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ORIGINAL ARTICLE

Myocardial recovery evaluation from ventricular assist device in patients with dilated cardiomyopathy

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Abstract

Aims The removal of left ventricular assist device (LVAD) after myocardial recovery can provide survival benefits with freedom from LVAD-associated complications. However, in the absence of standardization, the weaning evaluation and surgical strategy differ widely among centres. Therefore, we analysed the experiences of LVAD explantation with our protocol in dilated cardiomyopathy (DCM) patients and investigated the validity of our weaning evaluation and surgical strategy from the perspective of optimal long-term survival.

Methods and results All LVAD explantation patients in our institution between May 2012 and May 2020 were enrolled. All patients were evaluated by our three-phase weaning assessment: (i) clinical stability with improved cardiac function under LVAD support; (ii) haemodynamic stability shown by ramp-loading and saline-loading test; (iii) intraoperative pump-off test. Explant surgery involved removal of the whole system including driveline, pump, sewing ring and outflow-graft, and closure of an apical hole. Intra-operative, peri-operative, and post-operative outcomes, including all-cause mortality and LVAD associated major complications, were retrospectively analysed. A total of 12 DCM patients (DuraHeart, n = 2; EVAHEART, n = 2; HeartMate II, n = 6; HeartMate 3, n = 2) had myocardial recovery after a median 10 months [interquartile range (IQR); 6.3–15 months] support and qualified for our LVAD explantation study protocol [median age: 37 y, IQR; 34–41 years; 83% men]. The median left ventricular ejection fraction was 20% (IQR; 12–23%) at LVAD-implantation and 54% (IQR: 45–55%) before LVAD explantation ($P < 0.001$). There were no perioperative complications and median ICU stay was 4 days (IQR; 2–4 days). All patients were discharged after a median of 24 days (IQR: 17–28 days) postoperatively. No patient suffered from any cardiac event (heart failure hospitalization, re-implantation of LVAD, or heart transplantation) at a median of 40 months (IQR: 17–58 months) follow up. All patients are alive with NYHA functional class 1 with preserved left ventricular function.

Conclusions The evaluation of LVAD explant candidates by our weaning protocol was safe and effective. In the patients completing our protocol successfully, LVAD explantation is feasible and an excellent long-term cardiac event free-survival seems to be achieved.

Keywords Left ventricular assist device; LVAD explantation; Weaning protocol; Heart failure; Mechanical circulatory support

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Introduction

Long-term mechanical circulatory support (MCS) of left ventricular assist devices (LVAD) has increasingly become a treatment option in advanced heart failure (HF) with improving outcomes during the past two decades.[1,2]

LVAD implantation is chosen as a life-saving procedure for drug-refractory end-stage HF with severely LV dysfunction.[1,2]

Whereas most of LVAD patients are either bridged to transplantation (BTT) or destination therapy candidates, only a limited number of patients can reach a bridge to recovery (BTR) allowing LVAD explantation. Previously, low overall recovery rates (1–2%) was reported.[3] Pathophysiology and mechanisms of LV myocardial recovery secondary to LVAD support are not entirely explored; however, it is discussed that LV unloading can promote LV reverse re-

modelling, leading to improvement of LV function, in BTR patients.[4–10]

Furthermore, the evaluation of recovered patients is poorly standardized, with limited studies and small experiences. Despite suggested parameters that might be useful for assessment of sustained myocardial recovery and therefore long-term LVAD weaning success, standardized management for recovered patients has achieved no consensus so far.[11–13]

LVAD explantation seems meaningful in recovered patients, if it allows to eliminate VAD-associated major complications like infection, bleeding, or thromboembolic complications.[1,2] But surgical LVAD removal itself may be associated with a risk of recurrent cardiac failure due to 'invasive' redo-open heart surgery. Therefore, as 'less invasive' deactivation techniques, simplified surgical procedures ranging from driveline disruption to partial VAD explantation by thoracotomy with inflow occlusion using mechanical plugs have been reported.[14] However, the long-term safety and efficacy are unclear, because most studies have focused on short-term results in a small cohort study.

Thus, the aim of this study was to analyse our standardized evaluation with weaning protocol and develop an optimal evaluation which leads to a satisfied long-term survival and sustained cardiac function after LVAD explantation and surgical strategy (complete system removal) free from VAD-associated complications.

