Prediction of Cardiac Stability After Weaning From Left Ventricular Assist Devices in Patients With Idiopathic Dilated Cardiomyopathy

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Background—During ventricular assist device (VAD) unloading, cardiac recovery is possible even in patients with chronic heart failure (HF). We sought parameters predictive of cardiac stability after VAD removal.

Methods and Results—Among 81 patients weaned since March 1995, a homogenous group of 35 with idiopathic dilated cardiomyopathy weaned from left VADs was selected. We evaluated echo data obtained before left VAD implantation and during “off-pump” trials before explantation, histological changes, and serum anti-β1-adrenoceptor-autoantibody disappearance during unloading, duration of unloading, and HF duration. Postweaning 10-year survival with native hearts reached 70.7±9.2%. During the first 5 years, HF recurred in 13 patients (37.1%). Only 6 (17.1%) died after HF recurrence or noncardiac complications related to left VAD explantation. Comparison of patients with and without long-term cardiac stability showed that stable patients were younger, HF history and recovery time during unloading shorter, and preweaning left ventricular assessment revealed higher left ventricular ejection fraction, lower short/long axis ratios, and higher end diastolic relative wall thicknesses. For left ventricular ejection fraction ≥45% at end diastolic diameter of ≤55 mm, predictive value for ≥5-year cardiac stability was 87.5%. Left ventricular ejection fraction time course during the first 6 postweaning months appeared predictive for long-term stability. HF history >5 years and preweaning instability of cardiac improvement appeared predictive for HF recurrence.

Conclusions—In idiopathic dilated cardiomyopathy, left VAD removal can be successful for >12 years even with incomplete cardiac recovery. Pre-explantation left ventricular ejection fraction, left ventricular end diastolic diameter and relative wall thicknesses, stability of unloading-induced cardiac recovery, duration of left VAD support, and HF duration before left VAD insertion allow identification of patients able to remain stable for >5 years. Time course of left ventricular ejection fraction during the first 6 postweaning months allows prognostic assessment. 

Key Words: cardiomyopathy • echocardiography • heart failure • outcome • ventricular assist device

With progressive lengthening of waiting times on transplantation lists, the use of ventricular assist devices (VADs) as a bridge to transplantation has become a standard therapy in end-stage heart failure (HF).1 The detection of myocardial recovery during unloading, which in some patients allowed successful VAD explantation, opened up new perspectives for the use of VADs as potential bridges to recovery.1–10

Although myocardial recovery at cellular and molecular level has often been shown during VAD support, cardiac improvement detectable by echocardiography is less frequent and the probability of recovery to levels that allow patients to be weaned from VADs is relatively low.1,11 Recovery appears to be related to the etiology of myocardial damage and history lengths of HF.1,12 Cardiac recovery allowing weaning from VADs was more often detected after acute myocarditis and postcardiotomy HF, but it has been shown that recovery with long-term cardiac stability is also possible in idiopathic dilated cardiomyopathy (IDCM).3,4,7,8,12–14 However, greatly differing recovery rates after VAD implantation have been reported, especially for IDCM.12,15–17 These differences may arise from different medical treatments during mechanical unloading and differences in weaning criteria, but also from differences in patient selection for VAD implantation and differences in the mechanical systems used for ventricular support. Nevertheless, if cardiac recovery is detected, it is essential to have reliable tools for prediction of cardiac stability in the case of VAD explantation.

Worldwide, only few patients with chronic myocarditis or IDCM have been weaned from VADs.1,4,12,14–17 Of these, the
majority were weaned during the past 5 years. The fact that weaning is feasible only in patients with relevant cardiac recovery limits the value of clinical studies on myocardial recovery during ventricular unloading. Therefore, additional data from weaned patients, especially from those with cardiac stability for >5 years after VAD explantation, are necessary to improve future weaning decisions. Previous evaluation of data collected from our patients with IDC showed that certain “off-pump” echocardiographic data are useful to detect left ventricular (LV) recovery and predict cardiac stability for at least 3 years.12 Meanwhile, a larger number of our patients have reached at least 5 years of postweaning cardiac stability and it has become feasible to investigate whether long-term cardiac stability beyond 5 years can also be predicted before LV assist device (LVAD) explantation. Therefore, the present study aimed to identify weaning criteria that can predict long-term cardiac stability after LVAD removal to improve future weaning decisions and the further postweaning management of these patients.

