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Impact of pretransplant left ventricular assist device support duration on outcome after heart transplantation

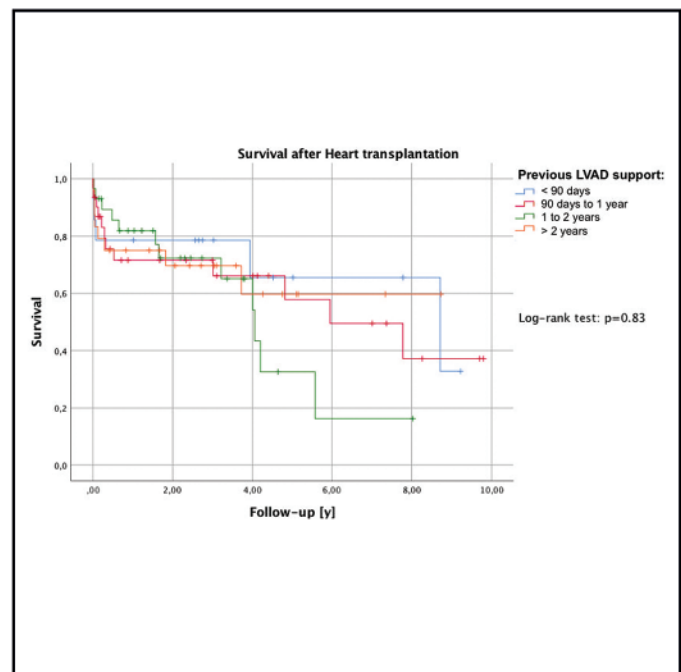
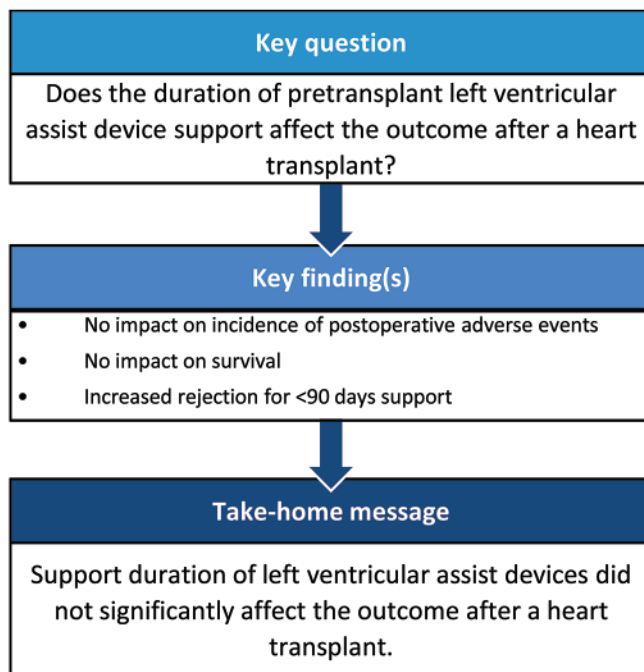
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Abstract

OBJECTIVES: Heart transplantation after left ventricular assist device (LVAD) implantation remains challenging. It is still unclear whether its support duration impacts the outcome after transplantation.

METHODS: All patients undergoing heart transplantation between 2010 and 2021 at a single department after previous left ventricular assistance were retrospectively reviewed and divided into 4 different study groups with regard to the duration of LVAD support to examine the impact on the postoperative morbidity and mortality.

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RESULTS: A total of $n = 198$ patients were included and assigned to the 4 study groups (group 1: <90 days, $n = 14$; group 2: 90 days to 1 year, $n = 31$; group 3: 1–2 years, $n = 29$; group 4: >2 years, $n = 24$). Although there were no differences between the 4 groups concerning relevant mismatch between the recipients and donors, the incidence of primary graft dysfunction was numerically increased in patients with the shortest support duration, and also those patients with >1 year of support (group 1: 35.7%, group 2: 25.8%, group 3: 41.4%, group 4: 37.5%, $P = 0.63$). The incidence of acute graft rejection was by trend increased in patients of group 1 (group 1: 28.6%, group 2: 3.3%, group 3: 7.1%, group 4: 12.5%, $P = 0.06$). Duration of LVAD support did not impact on perioperative adverse events (infections, $P = 0.79$; acute kidney injury, $P = 0.85$; neurological events, $P = 0.74$; thoracic bleeding, $P = 0.61$), neither on postoperative survival (1-year survival: group 1: 78.6%, group 2: 66.7%, group 3: 80.0%, group 4: 72.7%, $P = 0.74$).

