## ORIGINAL ARTICLES

# Experience with over 1000 Implanted Ventricular Assist Devices

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ABSTRACT  *Purpose:* The use of ventricular assist devices (VADs) in patients with chronic end-stage or acute heart failure has led to improved survival. We present our experience since 1987. *Subjects and Methods:* Between July 1987 and December 2006, 1026 VADs were implanted in 970 patients. Most of them were men (81.9%). The indications were: cardiomyopathy (n = 708), postcardiotomy heart failure (n = 173), acute myocardial infarction (n = 36), acute graft failure (n = 45), a VAD problem (n = 6), and others (n = 2). Mean age was 46.1 (range 3 days to 78) years. In 50.5% of the patients the VAD implanted was left ventricular, in 47.9% biventricular, and in 1.5% right ventricular. There were 14 different types of VAD. A total artificial heart was implanted in 14 patients. *Results:* Survival analysis showed higher early mortality (p < 0.05) in the postcardiotomy group (50.9%) than in patients with preoperative profound cardiogenic shock (31.1%) and patients with preoperative end-stage heart failure without severe shock (28.9%). A total of 270 patients were successfully bridged to heart transplantation (HTx). There were no significant differences in long-term survival after HTx among patients with and without previous VAD. In 76 patients the device could be explanted after myocardial recovery. In 72 patients the aim of implantation was permanent support. During the study period 114 patients were discharged home. Currently, 54 patients are on a device. *Conclusions:* VAD implantation may lead to recovery from secondary organ failure. Patients should be considered for VAD implantation before profound, possibly irreversible, cardiogenic shock occurs. In patients with postcardiotomy heart failure, a more efficient algorithm should be developed to improve survival. With increased experience, more VAD patients can participate in out-patient programs. doi: 10.1111/j.1540-8191.2008.00606.x
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Heart failure is a leading cause of death in the developed countries. Surgical procedures directed toward preserving the native heart have gained more and more acceptance in recent years: coronary artery bypass grafting in patients with impaired myocardial function and hibernating myocardium[1,2] and resection of postinfarction ventricular aneurysm.[3] So far these procedures can be performed only in patients in stable clinical condition. End-stage heart failure, especially with cardiogenic shock imminent or even present, requires heart replacement or use of a ventricular assist device (VAD) to support the native heart until heart transplantation (HTx) becomes possible.[4] The continuous increase in the number of patients with end-stage heart failure, the increasing complexity of surgery and therefore the increasing number of patients with postcardiotomy heart failure and, on the other hand, new concepts and developments in VAD technology have led to increasing numbers of VAD implantations. Currently, the aim of mechanical circulatory support at our institution is to keep patients alive and improve their general condition, with the possibility of further myocardial recovery, HTx, or permanent support. We present our experience from this point of view.

### METHODS AND STATISTICAL ANALYSIS

The data were analyzed using the VAD database of our institution, which contains the demographic, preoperative, postoperative, and long-term follow-up data of patients who have received mechanical circulatory support devices since July 1987.[5]

†This article is dedicated in deep mourning to our late co-worker Michael Jurmann, MD. He showed us how to fight but left us alone in this fight. Too early.

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**TABLE 1**
**Types and Numbers of VAD Implanted at the Deutsches Herzzentrum Berlin Since 1987 in Chronological Order of Their Introduction into Clinical Practice**

| Type | Number | Duration of Use | Configuration | Type of Flow | Placement |
|---|---|---|---|---|---|
| Bücherl Heart | 2 | Long-term | TAH | Pulsatile | Implantable |
| Berlin Heart | 620 | Long-term | BVAD/RVAD/LVAD | Pulsatile | Extracorporeal |
| Novacor LVAS | 116 | Long-term | LVAD | Pulsatile | Implantable |
| TCI (HeartMate) | 23 | Long-term | LVAD | Pulsatile | Implantable |
| MicroMed DeBakey | 40 | Long-term | LVAD | Axial | Implantable |
| Abiomed BVS 5000 | 47 | Short-term | BVAD/RVAD/LVAD | Pulsatile | Extracorporeal |
| Arrow LionHeart | 6 | Long-term | LVAD | Pulsatile | Implantable |
| Impella | 27 | Short-term | BVAD/RVAD/LVAD | Axial | Implantable |
| Incor | 119 | Long-term | LVAD | Axial | Implantable |
| DuraHeart | 8 | Long-term | LVAD | Centrifugal | Implantable |
| HeartMate II | 1 | Long-term | LVAD | Axial | Implantable |
| CorAide | 1 | Long-term | LVAD | Centrifugal | Implantable |
| CardioWest | 12 | Long-term | TAH | Pulsatile | Implantable |
| Levitronix | 3 | Short-term | BVAD/RVAD/LVAD | Centrifugal | Extracorporeal |
| Combination | 2 | Long-term | BVAD | Both | Both |
| **Total** | **1025** | | | | |

Combination–BerlinHeart RVAD was used with implantable LVAD TCI and INCOR for right heart failure;
TAH = total artificial heart.

