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# Clinical outcomes of HeartMate 3 left ventricular assist device support with a Bridge to Transplant vs a Destination Therapy strategy: a single-centre retrospective cohort

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## Summary

INTRODUCTION: Real-world outcomes with the HeartMate 3 left ventricular assist device (LVAD) depending on whether it's a bridge to transplantation (BTT) or destination therapy (DT) are poorly studied. We aimed to compare the profile and clinical outcomes of patients supported with HeartMate 3 according to a BTT or a DT pre-implantation strategy.

METHODS: All patients consecutively implanted with HeartMate 3 at our centre (University Hospital of Lausanne, Switzerland) in 2015–2022 were analysed in a retrospective observational study. Indications for HeartMate 3 implantation were advanced heart failure despite optimal medical treatment. Patients were treated with a vitamin K antagonist anticoagulant combined with antiplatelet therapy after HeartMate 3 implantation and were followed up monthly at our institution.

RESULTS: Among 71 patients implanted with HeartMate 3 between 2015 and 2022, 51 (71.8%) were implanted as a BTT and 20 (28.2%) as DT. Their median age was 58 (IQR: 52–69) years and 84% of patients were classified as INTERMACS profiles 2–4. The median follow-up duration was 18.3 (IQR: 7.5–33.9) months. Patients in the DT group were older than those in the BTT group ($p < 0.001$) and had more chronic renal failure ($p < 0.001$). They also had a lower 5-year survival rate (mean ± standard error: 87.3 ± 5.6% vs 49.4 ± 15.1%) and more adverse events such as renal dysfunction requiring temporary perioperative dialysis ($p = 0.08$) or bleeding ($p = 0.06$).

CONCLUSION: Although patients supported with HeartMate 3 have favourable survival, those with LVAD-DT have poorer outcomes. There is a need to better select patients eligible for LVAD-DT in order to limit the burden of adverse events and improve their prognosis.

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## Introduction

Heart failure (HF) is a common disease in developed countries with a prevalence of around 1–2% in adults [1–3]. Most HF patients progress to advanced HF and face a significant risk of mortality if treatment is only pharmacological. The use of left ventricular assist devices (LVADs) has transformed the management of advanced HF by offering two primary indications: bridge to transplantation (BTT) and destination therapy (DT) [4]. As a BTT, an LVAD provides temporary mechanical circulatory support to patients enabling them to maintain haemodynamic stability, improve peripheral organ function and enhance functional capacity while awaiting the availability of a suitable donor organ. As part of DT, the device is a long-term treatment option for patients who are not eligible for heart transplantation.

The HeartMate 3 LVAD (Abbott, Abbott Park, IL, USA) has significantly advanced the field of left ventricular assist device therapy using a continuous-flow centrifugal pump with a fully magnetically levitated rotor, wide blood flow passages and an intrinsic pseudopulse (which reduces blood stasis in the pump without generating noticeable pulsed pressure in the arterial circulation) [5]. This resulted in a significantly improved haemocompatibility profile, reducing complications such as pump thrombosis, stroke and bleeding compared to previous LVAD generations [6]. In the French-speaking part of Switzerland, an algorithm has been established for the care of advanced HF patients in need of long-term mechanical support [7]. Understanding the real-world results and implications of using the Heart-

**ABBREVIATIONS**

| | |
|---|---|
| **BTT** | bridge to transplantation |
| **DT** | destination therapy |
| **ECLS** | extracorporeal life support |
| **LVAD** | left ventricular assist device |
| **RV** | right ventricle |

Mate 3 device as a BTT or DT is essential to optimise patient selection and improve clinical decision-making.

We aimed to compare the profile and clinical outcomes of patients supported with a HeartMate 3 device in our institution according to a BTT or DT pre-implantation strategy.

## Methods

### Population

We evaluated, through an exploratory and retrospective observational study, all consecutive patients implanted with a HeartMate 3 LVAD at our centre (University Hospital of Lausanne, Switzerland) between November 2015 and October 2022. Patients supported during the same period with other implantable VADs such as Abbott HeartMate 2 (n = 2, implanted as isolated right ventricular [RV] assist device) were not included. No patients were excluded from the analysis. Indications for HeartMate 3 implantation have been described previously [7]. Briefly, patients with New York Heart Association (NYHA) class IIIB or IV symptoms with an ejection fraction ≤25% and a cardiac index ≤2.2 l/min/$m^2$ without inotropic support despite optimal medical management, or inotrope-dependent patients, or listed for heart transplant according to the recommendations of the International Society for Heart Lung Transplantation [8] were eligible. The DT programme at our institution was started in June 2017. Depending on transplant eligibility at the time of LVAD support, each patient was assigned to a pre-implantation strategy: BTT or DT. Patients with possible eligibility for transplantation (bridge to candidacy, n = 2) were analysed in the BTT group.

### Surgical technique

Immediately prior to HeartMate 3 implantation, transoesophageal echocardiography was always performed to exclude the presence of coexisting conditions requiring additional surgical procedure: moderate to severe aortic regurgitation, severe tricuspid regurgitation, patent foramen ovale, atrial septal defect or thrombus in the left ventricle after myocardial infarction. Valvular replacement with a bioprosthesis was performed in patients with a mechanical aortic prosthesis, whereas mechanical prostheses in mitral position were retained.

Surgical techniques have already been described [9]. Briefly, three different surgical approaches were used: “median sternotomy”, “double mini-thoracotomy” and “left thoracotomy”. In “median sternotomy” (the default approach) or “double mini-thoracotomy” (accessed through a left anterior mini-thoracotomy and an upper mini-sternotomy) [10], the left ventricular assist device was implanted between the left ventricular apex and the ascending aorta. In “left thoracotomy”, the outflow graft was implanted in the descending thoracic aorta via a left anterolateral thoracotomy [11]. The latter approach was preferred in patients with a history of cardiac surgery (especially coronary artery bypass grafting [CABG]) to avoid a high-risk resternotomy. All implantations were performed with central or peripheral cardiopulmonary bypass. No aortic cross-clamping was used, except in the case of concomitant left-sided cardiac procedures. The apical sewing ring was sutured to the apex of the left ventricle using the “core and sew with back stitch” technique [12]. The driveline was placed using the double tunnelling technique [13] and was stabilised immediately after surgery using the Hollister’s horizontal tube attachment device (Hollister Inc., Libertyville, IL, USA).