CONCLUSION: We cannot identify a significant impact of the duration of pretransplant LVAD support on postoperative outcome; therefore, we cannot recommend a certain timeframe for transplantation of LVAD patients.

Keywords: LVAD • Heart transplantation • Primary graft dysfunction • Acute rejection

ABBREVIATIONS

BTT	Bridge to transplant
HTx	Orthotopic heart transplantation
LVAD	Left ventricular assist device
va-ECMO	Veno-arterial extracorporeal membrane oxygenation

INTRODUCTION

For patients suffering from end-stage congestive heart failure, heart transplantation (HTx) offers the best therapeutic option with favourable long-term results [1, 2]. However, due to prolonged waiting lists for transplantation, left ventricular assist devices (LVAD) are often implanted as a bridge-to-transplant (BTT) therapy in patients waiting for a suitable donor organ [3, 4]. Heart transplantation in patients with BTT LVAD support remains surgically and immunologically challenging [5–7]. Therefore, the impact of previous LVAD implantation on the outcome after HTx is controversially discussed in the literature [5, 7–10].

While the occurrence of device-related complications did not seem to be associated with decreased postoperative survival after HTx, the impact of support duration remains another potential significant factor [7, 9, 10]. During LVAD therapy, patients often experience humoral sensitization leading to an increased risk of circulating human leukocyte antigen- and cytotoxic panel-reactive antibodies that may later trigger antibody-mediated rejection and carries the risk of development of cardiac allograft vasculopathy [6, 11–14]. In addition, LVAD implantation provokes intrathoracic adhesions, which may complicate the surgical procedure of the secondary HTx, e.g. by causing diffuse bleeding with need for re-thoracotomy and consecutively increased perioperative morbidity [15].

To investigate the possible association of prolonged duration of BTT LVAD support on the outcome after HTx, we retrospectively analysed all patients who underwent HTx after BTT LVAD implantation in our department within the past 10 years.

PATIENTS AND METHODS

Ethical statement

The reported study was carried out in accordance with the principles of the Declaration of Helsinki and was approved by the local university ethics committee (local study ID: 4567, approval

date: 31 January 2014). All patients gave their informed consent for the scientific use of their anonymized patient data prior to inclusion.

Patients and study design

All adult patients undergoing HTx between 2010 and 2021 in our department were prospectively enrolled and the medical record was entered into an institutional database. Data were retrospectively reviewed and patients with pretransplant ventricular assist device support were identified for further investigations. Patients with biventricular assist were excluded. The remaining patients were divided into 4 groups in regard to their previous LVAD support (group 1: <90 days, group 2: 90 days to 1 year, group 3: 1–2 years, group 4: >2 years) and examined in a retrospective single-centre study design (Fig. 1).

Study objectives and follow-up period

Donor and recipient parameters of the 4 groups were examined and the impact of duration of LVAD support on outcome in BTT patients undergoing HTx was analysed. Follow-up examinations were carried out on regular basis every 3 months throughout the whole study period. Postoperative survival was defined as the primary endpoint. Perioperative adverse events (infective complications, acute graft rejection, acute kidney failure, neurological complications, delayed chest closure and thoracic bleeding) were defined as secondary endpoints of the study.

Surgical procedure and perioperative management

Implantation of BTT LVAD with either axial flow (Abbott HeartMate IITM, ReliantHeart Heart Assist 5) or centrifugal flow (Abbot HeartMate IIITM, Medtronic HeartWare HVADTM) was performed by either full or partial sternotomy with additional left anterior thoracotomy. For the following HTx, orthotopic bicaval or Shumway technique was used. Primary immunosuppression regime followed a standardized institutional protocol, i.e. combination of tacrolimus, mycophenolate mofetil and prednisolone for all included patients. In case of acute graft rejection, induction therapy was initialized with high-dose prednisolone therapy for at least 3 consecutive days. In case of antibody-mediated rejection, additional treatment was carried out with immunabsorption or plasmapheresis, anti-T-lymphocyte IgG and intravenous IgM-enriched human immunoglobulin. Primary graft dysfunction was defined following the 2014 consensus statement of the