Methods

Patients and Ventricular Assist Devices

Between March 1995 and September 2007, 81 patients who received emergency VAD implantation because of terminal life-threatening HF unresponsive to medical treatment showed cardiac improvement after ventricular unloading, which allowed the removal of their VADs. Of the explanted VADs, 66 (81.5%) were LVADs, 12 (14.8%) were biventricular devices and 3 (3.7%) right ventricular assist devices. All patients consented to device implantation as a bridge to transplantation.

Because of great differences in the etiology of myocardial diseases, the kind of mechanical support, and patient age, to obtain reliable data, we focused our study on patients weaned from LVADs, and among these, we restricted the evaluation to those older than 14 years of age with IDC as the underlying cause for mechanical circulatory support. These criteria were fulfilled by 35 of the 37 patients with IDC in whom coronary disease was excluded by angiography, myocardial tissue specimens obtained before LVAD implantation showed no histological signs of acute myocarditis, and virological examinations did not reveal virus infections that could have caused myocardial damage. Two patients with IDC were excluded from evaluation because the devices they had were biventricular devices. Before LVAD insertion, all 35 evaluated patients had irreversible life-threatening end-stage HF and required continuous positive inotropic support.

During LV unloading, patients were treated with β-blockers, angiotensin-converting enzyme inhibitors, aldosterone antagonists, diuretics, and digitalis. Medication doses were individually adapted to reduce heart rate toward 55 to 60 beats/min and blood pressure to the lowest optimally tolerated value as well as to maintain optimal renal function. This treatment was continued after LVAD explantation. Of the 35 patients, 27 (77.1%) had Novacor LVADs, 3 (8.6%) TCI-LVADs, and 5 (14.3%) Berlin Heart LVADs (4 of them Incor axial flow pumps). Thus, 88.6% of the evaluated patients had pulsatile pumps.

LVAD implantation and explantation procedures have been previously described.8,12 During explantation, we aimed to maintain the recovered heart in a state as unmoistened as possible. Thus, the intrathoracic part of both cannulas was left in place after closing by ligation or blocking with a preformed plug. After operation, we also tended to avoid inotropic therapy and minimized volume loading. No special strategies other than those usually necessary for prevention of postoperative infections were applied unless patients already showed signs of infection before LVAD explantation or local infection became evident during surgery for LVAD removal. In these cases, anti-infection treatments were guided by the results of antibiograms and other microbiological tests.

Assessment of Cardiac Recovery for Weaning Decision

After LVAD implantation, before patients were discharged home, the effect of unloading on LV morphology and function was monitored weekly by echocardiography to select patients in whom cardiac recovery might allow LVAD removal. Thereafter, the frequency of follow-up examinations varied between 1 and 3 weeks. Table 1 shows the main echocardiographic parameters used for the assessment of cardiac recovery.

Since 1999, in addition to conventional echocardiography, pulsed wave tissue Doppler measurements of systolic wall motion peak velocities at the basal posterior wall were used for the evaluation of LV recovery. Methodological details of systolic wall motion peak velocity measurements were described previously.12,18

Off-pump trials evaluating the heart without LVAD support were started when the LV end diastolic diameter reduction reached 60 mm. In patients with pulsatile pumps, these trials consisted of pump frequency reduction to the lowest followed by intermittent pump stops lasting up to 10 minutes. Before, heparin was given to prevent thrombus formation inside the pump. Additionally, during the off-pump periods, the device was allowed to pump once a minute. In patients with axial flow pumps, in which stopping or low rotor speed leads to retrograde flow into the LV, which can be misleading for evaluation of cardiac function, we reduced the rotor speed to values that result in a zero net flow in one cardiac cycle. In patients with cardiac recovery, such trials were conducted weekly until the final decision for LVAD explantation was made.

<table>
<thead>
<tr>
<th>Table 1. Assessment of Cardiac Recovery by Echocardiography</th>
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<tr>
<td><strong>Parameters Obtained During Off-Pump Trials and Parameter-Derived Measurements</strong></td>
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<tr>
<td><strong>Echocardiographic Method</strong></td>
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<td>2-dimensional echocardiography</td>
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<td><strong>Trials and Parameter-Derived Measurements</strong></td>
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During recovery, as previously described, the working mode of the pumps was also changed to exert moderate load on the LV myocardium.\textsuperscript{7,8} To avoid excessive stimulation of the myocardium during recovery, in 34 of the 35 patients, stress echocardiography was not used during the off-pump trials. The decision for weaning was made electively in 30 patients. In another 5 patients, LVAD removal was performed by pump-related complications (thromboembolism, pump pocket infection, and/or intractable pain) when recovery was less than complete but seemingly sufficient for safe LVAD explantation.

