Myocardial recovery during mechanical circulatory support: weaning and explantation criteria

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ABSTRACT

For selected patients ventricular assist device explantation is feasible. Freedom from heart transplantation and VAD support for > 15 years following VAD removal is possible even if recovery is incomplete and the underlying cause for ventricular assist device implantation was a chronic form of cardiomyopathy. Echocardiography and rightheart catheterization are necessary to assess cardiac recovery. However, to date there is no gold standard for recovery assessment. Certain echocardiography parameters appeared highly predictive for long-term (≥5 years) post-weaning cardiac function and reliable for weaning decisions.

Keywords: heart failure, ventricular assist devices, ventricular function, myocardial recovery, survival, risk factors.

WEANING FROM MECHANICAL CIRCULATORY SUPPORT

After long controversy about the clinical relevance of unloading-promoted recovery from chronic heart failure (HF) and about the feasibility of elective weaning of patients from their ventricular assist device (VAD), taking into account the risk of early post-weaning HF recurrence, this topic has gained increasing interest over the past 10 years, especially after the publication of the first long-term weaning results in patients with chronic HF reversal after LVAD implantation (1-3).

Assessment of cardiac recovery

Temporary interruptions of mechanical unloading (‘‘off-pump trials’’) are mandatory for assessment of recovery, regardless of whether the assessment is performed at rest or during exercise. Short off-pump trials allow evaluation of the heart without mechanical support under the same circumstances that will exist after VAD removal. However, whereas pulsatile VADs allow optimal assessment of heart function during complete pump stops, complete stops of axial-flow pumps lead to retrograde flow into the LV followed by reduction of the diastolic arterial pressure that, by reducing...
the left ventricular (LV) afterload, can generate overestimations of LV systolic function. According to our observations, the misleading retrograde blood flow into the LV during off-pump trials is a major negative factor that can interfere with successful VAD explantation. Therefore, for such pumps, rotor-speed reduction to values resulting in close to zero flow in one cardiac cycle (3000–6000 rpm) is better than complete pump-stop (2–4). Before off-pump trials, heparin must be given (60–100 IU/kg according to the prothrombin time reported as INR) to prevent thrombus formation inside the pump (5, 6). Patients with heparin-induced thrombocytopenia should receive argatroban (synthetic thrombin inhibitor) infusions (2 μg/kg/min) which should be started 1 h before the off-pump trials (6).

Additionally, completely stopped pulsatile devices should be allowed to pump at least once a minute, or 3 bursts of pneumatic hand-pumping should be intercalated every 15 to 60 seconds to prevent blood stagnation (2, 4, 5, 7, 8). In patients with a biventricular assist device (BiVAD) it appeared appropriate to stop the right ventricular (RV) pump 30 seconds earlier than the LV pump; after both pumps are deactivated, evaluation of recovery can be performed (6). Duration of individual off-pump periods can vary between 3 and 15 minutes (4–6). In patients with insufficient recovery for possible VAD removal, as already shown during the first 3 minutes, there is no reason to further extend the off-pump trial (9).

With appropriate caution, the risk of interruption of unloading is low (4, 6, 9, 10). In weaning candidates it appears useful to conduct such trials weekly or every 2 weeks and to make the final decision for elective VAD explantation only after cardiac improvement has reached its maximum (no further improvement in at least 2 consecutive off-pump trials) (9). During recovery it appears useful to change the working mode of the pumps, in order to intensify the unloading if the ventricle size needs further reduction, or to exert moderate load on the ventricular myocardium after maximum improvement (1, 5, 7).

In addition to the retrograde blood flow into the LV during off-pump trials, which makes the evaluation of LV function very difficult, another factor that may impair successful VAD explantation in the subgroup of patients receiving continuous VAD is the usually great difficulty in maintaining the recovered heart in a state as unmolested as possible throughout explantation surgery. During VAD removal, which was performed on the beating heart in all our weaned patients, we aimed to leave the intrathoracic part of both cannulas in place after they were reliably occluded (6, 9). This was possible in 91% of patients with pulsatile pumps, but only in 57% of patients with continuous-flow pumps. Also, the heart-lung machine, which was used only in less than 10% of patients with pulsatile VADs, was required for all continuous-flow-pump explantations. Nevertheless, in our patients with non-ischemic chronic cardiomyopathy, there were no significant differences in the 3 year post-explant freedom from HF recurrence between patients weaned from pulsatile and those weaned from continuous flow pumps (9).