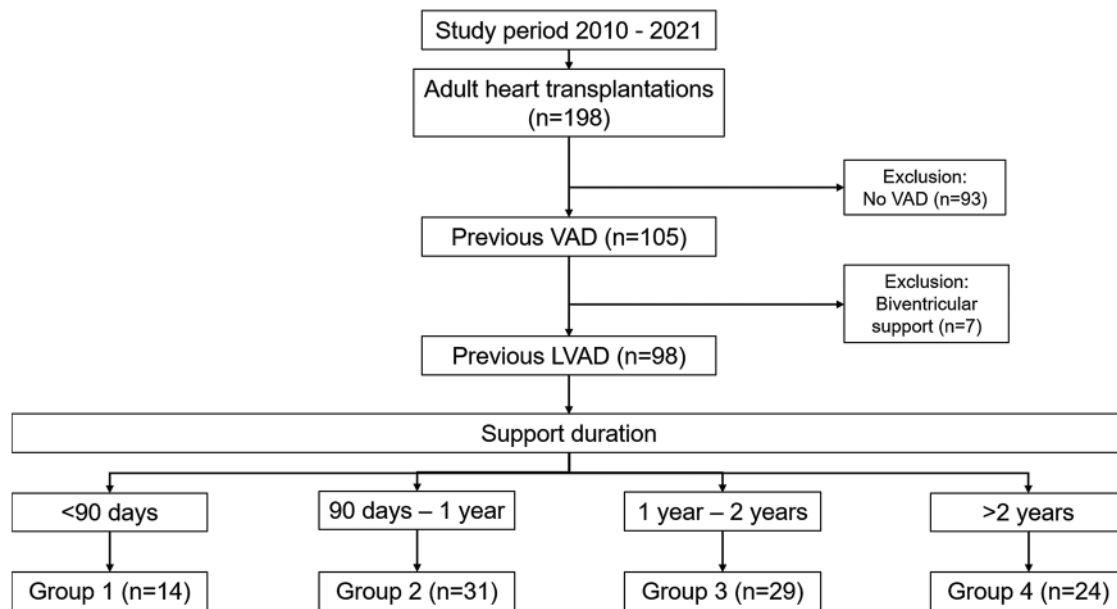


Figure 1: Study design. A total of $n = 198$ adult heart transplantations were retrospectively reviewed and $n = 98$ patients with previous left ventricular assist device implantation were included in the study. Selected patients were divided into 4 study groups with regard to their pre-transplant duration of left ventricular assist device support (group 1: <90 days, $n = 14$; group 2: 90 days to 1 year, $n = 31$; group 3: 1–2 years, $n = 29$; group 4: >2 years).

International Society of Heart and Lung Transplantation [16]. Patients suffering from primary graft dysfunction were treated following an institutional standard operating procedure covering adequate catecholamine therapy with epinephrine and norepinephrine, implantation of veno-arterial extracorporeal membrane oxygenation (va-ECMO) and a microaxial pump (Impella 5.0, Abiomed, Inc., Danvers, MA, USA).

Statistics

Statistical analyses were performed using SPSS Statistics 26 (IBM Corporation, Armonk, NY, USA) with non-parametric two-tailed Kruskal–Wallis trends tests. In case of statistically significant results ($P < 0.05$), additional *post hoc* analyses were by Bonferroni correction for continuous respectively Mann–Whitney U tests for categorical variables were performed. For analysing the direct impact of the previous LVAD support duration on the postoperative survival after HTx, a Cox regression analysis was performed. In addition, survival of the 4 groups was calculated according to the Kaplan–Meier method and compared by the log-rank test. Results of continuous variables are shown as median and interquartile range and categorical variables as percentage of the whole. Detailed information of the *post hoc* test is displayed in [Supplementary Material, Table S1](#).

RESULTS

Pre-transplant recipient and donor parameters

Detailed preoperative recipient parameters are displayed in Table 1. A total of $n = 198$ patients underwent HTx during the study period with $n = 98$ patients on previous BTT LVAD support that were included in the study and assigned to the 4 groups (group 1: <90 days, $n = 14$; group 2: 90 days to 1 year, $n = 31$; group 3: 1–2 years, $n = 29$; group 4: >2 years, $n = 24$). Most

common implanted device was Medtronic HeartWare HVAD™ ($n = 65$), followed by Abbot HeartMate III™ ($n = 22$) and Abbott HeartMate II™ ($n = 9$). The majority of cases were performed by full sternotomy ($n = 73$).

Demographic data of the 4 groups showed significant differences with recipients of group 3 containing the oldest patients and the lowest percentage of females. Predicted heart mass ratio of the recipients and donors was comparable indicating no relevant differences regarding organ size mismatch between the 4 study groups. Given by the study protocol, the pre-transplant duration of LVAD support differed markedly across the study groups, with patients of group 4 having a >27 times longer LVAD support than patients of group 1. Patients of group 1 were much likely to be transplanted after previous extracorporeal life support and mechanical ventilation than in the other groups. We did not observe relevant differences with regard to the percentage of patients suffering from severe device-related complications justifying high urgency waiting list status. However, patients of the different groups suffered from different kind of device-related complications, with right heart failure being predominant in group 1 and infective complications in groups 3 and 4. Whereas laboratory values did not show any differences between the 4 groups, patients of group 1 were more likely depended on chronic haemodialysis than the other ones. Donor data revealed no inter-group differences with gender distribution similar to the recipients as the only significant results (Table 2). There were no differences regarding the rate of marginal donors.

