The number of patients on the waiting list for a heart transplant in Germany declined each year from 1998 to 2001, but the trend then reversed direction, with a steady increase ever since. At the same time, the number of heart transplantations performed per year has gone down.

The causes of this development are multiple. One explanation may be that the introduction of better conservative treatments for end-stage heart failure, such as beta-blockers and biventricular pacemakers, at first led to a temporary decline in the demand for heart transplants, but that transplantation again became a desirable option later on in the course of the disease, once these treatments had been exhausted.

Another explanation can be found in the general demographic trend toward an increasing incidence of end-stage heart failure. Thus, it could be stated with certainty in 2001 that a patient on the heart transplantation waiting list would be able to undergo transplantation within one year. In 2008, in contrast, there were 873 patients on the waiting list, while only 382 transplantations were performed. As a consequence, many patients die while waiting for a transplant (Figure 1).

As early as the year 2000, a new allocation strategy was adopted to address this problem: priority in the allotment of transplants has been given since then to patients who need them urgently. Eight years ago, 30% (8 of 26) of the patients receiving heart transplants in Hannover were rated as "high urgency" (HU) candidates; the corresponding figure today is nearly 90% (28 of 32).

In September 2005, the HU criteria were made yet more stringent (1), and, even still, there are continually about 40 patients nationwide who are on this highest level of urgency. Patients with common blood groups and of normal body size have hardly any chance any more of receiving a heart transplant unless they are rated as HU. Some transplantation centers now only register patients for transplantation when they are in the HU category; generally, this means that the patient requires intensive care and is catecholamine-dependent.

If a patient in the HU category is in danger of dying while waiting for a transplant, ventricular assist devices (VAD) can be used as a temporizing measure until a transplantable organ becomes available. Although this strategy can be very successful in individual cases, it...
also worsens the imbalance between the number of potential organ recipients and the number of transplantable organs. Data from Europe show that, among all patients receiving a VAD as a temporary treatment, only 25% go on to receive a transplant within one year (2). This necessarily creates a state of chronic circulatory support with a left ventricular assist device (LVAD) for patients who are cared for on an ambulatory basis and who must live with such a device for an indefinite period of time. In this article—based on a literature search on the key words "total artificial heart," "BVAD" (biventricular assist device), "LVAD" (left ventricular assist device), and "rotary blood pumps" for the period 1970–2008—we will discuss the developments in LVAD technology that now enable patients to survive for several years with permanent circulatory support, and also the available ways of lessening the risks and invasiveness of interventions of this type.

The development of artificial heart technology
40 years ago, the functional replacement of the human heart was already a topic of intense public interest, not just because the first heart transplantation had been performed in December 1967, but also because the development and clinical application of artificial hearts was already underway even then. A pneumatically driven, two-chambered apparatus was then being developed for total heart replacement (3). Unlike heart transplantation, however, the artificial heart failed to become established in clinical practice in that early period (4), and the type of artificial heart that was then under development is in clinical use today in only a few special situations. The original type of artificial heart had major technical flaws, and the need to power it with a very large, extracorporeal console made it utterly impractical for permanent therapy as we know it today (5).

In order to address these technical problems, the artificial ventricles were moved outside the body (Figure 2). This step meant that what had originally been intended as an artificial heart was transformed into a ventricular assist device (6). This technology was successfully applied and is still in use today. Experience has shown that the functional replacement of both cardiac ventricles is not necessary in every case; rather, left ventricular assistance alone usually suffices (7).

In the 1990s, implantable, electrically powered left ventricular assist devices came onto the market. These large, heavy displacement pumps were implanted in a pocket below the diaphragm (8) and connected to the apex of the left ventricle and to the ascending aorta. They were connected to an external electric power supply through a percutaneous cable: this was the origin of the configuration that is still the most common one today (9), i.e., an implanted pump with a transcutaneous connection to a power supply (Figure 3). The unsatisfactory aspects of this solution were the size of the apparatus, the noise it made, the risk of infection, and limited mechanical durability. Using such a device as the sole method of treatment (destination therapy) was found to give patients a significantly higher chance of survival at one year than conservative treatment did (the REMATCH trial, [10]), yet the limited mechanical durability of the apparatus became a critical issue at two years, at which time the survival advantage was no more than marginal.

The second generation of left ventricular assistance devices (LVADs) consisted of axial pumps. The new technology opened up new possibilities: these LVADs provide continuous blood flow without valves, are relatively small and light, and remain mechanically stable for years. When they were first used, there were major

Figure 2: Systems for use in patients with biventricular heart failure
a) A Total Artificial Heart (SynCardia) that is implanted orthotopically and powered by a pneumatic console (photograph reproduced with the kind permission of SynCardia Systems, Inc. [www.syncardia.com])

b) An extracorporeal artificial ventricle (the Thoratec Paracorporeal Ventricular Assist Device [PVAD]), which can be used to assist the function of either the right or the left ventricle of the heart and is powered similarly to the Total Artificial Heart (photograph reproduced with the kind permission of the Thoratec Corporation)

The length of the waiting list and the number of heart transplantations performed each year in Germany, 1998–2008 (data from Eurotransplant, www.eurotransplant.nl)
problems relating to coagulation (11), but technical modifications and improved anticoagulation schemes have largely circumvented these difficulties. The incidence of infections and neurological complications is also much lower than before: first-generation LVADs were found, in the REMATCH trial (10), to be associated with 0.39 severe neurological disturbances per patient-year, while the comparable figure in a study of axial pumps (second-generation LVADs) was only 0.18 strokes per patient-year (12). The latter results were equaled by an incidence of 0.18 strokes per patient-year in a trial of a third-generation device (Ventracor) (13).