Patients were divided into three groups for survival analyses. Group I (n = 567) comprises patients who underwent emergency VAD implantation in profound cardiogenic shock (defined as presence of ongoing multiorgan failure requiring mechanical circulatory support in the next 12 hours). Group II (n = 230) had urgent VAD implantation (defined as surgery later than 12 hours after admission) during stable conditions without profound cardiogenic shock and multiorgan failure. Group III received VAD for postcardiotomy heart failure (n = 173), defined as low cardiac output due to myocardial failure that occurs immediately after cardiac surgery and leads to inability to wean the patient from cardiopulmonary bypass (CPB) or to hemodynamic instability after weaning. Patients who received a VAD for graft failure (n = 45) or an existing VAD problem (n = 6) were excluded from the analysis but are described below. The types and number of VAD used at the Deutsches Herzzentrum Berlin (DHZB) are shown in Table 1.

Statistical analysis was performed using SPSS 11.0 (SPSS Inc. Chicago, IL, USA). Quantitative data are presented as means and standard deviation, qualitative data as numbers and percent. The Pearson $\chi^2$ test was used to test for group differences in qualitative data. Actuarial survival was calculated using Kaplan-Meier estimates. To test for differences between groups a log rank test was used. A reference value of p of less than 0.05 was considered statistically significant.

## RESULTS

Between July 17, 1987, and December 20, 2006, 1026 ventricular assist devices (excluding Biomedicus centrifugal pumps and extracorporeal membrane oxygenation) were implanted in 970 patients. The mean age of the patients was 46.1 years (range three days to 78 years); 81 patients were younger than 18. There were 81.9% men. A total of 526 left ventricular assist devices (LVAD, 50.5%), 463 biventricular ventricular assist devices (BVAD, 47.9%), and 22 right ventricular assist devices (RVAD, 1.5%) were implanted. There were 15 artificial heart devices in all. Table 2 shows demographic characteristics and diagnoses in the population. The development of the VAD program at the DHZB year by year is illustrated in Figure 1 and the increasing number of LVADs implanted over the years is shown in Figure 2. Figure 3 presents the success of VAD therapy

**TABLE 2**
**Demographic Characteristics and Diagnoses Prior to VAD Placement According to Predominant Reasons for VAD Placement**

| | Number of Patients | Mean Age (Ranges) | Sex (m/f) | DCMP (n) | ICMP (n) | Others (n) |
|---|---|---|---|---|---|---|
| Bridge to HTx | 698 | 40.2 (0–69) | 591/107 | 400 | 208 | 90 |
| Postcardiotomy | 173 | 49.7 (0–78) | 129/44 | 16 | 97 | 60 |
| Permanent support* | 73 | 61.3 (40–76) | 60/13 | 28 | 39 | 6 |
| Graft failure | 45 | 44.5 (0–66) | 36/9 | 24 | 11 | 10 |
| Acute infarction | 36 | 51.2 (30–73) | 32/4 | 0 | 36 | 0 |

*The permanent support was a primary intention. Only three patients refused HTx after LVAD had been implanted.
DCMP = dilative cardiomyopathy; HTx = heart transplantation; ICMP = ischemic cardiomyopathy.
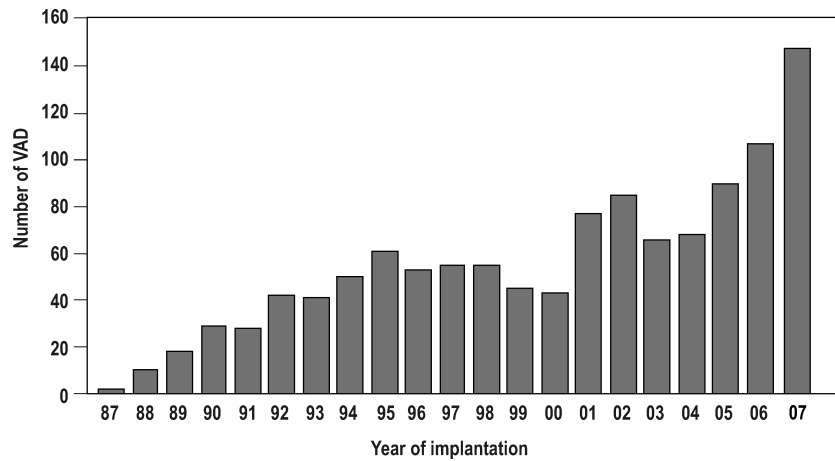
**Figure 1.** *Number of VADs implanted at the DHZB by year.*

in the study period, defined as 30-day survival or explantation of the device for myocardial recovery or HTx. The overall success rate for patients implanted with a BVAD was 57.2%, for patients implanted with an LVAD it was 69%, and for RVAD 42.9%. Survival analysis showed lower (p < 0.05) 30-day survival in Group III (49.1%) than in groups I (68.9%) and II (71.1%).

The reasons for device removal were: HTx in 270 patients, recovery of myocardial function in 76, switch from a short-term to long-term VAD in 16, thrombosis in six, infection in four, and technical problems with the VAD in six. On January 1, 2007, 54 patients were on support, 40 of them as outpatients.