Operative outcome

We did not observe any differences with regard to graft ischaemia time as well as postoperative hospital, intensive care unit or intermediate care unit stay (Table 3). However, there was a numerical discrepancy between the mechanical ventilation times, especially of group 2 (49 h) and group 3 (103 h). Similar numerical effects were observed with regard to the incidence of severe primary graft dysfunction requiring temporary mechanical support by va-ECMO

Table 1: Preoperative recipient parameters

Recipient variables	Group 1 (n = 14)	Group 2 (n = 31)	Group 3 (n = 29)	Group 4 (n = 24)	P-value
Age, years, mean (IQR)	51 (16)	57 (12)	62 (8)	56 (18)	<0.01
Female gender, n (%)	7 (50.0)	9 (29.0)	1 (3.4)	3 (12.5)	<0.01
Body mass index, kg/m ² , mean (IQR)	24.0 (4.8)	23.5 (5.4)	26.2 (5.2)	27.2 (5.6)	0.04 ^a
Predicted heart mass ratio, %, mean (IQR)	-0.6 (32.0)	4.7 (24.2)	-1.0 (17.6)	3.9 (25.4)	0.33
Aetiology					
Ischaemic cardiomyopathy, n (%)	7 (50)	13 (41.9)	14 (48.3)	13 (54.2)	0.85
Dilated cardiomyopathy, n (%)	7 (50)	18 (58.1)	15 (51.7)	11 (45.8)	
Ventricular assist device					
Support duration, days, mean (IQR)	36 (52)	216 (188)	498 (178)	1021 (360)	<0.01
Implantation technique					
Full sternotomy, n (%)	13 (92.9)	22 (75.9)	17 (58.6)	20 (83.3)	0.06
Partial sternotomy, n (%)	1 (7.1)	7 (24.1)	12 (41.4)	4 (16.7)	
Device flow					
Axial, n (%)	0 (0.0)	2 (6.7)	2 (6.9)	6 (25.0)	0.04 ^a
Centrifugal, n (%)	14 (100.0)	28 (93.3)	27 (93.1)	18 (75.0)	
Device-related adverse events causing high urgency wait list status, n (%)	8 (57.1)	11 (35.5)	17 (58.6)	13 (54.2)	0.27
Infection, n (%)	2 (14.3)	2 (6.5)	9 (31.0)	5 (20.8)	0.03
Thrombosis, n (%)	0 (0.0)	3 (9.7)	1 (3.4)	4 (16.7)	
Right heart failure, n (%)	4 (28.6)	0 (0.0)	2 (6.9)	0 (0.0)	
Stroke, n (%)	0 (0.0)	5 (16.1)	2 (6.9)	2 (8.3)	
Other, n (%)	2 (14.2)	1 (3.2)	3 (10.3)	2 (8.4)	
Concomitant diseases					
Diabetes mellitus, n (%)	1 (7.1)	5 (16.1)	8 (27.6)	7 (29.2)	0.58
Haemodialysis, n (%)	2 (14.3)	0 (0.0)	0 (0.0)	2 (8.3)	0.03
Myocardial infarction, n (%)	6 (42.9)	13 (41.9)	10 (34.5)	9 (37.5)	0.90
Smoking, n (%)	1 (7.1)	6 (19.4)	7 (24.1)	4 (16.7)	0.60
Dyslipidemia, n (%)	2 (14.3)	12 (38.7)	18 (62.1)	11 (45.8)	0.03
Arterial hypertension, n (%)	6 (42.9)	14 (45.2)	22 (75.9)	17 (70.8)	0.03
Pulmonary hypertension, n (%)	6 (42.9)	4 (12.9)	0 (0.0)	2 (8.3)	<0.01
Cardiopulmonary resuscitation, n (%)	5 (37.5)	5 (16.1)	4 (13.8)	2 (8.3)	0.16
Mechanical ventilation, n (%)	4 (28.6)	3 (9.7)	1 (3.4)	0 (0.0)	0.01
Extracorporeal life support, n (%)	2 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	0.02 ^a
Blood transfusion, n (%)	3 (21.4)	1 (3.2)	1 (3.4)	1 (4.2)	0.11
Panel-reactive antibodies, %, mean (IQR)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.62
Laboratory values					
Hemoglobin, g/dl, mean (IQR)	10.1 (1.8)	12.1 (3.9)	11.6 (3.1)	12.3 (3.1)	0.05
Bilirubin, mg/dl, mean (IQR)	0.5 (2.1)	0.5 (0.6)	0.5 (0.3)	0.4 (0.9)	0.95
Creatinine, mg/dl, mean (IQR)	1.1 (0.7)	1.1 (0.6)	1.1 (0.3)	1.3 (0.7)	0.29
Lactate dehydrogenase, U/l, mean (IQR)	283 (558)	248 (65)	259 (63)	256 (94)	0.79