The main diagnostic methods used to assess cardiac recovery are echocardiography and heart catheterization. Cardiopulmonary exercise testing is also increasingly used by some centers (4, 8).

**Echocardiography**

Echocardiography is the cornerstone for assessment of cardiac recovery allowing both selection of potential weaning candidates and decision-making in favor of or against VAD removal. After VAD implantation,
repeated transthoracic echocardiography (TTE) screenings with normal VAD function are necessary for selection of potential weaning candidates, i.e. patients with signs of relevant reverse remodeling who also seem to have their contractile function improved to levels deserving further evaluation. Such potential weaning candidates are those with LV end-diastolic diameter (LVEDD) < 55 mm (or 55-60 mm at BSA ≥1.8 m²) and fractional shortening (FS) > 15 %, no or ≤ grade I mitral and/or aortic regurgitation, no RV dilation and tricuspid regurgitation ≤ grade II (6).

Before the first off-pump trial, it is useful to perform stepwise pump-rate reductions under TTE monitoring, to verify whether complete interruption of unloading is possible. Thus, if incomplete unloading interruption already provokes symptoms (dizziness, sweating, etc.), complete interruption of unloading is senseless and risky. If the patient remains asymptomatic but the LVEDD increases beyond 60 mm, a complete interruption is also senseless, because such a patient is not yet a weaning candidate.

Echocardiographic assessment of recovery in weaning candidates is usually based on the results of repeated off-pump trials at rest (2, 4, 7, 9).

After months of intensive VAD support, even short periods of physiological loading by interruption of unloading may represent a serious challenge for a possibly incompletely-recovered ventricle. It therefore appears reasonable to avoid (at least initially) any risk of myocardial exhaustion, which might interfere with possibly still ongoing recovery. For this reason, all 119 patients

**Table 1 - Transthoracic echocardiographic measurements for evaluation of cardiac recovery during off-pump trials.**

| Echocardiographic Methods | Measurements                                                                 |
|---------------------------|------------------------------------------------------------------------------|
| **2D Echocardiography**   | LV end-diastolic and end-systolic diameters (LVEDD and LVESD, respectively)  |
|                           | LV end-diastolic short/long axis ratio (S/L ED)                              |
|                           | LV end-diastolic relative wall thickness (RWT ED)*                           |
|                           | LV fractional shortening (FS)                                               |
|                           | LV ejection fraction (LVEF) measured by biplane Simpson’s method            |
|                           | RV fractional dimensions (on parasternal and apical views)                  |
|                           | RV fractional area change (FAC) and ejection fraction (RVEF)                |
| **PW & Color Doppler**    | Doppler indices of LV diastolic function (transmitral flow, isovolumetric relaxation time) |
|                           | LV stroke volume (SV)**                                                     |
|                           | Regurgitation on mitral, aortic, tricuspid and pulmonary valves             |
| **CW Doppler**            | Pulmonary arterial systolic pressure estimation in patients with tricuspid valve regurgitation |
| **Tissue Doppler Imaging**| LV systolic wall motion peak velocity (Sm) at the basal posterior wall measured with the pulsed-wave tissue Doppler (PW-TD) |
|                           | Tricuspid lateral annulus peak systolic wall motion velocity (TAPS’) measured on apical 4-chamber views with the PW-TD |
| **Speckle Tracking 2D-Strain Imaging** | LV radial, circumferential and longitudinal strain and strain rate |
|                            | LV synchrony and synergy of contraction                                      |

*RWT ED = [interventricular septum thickness + posterior wall thickness] / LVEDD; **Product of time velocity integral measured with pulsed-wave Doppler at the LV outflow tract (LVOT) and cross-sectional area of the LVOT; LV = left ventricular.
who were weaned since 1995 in our center from long-term VADs primarily designed as a bridge-to-HTx or as permanent therapy underwent assessment of heart function exclusively at rest (6, 9, 10). Although at rest the conclusive value of assessments is limited by the lack of information about inotropic reserves and cardiac adaptation to stress, our weaning results appeared not to be relevantly affected by that, insofar as the results reported by groups who also used stress echocardiography and/or exercise testing were not better (4, 9, 11).

However, stress echocardiography can provide valuable information on inotropic reserves and adaptation to stress, which might be useful for weaning decisions. According to certain authors, an absolute EF increase by 5% during dopamine infusion indicates preservation of contractile reserve (4).