Methods

Data collection and follow-up

This single-centre study was approved by institutional Ethics Committee of the University of Tokyo [3031-(4)]. We included all patients from our institutional database qualifying for LVAD explantation for myocardial recovery. Clinical decisions were made in interdisciplinary heart team conferences consisting of cardiologists, cardiac surgeons, perfusionists, cardio-anaesthesiologists, psychologists, and VAD coordinators. As a BTT, a total of 190 patients were implanted with durable LVADs at our centre between November 2007 and April 2020 (Supporting Information, *Data S1*). Of those, 132 patients were retrospectively studied, who was diagnosed with idiopathic dilated cardiomyopathy (DCM) based on clinical and medical history and myocardial biopsy histology.[15] All types of devices have been included in this study, including DuraHeart (Terumo Heart, Ann Arbor, MI, USA), EVAHEART (Sun Medical technology Research Corp, Nagano, Japan), Jarvik 2000 (Jarvik Heart, New York, NY), HVAD (Medtronic, USA), HeartMate II (Abbott Medical, Abbott Park, USA), and HeartMate 3 (Abbott Medical, Abbott Park, USA) device. Demographics and clinical data also include invasive pressures recorded by right heart catheterization (RHC). We also collected imaging, laboratory values, cardiopulmonary exercise testing, and surgical data. Transthoracic echocardiography (TTE) was regularly performed 1, 6, and 12 months after LVAD explantation and subsequently every 6 months. The clinical follow-up was closed on 31 May 2021, when the last enrolled patient had completed 1 year of follow-up. Endpoints of the study were first re-hospitalization for HF or cardiovascular death. Re-hospitalization for HF was defined as new onset or worsening signs and symptoms of HF that required urgent therapy resulting in hospitalization.

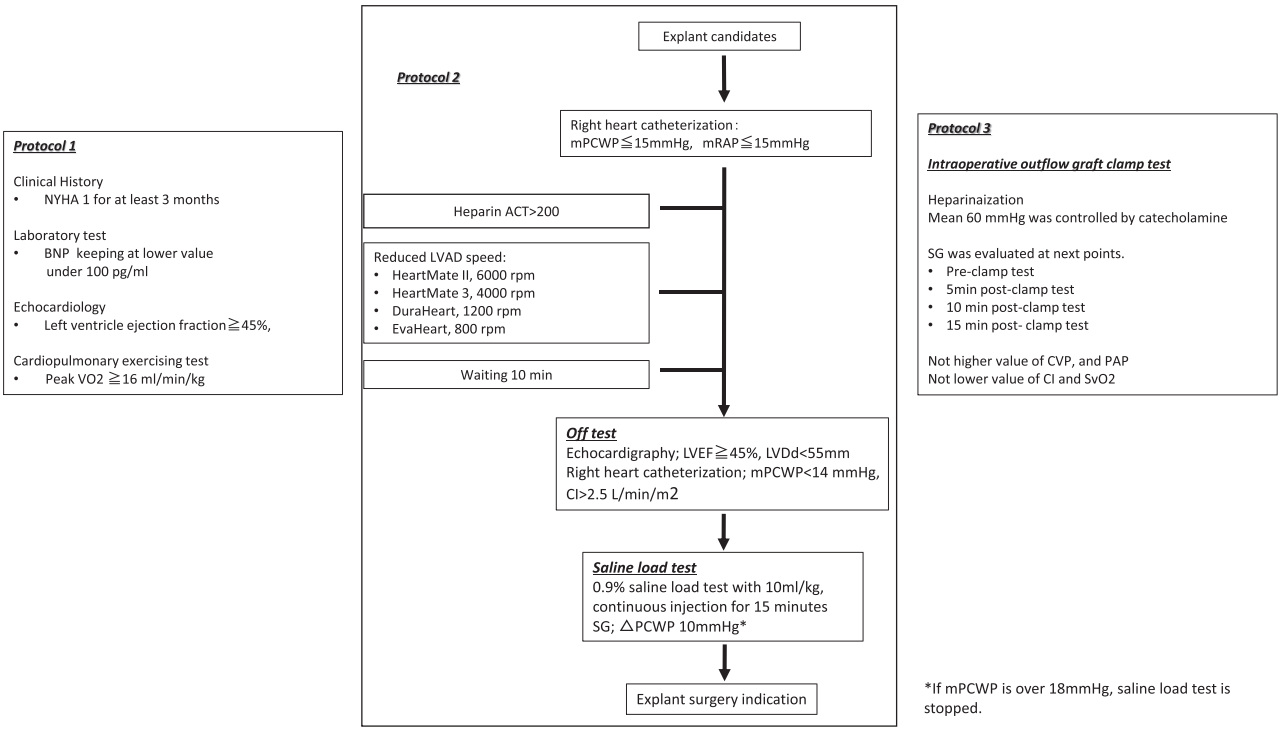
Standardized weaning protocol in our institution