In cases of severe postoperative right ventricular dysfunction, a temporary right ventricle support device was installed through a venoarterial extracorporeal life support (ECLS) (venous inflow cannula in the right atrium through a femoral vein and outflow cannula in the main pulmonary artery) [14]. Severe right ventricular dysfunction was defined as a right ventricular failure visually assessed by transoesophageal echocardiography associated with the inability to achieve a stable LVAD output ≥2.5 l/min despite adequate LVAD placement, sufficient volume loading and maximal inotropic and pulmonary vasodilator support.

### Antithrombotic treatment

Anticoagulation with intravenous heparin was started 6–12 h after surgery, with target anti-factor Xa activity of 0.3 to 0.45 IU/ml. Vitamin K antagonist (VKA) therapy was initiated after extubation and removal of chest drains with a target international normalised ratio (INR) of 2–3. In addition, in the absence of bleeding or thrombocytopenia, antiplatelet therapy as aspirin 100 mg/day was systematically added to the anticoagulation when patients were discharged from the intensive care unit. During follow-up, we bridged to low-molecular-weight heparin or unfractionated heparin (if estimated glomerular filtration rate was less than 30 ml/min/1.73 $m^2$) only when patients had an INR <1.8. The combination of vitamin K antagonist therapy and antiplatelet therapy was indicated lifelong in the absence of prohibitive bleeding risk such as the occurrence of a bleeding event leading to hospitalisation, in which case aspirin was definitely discontinued.

### Follow-up

After hospital discharge, patients were followed up every month at our outpatient Heart Failure Clinic by an experienced HF specialist to assess their clinical and biological status. A skin culture was also routinely taken from the driveline exit site at each visit. Driveline dressings were renewed three times per week in accordance with our local protocol.

### Data collection and outcomes

Baseline characteristics, intra- and peri-operative data, and clinical outcomes including follow-up data were retrospectively collected in a local database by reviewing patients’ electronic medical files. Data integrity was verified secondarily by one of the study investigators. Preoperative clinical profiles were established for each patient according to INTERMACS definitions [15] and assessed in the 24 hours prior to HeartMate 3 implantation. Patients with acute cardiogenic shock stabilised by venoarterial ECLS with recovery of peripheral organ function were classified as INTERMACS class 2. Outpatients treated with repeated (monthly) elective levosimendan infusions (administered at a dose of 0.1 µg/kg/min over 24 hours) were classified as INTERMACS class 4. Adverse events were reported as per the definitions of the Mechanical Circulatory Support Aca-

demic Research Consortium [16]. Postoperative infections were defined as VAD-specific or VAD-related in accordance with previous definitions [17]. Driveline infection was defined by the presence of drainage or inflammation around the driveline exit site associated with a positive culture. This study was conducted with the approval of the local ethics committee (CER Number 2019-00697).

### Statistical analysis

All patients were analysed within their initially assigned groups (BTT or DT) although three patients shifted from BTT to DT during follow-up because of contraindications to heart transplantation that emerged after LVAD implantation, namely refusal of heart transplantation, diagnosis of lung cancer and onset of a depressive syndrome. No crossovers were observed from DT to BTT. Categorical variables are presented as counts (percentages) and continuous variables as medians (interquartile ranges [IQR]). Comparisons between qualitative variables were made using the chi-square or Fisher's exact test, as appropriate. Continuous variables were compared using a Wilcoxon rank-sum test. Patient survival rates were estimated by the Kaplan-Meier method with its 95% confidence interval (CI). For patient survival estimates on HeartMate 3 support, patients were censored at the time of LVAD explantation (heart transplantation [n = 29] or device weaning [n = 1]) or at the date of last follow-up. Statistical comparisons of survival rates between the DT and BTT groups were not carried out due to the wide disparity between the two groups. All tests were 2-sided and conducted at a 0.05 level of significance. Statistical analyses were performed using SPSS BASE 17.0 statistical software (SPSS Inc., Chicago, IL, USA).

## Results

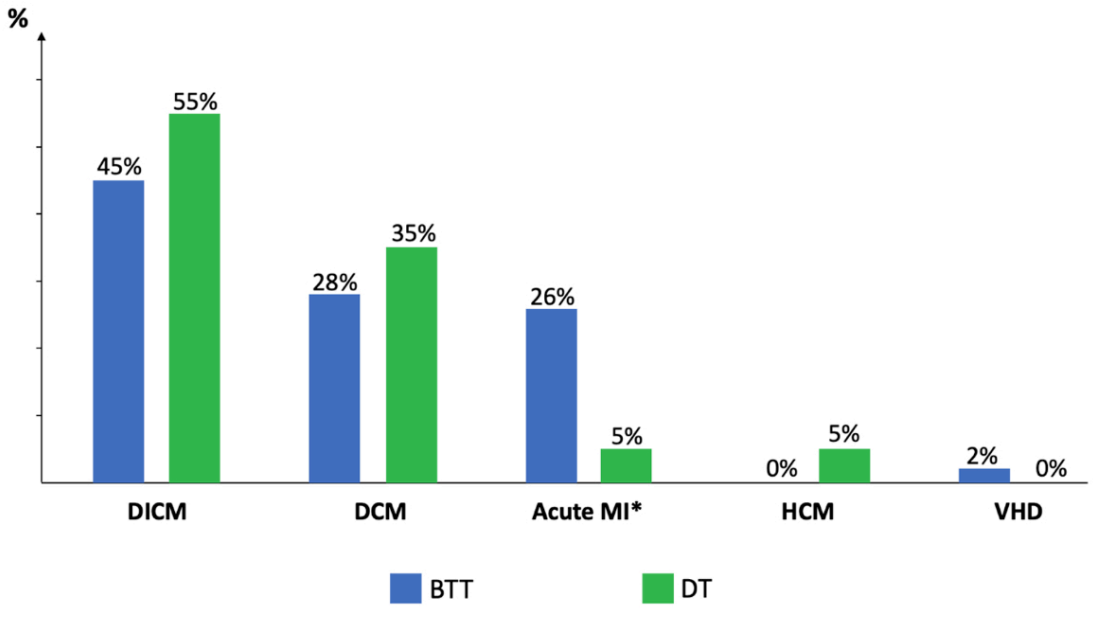
### Pre-implantation population characteristics