A possible limitation of dobutamine stress echocardiography can be, at least theoretically, the risk of myocardial exhaustion with negative impact on an ongoing myocardial recovery process. Further studies are therefore necessary to establish the real value of dobutamine stress echocardiography for weaning decisions.

In principle, off-pump TTE should be as comprehensive as possible, including tissue Doppler and strain imaging. Table 1 shows the TTE parameters we routinely measure in our department. However, not all these parameters can be reliably measured in all patients because of poor image quality in some patients with VAD support. Image

Table 2 - Main Left Ventricular Assist Device (LVAD) Explantation Criteria*.

| Examination          | Parameters and Parameter-Derived Measurements During the Last Off-Pump Trial Before LVAD Explantation** |
|----------------------|----------------------------------------------------------------------------------------------------------|
| **Echocardiography** |                                                                                                           |
| LV end-diastolic diameter (LVEDD) ≤55 mm                                                                 |
| LV ejection fraction (LVEF) ≥45%                                                                          |
| Stable pre-explant LVEF after maximum improvement                                                          |
| Stable pre-explant LVEDD after maximum improvement and during the final off-pump trial                   |
| Stable stroke volume (SV) during the final off-pump trial                                                 |
| Systolic wall motion peak velocity (Sm) ≥8 cm/s, stable after maximum improvement and during the final off-pump trial |
| No or less than grade II regurgitation at mitral and/or aortic valve                                       |
| No RV dilation (RVOT diameter < 35 mm, end-diastolic short/long axis ratio < 0.6)                          |
| No or maximum grade II regurgitation at the tricuspid and/or pulmonary valve                             |
| **RH Catheterization**                                                                                  |
| Cardiac index (CI) > 2.6 L/min/m²                                                                         |
| Pulmonary capillary wedge pressure < 13 mmHg                                                              |
| Right atrial pressure (mean) < 10 mmHg                                                                    |
| **Electrocardiography**                                                                                  |
| Sinus rhythm                                                                                              |
| Heart rate (HR) < 90 min                                                                                  |
| No more than 25% HR increase during off-pump trials                                                       |
| **Atrial Pressure**                                                                                       |
| Mean pressure ≥65 mmHg                                                                                    |

*These criteria used at present at the Deutsches Herzzentrum Berlin have evolved from a weaning experience of 18 years after explantation of 100 long-term VADs, primarily designed as bridge-to-HTx or permanent therapy (6, 9); **Measurements at rest, without inotropic support; †Since 2005 also speckle-tracking derived 2D-strain imaging parameters (global longitudinal strain and strain rate, intra-ventricular synchrony and synergy, including pre-explant stability of all these parameters after maximum improvement and during the final off-pump trial) were taken into consideration for weaning decisions (6).
quality was a serious limitation, especially for off-pump Doppler measurements that had to be performed during rotor-speed reduction instead of complete pump stop.

Off-pump right heart catheterization

Off-pump right heart catheterization (RHC) is also a cornerstone for recovery assessment (4, 9) and is necessary for final decisions in favor of or against VAD explantation. A final off-pump trial of ≥15 minutes in the operation room, with repeated measurements of hemodynamic parameters under continuous echocardiographic monitoring, is indispensable before the start of explantation surgery (9). RHC appeared also necessary before any preliminary decision-making in potential weaning candidates with borderline TTE data and/or relevant cardiac improvement only after > 6 months of unloading and/or long history duration (> 3 years) of HF (9). In patients with axial-flow pumps, such preliminary RHC appears more reliable if off-pump measurements are preceded by occlusion of the outlet cannula with a balloon (9). Balloon occlusion allows com-

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**Figure 1** - Usefulness of left ventricular (LV) peak systolic wall motion velocity (Sm) measurements at the basal posterior wall by pulsed-wave tissue Doppler to assess the stability of LV contractile function during and between off-pump trials and for detection of further cardiac improvement after left ventricular ejection fraction (LVEF) has reached its peak value. At the time when LVEF reached its maximum value (55%), Sm was 9 cm/s during full left ventricular assist device (LVAD) support (A) and remained stable during the off-pump trial (B). Although the LVEF remained unchanged, the Sm values with (C) and without (D) LVAD support increased during the next 3 weeks of unloading up to 11 cm/s (+22%). Thereafter, there was no further Sm improvement and the LVAD was successfully explanted.
VAD Explantation criteria

Complete pump stops without any misleading retrograde flow into the ventricle. Normal and stable hemodynamics during off-pump RHC trials is a necessary condition for a decision in favor of VAD removal, but not sufficiently predictive for long-term post-explant cardiac stability (6, 9).