Selection of weaning candidates at clinic visit (protocol 1) A weaning assessment is considered in all LVAD patients with (NYHA) functional class 1 for at least 3 months and treated on optimal guideline-directed HF therapy with consistent mean arterial pressure (MAP) adjustment at 60–80 mmHg. The routine follow-up protocol includes a TTE on 6 monthly to 1 yearly basis and blood tests with biomarkers such as brain natriuretic peptide (BNP) at each clinic visit. The improvement and stability of these tests (under 100 pg/mL and LVEF above 45%) are first required for a confidence of myocardial recovery. If that is the case, cardiopulmonary exercising test is secondary performed.[3,9,12] The acceptable result (peak VO_2 $\geq$16 mL/min/kg) in these screening tests allows us to identify patients who can proceed to subsequent protocol (*Figure 1*).

Left ventricular assist device speed reduction and saline loading test (protocol 2) First, RHC parameters are measured at a baseline speed. If the values of RHC are recorded as mean pulmonary capillary wedge pressure (PCWP) $<$ 15 mmHg and mean right atrium pressure (RAP) $<$ 15 mmHg, the test was continued.[3,9,12] Activated clotting time (ACT) after intravenous heparin bolus is assessed, and if it is $>$200, there is no need for extra anticoagulation. LVAD speed was reduced (DuraHeart: 1200 rpm, EVAHEART: 800 rpm, HeartMate II: 6000 rpm, and HeartMate 3: 4000 rpm, respectively). After a 10 min interval, the following measurements by TTE and RHC are recorded. If LVEF $>$40–45% and LVDd $<$55 mm in TTE in the parasternal view, mean PCWP $<$14 mmHg, and the cardiac index (CI) $>$ 2.2–2.5-L/min at the reduced speed, respectively, are observed, the test is considered positive. As next stage, a 0.9% saline (10 mL/kg) is continuously administered for 15 min.[3,9,12,16] If the range of mean PCWP differs within the value of 10 mmHg, LVAD explantation is subsequently scheduled[9,16] (*Figure 1*).

Intraoperative outflow graft occlusion test (protocol 3) When ACT $>$200 is confirmed after systemic heparinisation, LVAD speed is reduced to its minimum acceptable RPM before the outflow graft is clamped. Considering that there is an increased risk of thrombus formation, the clamp is re-

Figure 1 Weaning protocol sequence. BNP, brain natriuretic peptide; CI, cardiac index; CVP, central venous pressure; LVAD, left ventricular assist device; LVDd, left ventricular diastolic diameter; mPCWP, mean pulmonary capillary wedge pressure; mRAP, mean right atrium pressure; NYHA, New York Heart Association; PAP, pulmonary artery pressure; SvO_2, mixed venous oxygen saturation.



leased transiently for 5 s in every minute during the procedure. At this stage, the cardiac output can be accurately measured, because the flow through the graft is completely occluded. During this procedure, MAP (60 ± 10 mmHg) is controlled with support of catecholamine, if needed. RHC parameters including pulmonary artery pressure (PAP), CI, CVP, and mixed venous oxygen saturation (SvO_2) are recorded at post-clamp 5, 10, and 15 min, respectively (*Figure 1*). If the range of these variables are not changed, cardiopulmonary bypass (CPB) is established, and surgical procedures are subsequently performed.

Left ventricular assist device explantation surgery with ventricular restoration

All LVAD explantation procedures are performed on CPB and beating heart without cardioplegic arrest. Cautious dissection of intrapericardial tissue adhesions is performed. CPB is established by aortic cannulation in the proximal arch and venous cannulation via the SVC and IVC. LVAD drive is stopped, and the outflow graft is clamped at the level of aortic anastomosis. The next step is the detachment of the inflow cannula from the sewing ring with rigorous inspection of the LV cavity in order to exclude presence of thrombotic material in the LV. Afterwards, the sewing ring is removed, and an apical hole is directly closed with felt strips continuous 4–0 prolene running sutures. Next, the outflow graft is divided at 1 cm from the anastomotic site to the ascending aorta. The opening of the remaining short segment is oversewn. Finally, the driveline is completely removed.