We included a total of 71 HeartMate 3 patients: 51 (71.8%) were implanted as BTT and 20 (28.2%) as DT. The main reasons for DT were age ≥70 years in 17/20 (85%) patients, and chronic obstructive pulmonary disease, polyvascular disease and neurological conditions in the three others. Primary causes of heart failure by study group are shown in figure 1. The most common cause of heart failure was dilated ischaemic cardiomyopathy in 48% of patients, followed by primary dilated cardiomyopathy in 30% and recent acute myocardial infarction in 20%. There was a trend towards a higher frequency of recent acute myocardial infarction in the BTT patients than in DT patients (26% vs 5%, p = 0.09).

Baseline clinical characteristics of the study population are displayed in table 1. The median age was 58 (52–69) yearsand 63 (89%) patients were men**.** Patients in the BTT group were younger than those in the DT group (53 [47–60] years vs 71 [69–74] years, p <0.001). A total of 10 (14%) patients had a history of cardiac surgery, including coronary artery bypass grafting (n = 7, one with associated mitral annuloplasty), mechanical mitral valve replacement (n = 2) and mechanical aortic valve replacement (n = 1). Before implantation, 60 (84%) patients were classified as INTERMACS profiles 2–4, without differences between groups.

Baseline haemodynamics, laboratory and pre-implantation support data of the study population are listed in table 1. Median left ventricular ejection fraction, end-diastolic diameter and cardiac index were, respectively, 22 (17–28)%, 66 (59–70) mm and 2.2 (1.9–2.5) l/m$^2$/min. Patients in the BTT group had lower pulmonary vascular resistance than those in the DT group (2.2 [1.6–3.8] WU vs 2.4 [1.4–3.0]

**Figure 1:** Primary causes of heart failure by study group. Proportions of patients are expressed as percentages for each study group (blue bar for bridge to transplantation [BTT] and green bar for destination therapy [DT]). Comparisons between groups: Acute MI* (p = 0.09); DICM (p = 0.60); DCM (p = 0.57). DCM: dilated cardiomyopathy; DICM: dilated ischaemic cardiomyopathy; HCM: hypertrophic cardiomyopathy; MI: myocardial infarction; VHD: valvular heart disease. * myocardial infarction <3 months.



WU, p = 0.02). Most patients had chronic renal failure and 20 (28.2%) had creatinine levels ≥150 µmol/l. Patients in the DT group had more advanced chronic renal failure than those in the BTT group, as shown by higher creatinine values (respectively, 162 [139–193] µmol/l vs 107 [88–131] µmol/l, p <0.001) and urea values (respectively, 13 [9–17] mmol/l vs 7 [5–11] mmol/l, p <0.001). Hepatic cholestasis and/or hepatitis (defined as total bilirubin, aspartate aminotransferase or alanine transaminase values ≥3 upper limit of normal) was present in 29 (40.8%) patients, with lower alanine transaminase values in the DT group (34 [23–89] U/l vs 22 [17–36] U/l, p = 0.009). Regarding pre-implantation support, no difference was observed between groups.

### Intraoperative data

Intraoperative data are presented in table 2. Most patients (n = 60, 84%) were implanted by median sternotomy, four (6%) underwent a left anterolateral thoracotomy and seven (10%) were implanted by double mini-thoracotomy. The median cardiopulmonary bypass time was 64 (56–81) minutes and aortic crossclamp was performed in four patients because of concomitant cardiac procedures (aortic valve replacement in three and outflow graft anastomosis in one). There was no difference in intraoperative data between groups.

### Outcomes

#### *Patient survival*

The median follow-up duration was 18.3 months (IQR: 7.5–33.9 months). Among the 71 patients included, 13 (18.3%) died, 5/51 (9.8%) in the BTT group and 8/20 (40%) in the DT group. The overall patient survival rates on HeartMate 3 support were (mean ± standard error): 89.4 ± 3.8% [95% CI: 78.9–94.8%] at 1-year and 86.8 ± 4.5% [95% CI: 74.9–93.3%] at 2-year follow-up (figure 2). In the BTT group, patient survival rates at 1-year and 2-year were 91.3 ± 4.2% [95% CI: 78.2–96.7%] and 87.3 ± 5.6% [95% CI: 71–94.8%] respectively. In the DT group, patient survival rates at 1-year and 2-year were similar at 84.7 ± 8.1% [95% CI: 59.7–94.8%]. At 5-year follow-up, pa-

**Table 1:**
Baseline characteristics of the study population. Categorical variables are presented as counts (percentages) and continuous variables as medians (interquartile ranges).