**Exercise testing**

It was observed that, unlike non-recovered patients, those with unloading-promoted recovery show a significant LVEF increase in the 6-minute walking test (6MW) (4). Non-recovered patients showed a significant correlation between heart rate (HR) and mean arterial pressure (MAP) after 6MW, suggesting that HR increase was compensatory for MAP reduction, whereas recovered patients showed after the 6MW no correlation between HR and MAP, suggesting that HR increase was independent of MAP change and therefore a true inotropic reserve response (4). Harefield Hospital (UK) developed an algorithm for testing recovery that includes a 6MW test with repeated measurements afterwards to determine the inotropic reserve (4, 8). The same group also uses car-

![Figure 2 - Usefulness of speckle-tracking derived 2D-stain imaging for assessment of cardiac recovery after left ventricular assist device (LVAD) implantation. The comparison of recordings obtained before LVAD implantation (A and B) and several months later before LVAD explantation (C and D) showed a striking improvement of systolic global longitudinal strain (myocardial longitudinal shortening) and strain-rate (velocity of myocardial longitudinal shortening) which increased during LVAD support from 4% (A) and 0.3/s (B), respectively to 17.5% (C) and 9.6/s (D), respectively. The global early diastolic strain rate (early relaxation velocity) also increased from 0.7/s (B) to 1.6/s (D) and image D also shows a normalization of early/late strain-rate ratio.](image-url)
diopulmonary exercise testing with oxygen uptake (VO₂) as a parameter for weaning decisions (4).

**Decision-making in favor of VAD explantation**

Our weaning criteria that have evolved during nearly 20 years of weaning experience are summarized in Table 2. Essential criteria are, in addition to a stable off-pump LVEF ≥45%, normal and stable LV size and shape, as well as high stability of hemodynamic parameters measured during the off-pump right heart catheterization (RHC) trials (6, 9). Even in patients with good recovery, it appears useful to explant VADs only after the recovery has reached its maximum (no further improvement during the next 2-4 weeks) (9). If a relevant LVEF reduction and/or LV enlargement occurs during the next 2-4 weeks after maximum cardiac recovery, it can be risky to explant the VAD, even if the LVEF did not fall below 45% and the LVEDD did not increase beyond 55 mm (6).
The weaning criteria used by the Harefield group include fewer TTE parameters; instead they use the 6MW-test and the peak oxygen consumption (VO_{2}) (optimal: > 16 mL/kg/min or > 65% predicted) (4). However, it is important to emphasize that they also do not explant LVADs in patients with LVEF < 45% (4, 6, 9).

For more reliable evaluation of cardiac recovery, since 2005 we have also used tissue Doppler and speckle-tracking-derived 2D-strain imaging (12, 13).

The potential usefulness of tissue Doppler wall motion velocity measurements is shown in Figure 1.

The advantages of strain imaging are its ability to differentiate between active and passive movement of myocardial segments, the angle independency of deformation-velocity measurements, and the possibility to quantify intra-ventricular asynchrony and dyssynergy and to evaluate components of myocardial function, such as longitudinal myocardial shortening, that cannot be visually assessed (12).

Unfortunately, as 2D-strain imaging is a new method, the available off-pump data are insufficient for reliable assessment of their predictive value for long-term post-explant cardiac stability.

However, in borderline cases, off-pump data on deformation velocity as well as on intraventricular synchrony and synergy of contraction, including their stability after maximum improvement, can be useful for weaning decisions.

The major limitation of this method is its dependence on image quality. Figures 2 and 3 show the potential usefulness of 2D-strain imaging for assessment of recovery after LVAD implantation.

CONCLUSION

Echocardiography is the mainstay for assessment of unloading-promoted cardiac recovery. Off-pump LVEF ≥45% plus normal LVEDD at rest are basic weaning requirements and their stability after maximum improvement over the next 2 to 4 weeks during and between additional off-pump tests is predictable for long-term post-explant patient outcome.

Tissue Doppler and strain imaging data are useful for decision making especially if their stability after maximum remission is also considered.

After maximum improvement, stable size, geometry and function also during moderate loading of the ventricle by pump speed reduction for several days can be helpful for weaning decisions.

Stable normal off-pump hemodynamics is necessary for weaning decision, but insufficiently predictive for long-term cardiac stability after VAD removal.

Cardio-pulmonary exercise testing (with VAD support and during off-pump trials) provides information on inotropic reserve and can be useful for weaning decisions.

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