LVAD removal was performed if, during repeated off-pump trials performed over several days, the maximum LV internal diastolic (end diastolic) diameter (LVIDd) was 55 mm and the minimum left ventricular ejection fraction (LVEF) 45\%, whereas the right ventricular diameters and function remained stable. In patients without restrictive transmural flow patterns, normal stroke volume and no relevant LV geometry alteration (relative wall thickness [RWT] >0.30 and sphericity index <0.8) during final off-pump trials, less recovery in LV size and/or LVEF was also accepted as being sufficient for safe LVAD explantation if right heart catheterization with off-pump hemodynamic measurements revealed no relevant pulmonary arterial and/or central venous pressure increase beyond the normal ranges. Thus, in 8 of the 30 electively weaned patients, LVAD removal was performed although off-pump LVIDd was 56 to 60 mm and/or LVEF 30\% to 44\%. All weaned patients with IDCM had sinus rhythm before LVAD explantation.

To monitor myocyte recovery during LV unloading, we also looked for anti-\(\beta_1\)-adrenocceptor autoantibodies (A-\(\beta_1\)-AABs) before LVAD implantation and thereafter weekly during the entire period of LVAD support. The underlying principle of the bioassay for A-\(\beta_1\)-AAB measurement was described previously.\textsuperscript{7,19} However, due to the lack of data on impact of A-\(\beta_1\)-AAB disappearance on cardiac recovery during mechanical unloading, weaning decisions were made independently of A-\(\beta_1\)-AAB measurements results. Weaning decisions were also independent of histological data because after LVAD implantation, no routine myocardial biopsies for monitoring histological changes during mechanical unloading were performed.

**Follow-Up Examinations After Left Ventricular Assist Device Explantation**

Echocardiography remained the major tool for monitoring cardiac function after LVAD removal. During the first postweaning week, echocardiographic follow-up was performed daily and thereafter each second day. During rehabilitation, follow-up controls were performed weekly. In outpatients, the frequency of scheduled follow-up visits varied in accordance with the postweaning time between monthly (during the first postweaning year) and every 6 months (after 3 years).

Exercise tolerance was evaluated by a maximum (symptom-limited) incremental treadmill exercise test according to Naughton’s protocol. However, this examination was not performed before 2 to 3 months postoperatively. During the last 5 years, at each follow-up examination, NT-proBNP plasma levels were also measured.

**Predictability of Cardiac Stability Without Left Ventricular Assist Device Support**

With regard to potential prediction of weaning success, we evaluated echocardiographic data obtained during “off-pump” trials before LVAD explantation, histological changes, serum A-\(\beta_1\)-AAB disappearance during unloading, duration of mechanical support, and duration of HF before LVAD implantation (Table 2).

**Statistics**

Statistical analysis was performed using SPSS 12.0 for Windows (SPSS Inc, Chicago, Ill). Quantitative data, representing patient characteristics before LVAD implantation and at the time of LVAD removal, were expressed as means and SEM, because the distribution of data was not skewed. However, because we dealt with small data sets (small number of subjects) with nonnormally distributed data, differences between patients with lasting recovery and those with recurrence of HF (independent groups) were analyzed using the nonparametric Mann-Whitney \(U\) test. LVEF and LV end diastolic diameter values measured at the time of LVAD explantation were compared with those measured at 1 month, 3 months, and 6 months after LVAD removal (paired groups) using the nonparametric Wilcoxon signed rank test. For all tests, differences between groups were considered significant for 2-sided \(P<0.05\). Sensitivity, specificity, and predictive values were calculated for selected echocardiographic parameters and time parameters related to HF history and cardiac recovery during LVAD support according to prespecified cut points and were expressed as percentages. Receiver-operating characteristic curves were used to evaluate the discriminatory value of different parameters to test their prognostic accuracy in prediction of HF recurrence after weaning. Kaplan-Meier curves were applied for survival analysis and for freedom from transplantation after LVAD explantation. The probability of survival and the probability of freedom from transplantation at a given point of time as derived from the Kaplan-Meier estimation were expressed in percent±SE.

All authors have read and agree to the manuscript as written. The authors had full access to and take full responsibility for the integrity of the data.

**Results**

LVAD explantation was performed in 35 (18.6\%) of the 188 patients with IDCM older than 14 years of age who received an LVAD as a bridge to transplantation.