Patients undergoing heart transplantation after LVAD implantation were divided into 4 study groups with regard to the duration of pre-transplant LVAD support (group 1: <90 days, n = 14; group 2: 90 days to 1 year, n = 31; group 3: 1–2 years, n = 29; group 4: >2 years). Results of continuous variables are shown as median and interquartile range and categorical variables are shown as percentage of the whole.

LVAD: left ventricular assist device.

^aPost hoc analysis revealed no statistically significant inter-group differences. Detailed results for post hoc analysis are displayed in [Supplementary Material, Table S1](#).

(group 2: 25.8%; group 3: 41.4%). The incidence of perioperative severe adverse events, e.g. infective complications (e.g. sepsis, severe wound infections requiring surgical revision), acute kidney injury with consecutive haemodialysis on intensive care unit, neurological events (e.g. transient ischaemic attack and stroke) as well as rethoracotomy for bleeding, was all comparable between the study groups. In addition, there was no statistical difference regarding the incidence of acute graft rejection in patients with short (group 1: 28.6%), intermediate (group 2: 3.3% and group 3: 7.1%) and long duration (group 4: 12.5%) of LVAD support.

Postoperative survival

The median follow-up period was 2.32 years (IQR: 3.83) with a maximum of 9.8 years. The duration of LVAD support had no impact

on 30-day ($P = 0.48$) no on 1-year survival ($P = 0.74$) (Table 3). Kaplan–Meier survival analysis confirmed this results for longer-term follow-up ($P = 0.83$). Within the first 4 years after HTx, survival curves were more or less identical for all study groups, indicating no relevant impact of prolonged pre-transplant LVAD support (Fig. 2). In addition, Cox regression analysis of the whole cohort of 98 patients did not show any significant impact of the duration of LVAD support on postoperative survival ($P = 0.73$).

DISCUSSION

Patients suffering from severe heart failure with BTT LVAD implantation may experience decreased postoperative outcome after HTx. In the present study, our investigation is focused on the impact of duration of LVAD support as a possible mediator for impaired survival

Table 2: Donor parameters

Donor variables	Group 1 (n = 14)	Group 2 (n = 31)	Group 3 (n = 29)	Group 4 (n = 24)	P-value
Age, years, mean (IQR)	46 (18)	48 (17)	39 (19)	42 (22)	0.13
Female gender, n (%)	10 (66.7)	17 (56.7)	6 (18.8)	8 (34.8)	0.01
Cardiopulmonary resuscitation, n (%)	5 (35.7)	4 (12.9)	11 (37.9)	5 (20.8)	0.11
Duration, min, mean (IQR)	14 (20)	20 (39)	16 (18)	6 (6)	0.13
Norepinephrine, µg/kg/min, mean (IQR)	0.10 (0.73)	0.08 (0.21)	0.10 (0.15)	0.05 (0.08)	0.69
Ejection fraction, % (IQR)	60 (10)	65 (12)	60 (10)	61 (10)	0.54
Concomitant diseases					
Coronary artery disease, n (%)	0/1 (0.0)	0/11 (0.0)	1/10 (10.0)	0/10 (0.0)	0.99
Arterial hypertension, n (%)	8/10 (80.0)	10/16 (62.5)	9/17 (52.9)	2/9 (22.2)	0.08
Diabetes mellitus, n (%)	1/4 (25.0)	2/18 (18.2)	1/10 (10.0)	0/8 (0.0)	0.63
Smoking, n (%)	7/13 (53.8)	14/25 (56.0)	17/26 (65.4)	9/21 (42.9)	0.51
Alcohol abuse, n (%)	5/13 (38.5)	9/26 (34.6)	9/24 (37.5)	9/23 (39.1)	0.99
Drug abuse, n (%)	1/13 (7.7)	3/26 (11.5)	4/25 (16.0)	2/22 (9.1)	0.86
Laboratory values					
Hemoglobin, g/dl, mean (IQR)	11.2 (2.9)	9.6 (2.5)	9.2 (4.2)	11.1 (5.4)	0.15
Lactate dehydrogenase, U/l, mean (IQR)	310 (872)	282 (183)	340 (325)	332 (390)	0.86