Of 173 patients requiring a VAD for postcardiotomy heart failure, 26 (15%) could be weaned from support, in 14 (8.1%) patients HTx was performed, and in six (3.5%) patients the short-term VAD was exchanged for a long-term system. In total, 71 patients (41%) survived more than 30 days.

Among 438 adult patients with dilative cardiomyopathy (DCMP) implanted with an LVAD, 46 could be weaned from VAD support. In 30 patients myocardial function remained stable over the years; seven died for noncardiac reasons after VAD removal. In 16 patients

deterioration of myocardial function occurred, 12 patients underwent HTx, three received renewed VAD implantation and one patient died on the waiting list. As reported by our working group, among the parameters evaluated only duration of heart failure (2 ± 1 vs 8 ± 4 years, p = 0.008), left ventricular ejection fraction (48 ± 3 vs 39 ± 9%, p = 0.005) and left ventricular end-diastolic diameter before explantation (50 ± 5 vs 58 ± 7 mm, p = 0.007) differed significantly between patients with sustained cardiac recovery for longer than two years and those with deteriorating cardiac function.[6]

There were no differences in long-term follow-up after HTx with previous VAD implantation (n = 270, including five patients with VADs implanted in three other hospitals) and without (n = 1326) previous VAD implantation (p = 0.86). The analysis of patients transplanted since 1996, when our strategy had largely changed in favor of HTx after complete recovery of organ function and of more LVAD implantations, also showed no differences (p = 0.51) between patients with and without previous VAD support (Fig. 4).

Since 1997 VADs have been implanted for permanent support, as primary intention, in 72 patients with
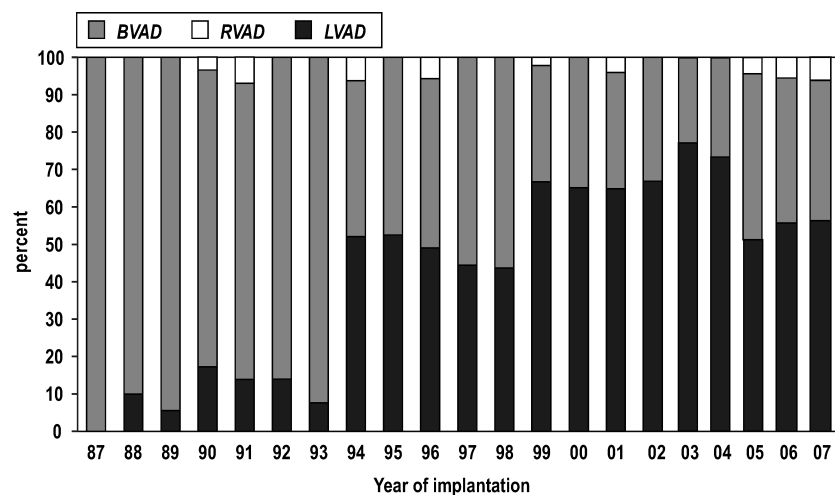


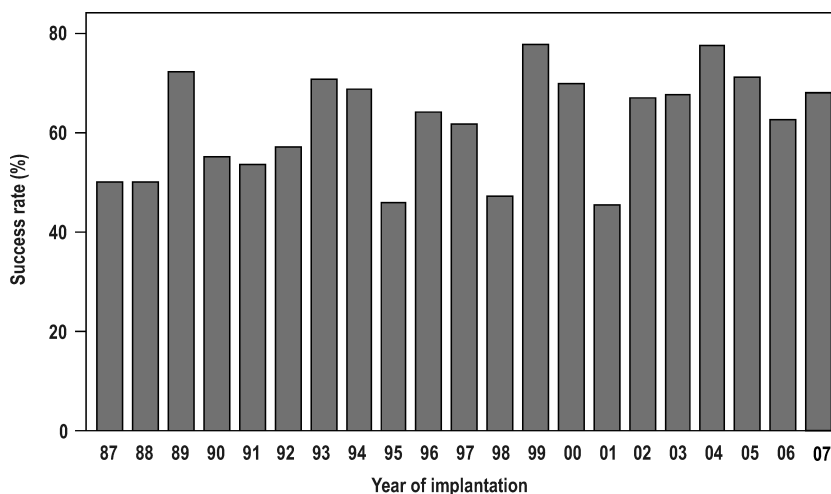**Figure 2.** *Increasing number of left ventricular assist devices implanted over the years.*