**Weaned Patient Characteristics Before Left Ventricular Assist Device Implantation**

At LVAD implantation, of the 35 evaluated patients (33 men, 2 women), 16 (45.7\%) were <40 years old, 11 (31.4\%) were 40 to 55 years old, and 8 (22.9\%) were between 56 and 65 years. Before LVAD implantation, all 35 weaned patients had severely dilated LV (end diastolic diameters between 64 mm and 93 mm) and extremely low LVEF (between 10\% and
None had undergone previous resynchronization therapy. The mean duration of HF before LVAD insertion (calculated from onset of HF symptoms) was 4.0±0.6 years. Weaned patient characteristics before LVAD implantation are shown in Table 3. There were no differences in pre-LVAD implantation LVIDd and LVEF between the 35 weaned patients and the other patients with IDCM who could not be weaned from their LVADs because of lack of cardiac recovery during mechanical unloading.

For the assessment of long-term (>5 years) postweaning cardiac stability, only 27 of the 35 weaned patients with IDCM could be considered because 3 patients with stable cardiac function after LVAD removal had not reached the fifth postweaning year at the time of evaluation and another 5 patients without HF recurrence were lost to follow-up after they died during the first 5 postweaning years due to noncardiac causes.

Before LVAD implantation, between the 15 patients with and the 12 without long-term (>5 years) postweaning freedom from HF recurrence, there were no significant differences in LVEF or LVIDd (Table 3). There were, however, significant differences (P<0.05) between patients with and without recurrence of HF during the first 5 years after LVAD removal with regard to their age and history of HF before LVAD implantation (Table 3). Thus, patients with long-term postweaning cardiac stability were younger and had a shorter history of HF before LVAD implantation.

Of 35 weaned patients, 34 (97.1%) tested positive for A-β1-AAbs before LVAD insertion. During LV unloading, the A-β1-AAbs tended to disappear and before LVAD explantation, only one patient tested positive for A-β1-AAbs. Comparing the pre-LVAD implantation A-β1-AAbs serum levels between patients with and without HF recurrence during the first 5 years after LVAD removal, no differences were found (Table 3).

### Duration of Left Ventricular Assist Device Support and Clinical Features Before Left Ventricular Assist Device Explantation

For the 35 weaned patients, the duration of LVAD support necessary for cardiac improvement allowing LVAD explantation was 4.3±0.7 months. Table 4, which includes the main data obtained from the 27 patients evaluated for long-term (>5 years) postweaning cardiac stability, shows that in

### Table 3. Patient Characteristics at Time of LVAD Implantation and Comparison of Patients With HF Recurrence During the First 5 Years After LVAD Removal With Those Who Exhibited Long-Lasting Cardiac Recovery

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Values* in All IDCM Patients Weaned From LVADs (n=35)</th>
<th>Values* in Patients Evaluated for Long-Lasting Recovery (n=27†)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>40.8±2.3</td>
<td>47.2±2.8</td>
<td>0.02</td>
</tr>
<tr>
<td>History of heart failure, years</td>
<td>4.0±0.6</td>
<td>6.1±1.3</td>
<td>0.01</td>
</tr>
<tr>
<td>LVIDd, mm</td>
<td>74.0±1.2</td>
<td>76.0±2.0</td>
<td>0.15</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>15.0±0.5</td>
<td>15.6±0.9</td>
<td>0.75</td>
</tr>
<tr>
<td>Serum A-β1-AAbs, LU</td>
<td>5.2±0.4</td>
<td>5.1±0.6</td>
<td>0.98</td>
</tr>
</tbody>
</table>

*Values are means±SEM.
†Patients with stable cardiac function lost to follow-up during the first 5 postweaning years and those who were weaned <5 years before this evaluation were not included.

### Table 4. Patient Characteristics at Time of LVAD Explantation and Comparison of Patients With IDCM With HF Recurrence During the First 5 Years After Weaning With Those Who Exhibited Long-Lasting Cardiac Recovery