Patients undergoing heart transplantation after LVAD implantation were divided into 4 study groups with regard to the duration of pre-transplant LVAD support (group 1: <90 days, n = 14; group 2: 90 days to 1 year, n = 31; group 3: 1–2 years, n = 29; group 4: >2 years). Results of continuous variables are shown as median and interquartile range and categorical variables as percentage of the whole. Detailed results for *post hoc* analysis are displayed in [Supplementary Material, Table S1](#). LVAD: left ventricular assist device.

Table 3: Operative outcome

Outcome variables	Group 1 (n = 14)	Group 2 (n = 31)	Group 3 (n = 29)	Group 4 (n = 24)	P-value
Total graft ischaemic time, min, mean (IQR)	216 (67)	206 (49)	224 (48)	212 (59)	0.41
Transport time, min, mean (IQR)	149 (55)	147 (45)	157 (41)	162 (63)	0.58
Primary graft dysfunction					
Peak catecholamine					
Dobutamine, µg/kg/min, mean (IQR)	5.93 (7.02)	4.44 (1.51)	4.63 (1.87)	3.90 (2.91)	0.48
Epinephrine, µg/kg/min, mean (IQR)	0.25 (0.22)	0.24 (0.16)	0.25 (0.30)	0.15 (0.20)	0.10
Norepinephrine, µg/kg/min, mean (IQR)	0.34 (0.41)	0.25 (0.22)	0.27 (0.36)	0.25 (0.38)	0.94
va-ECMO, n (%)	5 (35.7)	8 (25.8)	12 (41.4)	9 (37.5)	0.64
Died on support, n (%)	1/5 (20.0)	3/7 (42.9)	2/12 (16.7)	4/9 (44.4)	0.50
Postoperative morbidity					
Infective complications, n (%)	4/14 (28.6)	8/30 (26.7)	6/28 (21.4)	4/24 (16.7)	0.79
Acute graft rejection, n (%)	4/14 (28.6)	1/30 (3.3)	2/28 (7.1)	3/24 (12.5)	0.06
Hemodialysis on ICU, n (%)	6/14 (42.9)	16/30 (53.3)	15/29 (51.7)	14/24 (58.3)	0.85
Neurological complications, n (%)	3/14 (21.4)	8/30 (26.7)	4/28 (14.3)	5/24 (20.8)	0.74
Delayed chest closure, n (%)	1/14 (7.1)	0/30 (0.0)	4/28 (14.3)	3/24 (12.5)	0.22
Re-thoracotomy, n (%)	3/14 (21.4)	9/31 (29.0)	9/28 (32.1)	10/24 (41.7)	0.61
Postoperative hospital stay, days, mean (IQR)	36 (27)	35 (22)	35 (38)	32 (23)	0.59
Postoperative ICU/IMC stay, days, mean (IQR)	16 (18)	15 (20)	20 (17)	12 (26)	0.24
Mechanical ventilation, h, mean (IQR)	96 (61)	49 (102)	103 (268)	60 (241)	0.19
Blood transfusion					
Packed red blood cells, ml, mean (IQR)	2565 (2498)	2160 (3645)	2295 (2835)	2160 (3780)	1.00
Fresh frozen plasma, ml, mean (IQR)	3125 (2688)	4000 (5313)	3625 (6500)	3500 (9500)	0.60
Platelets, ml, mean (IQR)	220 (990)	330 (1100)	440 (1760)	440 (1320)	0.80
30-Day survival, n (%)	11/14 (78.6)	27/30 (90.0)	27/29 (93.1)	20/24 (83.3)	0.55
1-Year survival, n (%)	11/14 (78.6)	16/24 (66.7)	20/25 (80.0)	16/22 (72.7)	0.74

Patients undergoing heart transplantation after left ventricular assist device implantation were divided into 4 study groups in regard to their pretransplant left ventricular assist device duration (group 1: <90 days, n = 14; group 2: 90 days to 1 year, n = 31; group 3: 1–2 years, n = 29; group 4: >2 years). Results of continuous variables are shown as median and interquartile range and categorical variables as percentage of the whole.

ICU: intensive care unit; IMC: intermediate care unit; LVAD: left ventricular assist device; va-ECMO, veno-arterial extracorporeal life support.

after HTx. For this investigation, we have retrospectively analysed all patients undergoing HTx in the recent 10 years after prior BTT LVAD implantation at our department.