| | | | All patients | Bridge to transplantation | Destination therapy | p value |
|---|---|---|---|---|---|---|
| | | | **n = 71** | **n = 51** | **n = 20** | |
| Clinical characteristics | Age in years | | 58 (52–69) | 53 (47–60) | 71 (69–74) | **<0.001** |
| | Male sex | | 63 (89%) | 47 (92%) | 16 (80%) | 0.21 |
| | Body surface area, in $m^2$ | | 2.0 (1.8–2.1) | 2.0 (1.8–2.1) | 1.9 (1.8–2.1) | 0.42 |
| | Diabetes mellitus | | 18 (25%) | 14 (28%) | 4 (20%) | 0.76 |
| | History of stroke | | 11 (16%) | 6 (12%) | 5 (25%) | 0.28 |
| | Previous cardiac surgery | | 10 (14%) | 6 (12%) | 4 (20%) | 0.45 |
| | INTERMACS profiles | | | | | 0.90 |
| | | 1 | 9 (13%) | 7 (14%) | 2 (10%) | |
| | | 2 | 14 (20%) | 10 (20%) | 4 (20%) | |
| | | 3 | 21 (29%) | 14 (27%) | 7 (35%) | |
| | | 4 | 25 (35%) | 18 (35%) | 7 (35%) | |
| | | 5 | 2 (3%) | 2 (4%) | 0 | |
| Haemodynamics | LVEF, in % | | 22 (17–28) | 22 (16–29) | 22 (18–28) | 0.27 |
| | LVEDD, in mm | | *[n = 61/71]:* 66 (59–70) | *[n = 42/51]:* 65 (58–70) | *[n = 19/20]:* 69 (63–71) | 0.30 |
| | MAP, in mm Hg | | *[n = 50/71]:* 79 (68–88) | *[n = 37/51]:* 72 (66–85) | *[n = 13/20]:* 87 (77–95) | 0.17 |
| | CVP, in mm Hg | | *[n = 47/71]:* 10 (6–12) | *[n = 31/51]:* 11 (7–12) | *[n = 16/20]:* 8 (6–12) | 0.79 |
| | PCWP, in mm Hg | | *[n = 54/71]:* 23 (19–32) | *[n = 37/51]:* 25 (19–32) | *[n = 17/20]:* 22 (17–32) | 0.57 |
| | PVR, in Woods units | | *[n = 54/71]:* 2.4 (1.5–3.0) | *[n = 37/51]:* 2.4 (1.4–3.0) | *[n = 17/20]:* 2.2 (1.6–3.8) | **0.02** |
| | CI, in l/$m^2$/min | | *[n = 54/71]:* 2.2 (1.9–2.5) | *[n = 37/51]:* 2.2 (1.9–2.7) | *[n = 17/20]:* 2.2 (1.8–2.3) | 0.65 |
| Laboratory | Sodium, in mmol/l | | 139 (136–141) | 139 (136–141) | 138 (131–140) | 0.59 |
| | Creatinine, in µmol/l | | 116 (95–160) | 107 (88–131) | 162 (139–193) | **<0.001** |
| | Blood urea nitrogen, in mmol/l | | *[n = 70/71]:* 9 (6–13) | *[n = 50/51]:* 7 (5–11) | *[n = 20/20]:* 13 (9–17) | **<0.001** |
| | White blood cell count, in $10^9$/l | | 7.8 (6.2–10.4) | 8.1 (6.5–10.5) | 6.6 (6.0–10.3) | 0.14 |
| | Platelet count, in $10^9$/l | | 218 (166–262) | 222 (178–269) | 192 (149–255) | 0.20 |
| | Haematocrit, in % | | 35 (31–40) | 35 (32–40) | 33 (29–40) | 0.31 |
| | Total bilirubin, in µmol/l | | *[n = 70/71]:* 12 (9–19) | *[n = 50/51]:* 13 (9–21) | *[n = 20/20]:* 11 (8–16) | 0.39 |
| | Aspartate aminotransferase, in U/l | | 28 (19–54) | 27 (19–60) | 29 (18–43) | 0.40 |
| | Alanine transaminase, in U/l | | 31 (21–69) | 34 (23–89) | 22 (17–36) | **0.009** |
| | Albumin, in g/l | | *[n = 65/71]:* 36 (29–41) | *[n = 46/51]:* 36 (31–41) | *[n = 19/20]:* 35 (26–40) | 0.32 |
| | Lactates, in mmol/l | | *[n = 70/71]:* 1.1 (1.0–1.5) | *[n = 50/51]:* 1.1 (1.0–1.9) | *[n = 20/20]:* 1.0 (1.0–1.2) | 0.17 |
| Pre-implantation support | In intensive care unit | | 25 (35%) | 20 (39%) | 5 (25%) | 0.29 |
| | Preoperative mechanical ventilation | | 16 (23%) | 13 (26%) | 3 (15%) | 0.53 |
| | Preoperative MCS | IABP | 5 (7%) | 5 (10%) | 0 | 0.31 |
| | | ECLS / CentriMag | 10 (14%) | 9 (18%) | 1 (5%) | 0.26 |
| | Haemofiltration / dialysis | | 8 (11%) | 4 (8%) | 4 (20%) | 0.21 |

CI: cardiac index; CVP: central venous pressure; ECLS: extracorporeal life support; IABP: intra-aortic balloon pump; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MAP: mean arterial pressure; MCS: mechanical circulatory support; PCWP: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance.

tients in the BTT group had numerically better survival on HeartMate 3 support than those in the DT group [87.3 ± 5.6% (95% CI: 71–94.8%) vs 49.4 ± 15.1% (95% CI: 19.2–74%)] (figure 3).

A total of 30 (42.2%) patients underwent LVAD explantation: 29 (41%) had heart transplantation and one (1.4%) had device weaning for recovery from peripartum cardiomyopathy. The overall median duration of postoperative mechanical ventilation was 3 (1–3) days without difference between groups. Patients in the BTT group tended to have a shorter intensive care unit stay (6 [4–18] days vs 13 [5–40] days, p = 0.09) and a shorter mean hospital stay (29 [22–66] days vs 69 [25–113] days, p = 0.05).

*Adverse events*

Adverse events observed during support are listed in table 3. We did not identify any cases of pump thrombosis or technical malfunction during follow-up.