**Figure 3.** *Success of VAD therapy over the years defined as 30-day survival or removal of the device due to myocardial recovery or heart transplantation.*

a mean age of 61.3 (range 40–76) years; nine of them are currently on support. The reason for this decision was most often advanced age (n = 58), followed by diseases precluding HTx (fixed high pulmonary vascular resistance, peripheral arterial disease, extreme obesity). In one patient a VAD was implanted for permanent support for toxic cardiomyopathy arising after chemotherapy for malignancy, which precluded HTx. In one patient a hypophysis tumor with acromegaly precluded HTx. Three patients refused HTx after VAD implantation. In all except five patients with a Cardio West total artificial heart and one patient with a Berlin Heart Excor BVAD (Berlin Heart GmbH, Berlin, Germany), LVADs were implanted for permanent use (Berlin Heart Excor n = 10, MicroMed DeBakey VAD n = 20 [MicroMed Cardiovascular Inc., Houston, TX, USA], Novacor LVAS n = 6 [World Heart Inc., Oakland, CA, USA], LionHeart n = 6 [Arrow International, Inc., Reading, PA, USA], DuraHeart n = 2 [Terumo Heart Inc., Ann Arbor, MI], and Incor n = 22 [Berlin Heart Gmbh]). The mean duration of support was 301 days and maximal duration 1876 days. In three patients a Novacor LVAD was exchanged electively due to defective bearings after two to 4.5 years. Among patients permanently treated with a VAD, 16 patients have been supported for more than one year. Seven were supported for more than three years (Novacor LVAS n = 3, Berlin Heart n = 2, Incor 2) and the five with Novacor LVAS and Berlin Heart for more than four years.[7]

Between January 1996, when the outpatient program was started, and December 2006, a total of 114 patients were discharged home. The mean time on support was 602 (range 77–1731) days. The mean age was 46.1 (range 10–78) years. There were 56 patients supported by a Berlin Heart VAD (BVAD n = 20, LVAD n = 36), 29 by Novacor LVAS, 14 by Incor, nine by a MicroMed DeBakey VAD, four by HeartMate I [Thoratec Corp., Pleasanton, CA, USA], one by DuraHeart, and one by Arrow LionHeart). Patients spent a mean period at home of 301 days out of a total of 503 days on

support (59.8%). Fifty-five patients were transplanted after a mean of 502 days.

## DISCUSSION

Our experience shows that VAD implantation conserves the lives of patients with life-threatening cardiogenic shock and leads to recovery from secondary organ failure. Moreover, it is a successful approach for bridge to transplantation or to myocardial recovery and has emerged as a realistic option for permanent support for nontransplantable patients. However, patients should be considered for implantation of a VAD before profound, possibly irreversible, cardiogenic shock occurs.

In the past 19 years a number of different VADs were used in our institution (Table 1). Recently, almost two-thirds of implantations were of LVADs (Fig. 2). The phi-
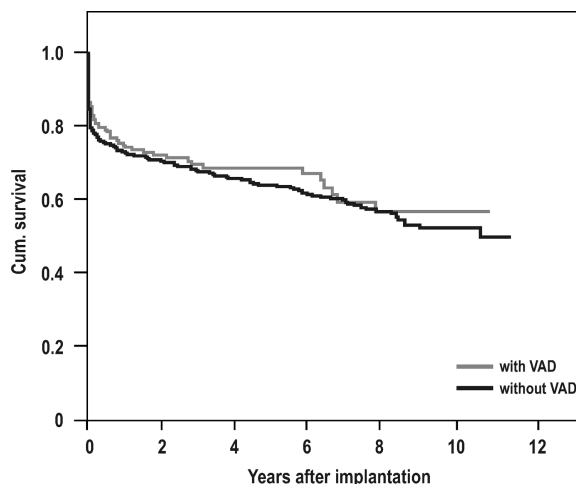


**Figure 4.** *Kaplan-Meier analyses in the patients receiving heart transplantation after 1996, after our strategy had largely been changed in favor of transplantation after complete recovery of organ function and in ambulatory patients.*
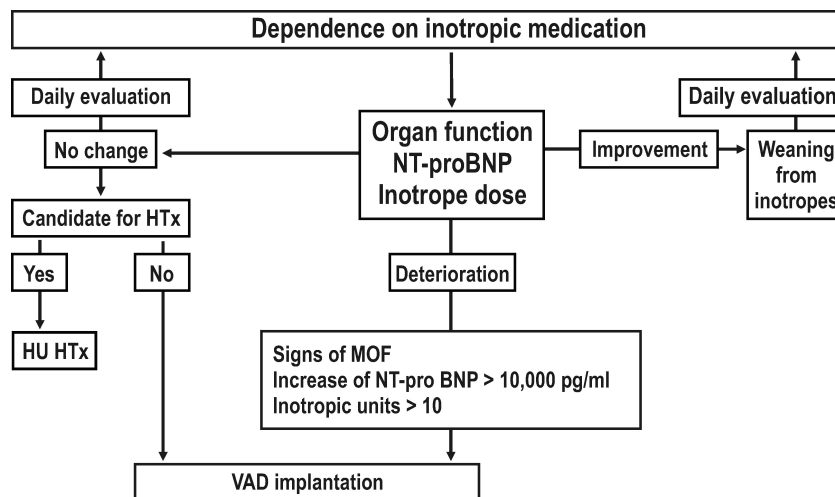
**Figure 5.** *Our current strategy for the management of patients with chronic end-stage heart failure, on inotropes and scheduled for high urgency HTx. In non-HTx candidates LVAD implantation should be performed without delay to decrease risk for right heart failure and multiorgan dysfunction. This strategy is based on a number of studies and experience gained in the past 20 years. The calculation of inotropic units has been described by Kormos and modified by Potapov.[19]*

losophy of LVAD support received a boost with the use of the first implantable LVADs: in November 1993 the Novacor LVAS and in May 1994 the HeartMate I. Further, the number of LVAD implantations has risen due to many developments including the introduction of inhaled nitric oxide in 1996;[8] the implantation of the LVAD through lateral thoracotomy in patients with previous sternotomy since 1997;[9,10] the introduction of a large apical cannula for the Berlin Heart system, which allows better unloading of the left ventricle; the use of miniaturized axial flow pumps since 1998 and the development of the novel magnetically suspended axial flow LVAD Incor;[11] and the improvements in preventing postoperative right heart failure.[12,13]

