; NO, nitric oxide; LVAD, left ventricular assist device

The MVAD is based on the same proprietary 'contactless' impeller suspension technology used in the HVAD, with its single moving part held in place through a combination of passive magnetic and hydrodynamic forces. *In vitro* and *in vivo* studies showed promising results. Within one *in vivo* study the MVAD was implanted in an ovine model (n = 9) for 90 days. Results demonstrated the safety, reliability, hemocompatibility, and biocompatibility of the MVAD. Nine animals were implanted for 90 ± 5 days. No complications occurred during surgical implantation. Seven of the nine animals survived until elective sacrifice. Each sheep that survived to the scheduled explant appeared physically normal, with no signs of cardiovascular or other organ compromise. Even a transapical implantation approach was tested [13]. A new cannula configuration has been developed for transapical implantation, where the outflow cannula is positioned across the aortic valve. The two primary objectives for this feasibility study were to evaluate anatomic fit and surgical approach, and efficacy of the transapical MVAD configuration. Anatomic fit and surgical approach were demonstrated using human cadavers (n = 4). Efficacy was demonstrated in acute (n = 2) and chronic (n = 1) bovine model experiments and assessed by improvements in hemodynamics, biocompatibility, flow dynamics, and histopathology. Potential advantages of the MVAD pump include flow support in the same direction as the native ventricle; elimination of cardiopulmonary bypass, and minimally invasive implantation.

THERAPY FOR PULMONARY HYPERTENSION (THE VIENNA MODEL)

LVAD support, when used as a BTT, effectively improves pulmonary hemodynamics in patients with end-stage heart failure. Pulmonary hypertension is a common complication of severe long-standing heart failure. Approximately 72% of patients with terminal heart failure who are eligible for cardiac transplantation have PH (Fig. 14) [14].

CONCLUSION

Vienne strategy is a distribution of patients in two groups: the heart transplant recipients and patients receiving LVADs as a BTT. The second group included patients approved and listed for transplant, patients who are unable to survive until transplantation without VAD, patients who might profit from VAD therapy (rehabilitation). Balance between LVAD and heart transplantation depended on: infrastructure of the center; law (informed or presumed consent); the individual risk of the patient.

The authors declare no conflict of interest.

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