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Values* for All IDCM Patients Weaned From LVADs (n=35)</th>
<th>Values* for Patients Evaluated for Long-Lasting Recovery (n=27†)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of LVAD support, months</td>
<td>4.3±0.7</td>
<td>6.9±1.7</td>
<td>0.02</td>
</tr>
<tr>
<td>LVIDd, mm</td>
<td>51.7±1.1</td>
<td>56.7±1.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVIDd change, % of best value</td>
<td>9.8±1.9</td>
<td>19.9±4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RWT</td>
<td>0.40±0.01</td>
<td>0.33±0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RWT change during off-pump trials, %</td>
<td>-9.4±1.2</td>
<td>-16.6±2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>47.0±1.0</td>
<td>42.6±1.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVEF change, % of best value</td>
<td>-7.7±1.4</td>
<td>-4.2±1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV sphericity index, short/long axis ratio</td>
<td>0.66±0.02</td>
<td>0.72±0.02</td>
<td>0.04</td>
</tr>
<tr>
<td>Time to disappearance of serum A-β1-AAbs, months</td>
<td>2.5±0.02</td>
<td>2.6±0.5</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*Values are means±SEM.
†Only 27 of the 35 weaned patients with IDCM because patients with stable cardiac function lost to follow-up during the first 5 postweaning years and those who were weaned <5 years before this evaluation were not included.
patients with HF recurrence during the first 5 postweaning years, the duration of LVAD support necessary for recovery was significantly longer (P=0.02) than in patients with postweaning cardiac stability for >5 years. The LVEF and LVIDd values measured in the 35 weaned patients during final off-pump trials before LVAD removal ranged from 35% to 60% and from 40 to 62 mm, respectively. As shown in Table 4, in patients with postweaning cardiac stability for >5 years, before LVAD removal, the LVEF was higher and the LVIDd smaller than in the patients with HF recurrence during the first 5 postweaning years (P<0.01).

There were no differences in Doppler parameters or Doppler-derived indices of diastolic function measured at final off-pump trials in patients with and without HF recurrence after weaning.

In 33 of 34 weaned patients who tested positive for A-β-AABs before LVAD implantation, the autoantibodies disappeared after 3 to 31 weeks of LV unloading. Between patients with and without HF recurrence during the first 5 postweaning years, there were no differences for the disappearance time of A-β-AABs during LVAD support (Table 4).

Comparative histomorphometry showed a 32.5±28.7% reduction of the relative content of fibrosis during unloading. Reduction of fibrosis was shown in 82% and regression of myocardial hypertrophy in 91% of the weaned patients in whom comparative histological evaluations were possible.

**Patient Outcome After Left Ventricular Assist Device Explantation**

Without inclusion of the posttransplant survival for those who underwent heart transplantation after HF recurrence, the postweaning 5-year and 10-year survival with native hearts was 76.2±8.1% and 70.7±9.2%, respectively (Figure 1A). To date, 11 patients with IDCM with postweaning times >6 years still have their native hearts without the necessity of heart transplantation. Of these, 3 patients have reached postweaning survival times of >12 years. The overall 5-year and 10-year survival after LVAD removal including posttransplant survival for patients with HF recurrence were 79.1±7.1% and 75.3±7.7%, respectively (Figure 1B). Detailed description of patients’ outcome after LVAD explantation is shown in Figure 2. Among the 35 weaned patients, there were no differences in survival between the 16 patients with and the 19 patients without recurrence of HF after LVAD explantation.

Of the 19 patients with postweaning cardiac stability, 5 died during the first 5 years after LVAD explantation due to extracardiac complications. Of these 5 patients, 3 died during the first 6 postweaning months (one early after LVAD explantation due to septic shock because of infection at the LVAD conduits already detected before weaning, the other 2 patients later, between the fourth and fifth postweaning months, due to acute pulmonary emboli and pulmonary bleeding, respectively). The other 2 patients’ deaths despite stable heart function occurred beyond the second postweaning year. Thus, one patient died 2.5 years after weaning due to infection at the residual apical inflow conduit and the other 3.5 years after LVAD explantation due to sequelae of cerebral bleeding that had occurred before LVAD removal.

Of the 16 patients with HF recurrence, 12 were transplanted, one is on the heart transplant waiting list (after second LVAD implantation), and 3 patients died before LVAD reimplantation or heart transplantation was possible. One of the 3 deaths due to recurrence of HF occurred on the third postweaning day in a patient in whom neither a second VAD implantation nor heart transplant was indicated because of severe cerebral lesions and pump pocket infection, which were already present before LVAD removal. The other 2 patients who died due to HF recurrence had more than 2 and 5 years, respectively, of stable postweaning cardiac function before the onset of relatively rapid worsening of cardiac function.

Of the 16 patients with HF recurrence, 15 were listed for heart transplantation. Of these 15 patients, 2 (13.3%) died before donor hearts became available. The decision for listing (or relisting) was taken if LVEF dropped to <30% and exercise tolerance became irreversibly worse (New York Heart Association ≥III) despite maximum intensification of HF therapy. If intravenous inotropic support became necessary or the worsening of heart function progressed very rapidly, urgency or high-urgency listing was requested. A second LVAD implantation necessary for bridging to heart transplant was well tolerated by the 3 patients who underwent this procedure.