Implantable wearable electrical LVADs give patients greater mobility and quality of life, while implantation of a BVAD requires more extensive surgery, the blood is exposed to a greater area of foreign surface, and the drive units are larger, restricting the patient's ability to walk around freely. However, as this type of LVAD is only able to support the left ventricle, impending right heart failure has been a major concern in these patients. Prediction of right ventricular dysfunction after LVAD implantation is extremely difficult.[8,14,15] Echocardiography is currently the most powerful tool for evaluation of right ventricular function. Tricuspid regurgitation and geometry of the right ventricle are of particular importance and may help to predict right ventricular function after LVAD implantation. As yet no definitive criteria for device selection have been established.[16-18] Patients with severe ventricular arrhythmia and signs of multiorgan failure (indicated by metabolic acidosis; oliguria or anuria; increasing serum creatinine, transaminases, or bilirubin; or requiring mechanical ventilation for lung edema or high doses of catecholamines, especially epinephrine) require biventricular support. Our current strategy in the management of patients with chronic end-stage heart failure on inotropes scheduled for high urgency HTx is presented in Figure 5. It is fairly difficult to achieve the right balance between a

stable situation allowing high urgency listing for HTx and the implantation of a mechanical circulatory support for bridge to HTx in case of or just before deterioration of the hemodynamics with threatening cardiogenic shock. For decision making, we focus on the development of signs of organ dysfunction, NT-pro-BNP level, and inotropic support.[19] In non-HTx candidates the LVAD implantation should be performed without delay to decrease the risk for right heart failure and multiorgan dysfunction. For some parameters there are evidence-based[19,20] and for some experience-based cut-off values. Further studies are necessary to support and improve such algorithms. Equally unresolved is the question of the depths of cardiogenic shock from which an organism can be brought back to fully restored function of all organs if supplied with adequate blood circulation by a device. Despite some established indicators that the downhill course is irreversible, there are also many examples of a surprising return to life of a seemingly moribund body.

Further investigations are necessary to establish criteria to predict the possibility of organ recovery in patients with profound cardiogenic shock.

In recent years, VADs have progressed from being bulky, pneumatically driven extracorporeal devices through implantable electrical pulsatile devices to miniaturized magnetically levitated axial or centrifugal flow pumps.[21] Using the different types of VAD and experience gained in the past 19 years we are now able to offer VAD therapy tailored to the individual patient.

