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Clinical outcome in patients with end-stage heart failure who underwent continuous-flow left ventricular assist devices in a single center

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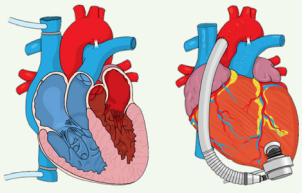
Patients



50 Chronic end-stage heart failure
continuous flow left ventricular assist device (cf-LVAD)

BTT (Bridge to transplantation)	BTC (Bridge to candidacy)	DT (Destination therapy)
28	2	20

Outcomes

In-hospital mortality	0%
All-cause mortality	22%
Cause of death Hemorrhagic stroke	27%
Post-LVAD complication Major bleeding	44%
Re-hospitalization Gastrointestinal bleeding	76%

Conclusion

With creditable survival and adverse event rates, our results support the use of LVAD for bridge to transplantation and destination therapy.

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Background/Aims: The continuous flow left ventricular assist device (cf-LVAD) has improved the survival of chronic end-stage heart failure (HF) patients. Here we describe our clinical experience of the initial 50 LVAD patients from a single center.
Methods: A total of 50 patients underwent LVAD implantation as bridge to transplantation (BTT; n = 28, 56%), bridge to candidacy (BTC; n = 2, 4%), or as destination therapy (DT; n = 20, 40%) from 2012 to 2019. Pre-implant characteristics and clinical outcomes were compared between BTT/BTC and DT.
Results: The median age of patients was 67 years (range, 59 to 73). Men were more likely to receive LVAD (76% vs. 24%) than women. DT patients were older, had smaller body surface area, and worse laboratory profiles than BTT/BTC patients. There was no in-hospital mortality. During an average of 14 months (range, 8 to 23), the all-cause mortality was 22%. The first-year survival was 86 and 90% in BTT/BTC and DT groups, respectively. Hemorrhagic stroke was the most common cause (27%) of death. In the BTT/BTC group, 22 patients successfully underwent heart transplantation during median duration of 10 months (range, 7 to 14). The most common post-LVAD complication during the first year of LVAD implantation was major bleeding (44%). A significant proportion (76%) of patients experienced rehospitalization with gastrointestinal bleeding as the most common cause.
Conclusions: We describe short-term clinical outcome of LVAD patients from a single center for the first time in Korea. With the newer generation LVAD and a dedicated team approach, improved clinical outcomes of LVAD for end-stage HF are expected.

Keywords: Ventricular assist device; Left ventricular assist device; Heart failure

INTRODUCTION

End-stage heart failure (HF) patients are a steeply increasing burden in Korea [1,2]. Heart transplantation (HTx) is the treatment of choice in end-stage HF, however, only a limited number of patients undergo HTx due to strict eligibility criteria and a shortage of donors [1,3-5]. According to the latest annual report from the Korean Network for Organ Sharing, the median wait time was 50 months before receiving HTx [6]. For end-stage HF patients who are not eligible for HTx or are not expected to survive the waiting time because of severe cardiac dysfunction, continuous flow left ventricular assist devices (cf-LVADs) have been shown to increase survival for those who undergo LVAD as bridge to transplant (BTT) or destination therapy (DT) [7]. For patients who undergo LVAD as BTT, LVAD treatment has improved the survival time to HTx, facilitated better use of donor organs, and enhanced post-HTx survivals [8,9]. As the device has become more durable and portable, LVAD implantation as DT is increasing and recent trials have shown better functional capacity and quality of life in DT patients when compared to patients with other medical treatment [10,11].

In Korea, after the first few successful cases [12,13], the cases of LVAD implantation are increasing since the approval system for reimbursement under the national health insurance has been introduced for LVAD in October, 2018. Considering the rapidly growing volume of LVAD implantation patients in Korea, we aimed to describe the clinical outcomes of the initial 50 cases from a single center.

METHODS

Study population

This study was a retrospective analysis using data from a single center registry. A total of 50 end-stage HF patients who remained symptomatic despite medical therapy underwent cf-LVAD implantations at Samsung Medical Center from August 2012 to December 2019 (Fig. 1). Informed consent was received from all relevant and the study was approved by the Institutional Review Board of Samsung Medical Center (No. 2017-08-044 and No. 2017-08-167). All patients were followed up until death, HTx, or the censor date, August 2020.