Moreover, it has become clear that continuous blood flow, with loss of the pulse, is physiologically entirely unproblematic (14). The neurocognitive disturbances associated with severe heart failure can be improved with pulseless LVADs, just as they can with pulsatile devices (16). The patient also remains able to compensate for the increasing physical stress of exercise after the native heart has been relieved of its functional burden (17).

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<td>Advantages and disadvantages of heart transplantation versus cardiac assistance systems</td>
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| Advantages | ● Definitive treatment  
● Normal physical activity possible  
● Good long-term prognosis | ● Immediately available  
● Planned intervention  
● Good level of physical activity achievable  
● Recovery of native heart possible (ca. 8%) |
| Disadvantages | ● Lack of donor organs  
● Disease can arise in the donor organ  
● Risk of transplant vasculopathy  
● Immune suppression: – renal failure  
– neoplasia  
– susceptibility to infection  
– diabetes mellitus  
– hypertension | ● Dependency on device  
● Device must be continually supplied with power  
● Cardiac arrhythmia  
● Anticoagulation (hemorrhage, stroke)  
● Risk of infection (Driveline*) |

* percutaneous cable connection
Because of potential problems in the non-invasive measurement of blood pressure, as well as the inability to record a capillary pulse, the usual treatment modalities need to be altered for patients bearing pulseless LV ADs. In particular, when medical or surgical treatments are needed independently of the cardiac situation, consultation with an implanting center is recommended. These patients also have an elevated tendency to bleed, e.g., during dental or surgical procedures, partly because of the necessary anticoagulation, partly because of acquired platelet dysfunction, and perhaps also because of an acquired von Willebrand syndrome (18). It follows that such procedures should only be performed in specialized centers. These patients often do not lose consciousness even when they go into atrial fibrillation. One can well imagine the consternation of emergency medical personnel who are called to see such patients and then find them pulseless, but alert and talking!

**Indications and results**

In the past, artificial cardiac support systems were only implanted in patients who would otherwise have had no chance of survival. Accordingly, the high perioperative morbidity and mortality were not solely due to the dangers of the device itself and its implantation, but also in large measure to the preexisting cardiac shock and the consequent multiple organ failure. Unlike heart transplantation, which, at present, can no longer be ethically or legally offered to patients with a very poor prognosis in view of the lack of transplantable organs, ventricular assist devices are, in principle, available for use in all patients at all times (Table). It follows that the extreme reluctance to use VADs prevailing in Europe today can only be understood as a product of the historical setting.

Risk assessment has been attempted in order to determine how the patient’s preoperative condition affects the postoperative outcome of VAD implantation.

In this connection, the finding reported by Lietz et al. (19) in 2007 needs to be emphasized: even a moderate degree of two-organ or multiple organ failure massively affects the outcome after an assist device has been implanted (Figure 4). Patients with a risk score below 17 achieve greater than 70% survival at one year, while those with a risk score of 17 or higher have a one-year survival rate no higher than 30%. Thus, a patient with a platelet count below 148 000 per microliter and a plasma albumin concentration below 3.3 g/dL, under afterload-reducing treatment and with a moderately elevated blood urea nitrogen concentration, is already in a high-risk category even if no intravenous inotropic agents are being administered. The decision to use a ventricular assist device must be made in timely fashion, before multiple organ failure sets in, if a successful outcome is to be achieved (20).

The hypothesis guiding this article is that the lower invasiveness of the implantation of modern support systems and the possibility of permanent therapy with them can lead to more timely decisions to treat, and thus to better outcomes. The risk to the patient is greatest in the perioperative phase, it is largely a function of the patient’s preoperative condition (Figure 5). Device failure—such as is still encountered with pulsatile LVADs (10)—has little influence on outcomes later on in the course of treatment (2).

At the Hannover Medical School, the decision to treat early has already reduced the perioperative mortality from 25% (18 of 70 patients) in 2004–2006 to 12% in 2007 and 10% (2 of 22 patients) in the first half of 2008 (p < 0.05). As described by Lietz et al. (19), it is important that the decision to treat should be mainly based, not on hemodynamic parameters, but rather on indicators of incipient organ dysfunction (the international normalized ratio [INR]), the serum albumin concentration, renal function parameters, and the platelet count (Figure 4). Moreover, the markedly improved outcomes that are currently seen have come about through the establishment
of interdisciplinary teams and integrated patient care at clinical institutions with active cardiac support programs. The improved outcomes also clearly indicate that this type of treatment is becoming established as permanent therapy. Although the one-year survival after heart transplantation around the world has remained well over 80% for several years now (as documented by the International Society for Heart and Lung Transplantation, with data from 76,538 transplants performed up to 2006), the corresponding figure for Germany in 2007 was only 73% among 252 heart transplants (data from the German Federal Quality Assurance Office, Bundesgeschäftsstelle Qualitätssicherung [BQS]). A major factor leading to this relatively low figure is in-hospital lethality, which has risen over the last three years to the latest figure of 22.2%. Potential causes of this development include the lack of transplantable organs in Germany and the allocation of transplants to recipients in intensive care units who are already suffering from multiple organ failure.