A temporary right ventricle support device was implanted in a quarter of patients during the initial left ventricular as-

**Figure 2:** Overall estimates of patient survival after HeartMate 3 left ventricular assist device (LVAD) implantation.

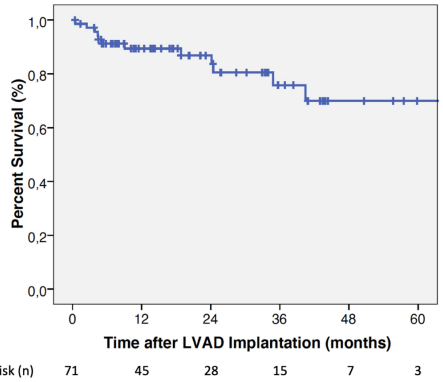



**Table 2:**
Intraoperative data. Categorical variables are presented as counts (percentages) and continuous variables as medians (interquartile ranges).

| | | All patients | Bridge to transplantation | Destination therapy | p value |
|---|---|---|---|---|---|
| | | n = 71 | n = 51 | n = 20 | |
| Incision | Median sternotomy | 60 (84%) | 43 (84%) | 17 (85%) | >0.99 |
| | Left thoracotomy | 4 (6%) | 2 (4%) | 2 (10%) | 0.31 |
| | Double mini-thoracotomy | 7 (10%) | 6 (12%) | 1 (5%) | 0.66 |
| | CPB time, in min | 64 (56–81) | 62 (54–78) | 71 (57–88) | 0.18 |
| | Aortic crossclamp | 4 (6%) | 3 (6%) | 1 (5%) | >0.99 |
| | Duration of aortic crossclamp, in min | 41 (29–55) | 45 (33–55) | 36 (–) | >0.99 |
| Left ventricular assist device outflow | Ascending aorta | 67 (94%) | 49 (96%) | 18 (90%) | 0.31 |
| | Descending thoracic aorta | 4 (6%) | 2 (4%) | 2 (10%) | – |
| Concomitant cardiac procedures | AV replacement | 3 (4%) | 2 (4%) | 1 (5%) | >0.99 |
| | Perioperative ASD closure | 4 (6%) | 3 (6%) | 1 (5%) | >0.99 |

ASD: atrial septal defect; AV: aortic valve; CPB: cardiopulmonary bypass.

**Table 3:**
Adverse events observed during mechanical circulatory support. Categorical variables are presented as counts (percentages) and continuous variables as medians (interquartile ranges).

| | | | All patients | Bridge to transplantation | Destination therapy | p value |
|---|---|---|---|---|---|---|
| | | | n = 71 | n = 51 | n = 20 | |
| RVAD support | Temporary RVAD support | | 18 (25%) | 10 (20%) | 8 (40%) | 0.13 |
| | – Duration of RVAD support, in days | | 8 (6–9) | 8 (4–9) | 7 (6–8) | 0.34 |
| | Durable RVAD support | | 0 | 0 | 0 | – |
| Renal dysfunction requiring temporary dialysis | | | 12 (17%) | 6 (12%) | 6 (30%) | 0.08 |
| Pump thrombosis | | | 0 | 0 | 0 | – |
| Technical malfunction | | | 0 | 0 | 0 | – |
| Bleeding | Any bleeding event *[/ patient/year]* | | 35 (50%) *[0.27]* | 21 (42%) *[0.24]* | 14 (70%) *[0.30]* | 0.06 |
| | Bleeding requiring surgery | | 23 (32%) | 14 (28%) | 9 (45%) | 0.17 |
| | GI bleeding *[/patient/year]* | | 14 (20%) *[0.11]* | 8 (16%) *[0.09]* | 6 (30%) *[0.13]* | 0.20 |
| Infection | VAD-specific *[/patient/year]* | | 50 (70%) *[0.38]* | 36 (71%) *[0.41]* | 14 (70%) *[0.31]* | 0.45 |
| | | Driveline culture >0 | 48 (68%) | 34 (67%) | 14 (70%) | – |
| | | Driveline surgical | 10 (14%) | 6 (12%) | 4 (20%) | – |
| | | Pump | 2 (3%) | 2 (4%) | 0 | – |
| | VAD-related (mediastinitis) | | 4 (6%) | 2 (4%) | 2 (10%) | 0.31 |
| Neurological complications | TIA / Ischaemic stroke *[/patient/year]* | | 8 (12%) *[0.06]* | 4 (8%) *[0.05]* | 4 (22%) *[0.09]* | 0.19 |
| | Disabling ischaemic stroke | | 1 (1.4%) | 1 (2%) | 0 | – |
| | Ischaemic stroke-related death | | 1 (1.4%) | 1 (2%) | 0 | – |
| | Haemorrhagic stroke | | 0 | 0 | 0 | – |
| | Post-traumatic IC bleeding *[/patient/year]* | | 2 (3%) *[0.02]* | 0 *[0]* | 2 (10%) *[0.04]* | 0.08 |

GI: gastrointestinal; IC: intracranial; RVAD: right ventricular assist device; TIA: transient ischaemic attack; VAD: ventricular assist device.

sist device implantation procedure. The need for right ventricle support tended to be higher in the DT group with 8 out of 20 patients (40%) requiring support compared to 10 out of 51 patients (20%) in the BTT group (p = 0.13). All patients who received temporary right ventricle support were successfully weaned after a median support time of 8 (6–9) days without any differences between groups, and none of them required a permanent RV device. No instance of severe right ventricle dysfunction was observed during the follow-up period.