**Cardiac Function After Left Ventricular Assist Device Removal**

HF recurrence occurred in 16 (45.7%) of the 35 weaned patients (Figure 2). At the end of the fifth postweaning year, we found a probability of 61.3±9.0% for freedom from HF recurrence (Figure 1C). Of all 16 HF recurrences, 9 (56.3%) occurred during the first year after LVAD removal and the other 7 (43.7%) later, beyond the second postweaning year. All patients with HF recurrence during the first postweaning year were weaned during the initial phase of our weaning program, before September 2000. In patients who survived the first postweaning year without HF recurrence, the probability for freedom from HF recurrence at the end of the fifth and tenth years after LVAD explantation was as high as 84.2±8.4% and 61.8±11.4%, respectively. Among the 15 patients without cardiac alterations during the first 5 years after LVAD removal, 13 (86.7%) were in functional New York Heart Association Class ≤II with only slightly elevated NT-proBNP levels (152.8±90.3 pg/mL) and only 2 (13.3%) in New York Heart Association Class II/III at the end of the fifth postweaning year.

Since 1999, when tissue Doppler imaging was introduced in our weaning protocol, all patients with postweaning cardiac stability showed systolic radial and longitudinal wall motion peak velocities (measured at the basal posterior wall) of >8 cm/s.

**Risk Factors for Heart Failure Recurrence After Left Ventricular Assist Device Removal**

In addition to the already mentioned patient age and HF duration before LVAD implantation, at the time of LVAD removal, patients with cardiac stability during the first 5
Figure 1. Outcome of patients with IDCM after LVAD removal. A, Survival with the native heart. B, Overall survival with inclusion of post-heart-transplant survival in patients with HF recurrence. C, Freedom from HF recurrence.
postweaning years also showed differences in LV size, geometry, and systolic function in comparison to patients with postweaning HF recurrence (Table 4). Thus, in patients with postweaning cardiac stability, the LVs had smaller end diastolic diameters, were less spherical, and showed higher RWT and ejection fractions. There were also significant differences between patients with long-term postweaning cardiac stability and those with HF recurrence in the time course of LV end diastolic diameter and LVEF during mechanical unloading. Thus, patients with postweaning HF recurrence required longer mechanical support for recovery and already showed partial reversibility of cardiac improvement (worsening of LVEF and LVIDd increase) before LVAD removal. Patients with postweaning HF recurrence also had larger RWT alterations (LVIDd increase and end diastolic wall thinning) during final off-pump trials (Table 4).

After LVAD removal, the time course of LVEF and LVIDd was different between patients with and without cardiac stability during the first 3 postweaning years. Thus, those without HF recurrence showed no LVEF changes during the first 6 postweaning months and their LVIDd remained relatively stable between the first and sixth postweaning months (Figure 3). LVEF reduction during the first 6 months of >10% of preweaning values showed a predictive value of 75.0% for HF recurrence during the first 5 years.

Our data revealed several risk factors for HF recurrence (Table 5; Figure 4). At certain cutoff values that also provide good balanced sensitivity and specificity, the presence of these risk factors appeared associated with high probabilities for HF recurrence after LVAD removal. Thus, pre-explantation off-pump LVEF <45%, LVIDd >55 mm, and LV end diastolic RWT <0.38 as well as end diastolic RWT increase of >10% during the final off-pump trial revealed predictive values between 81.8% and 88.9% for HF recurrence during the first 3 and between 87.5% and 90.0% for HF recurrence during the first 5 postweaning years. Also preweaning LVEF and/or LVIDd alterations of >10% of the best off-pump value as well as history of HF >5 years and mechanical support of >6 months appeared to be relevant risk factors for weaning. LVEF of <40% showed a 100% predictive value for HF recurrence already during the first 3 postweaning years. Although patients with HF recurrence had higher sphericity indexes (Table 4), higher values of this index appeared less predictive for HF recurrence.

Figure 2. Outcome of the patients with IDCM after LVAD removal. *One patient with a second LVAD as bridge to transplant; †one patient died of causes unrelated to LVAD removal; ‡unrelated to LVAD removal.

Prediction of Long-Term Postweaning Cardiac Stability
Pre-explantation off-pump LVEF of ≥45% in relation to LV size and RWT showed positive predictive values for cardiac stability during the first 3 and 5 postweaning years of between 85.7% and 94.7% and between 73.7% and 87.5%, respectively (Table 6). The highest predictive values were obtained for LVEF ≥45% at LVIDd ≤55 mm and for LVEF ≥45% at LV end diastolic RWT ≥0.38.