The preoperative data of the HTx recipients displayed a heterogeneous cross-section of LVAD patients [3, 17]. Although

gender distribution differed between the groups, the predicted heart mass ratio of recipients and respective donors were comparable disproving relevant differences regarding mismatch [18]. The overall incidence of device-related complications justifying high urgency status on the waiting list was comparable between

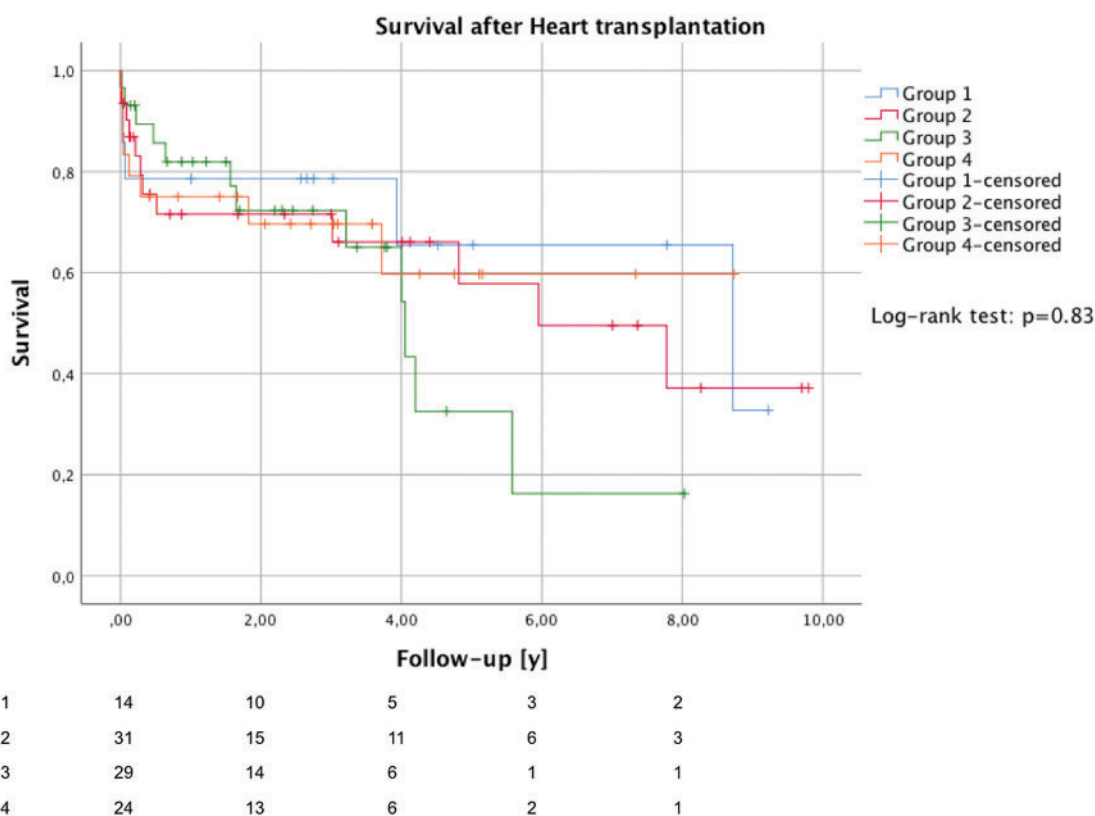


Figure 2: Kaplan-Meier survival curve for patients of the 4 study groups. Patients were divided into 4 study groups in regard to the duration of pre-transplant left ventricular assist device support (group 1: <90 days, $n = 14$; group 2: 90 days to 1 year, $n = 31$; group 3: 1–2 years, $n = 29$; group 4: >2 years).

the 4 groups with no association with prolonged duration of support, indicating a linear relationship between support duration and the incidence of device-related adverse events as supported by the literature [19]. In contrast to that, the observed kind of device-related complications differed between the 4 groups. However, in a previous published two-centre study, we were able to show that the different device-related complications such as right heart failure, infections, stroke or thrombosis do not impact the outcome after HTx [10].

The incidence of postoperative primary graft dysfunction with the need of temporary mechanical assistance by va-ECMO was in general high in all study groups, which is caused by a relatively liberal institutional regime with early va-ECMO implantation [20–22]. As a consequence, weaning and survival on va-ECMO support was distinctly improved compared to the literature [23]. With regard to the duration of preoperative LAVD support, we observed only numerical differences with patients with 1–2 years of support (group 3) having the highest and patients with 90 days to 1 year support (group 2) having the lowest risk. Eventually, while patients with very short support duration may still be affected by the previous LVAD implantation, patients with a support longer than 1 year might be affected by the prolonged support duration itself. However, more evidence to support the latter hypothesis is still missing in the literature.