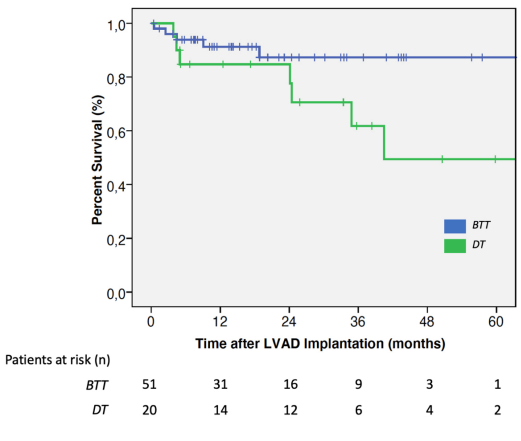
A total of 12 patients (17%) required immediate postoperative dialysis. Patients in the DT group tended to have more perioperative renal dysfunction requiring dialysis than those in the BTT group (12% vs 30%, p = 0.08). All patients were weaned off dialysis prior to hospital discharge.

Bleeding complications were observed in half of patients and predominantly occurred during the perioperative period. A total of 23 (32%) patients required surgical re-exploration, which confirmed that bleeds were related neither to the inflow or outflow sutures nor to the pump connections. Non-surgical bleeding occurred in 12 (16.9%) patients and were mainly of gastrointestinal origin (n = 9/12, 75%). Patients in the DT group displayed a higher tendency for bleeding complications compared to those in the BTT group (70% vs 42% p = 0.06).

A VAD-specific infection was diagnosed in 50 (70%) patients: 48/50 (96%) had a driveline infection and 2/50 (4%) had a pump infection confirmed by surgical or percutaneous CT-guided drainage. Among patients with driveline infection, 38 (79.2%) were successfully treated using local wound care and culture-directed antibiotic therapy, while 10 (20.8%) required surgical debridement and relocation of the driveline exit site. The two patients with a pump infection were placed on the emergency transplantation list and ultimately underwent successful transplantation, without post-transplant mediastinal infections. There were no differences between groups regarding infection-related adverse events.

Ischaemic neurological complications (stroke or transient ischaemic attack) occurred in 8 (12%) of the study population, including one patient with a fatal ischaemic stroke in the BTT group. No spontaneous haemorrhagic stroke occurred. The rate of neurological complications was similar in both groups.

**Figure 3:** Estimates of patient survival after HeartMate 3 LVAD implantation by study group. BTT: bridge to transplantation; DT: destination therapy; LVAD: left ventricular assist device.




## Discussion

The main results of this study are: (1) Patients with advanced heart failure supported with a HeartMate 3 LVAD device had a favourable 2-year patient survival rate; (2) Adverse events remain high, mainly due to driveline infections and bleeding; and (3) Patients with LVAD-DT experience worse outcomes and more adverse events than those with LVAD-BTT.

We reported our 7-year experience with the HeartMate 3 LVAD used as BTT or DT through a single-centre study. Despite a retrospective observational design, all patients were consecutively included and were representative of real-world conditions. Indeed, our population study shares comparable characteristics at baseline to those of previously published studies, with a clear majority (84%) having a pre-implant INTERMACS clinical profile of 2–4. This is in line with the ELEVATE registry [18] and the CE Mark study [19], in which 88% and 92% of patients, respectively, were in the same INTERMACS class. Post-implantation patient survival rates in our population were 89.4% at 1-year and 86.8% at 2-year follow-up. These results are quite favourable and comparable to patient survival observed in the MOMENTUM 3 trial (86.6% and 79% in the HeartMate 3 group at 1- and 2-year follow-up, respectively) (20), the CE Mark study (81% and 74% at 1- and 2-year follow-up, respectively) (19) and the ELEVATE registry (83.4% at 2-year follow-up) [18].

Although we observed satisfactory patient survival, the incidence of adverse events remained substantial. Infection-related adverse events were frequent with 70% of patients experiencing VAD-specific infections. Primarily related to driveline infections, this highlights the importance of rigorous exit site care and meticulous hygiene practices to prevent this adverse event. However, the majority of these infections were successfully treated using local wound care and culture-directed antibiotic therapy, emphasising the benefits of early detection and aggressive management of driveline infections. The development of durable and exclusively internal heart pumps, eliminating the need for a driveline, would be a major step forward in this regard. Bleeding complications were also common with half of the patients experiencing bleeding events, mostly during the perioperative period. Bleeding risk remains a major clinical challenge after HeartMate 3 LVAD implantation, notably because of the high risk of gastrointestinal bleeding during follow-up [6, 18, 19]. While the aetiology of bleeding complications associated with left ventricular assist device is acknowledged to be multifactorial, the combined use of and antiplatelet agents is a well-known risk factor. This antithrombotic regimen continues to be recommended [21] even for state-of-the-art devices such as the HeartMate 3, despite advances in device engineering lowering the risk of pump thrombosis and improving haemocompatibility profiles compared with axial-flow pumps [20]. Nevertheless, the recent ARIES-HM3 trial [22] showed that in patients with advanced heart failure supported with HeartMate 3 LVAD and anticoagulated with a vitamin K antagonist, the placebo was noninferior to daily aspirin with respect to the composite endpoint of bleeding and throm-

botic events at 1 year. It therefore seems reasonable to assume that the optimal antithrombotic treatment regimen in HeartMate 3 patients should be based on anticoagulation alone. This is more so true for HeartMate 3 LVAD patients with advanced heart failure due to cardiomyopathy of non-ischaemic origin. In addition, some small observational studies have shown that the use of a direct oral anticoagulant appears to be safe and could reduce the risk of bleeding compared with vitamin K antagonists in left ventricular assist device patients [23, 24]. Nevertheless, in the absence of a randomised controlled phase 3 trial, the standard of care remains vitamin K antagonists. The results of the ongoing DOAC LVAD Phase 2 study [25] will provide further information on the safety and feasibility of anticoagulant therapy with apixaban in HeartMate 3 patients. Notably, we have not identified any cases of pump thrombosis or technical malfunction during follow-up, suggesting the reliability and durability of the HeartMate 3 LVAD.