Follow up

In a follow-up period, daily quality of life and functional status were assessed thoroughly. Finally, TTE and RHC were repeated to ensure sustained myocardial recovery. After LVAD explantation, clinical follow-up and TTE were performed at 1, 3, 6, and 12 months after the LVAD explantation for the first year.

Statistical analysis

Results are expressed as median +25th–75th percentile interquartile range for continuous variables, and frequency and percentage for categorical variables as appropriate. Univariable comparisons were performed with a Student's unpaired *t*-test for continuous normally distributed data. A

Mann–Whitney *U* test was used for comparisons of non-parametric data and Fisher's exact test for categorical variables. The data in paired two groups were analysed with a Wilcoxon–Mann–Whitney test. Friedman test was used, comparing between paired three groups with nonparametric nature of data. A *P*-value of <0.05 was considered statistically significant, and all reported *P*-values are two-sided. All statistical analyses were performed using R (The R Project for Statistical Computing; The R Foundation).

Results

A total of 12 DCM-patients ($n = 10$, implantation in our hospital, and $n = 2$, in other institutions) completed our standardized study protocol to test LVAD system explantation (Supporting Information, *Data S1*). Patient baseline characteristics at the time of LVAD implantation and explantation are summarized in *Table 1*.

Characteristics at the time of left ventricular assist device implantation

At the time of LVAD implantation, the distribution of Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) status was as follows: INTERMACS II ($n = 7$) and INTERMACS III ($n = 5$). One patient in INTERMACS III was clinically stable with a support of papracorporeal pulsatile LVAD. All patients underwent LVAD implantation initially as BTT strategy. Eight patients needed concomitant valve surgery (aortic, mitral, and tricuspid valve repair) at LVAD implantation. One patient in other hospital concomitantly required temporary right VAD (RVAD) but could be weaned from the RVAD at day 7 (*Table 1*).

Patient characteristics at the time left ventricular assist device explantation

A total of 12 patients experienced LVAD explantation in our centre after a median support duration of 10 (IQR: 6.3–15) months. Median age at LVAD explanation was 39 (IQR: 35–42) years and NYHA class improved to functional class I in all 12 patients. Two patients had a history of minor non-disabling strokes while on LVAD, but none had disabling stroke. Three patients needed re-admission due to driveline infection for surgical debridement and antibiotic therapy. LVEF at the time of LVAD explanation improved up to more than 40% in 11 patients (*Table 1*). In particular, LV function significantly improved at 6 months after LVAD implantation ($P < 0.005$).

The evaluation with saline load test and outflow graft clamp test

The stability of the parameters of TTE and RHC evaluated at ramp test and saline loading test was necessary to pass our explant criteria (*Figure 1*, and *Table 2A*). After infusion of 0.9% saline solution with speed of 10 mL/kg for 15 min, parameters showing volume loading significantly increased, but CI was not different.

In our 12 patients, who finally passed saline loading test by our protocol, the parameters showing cardiac function during outflow graft clamp test in protocol 3 were not statistically different at every point (*Table 2B*). Therefore, all 12 patients proceeded surgical VAD explantation.

Consequently, an elective surgical LVAD removal was performed without any complication in all the patients. Seven patients had their LVAD explanted within their first year, while the remaining five patients were on LVAD support for longer than 1 year.

Perioperative results and follow-up

Perioperative outcomes are summarized in *Table 3*. No one required temporary MCS such as ECMO and IABP after LVAD explanation. In the perioperative period, complications including cerebrovascular accident, HF, bleeding, and infection were not observed, and all 12 patients survived and were discharged home. A median stay in an intensive care unit was 4 (IQR; 3–4) days and a median total hospital stay was 24 (IQR; 18–30) days.

During a median of 43 (IQR; 20–61) months follow-up, there was no cardiac-related or non-cardiac-related death. No patient required re-hospitalization for recurrent left HF or a new onset of right HF, or invasive treatment such as MCS and heart transplantation. Anti-coagulation therapy was stopped 3 months after VAD explantation, if there was no specific medical indication, and no anticoagulation associated complication was observed during follow-up in our study cohort, such as gastrointestinal bleeding, stroke, or procedure-related infections (*Table 3*). Overall survival after LVAD explantation was 100% at any point (*Figure 2*). They remained in NYHA functional class I with ongoing medical management (i.e. beta-blocker and ACEI or ARB were used in all the patients).