Postoperative severe adverse events were most likely not associated with the duration of previous BTT LVAD support. Interestingly, preoperatively we observed differences in the incidence of haemodialysis between the 4 groups. Patients with either short (<90 days) or long term (>2 years) LVAD support had a numerically increased incidence of haemodialysis, which is

supported by the literature and might be caused by the impact of the continuous flow of the LVAD on the renal vessels [24]. However, postoperatively these effects seemed to vanish. Neurological outcome was similar in the 4 study groups indicating once again no correlation with prolonged LVAD support. These results are supported by data recently presented by Suarez-Pierre *et al.* [25] who described a similar outcome for patients with or without any LVAD support after HTx.

HTx after BTT LVAD is surgically challenging because of intrathoracic adhesions possibly causing relevant diffuse bleeding complications [5, 15]. Nevertheless, we did not observe differences concerning delayed chest closure or re-thoracotomy rate because of hemothorax or pericardial effusion indicating no additional correlation with the support duration. In contrast to that the latter findings, we observed a trend towards increased incidence of acute graft rejection in patients with either very short (<90 days) or very long (>2 years) duration of BTT LVAD therapy. As mentioned before, human leukocyte antigen sensitization is common in LVAD patients possibly increasing the risk for later organ rejection [6, 11–14]. In patients with short-term LVAD support, potential effects of recent perioperative blood transfusion along the LVAD implantation may further increase the risk of rejection, which is supported by our preoperative data [26]. In contrast to that, in patients with prolonged LVAD support duration the impact of potential device-related infective complications throughout the LVAD therapy may induce high panel-reactive antibodies, which were also observed in our cohort [27].

Finally, we did not observe differences in survival after HTx with regard to the duration of previous LVAD support. Neither Cox-regression analysis of the whole cohort nor log-rank test of

the 4 individual study groups revealed any disadvantages for patients within a particular support duration category. These results are contrary to some of previously published data that have reported a decreased survival for patients undergoing HTx after prolonged LVAD therapy [7, 9]. Regardless the fact that we do not observe any impact of the duration of LVAD support on outcome after HTx, we do observe a negative impact of LVAD therapy itself on outcome after HTx. This finding is still divergent with registry data that could not report any impact of LVAD therapy on post-transplant outcome at all [5, 8, 10].

Limitations

The reported study is limited by its single-centre and retrospective design. Because of the limited group sizes propensity score matching was not possible, thus leading to heterogeneous groups and potential effects may not have been found. Furthermore, because of the short follow-up period of the majority of patients, the known disproportionately high first-year mortality after HTx most likely underestimates the longer-term survival of the cohort assessed by the Kaplan–Meier method. In addition, the high number of previously censored patients and the consecutive relatively small remaining follow-up cohort may represent a bias with an impact on potential differences beyond the fourth post-operative year.

CONCLUSION

Heart transplantation after previous LVAD support remains surgically and immunologically challenging. Really short and really long support durations seem to be associated with an increased risk for early graft rejection. In addition, patients with >1 year of LVAD support may more likely experience severe primary graft dysfunction. However, a liberal regime with early va-ECMO implantation can successfully protect the recipients' organ function, prevent perioperative morbidity, and preserve good early survival after HTx. Therefore, in the given circumscribed study cohort, we cannot identify a significant impact of duration of pre-transplant LVAD support on the postoperative outcome and can support the HTx of BTT LVAD patients at any support time.

SUPPLEMENTARY MATERIAL

[Supplementary material](#) is available at *ICVTS* online.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Author contributions

Moritz Benjamin Immohr: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing—original draft; Writing—review & editing. **Hug Aubin:** Conceptualization; Project administration; Supervision; Validation; Writing—review & editing. **Sophiko Erbel-Khurtsidze:** Conceptualization; Data curation; Validation; Writing—review & editing. **Hannan Akhyari:** Data curation; Validation; Writing—review & editing. **Raphael Romano Bruno:** Data curation; Validation; Writing—review & editing. **Ralf Westenfeld:** Data curation; Validation; Writing—review & editing. **Igor Tudorache:** Data curation; Validation; Writing—review & editing. **Payam Akhyari:** Data curation; Methodology; Project administration; Supervision; Validation; Writing—review & editing. **Udo Boeken:** Conceptualization; Data curation; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing—review & editing. **Artur Lichtenberg:** Conceptualization; Data curation; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing—review & editing.

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