Regarding outcomes, the BTT group showed higher patient survival rates at 5-year follow-up than the DT group. Given that a pre-transplant continuous-flow mechanical circulatory support strategy with subsequent orthotopic heart transplantation provides post-transplant outcomes not different to those of direct heart transplantation [26], HeartMate 3 implantation as bridge to transplantation is a valid option in this high-risk population. We also observed a disparity between the two study groups in terms of the occurrence of adverse events: patients in the DT group experienced a higher incidence of adverse events than patients in the BTT group, which is consistent with other published data [27]. This difference may be attributed to the fact that patients in the BTT group are generally in a relatively better clinical state at the time of LVAD implantation, as they are considered suitable candidates for heart transplantation. In contrast, patients in the DT group have a more complex clinical profile characterised by older age, a higher prevalence of comorbidities and a more advanced stage of heart failure. These factors predispose them to poorer outcomes than patients implanted as bridge to transplantation. Indeed, clinical frailty has been associated with prolonged time to extubation, extended hospital stays and increased long-term mortality in LVAD implantation when compared to non-frail individuals [28]. The challenge is to optimise the selection of patients with a pre-implantation destination therapy strategy by limiting LVAD implantation to those whose comorbidities and frailty could improve after LVAD haemodynamic restoration. As previously reported by Cain et al. [29], it is necessary to identify two types of frailty in LVAD-DT eligible patients: the "LVAD-responsive frailty", which may improve with ventricular assistance and does not represent a barrier to LVAD implantation, and "LVAD-independent frailty", which may persist despite LVAD implantation and for which this procedure should be avoided.

## Limitations

The main limitations of this hypothesis-generating study are the relatively small sample size and its retrospective observational design. Therefore, the results of statistical analyses should be interpreted with caution. By definition, there is a misbalance favouring patient survival on HeartMate 3 support in the BTT group over the DT group, related to the competing risk of heart transplantation (exposure to HeartMate 3 support was lower for patients in the BTT group than for those in the DT group). All implant procedures were exclusively conducted at a single institution, potentially impacting the generalisability of our findings and their susceptibility to institutional biases.

## Conclusion

Although HeartMate 3 LVAD demonstrates favourable survival in patients with advanced heart failure, patients with LVAD-DT have a poorer prognosis compared to those with LVAD-BTT. A careful selection of patients eligible for an LVAD-DT and diligent post-implantation management are essential to improve outcomes and limit the occurrence of adverse events which remain high in this population.

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**References**

1. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. Heart. 2007 Sep;93(9):1137–46. doi: http://dx.doi.org/10.1136/hrt.2003.025270.
2. Roger VL. Epidemiology of heart failure. Circ Res. 2013 Aug;113(6):646–59. doi: http://dx.doi.org/10.1161/CIRCRESAHA.113.300268.
3. Smeets M, Vaes B, Mamouris P, Van Den Akker M, Van Pottelbergh G, Goderis G, et al. Burden of heart failure in Flemish general practices: a registry-based study in the Intego database. BMJ Open. 2019 Jan;9(1):e022972. doi: http://dx.doi.org/10.1136/bmjopen-2018-022972.
4. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al.; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep;42(36):3599–726. doi: http://dx.doi.org/10.1093/eurheartj/ehab368.
5. Pinney SP, Anyanwu AC, Lala A, Teuteberg JJ, Uriel N, Mehra MR. Left Ventricular Assist Devices for Lifelong Support. J Am Coll Cardiol. 2017 Jun;69(23):2845–61. doi: http://dx.doi.org/10.1016/j.jacc.2017.04.031.
6. Mehra MR, Goldstein DJ, Cleveland JC, Cowger JA, Hall S, Salerno CT, et al. Five-Year Outcomes in Patients With Fully Magnetically Levitated vs Axial-Flow Left Ventricular Assist Devices in the MOMENTUM 3 Randomized Trial. JAMA. 2022 Sep;328(12):1233–42. doi: http://dx.doi.org/10.1001/jama.2022.16197.
7. Hullin R, Meyer P, Yerly P, Kirsch M. Cardiac Surgery in Advanced Heart Failure. J Clin Med. 2022 Jan;11(3):773. doi: http://dx.doi.org/10.3390/jcm11030773.
8. Mehra MR, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA, et al.; International Society for Heart Lung Transplantation (ISHLT) Infectious Diseases, Pediatric and Heart Failure and Transplantation Councils. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. J Heart Lung Transplant. 2016 Jan;35(1):1–23. doi: http://dx.doi.org/10.1016/j.healun.2015.10.023.
9. Nowacka A, Hullin R, Tozzi P, Barras N, Regamey J, Yerly P, et al. Short-term single-centre experience with the HeartMate 3 left ventricular assist device for advanced heart failure. Eur J Cardiothorac Surg. 2020 Sep;58(3):511–8. doi: http://dx.doi.org/10.1093/ejcts/ezaa075.
10. Schmitto JD, Molitoris U, Haverich A, Strueber M. Implantation of a centrifugal pump as a left ventricular assist device through a novel, minimized approach: upper hemisternotomy combined with anterolateral thoracotomy. J Thorac Cardiovasc Surg. 2012 Feb;143(2):511–3. doi: http://dx.doi.org/10.1016/j.jtcvs.2011.07.046.
11. Pfister R, Tozzi P, Hullin R, Yerly P, Jahns FP, Prêtre R et al. HeartMate 3 implantation via left antero-lateral thoracotomy to avoid resternotomy