Haemodynamics

A post-LVAD removal assessment by TTE ± RHC was performed at different time points. These values demonstrated significant improvement at the time of LVAD explantation when compared with those recorded at the

Table 1 Baseline characteristics at LAD implantation and explantation; *n* (%) if not otherwise specified

Baseline characteristics	*n* = 12
At the time of LVAD implantation	
Age, median (years)	37 (IQR: 34–41)
Male gender	10 (83)
Body mass index, median (kg/m^2)	23 (IQR: 20–25)
Body surface area (m^2)	1.77 (IQR: 1.6–1.90)
Hypertension	2 (17)
History of stroke	1 (8.3)
Chronic obstructive lung disease	0 (0)
Diabetes mellitus	3 (25)
Previous cardiac resynchronization therapy	0 (0)
Previous cardiac surgery	1 (8.3)
INTERMACS level	2 (IQR: 2–3)
Time between First HF and LVAD implantation (months)	4 (IQR: 1.75–7.0)
Echocardiography	
Left ventricle ejection fraction (%)	18 (IQR: 12–23)
Left ventricular end-diastolic diameter (mm)	71 (IQR: 64–73)
Left ventricular end-systolic diameter (mm)	65 (IQR: 57–66)
Medication	
Beta-blocker	11 (92)
ACE inhibitor/ARB	8 (67)
Mineralocorticoid receptor antagonist	9 (75)
Temporary MCS use	
Intra-aortic balloon pumping	6 (50)
Extracorporeal membrane oxygenation	0 (0)
Impella	0 (0)
Paracorporeal-LVAD implantation	1 (8.3)
Implanted LVAD model	
DuraHeart	2 (17)
EVAHEART	2 (17)
HeartMate II	6 (50)
HeartMate 3	2 (17)
Simultaneous valve surgery performed	
Aortic valve replacement	1 (8.3)
Mitral valve repair	2 (17)
Tricuspid valve repair	5 (42)
Temporary right ventricular assist device support	1 (8.3)
At the time of LVAD explantation	
Age, median (years)	39 (IQR: 35–42)
New York Heart Association functional class, median	1 (IQR: 1–1)
Median time between LVAD implantation and LVAD explantation (months), median	10 (IQR: 6.3–15)
LVAD complication	
Drive line infection	3 (25)
Cerebrovascular accident	2 (17)
Cardiopulmonary exercising test	
Peak VO_2 (mL/kg/min)	18.5 (IQR: 16.8–19.6)
Peak VO_2 age-adjusted %	63 (IQR: 60.5–68)
Echocardiography	
Left ventricle ejection fraction (%)	51 (IQR: 42.5–55)
Left ventricular end-diastolic diameter (mm)	50 (IQR: 45–58)
Left ventricular end-systolic diameter (mm)	38 (IQR: 33–42)
Laboratory test	
Creatinine (mg/dL)	0.87 (IQR: 0.78–0.90)
Estimated glomerular filtration rate (mL/min)	79.4 (IQR: 76.63–86.65)
Brain natriuretic peptide (pg/mL)	48.2 (IQR: 35.28–63.2)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; IQR, interquartile range; LVAD, left ventricular assist device.

time of LVAD implantation. In addition, TTE demonstrated sustained improved LV function after LVAD explantation. CI increased before LVAD explantation and to remain at this improved level from perioperative period through late follow-up. No statistical difference in mean PCWP and pulmonary vascular resistance (PVR) is also identified (*Table 4*).

Discussion

In our study, we showed an extremely satisfied long-term survival rate [100% at median 3 (IQR; 1–4) years follow-up] and freedom rate from cardiac events [100% at the same time above] in LVAD explantation patients, who successfully passed our weaning protocol to evaluate LVAD explanation

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Table 2 Haemodynamic change during protocol 2 and protocol 3

A. Change of right heart catheter parameters at each point during saline load test in protocol 2; *n* (IQR: interquartile range) if not otherwise specified. *P*-value; comparison between 4 points including low rpm, 5 min, 10 min, and 15 min after saline load test, respectively.