A number of studies have already shown better one-year survival figures after LVAD implantation than after heart transplantation in Germany (13), yet the comparability of the patient groups is highly questionable. The most pertinent figures for survival after LVAD implantation are those of a retrospective European study (2): the one-year survival in this study, just over 70%, was on the same order of magnitude as that of heart transplantation in Germany.

The treatment algorithm for end-stage heart failure should take risk scores into account, both for transplantation and for LVAD implantation. This carries the potential of considerably improving the overall outcome for these high-risk patients, whichever of the two treatments they receive.

Health-related quality of life

There are major differences between heart transplant recipients on the one hand and artificial heart recipients on the other. Heart transplantation carries with it a lifelong need for immunosuppressive treatment, with the attendant major side effects. Permanent treatment with an LVAD necessitates both anticoagulation and the continuous provision of electric current to the device. The patient’s perception of these restrictions on his or her quality of life depends not only on the course of disease before and after surgical treatment, but also on personal coping ability.

A current study from the Netherlands shows that even patients with first-generation support devices experience a marked improvement of physical performance, with little or no restriction of their aerobic capacity. Patients who had received heart transplants did even better (22). Some of the devices used in this study, however, must be regarded as out of date.

To address the question of physical performance and quality of life in patients with modern cardiac support systems, the authors used spiroergometry to monitor the physical functioning of the heart transplant patients whom they cared for as outpatients, as well as that of their patients with artificial heart systems as permanent treatment, and also monitored their psychosocial competence (health-related quality of life, HRQoL) using the Medical Outcomes Study Short-Form General Health Survey (SF-36). Furthermore, in an as yet unpublished study of the Department of Cardiothoracic, Transplant, and Vascular Surgery at the Hannover Medical School, 53 heart-transplant patients and 21 LVAD patients were examined six to nine months after the surgical procedure.

Both groups were composed exclusively of men, most of whom suffered from dilated cardiomyopathy. The mean age was 52 ± 12 years in the heart transplantation (HTx) group and 47 ± 13 years in the LVAD group (p = 0.07). With regard to cardiopulmonary performance, the maximal performance capacity in the HTx group was found to be 84 ± 27 W (watts), as compared to 105 ± 16 W in the LVAD group (p < 0.026). In both groups, these figures corresponded to 52% of the age-adjusted norm. The maximal oxygen consumption (VO2 max in mL/min/kg) was 17.4 ± 3.5 in the HTx group and 20.5 ± 4.6 in the LVAD group (p < 0.04).

We interpret these data as showing that both forms of treatment can lead to an acceptable outcome in terms of cardiopulmonary performance, with slightly better results for LVAD. The latter are possibly accounted for by the somewhat younger age of the LVAD patients and by their markedly shorter disease course before treatment, in consequence of which they have not yet undergone severe muscular deconditioning during their period of
their heart failure. With regard to physical performance ability after heart transplantation, it is known from earlier studies that muscular deconditioning (23) is difficult to reverse after transplantation, and that improvement is only possible through a continuous program of muscle training. The inhibitory effect of immune suppression on the skeletal musculature may also contribute to deconditioning (24).

With regard to the quality of life, as assessed on a scale from 0 to 100, no differences were found in the two groups' overall self-ratings: 50 ± 30 in the HTx group and 49 ± 27 in the LV AD group. The heart transplant patients, however, gave themselves higher ratings than the LVAD patients in the SF-36 subanalyses concerning "physical functioning" (p<0.04), "vitality" (p<0.03), and "mental health" (p<0.01).

**Perspectives**

In view of the demographic trend toward an aging population, waiting lists for heart transplantation can be expected to grow longer. It would be desirable for this development to be met by a correspondingly greater willingness on the part of the public to donate organs.

The technology of permanent mechanical circulatory support has now developed onward into the third generation of assist devices (centrifugal pumps) (Figure 6). These new LVADs are smaller and more efficient than those previously in use: they weigh only 140 g and can completely assume the tasks of the left ventricle of the heart with an energy consumption of less than 5 W. Systems are also now available for partial circulatory support with flow rates from 1.5 to 2 liters/minute. These systems are attractive because they can be implanted in relatively non-invasive fashion and because they consume very little energy.

The quality of the external components, such as batteries and cable connections, could still use marked improvement. We cannot yet expect completely implantable LVADs (25) to become available any time soon, in view of the complexity and lack of durability of these devices. Rather, the next avenue of investigation at present is the transcutaneous generation of current by induction, which will permit the elimination of the cable that now connects the external and internal components of the device. This should improve the patients' quality of life and reduce the incidence of life-threatening complications.
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