**Postcardiotomy heart failure**

Postcardiotomy heart failure occurs in 2% to 6% of all adult cardiac operations and is a frustrating clinical entity because of its high mortality rate.[2] Despite maximal medical treatment and use of the intra-aortic balloon pump (IABP), some patients remain in low output status with subsequent impairment of organ perfusion. We showed the usefulness of a score value after IABP
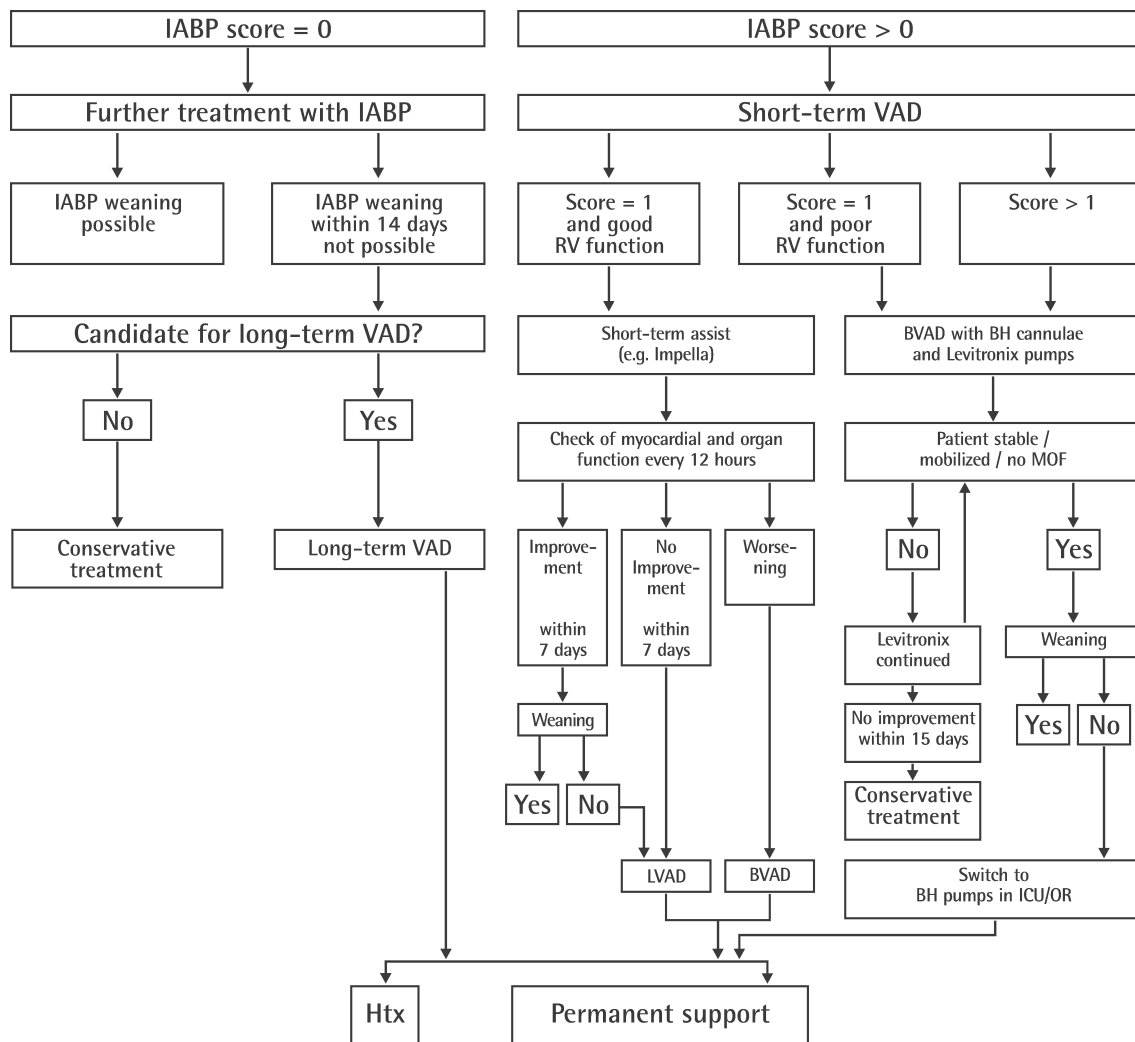
**Figure 6.** *The algorithm used in the operating room to improve survival in patients with postcardiotomy heart failure. This algorithm is based on the intra-aortic balloon pump (IABP) score (2) and recommends, for patients with more pronounced heart failure, early support with a short-term VAD employing cannulae from the long-term Berlin Heart VAD. This strategy eliminates the need for a second operation in the case of organ recovery but not of myocardial recovery with subsequent need for long-term support. Most patients will require biventricular support.*

implantation (IABP score) to predict outcome in these patients. In patients with a high IABP score, a short-term VAD that unloads the failed heart and provides adequate organ perfusion should be implanted, employing cannulae of a long-term device.[22] The goal is to support the heart until it recovers.[22-25] If it does not recover, although multiorgan dysfunction resolves and no neurological deficits can be seen under mechanical support, the short-term VAD should be switched to a long-term assist device in the ICU without reopening of the chest.[22] However, one needs to remember that most of these patients can be saved only by HTx and therefore it is reasonable to restrict VAD implantation to those patients who qualify for HTx. Our current strategy in patients with postcardiotomy heart failure is based on IABP score and is presented in Figure 6.

**Myocardial recovery**

Recovery of myocardial function on VAD support in patients with DCMP remains a fascinating phe-

nomenon.[26] Since 1995, in 46 patients the previously implanted LVAD could be removed and in 30 of them myocardial function remained stable for maximal follow-up of over 10 years (Fig. 5).[6]

In our institution all patients with DCMP implanted with LVADs are routinely evaluated by echocardiography for recovery of myocardial function. As yet no preoperative biochemical or histological predictors for this phenomenon are known.[27-30] However, patients presenting myocardial recovery showed a shorter history of the disease. The indication for explantation is improvement of left ventricular ejection fraction to over 45%, decrease of left ventricular end-diastolic diameter to 55 mm or less, and improvement of the systolic wall motion of the left ventricle to over 8 cm/s measured during pump stop. After device removal, all patients continue to receive heart failure medication including ACE inhibitors, beta blockers, aldactone, vitamins and antioxidants, and, if necessary, diuretics and digitalis.[31]

In selected patients, administration of clenbuterol may enhance myocardial recovery as advocated by

Yacoub and associates.[32] This treatment and the intra-operative application of stem cells are currently under clinical investigation in our institution.