	Standard	Low rpm	5 min	10 min	15 min	*P*-value
CI, L/min/m^2	2.64 (2.51–2.82)	2.57 (2.25–2.82)	2.68 (2.55–2.91)	2.64 (2.49–2.91)	2.68 (2.45–2.80)	0.72
mPAP, mmHg	7 (5.5–8.25)	8.5 (8–10)	10 (8.5–12)	11 (9–14)	12 (10–15)	<0.005
mRAP, mmHg	4 (4–6.5)	5.5 (4.75–6.25)	7 (6–8)	8 (6.5–8)	8.5 (8–10.25)	<0.005
mPCWP, mmHg	7.0 (5.5–8.25)	8.5 (8–10)	10 (8.5–12)	11 (9–14)	12 (10–15)	<0.005

B. Change of right heart catheter parameters at each point after outflow graft clamp in protocol 3; *n* (IQR: interquartile range) if not otherwise specified. *P*-value; comparison between each point including pre-outflow graft clamp, 5 min, 10 min, and 15 min, respectively.

	Pre-outflow graft clamp	5 min	10 min	15 min	*P*-value
CI, L/min/m^2	2.1(2.-2.2)	2.4 (2.15–2.)	2.4 (2.05–2.95)	2.55 (2.05–2.98)	0.24
mPAP, mmHg	15 (10–17)	16 (15–18)	15 (15–15)	16 (13–19)	0.59
SvO_2, %	79 (73–81)	77 (71–81)	80 (74–81)	79 (76–81)	0.51
CVP, mmHg	7 (6.5–8)	7 (6–8)	7 (6–8.5)	7 (6–7.8)	0.90

CI, cardiac index; CVP, central venous pressure; mPAP, mean pulmonary artery pressure; mPCWP, mean pulmonary capillary wedge pressure; mRAP, mean right atrium pressure; SvO_2, mixed venous oxygen saturation.

Table 3 Intraoperative and postoperative outcomes; *n* (%) if not otherwise specified

	N = 12
Intraoperative and perioperative outcomes	
Anaesthetic time, min	486 (IQR: 461–506)
Operation time, min	367 (IQR: 346–384)
Cardiopulmonary bypass time, min	111 (IQR: 104–124)
Intensive care unit stay, day	4 (IQR: 2.8–4.3)
In-hospital stay, day	24 (IQR: 18–30)
Medication at discharge	
ACE inhibitor/ARB	12 (100)
Beta-blocker	12 (100)
Mineralocorticoid receptor antagonist	8 (67)
Long-term follow up	
All-cause mortality	0 (0)
MACCE	0 (0)
Cardiac death	0 (0)
Cerebrovascular accident	0 (0)
Re-VAD implantation	0 (0)
Heart transplantation	0 (0)
Re-admission due to heart failure	0 (0)
Infection (sepsis)	0 (0)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; IQR, interquartile range; MACCE, major adverse cardiovascular or cerebrovascular events.

eligibility. In the literatures, cardiac and physical functional capacity in patients with LVAD explantation was well maintained compared with those with LVAD therapy or heart transplantation.[17] As the reasons for increased mortality in ongoing VAD patients are VAD-related complications, we consider that LVAD explantation should be aimed at if possible.

However, it is currently not standardized how to evaluate these patients, and there are no consensus regarding indications for LVAD explantation, because of limited clinical experiences and studies of LVAD explantation. Moreover, no criteria for successful LVAD explantation have been validated without any promising workflow of LVAD explantation being confirmed or substantiated by scientific evidence. In addition to a lack of a global consensus on an explantation protocol, surgical explantation techniques varied between institutions and depended on an individual experience, further leaving an uncertainty regarding long-term results and survival.

Dandel *et al*. reported a post-explant survival in 53 weaned LVAD patients of 73% at 5 years and of 67% at 10 years, respectively.[18] However, these data also include patients that underwent heart transplantation during the follow-up period for recurrent worsening of HF, that reduced a HF free-survival substantially. Since then, diverse approaches for LVAD weaning have been proposed in various published articles, but a reliable and robust evaluation protocols that yield a satisfied outcome after LVAD weaning are lacking.[5–10] Our standardized evaluation method for a surgical total explantation of the device in LVAD patients with myocardial recovery results in 5 year survival of 100% therefore seems to be more robust than other studies.[5–10,18] Importantly, no one had re-admission due to recurrent HF or cardiac events during a study period. Pan *et al*. identified some predictors of myocardial recovery after durable LVAD implantation including younger age, female sex, lower body mass index, non-ischaemic cause, and short interval of HF before LVAD implantation.[4] Certainly, many of the aforementioned predictors may correspond to characteristics in our cohort. An explanation rate in our study [5.6% (*n* = 10/181) in adult BTT cohort, and 7.6% (*n* = 10/132) in DCM cohort alone)] is higher than in published study cohort (Supporting Information, *Data S2*). In our cohort, clinical follow-up and TTE were regularly performed in all patients, and it was repeated to ensure sustained myocardial recovery (protocol 1). Myocardial recovery was observed with TTE and low value of BNP; invasive evaluations were made in these patients (protocol 2). This makes explanation why we could find the explant candidates