in high risk patients. Multimed Man Cardiothorac Surg. 2018 Apr;2018 doi: http://dx.doi.org/10.1510/mmcts.2018.026.
12. Hanke JS, Krabatsch T, Rojas SV, Deniz E, Ismail I, Martens A, et al. In Vitro Evaluation of Inflow Cannula Fixation Techniques in Left Ventricular Assist Device Surgery. Artif Organs. 2017 Mar;41(3):272–5. doi: http://dx.doi.org/10.1111/aor.12735.
13. Schibilsky D, Benk C, Haller C, Berchtold-Herz M, Siepe M, Beyersdorf F, et al. Double tunnel technique for the LVAD driveline: improved management regarding driveline infections. J Artif Organs. 2012 Mar;15(1):44–8. doi: http://dx.doi.org/10.1007/s10047-011-0607-3.
14. Lenoir M, Quessard A, N'guyen A, Kirsch M. Simplified temporary right ventricular support after implantation of a left ventricular assist device. Heart Surg Forum. 2013 Jun;16(3):E152–4. doi: http://dx.doi.org/10.1532/HSF98.20131003.
15. Stevenson LW, Pagani FD, Young JB, Jessup M, Miller L, Kormos RL, et al. INTERMACS profiles of advanced heart failure: the current picture. J Heart Lung Transplant. 2009 Jun;28(6):535–41. doi: http://dx.doi.org/10.1016/j.healun.2009.02.015.
16. Kormos RL, Antonides CF, Goldstein DJ, Cowger JA, Starling RC, Kirklin JK, et al. Updated definitions of adverse events for trials and registries of mechanical circulatory support: A consensus statement of the mechanical circulatory support academic research consortium. J Heart Lung Transplant. 2020 Aug;39(8):735–50. doi: http://dx.doi.org/10.1016/j.healun.2020.03.010.
17. Hannan MM, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR, et al.; International Society for Heart and Lung Transplantation. Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. J Heart Lung Transplant. 2011 Apr;30(4):375–84. doi: http://dx.doi.org/10.1016/j.healun.2011.01.717.
18. Zimpfer D, Gustafsson F, Potapov E, Pya Y, Schmitto J, Berchtold-Herz M, et al. Two-year outcome after implantation of a full magnetically levitated left ventricular assist device: results from the ELEVATE Registry. Eur Heart J. 2020 Oct;41(39):3801–9. doi: http://dx.doi.org/10.1093/eurheartj/ehaa639.
19. Schmitto JD, Pya Y, Zimpfer D, Krabatsch T, Garbade J, Rao V, et al. Long-term evaluation of a fully magnetically levitated circulatory support device for advanced heart failure-two-year results from the HeartMate 3 CE Mark Study. Eur J Heart Fail. 2019 Jan;21(1):90–7. doi: http://dx.doi.org/10.1002/ejhf.1284.
20. Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, et al.; MOMENTUM 3 Investigators. A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. N Engl J Med. 2019 Apr;380(17):1618–27. doi: http://dx.doi.org/10.1056/NEJMoa1900486.
21. Saeed D, Feldman D, Banayosy AE, Birks E, Blume E, Cowger J, et al. The 2023 International Society for Heart and Lung Transplantation Guidelines for Mechanical Circulatory Support: A 10- Year Update. J Heart Lung Transplant. 2023 Jul;42(7):e1–222. doi: http://dx.doi.org/10.1016/j.healun.2022.12.004.
22. Mehra MR, Netuka I, Uriel N, Katz JN, Pagani FD, Jorde UP, et al.; ARIES-HM3 Investigators. Aspirin and Hemocompatibility Events With a Left Ventricular Assist Device in Advanced Heart Failure: The ARIES-HM3 Randomized Clinical Trial. JAMA. 2023 Dec;330(22):2171–81. doi: http://dx.doi.org/10.1001/jama.2023.23204.
23. Meredith T, Schnegg B, Hayward C. The use of direct oral anticoagulants in patients with ventricular assist devices: is there hope for Factor Xa inhibition? Artif Organs. 2021 May;45(5):E123–9. doi: http://dx.doi.org/10.1111/aor.13848.
24. Whitehouse KR, Avula D, Kahlon T, Costelle D, Dunbar-Matos C, Pahwa S, et al. Apixaban: Alternative Anticoagulation for HeartMate 3 Ventricular Assist Device. ASAIO J. 2022 Mar;68(3):318–22. doi: http://dx.doi.org/10.1097/MAT.0000000000001650.
25. Dimond M, Looby M, Shah B, Sinha SS, Isseh I, Rollins AT, et al. Design and Rationale for the Direct Oral Anticoagulant Apixaban in Left Ventricular Assist Devices (DOAC LVAD) Study. J Card Fail. 2023 Nov;S1071-9164(23)00863-1
26. Hullin R, Abdurashidova T, Pitta-Gros B, Schukraft S, Rancati V, Lu H, et al. Post-transplant survival with pre-transplant durable continuous-flow mechanical circulatory support in a Swiss cohort of heart transplant recipients. Swiss Med Wkly. 2023 Dec;153(12):3500. doi: http://dx.doi.org/10.57187/s.3500.
27. Goldstein DJ, Naka Y, Horstmanshof D, Ravichandran AK, Schroder J, Ransom J, et al. Association of Clinical Outcomes With Left Ventricular Assist Device Use by Bridge to Transplant or Destination Therapy Intent: The Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3 (MOMENTUM 3) Randomized Clinical Trial. JAMA Cardiol. 2020 Apr;5(4):411–9. doi: http://dx.doi.org/10.1001/jamacardio.2019.5323.
28. Tse G, Gong M, Wong SH, Wu WK, Bazoukis G, Lampropoulos K, et al.; International Health Informatics Study (IHIS) Network. Frailty and Clinical Outcomes in Advanced Heart Failure Patients Undergoing Left Ventricular Assist Device Implantation: A Systematic Review and Meta-analysis. J Am Med Dir Assoc. 2018 Mar;19(3):255–261.e1. doi: http://dx.doi.org/10.1016/j.jamda.2017.09.022.
29. Cain MT, Firstenberg MS, Cleveland JC Jr. Heart Transplant and Ventricular Assist: Cardiac Surgery and Heart Failure Perspective. US Cardiol. 2021 Sep;15:e16. doi: http://dx.doi.org/10.15420/usc.2021.11.