Routine follow-up including echocardiographic studies should be performed after device removal. If necessary, the patients presenting deterioration of myocardial function should be referred for HTx.[33-35]

### Bridge to transplantation

In candidates for HTx with rapid deterioration of cardiac function, implantation of a long-term VAD should be considered. Most of these patients present with acute cardiogenic shock and signs of multiorgan failure. Emergency implantation of a BVAD or TAH is required to support the circulation and keep the patient alive. Patients with optimized treatment of heart failure presenting with marginal, but stable, hemodynamic conditions under intravenous (IV) catecholamines are immobilized and may suffer rapid decompensation with acute multiorgan failure or sudden death due to arrhythmia. In these patients early implantation of a VAD is a better option than IV catecholamines in order to keep them in a marginal condition until HTx.[36] Moreover, implantation in stable patients mostly allows the use of an implantable LVAD even in the case of pulmonary hypertension,[37] with subsequently better survival and better quality of life. The survival rates after HTx in patients with and without previous VAD implantation are, in our experience,[35] similar (Fig. 4). Aaronson et al. even showed a superior survival rate for patients bridged with VADs.[36] This might be explained by normalized organ function following improved hemodynamic status.[16,38,39] In the 1980s we strove for high urgency transplantation immediately after VAD implantation. With increased understanding of shock pathophysiology and improvements in VAD technology leading to a subsequent decrease in the complication rates (e.g., bleeding and thromboembolism),[35,40,41] and, more importantly, having seen a number of donor organs wasted in recipients with multiorgan failure, we changed our strategy in favor of HTx in VAD patients in stable hemodynamic condition, with normal organ function and preferably discharged home. These patients are on the normal waiting list and acquire high-urgency status only if VAD complications occur.

The use of the VAD as a bridge to transplantation does not solve the main problem of the shortage of donor organs.[4] However, this concept has led to the definition of indications for, and limits of, mechanical circulatory support. The widespread use of VADs has stimulated continuous improvements in this technology with a subsequent decrease in complication rates. Further, more and more patients and physicians accept and trust in this technology. In a large number of patients on the waiting list, different types of VAD are successfully used for months and years.[42] The patients are discharged home and can enjoy life with their families; some of them have even returned to work.[41] From this experience, use of the implantable LVAD for permanent support seems to be an appropriate solution for a large cohort of patients with end-stage heart failure and contraindications for HTx.

### VAD for permanent support

The number of patients with end-stage heart failure is far larger than the number of donor hearts available.[4,43,44] The mortality rate of this disease is worse than that of most forms of cancer.[43,44] Additionally, an increased number of patients survive acute heart failure and high-risk cardiac surgery but develop end-stage heart failure some years later. However, high pulmonary vascular resistance, peripheral arterial disease, extreme obesity, and mostly advanced age, as in almost 80% of cases in our experience, eventually preclude listing for HTx. In this scenario, a VAD for definitive therapy may be an option that also significantly lowers hospital costs.[45] Such a VAD should be durable and without technical wear for at least five years. The blood contact surface and the construction of the blood pumping unit should be nonthrombogenic and the blood flow characteristics not detrimental to the vessels and end-organs. The device should be fully implantable and the energy transfer and control transcutaneous, without leads penetrating the skin. The device should be noiseless, small, and easy to implant. Low energy consumption would allow a longer period without an external energy supply. Last, but not least, low costs would allow widespread use of this device. None of the currently available devices fulfill all these requirements. The preliminary results with various rotary blood pumps such as Jarvik 2000 (Jarvik Heart, Inc., New York, NY, USA), VentrAssist (Ventacor, Chatswood, Australia), DuraHeart, and Incor as devices for definitive therapy are encouraging but still not conclusive. In our experience, most of the patients receiving a VAD as a definitive therapy have had previous median sternotomy and require implantation of the device through lateral thoracotomy. In this situation firstly the extracorporeal pulsatile Berlin Heart Excor and later the axial MicroMed DeBakey VAD and Incor have been successfully used.[7,9,10]

### Experience with outpatients

With the decreasing number of available donor hearts and increasing numbers of potential heart recipients, the waiting period for HTx has lengthened and is currently, depending on the country, up to several months. Anticipating prolonged duration of VAD treatment, a policy of discharging patients home has been instituted. A comparison between patients supported by different types of VAD discharged home and remaining hospitalized showed better survival and quality of life in discharged patients. In our experience 114 outpatients spent two-thirds of the waiting time at home. The readmission rate after discharge was 3.1 per patient and comparable with the experience of other centers.[41,46-48] In more than half of the cases (56.3%), the reason for readmission was unrelated to VAD, followed by wound infection (20.9%), coagulation disorders (10.9%), and cerebral embolism (7.7%).

Our experience demonstrates that patients on a VAD can be discharged home without increased risk of mortality or morbidity, with an acceptable readmission rate and good quality of life.[41] Samuels also reported an improvement in mood, psychosocial conditions, and a positive shift in relations with family and friends after discharge.[49] Moreover, noiseless continuous flow pumps offer better quality of life and a lower infection rate.[50-52]

Recently, over 50% of VAD patients have been outpatients supported by their family, social workers, and family physician, who are monitored in our outpatient department every two to six weeks. For emergency cases a perfusionist/physician hotline has been established.

The positive experience with outpatients[41,46-48] was one of the leading factors in promoting the LVAD for permanent support.[42] However, this experience shows that currently available VADs are not yet real alternatives to HTx, although they have emerged as a realistic option for nontransplantable patients, with steadily improving quality of life. Major concerns are the mechanical durability of the devices, the need for anticoagulation, and the elevated risk of thromboembolic and bleeding complications. The problems with infection and limited mobility of the patients have been alleviated using small continuous flow devices and in the future they may be minimized using transcutaneous energy transfer systems.