Also, the history of HF appeared relevant for cardiac stability after LVAD removal. In patients with history of HF <5 years, pre-explantation off-pump LVEF of ≥45% showed high predictive values for cardiac stability during the first 3 and 5 postweaning years (94.4% and 81.25%, respectively). There was no recurrence of HF during the first 4 years after LVAD removal in patients with LVEF ≥45% at LVIDd ≤55% and history of HF <5 years.
In patients with off-pump LVEF of ≥45%, also, the stability of LVEF after maximum improvement during unloading both before LVAD explantation and during the first 6 months after weaning appeared predictive for cardiac stability during the first 3 and 5 postweaning years (Table 6). Pre-explantation off-pump LVEF of ≥40% alone showed low predictability for cardiac stability after LVAD removal. However, in relation to LV size and RWT, also, LVEF ≥40%
appeared predictable for cardiac stability, especially during the first 3 postweaning years.

Discussion

Although relevant improvements in anatomic, hemodynamic, and electrophysiological properties are known to occur during mechanical unloading, the number of patients with chronic HF who underwent VAD removal for cardiac recovery/improvement in published studies is low (worldwide <65 patients).\textsuperscript{1,11,12,16} Besides the low rate of cardiac recovery, which might in principle allow patients’ weaning from VADs, the limited long-term outcome data after weaning and the lack of data on predictability of weaning results are major contributors to the low number of VAD explanations performed in patients with chronic HF.

In our patients, the postweaning 5-year and 10-year survival rates with native hearts were higher than 70%, although only 3 (8.6%) of the 35 weaned patients had pre-explantation off-pump LVEF of >50%. Even the 3 patients with post-weaning cardiac stability of >12 years had pre-explantation LVEF of only 45%, 46%, and 55%, respectively. With the option of heart transplantation, 71% of our weaned patients were alive at the end of the fifth postweaning year (73% of them with their native hearts). This survival rate is better than that expected after heart transplantation.\textsuperscript{20} Our data support the supposition that complete cardiac recovery is not indispensable for LVAD explanation and that weaning is feasible also without normalization of cardiac function.\textsuperscript{1,7,10,12} In our cohort of 35 weaned patients with IDCM, the high proportion of those with incomplete recovery might be a reason for the relatively high recovery rates reported by us in comparison to others.\textsuperscript{1,10,12} As already postulated, partial recovery by LVADs may indeed provide the necessary conditions for device explanation in a larger group of patients if living with a lower degree of HF but with adequate functional class is accepted.\textsuperscript{1}

The present study focused mainly on the potential prediction of postweaning outcome. Our data allowed the identification of several risk factors for HF recurrence in patients with IDCM after LVAD removal. In addition to previously detected risk factors for early postweaning cardiac worsening (pre-explantation LVEF <45% and LVIDd >55 mm plus HF duration of >5 years before LVAD implantation), the present study revealed also pre-explantation LV end-diastolic RWT of <0.38 as another relevant risk factor. Altered LV geometry appeared to be a potential risk factor for HF recurrence even in patients with preweaning LVEF ≥45%. Also, LV end-diastronic RWT decrease of >10% during pre-explantation off-pump trials appeared to be a risk factor for HF recurrence. This is not surprising because RWT reduction is associated with wall stress increase.\textsuperscript{21} In addition to the duration of mechanical support of >6 months, our data also revealed preweaning instability of unloading-induced cardiac recovery as a risk factor for postweaning HF recurrence. Thus, if after maximum improvement, further unloading is followed by LVEF alteration and/or LVIDd increase of >10% of best value, the risk of HF recurrence is high.

Prediction of postweaning long-term cardiac stability also became possible. The highest predictive values for >5-year cardiac stability were found in patients with pre-explantation LVEF ≥45% and either LVIDd ≤55 mm or RWT ≥0.38 (Table 6). Also, pre-explantation LVIDd stability after maximum improvement in patients with pre-explantation LVEF ≥45% appeared predictive for long-term (<5 years) cardiac stability after LVAD removal.
Although all patients without HF recurrence after weaning showed systolic wall motion peak velocities of >8 cm/s at the basal posterior wall, the data available at present are insufficient for reliable conclusions. The predictive value of tissue Doppler parameters remains to be established by future studies.

The time course of LVIDd and LVEF early after weaning showed important prognostic value. Patients without HF recurrence showed no relevant LVEF changes during the first 6 postweaning months, whereas those with HF recurrence within the first 3 years showed continuous LVEF and LV end diastolic diameter alterations throughout this period. Therefore, more frequent follow-up examinations during the first 6 months after weaning make sense.