Figure 2 Overall survival after LVAD explantation. Kaplan–Meier curves for freedom from al cause mortality, showing 100% survival rate at 1 year after LVAD explantation. All patient survived at median 3 years (IQR; 1–4 years) follow-up.

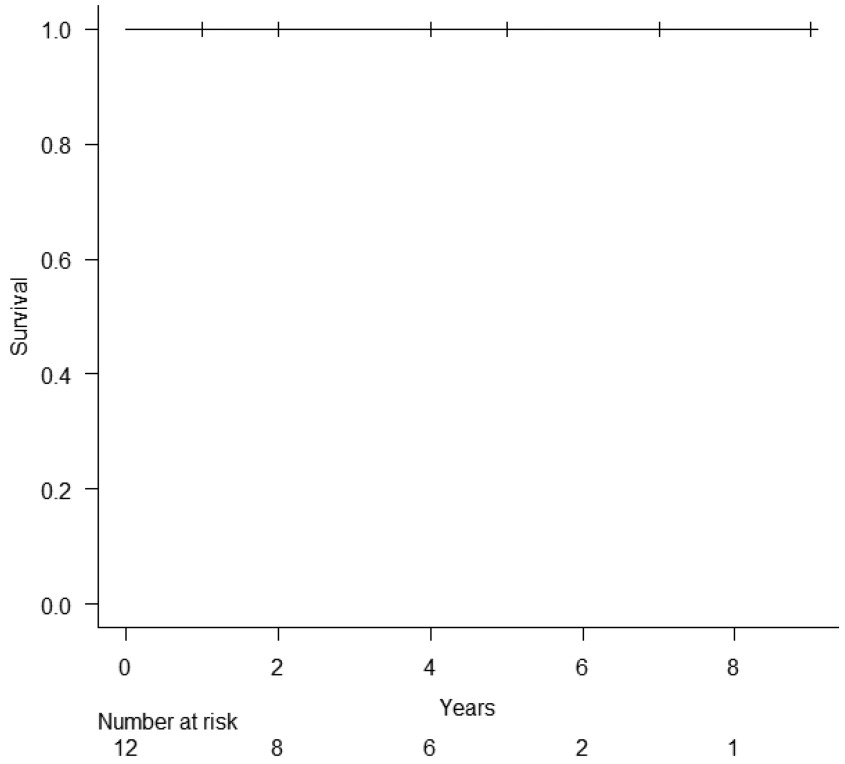

Table 4 Comparison of at LVAD implantation, at pre-LVAD explantation and postoperative values of transthoracic echocardiography (TTE) and right heart catheterization (RHC) at each point (at discharge, and follow-up at 12 months and late months after LVAD explantation). *n* (IQR) if not otherwise specified

Variables	Pre-implantation	Pre-explanation	*P*-value	Post-explantation at discharge	*P*-value*	1 year	Late follow	*P*-value#
TTE								
LVEF, %	18 (12–23)	51 (43–55)	<0.005	48 (43–53)	0.441	50 (49–54)	51 (47–54)	0.61
LVDd, mm	71 (64–73)	50 (45–58)	<0.005	53 (49–56)	0.441	53 (50–56)	53 (48–61)	0.83
LVDs, mm	65 (57–66)	38 (33–42)	<0.005	40 (38–43)	0.201	39 (38–42)	40 (37–44)	0.49
RHC								
mRAP, mmHg	12 (8–13)	4.5 (4–6)	0.017	7 (6–9)	0.239	-	-	-
mPAP, mmHg	36 (28–38)	13.5 (12–16)	0.0059	14 (12–15)	1	-	-	-
mPCWP, mmHg	30 (23–31)	6.5 (4–9.25)	0.0059	8 (6–9.5)	0.35	-	-	-
PVR, wood unit	2 (1.91–2.44)	1.41 (1.23–1.80)	<0.005	1.41 (0.99–1.86)	1	-	-	-
CI, L/min/m^2	1.57 (1.52–1.87)	2.62 (2.34–2.8)	<0.005	2.47 (2.29–2.7)	0.79	-	-	-