## Differences between pulsatile and axial flow pumps

Discussion of the impact of continuous flow on organ function is as old as the use of the heart-lung machine. This question arises again with long-term use of continuous flow VADs. These pumps have enormous advantages over bulky pulsatile pumps.[21] The small size and low weight, which is only 20% to 30% of that of the pulsatile pumps, make the pump pocket—the main source of infection and bleeding— unnecessary. These pumps are noiseless and easy to implant; they need less energy and seem to be durable, especially the Jarvik 2000 with the newly designed ceramic bearings[53] and Incor with its magnetically suspended impeller.[50] Implantable centrifugal pumps (Terumo DuraHeart, VentrAssist) with magnetic or hydrodynamic levitation are larger, but also offer low rates of thromboembolic events and good durability. In a previous study, we showed that in patients with an axial flow pump, after the left ventricle has been unloaded and some recovery of myocardial function and contractility has occurred, the flow becomes slightly pulsatile.[54] In our experience with over 250 patients implanted with continuous flow pumps there are no differences in postoperative recovery of organ function.[55] However, the long-term effect of less pulsatile flow on the endothelium and on end-organs remains unknown.

The impeller with its high-speed rotation (2000–3000 rpm for centrifugal and 7000–10,000 rpm for axial pumps) has a different impact on coagulation and the inflammatory systems from the pulsatile pump,[56,57] while the postoperative bleeding and thromboembolic complications are more influenced by GP IIb/IIIa polymorphism than by the type of pump.[58]

## Ongoing challenges

Despite enormous progress in mechanical circulatory support, there are still challenging questions in patient selection for VAD implantation. The improved results of bridging to HTx using optimal pharmacological heart failure therapy in patients with New York Heart Association (NYHA) Class III and still existing complications related to the device and to surgery so far preclude the use of VADs in this cohort of patients. In our opinion, LVAD implantation is the treatment of choice for bridging to HTx in an NYHA Class IV patient who is stable but dependent on IV medical treatment with catecholamines.[36,38] At the other end of the spectrum is the patient with severe cardiac and multiorgan failure, needing biventricular support, in whom the success is limited by the degree of irreversible organ damage.

The optimal time-point for VAD implantation in patients on IV inotropes may easily be missed because of the mostly rapid decline into cardiogenic shock and multiorgan failure. In this situation serial measurement of BNP or NT-pro-BNP and/or inflammatory parameters may be helpful.[19] It seems that advanced age is a major risk factor for mortality after VAD implantation;[58] however, the majority of our patients received the VAD for permanent support because of advanced age.[59] A network involving the cardiology departments of local hospitals and hub heart centers can be life-saving for ongoing cardiogenic shock patients.[60]

## Anticoagulation on VAD

During long-term VAD therapy one of the important issues is balanced anticoagulation. Despite new data concerning coagulatory processes during long-term VAD support[57] and the use of extended control tests such as the international normalized ratio, the thrombocyte aggregation tests and thrombelastography, thromboembolic, and bleeding complications remain major limitations for long-term VAD support.[42]

Currently, sophisticated anticoagulation strategies tailored to different types of VAD are used in different centers[41,58,61] but as yet no standard anticoagulation protocols have been developed. For patients on the HeartMate I LVAD only acetylsalicylic acid (ASA) is suggested for long-term anticoagulation to minimize the rate of thromboembolic events, while for other devices most centers recommend also warfarin. In patients with a continuous flow VAD, the anticoagulation protocols mostly include warfarin, ASA, and optional clopidogrel and dipyridamol.[41,57,61,62] Our study showed a significant association of the PlA A1A1 genotype with bleeding and of A1A2 with thromboembolic complications during long-term follow-up in patients implanted with a VAD. The type of LVAD and use of clopidogrel did not influence the complication rate. Determination of PlA polymorphism in VAD patients and corresponding adjustment of platelet inhibitor doses may therefore reduce bleeding and thromboembolic complications.[63]

A frequent complication is heparin-induced thrombocytopenia (HIT) with detrimental results when

occurring after implantation. Our recent experience has shown an improvement in the outcome of such patients through the early detection of HIT antibodies before and shortly after the implantation and the immediate implementation of an alternative anticoagulation regimen that advocates the use of lepirudin and now also tirofiban.[64]

## CONCLUSION

As yet, the VAD is not an alternative to HTx. The "bridge-to-transplant" mechanical circulatory support concept may be life-saving for the individual patient but it does not solve the problem of organ shortage; however, it has stimulated the development of long-term systems. The use of long-term systems allowed the introduction of the "bridge-to-recovery" concept, which has become a possible, although still unpredictable, course with excellent long-term results in a still-limited proportion of patients. Further, the discharge home of patients with a VAD is safe and improves their quality of life. Finally, permanent support has emerged as a realistic treatment for nontransplantable patients, relieving the symptoms of heart failure and steadily improving quality of life.

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