Other important aspects besides HF recurrence are potential complications related to the LVAD explantation itself. The residual apical inflow conduit left in place after LVAD removal produced complications (local infection) in 3 (8.6%) of the 35 weaned patients with IDCM (in one patient early after LVAD removal; in the other 2 unexpectedly late, after 2.5 and 4 years, respectively). One of these 3 patients recovered completely after removal of the residual apical cannula and is now, after >12 years since LVAD removal, still asymptomatic. Infection was a major postweaning problem in 2 patients, but in both, it was already present before LVAD removal. Bleeding complications occurred in only one patient (lethal pulmonary bleeding 4 months after LVAD removal). None of the 35 patients with the residual apical conduit left in place after LVAD removal had stroke or extracerebral embolic complications arising from the LV. Thus, HF recurrence was the most frequent complication after LVAD removal in our patients and therefore, further improvement of patients’ outcome after LVAD explantation will depend mainly on better prediction of postweaning cardiac stability.

Limitations
Data were obtained from a single-center retrospective study of prospectively gathered information. The relatively small cohort and the lack of randomization also limited our study.
Weaning from LVADs is a clinical option with potentially successful results for \( >12 \) years even in patients with IDCM without relevant myocardial improvement.

A potential limitation is also the fact that the majority of evaluated patients had pulsatile pumps, which are not used in large numbers today because the trend is toward rotary pumps that most likely operate differently with respect to unloading conditions. However, echocardiographic measurements for evaluation of myocardial recovery were performed during “off-pump” conditions on ventricles working for a limited time without mechanical support, which allowed morphological and functional evaluation of the heart under the same circumstances that will exist after LVAD removal.

### Conclusions

Weaning from LVADs is a clinical option with potentially successful results for \( >12 \) years even in patients with IDCM with incomplete cardiac recovery during unloading. Echocardiographic data obtained during off-pump trials are reliable for the detection of cardiac improvement. Pre-explantation LVEF, end diastolic LV diameter and RWT, stability of unloading-induced cardiac improvement, duration of mechanical support, and duration of HF before LVAD implantation allow the distinction between patients with and without the potential to maintain cardiac stability for \( >5 \) years after weaning. The time course of LVEF during the first 6 postweaning months is helpful in prognostic assessment.

### Acknowledgments

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### Disclosures

None.

### References


### Table 6. Echocardiographic Prediction of Long-Term Cardiac Stability After LVAD Removal in Patients With IDCM

<table>
<thead>
<tr>
<th>Selected Parameters and Cutoff Values</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final* off-pump LVEF ( \geq 45% )</td>
<td>94.74</td>
<td>70.00</td>
<td>85.71</td>
</tr>
<tr>
<td>At LVIDd ( &gt;55 ) mm</td>
<td>94.74</td>
<td>90.00</td>
<td>94.74</td>
</tr>
<tr>
<td>At RWT ( \geq 0.38 )</td>
<td>98.47</td>
<td>90.00</td>
<td>94.44</td>
</tr>
<tr>
<td>Without preweaning LVIDd increase ( 10% ) of best value†</td>
<td>68.42</td>
<td>80.00</td>
<td>86.67</td>
</tr>
<tr>
<td>Not ( &gt;10% ) below best LVEF value†</td>
<td>84.21</td>
<td>72.73</td>
<td>88.89</td>
</tr>
<tr>
<td>With history of HF ( &lt;5 ) years</td>
<td>89.47</td>
<td>90.00</td>
<td>94.44</td>
</tr>
<tr>
<td>At LVIDd ( \geq 60 ) mm</td>
<td>94.74</td>
<td>70.00</td>
<td>85.71</td>
</tr>
<tr>
<td>Final* off-pump LVEF ( \geq 40% )</td>
<td>100</td>
<td>30.00</td>
<td>73.08</td>
</tr>
<tr>
<td>With history of HF ( &lt;5 ) years</td>
<td>94.74</td>
<td>90.00</td>
<td>94.74</td>
</tr>
<tr>
<td>At LVIDd ( &gt;55 ) mm</td>
<td>94.74</td>
<td>80.00</td>
<td>90.00</td>
</tr>
<tr>
<td>Not ( &gt;10% ) LVEF reduction during the first 6 postweaning months</td>
<td>84.21</td>
<td>71.43</td>
<td>88.89</td>
</tr>
</tbody>
</table>

*Last pump stop before LVAD explantation.
†Best of all off-pump values before weaning.


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