CI, cardiac index; LVAD, left ventricular assist device; LVDd, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; mPAP, mean pulmonary artery pressure; mPCWP, mean pulmonary capillary wedge pressure; mRAP, mean right atrium pressure; PVR, pulmonary vascular resistance; RHC, right heart catheter.
**P*-value; comparison between pre-LVAD explantation and post-LVAD explantation at discharge.
#P-value; comparison between pre-LVAD explantation, at discharge, follow up at 12 months, and late months after LVAD explantation.

with this higher rate. In addition, our evaluation with protocol 2 (saline loading test) seems to be more reliable to judge the indication to surgical LVAD explantation than the protocols suggested in other publications. It is notable that all patients evaluated successfully in protocol 2 accomplished the intraoperative clamp test successfully, which reflect on the recovered myocardial function. Some authors reported that the patients evaluated with bicycle stress test (125 Watts, 2 min with pump stop) successfully could accomplish surgical LVAD explantation with stable circulation, and no one died due to cardiac events at 1 year follow up.[19] However, in some patients with skeletal or muscle weakness and with disable/non-disable condition after cerebral vascular accident, this evaluation method may not be applicable. We hope that var-

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ious evaluation strategies will be compared in a multi-centre study; thereby, more robust evaluation method will be established.

Surgical technical recommendations on 'how to successfully explant' LVAD are under intense discussion. Baldwin *et al*. reported four possible surgical approaches for LVAD explantation, consisting of a plug placement, ligation, subxiphoid ligation, and driveline transection in 27 patients mainly implanted with the HeartMate II device.[20] These techniques may be less invasive and easier to perform but may lead to a risk of complications such as thromboembolic events or infection over time. In this context, the authors reported that 4/27 (15%) patients had neurologic events and 7/27 (26%) patients required reoperation for infection after the initial procedure.[20] Moreover, plug replacement is not an approved medical device procedure and leaving the driveline never preclude an infectious risk, because the exposed cables contained in a driveline is not sterile. Based on this concept, Morshuis *et al*. reported complete LVAD removal technique with ventricular double-patch plasty.[19] In this context, no major adverse cardiovascular event, including stroke or infection, occurred after this strategy through median 10 months follow-up period, as in our series. Certainly, LV restoration using patch plasty is also under debate, as it represents a more invasive procedure. LV dimension remained stable after LVAD explantation, yet the LV apical wall motion seems to be restrictive due to double-patch technique.[19] This may lead to recurrent LV-HF during a long-term follow-up. In our cohort, LV linear closure technique was selected not to restrict apical wall motion in all the patients. During a median follow-up period of 43 months, LV function and dimension are stable in all patients without any sign of worsening compared with those at the device explant (*Table 4*).

Most importantly, there is always a risk for recurrent HF, even if primary explantation was successful. Fortunately, myocardial recovery was persistently preserved throughout the complete follow-up (*Table 4*). All the patients were treated with beta-blocker and ACEI/ARB during the study period. This guideline direct medical therapy is considered to be mandatory to keep LV function after myocardial recovery, and this theory is actually under discussion and should be evaluated with confidence in the future.[21]

Limitations

There are several limitations in our study. First, this is a retrospective, single centre study with a limited number of patients. Second, our protocol might be too strict to identify weaning candidates. There is a risk of missing candidates that may successfully reach to LVAD explantation. Finally, it should be noticed that only DCM population is enrolled in this study. Even though this study does not allow for generalized statements, we are still able to report good outcomes for this cohort.

Conclusions

Although myocardial recovery in continuous flow VAD patients occurred only in a limited number of cases, the selected patients may enjoy a long-term cardiac event free-survival. There may be two key components for a successful VAD explantation. One is to confirm the optimal requirements for VAD explantation by evaluation with a standardized weaning protocol. The other is a complete removal of the VAD system to completely eliminate the VAD associating complications such as thromboembolic event and infection.

Conflict of interest

All authors declare no conflict of interest in context with this study.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Flow chart for selection of patients.
Data S2. Summary of the rate of explantation and the outcomes in published studies.

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