The criteria for LVAD implantation were in accordance with the current LVAD reimbursement indications, which are based on the patient selection criteria from previous LVAD trials (Supplementary Table 1) [14-16]. The HeartWare Ventricular Assist Device (HVAD) pump (HW; Heartware, Framingham, MA, USA) was implanted in 17 (34%)

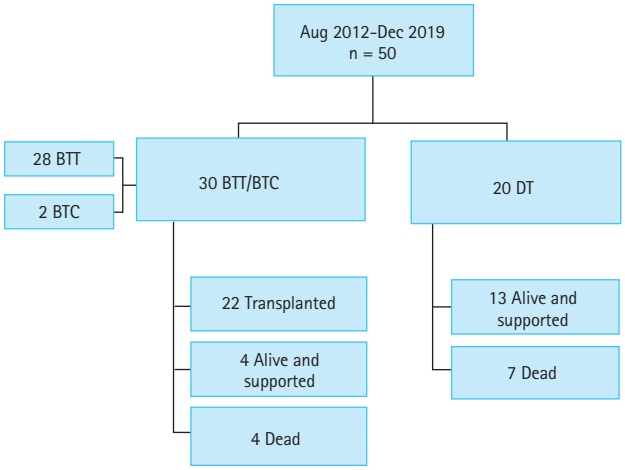

Figure 1. Study population. From August 2012 to December 2019, 50 consecutive patients were enrolled. Patients were divided by implant strategy: bridge to transplantation/bridge to candidacy (BTT/BTC) as a group and destination therapy (DT). Depicted are the outcomes at the point of follow-up (August 2020).

patients, while HeartMate II (HMII; Thoratec, Pleasanton, CA, USA) was implanted in 33 (66%) patients. Patients were categorized by the intention for LVAD implantation (BTT/bridge to candidacy [BTC]: n = 30 [60%] vs. DT: n = 20 [40%]). In subanalysis, patients were divided by the period before and after reimbursement initiation by the national insurance, which took place on October, 2018. Detailed information on patient demographics, preoperative risk factors, laboratory parameters, hemodynamic measurements including echocardiography and cardiac catheterization, as well as preoperative risk factors were compared. All patients were maintained on aspirin and warfarin treatment unless contraindicated by serious bleeding.

Multidisciplinary team

All patients underwent comprehensive assessment by a multidisciplinary team to determine indications for LVAD therapy. Our LVAD team maintains a high level of interaction through constant communication and consists of: cardiologists and cardiac surgeons specializing in HF, cardiac intensivist, nurse specialists including device coordinator, staff nurses of the cardiac and cardiothoracic surgical intensive care unit, perfusionist, cardiac rehabilitation team, pharmacist, psychologist, and social service worker. Family dynamics and support as well as medical, socioeconomic condition were carefully evaluated before surgery. After discharge, patients were provided advice and physician contact when needed through a 24/7 hotline by nurse specialists.

Definitions and outcomes

Definitions of associated comorbidities and major adverse outcome are described in Supplementary Table 2 [17-26]. All definitions were in accordance with the International Society for Heart and Lung Transplantation (ISHLT) Mechanically Assisted Circulatory Support (IMACS) registry and previous studies [17-21,27]. Major adverse events included major bleeding, cardiac arrhythmia, device thrombosis, hemolysis, hepatic dysfunction, major infection, neurologic dysfunction, renal dysfunction, respiratory dysfunction, and right heart failure (RHF) (Supplementary Table 2). Infections were also categorized according to the ISHLT standard definition of infection in LVAD patients [26]. All-cause mortality, major adverse events, and rehospitalizations after LVAD implantation were analyzed.

Statistical analysis

Categorical variables are expressed as percent (frequency) and continuous variables as median (interquartile range [IQR]). Comparisons of continuous and categorical data between groups were performed using unpaired *t* tests and Fisher exact tests, respectively. The Kaplan-Meier method and log-rank test were used for time-to-event analysis. Statistical significance was considered at a $p < 0.05$. Statistical analysis was performed using SPSS version 26 (IBM Co., Armonk, NY, USA).

RESULTS

Baseline characteristics

Median follow-up was 14 months (IQR, 8 to 23). Clinical characteristics, laboratory, and hemodynamic findings are shown in Table 1. The median patient age was 67 years (IQR, 59 to 73) and 76% were men. The etiology of end-stage HF was ischemic heart disease in 28 (56%) patients, and 16 (32%) patients had prior history of cardiac surgery. Upon LVAD implantation, 86% had New York Heart Association (NYHA) class IV HF symptoms and 60% patients were at the level of Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile three (60%). When compared according to intention of LVAD implantation, the DT group had a significantly smaller body surface

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Table 1. Baseline characteristics at LVAD implantation by implant strategy

Variable	Total (n = 50)	DT (n = 20)	BTT/BTC (n = 30)	*p* value
Clinical characteristics				
Age, yr	67.0 (59.0–73.3)	75.0 (72.3–77.0)	62.0 (50.5–66.3)	< 0.001
Male sex	38 (76.0)	14 (70.0)	24 (80.0)	0.506
Body mass index, kg/m^2	23.0 (21.2–24.7)	23.1 (21.0–24.6)	22.8 (21.5–25.0)	0.994
Body surface area, m^2	1.7 (1.6–1.9)	1.7 (1.5–1.7)	1.8 (1.6–1.9)	0.015
Severe diabetes mellitus	15 (30.0)	8 (40.0)	7 (23.3)	0.208
Chronic renal disease	23 (46.0)	10 (50.0)	13 (43.3)	0.643
COPD	11 (22.0)	7 (35.0)	4 (13.3)	0.090
Major stroke	10 (20.0)	4 (20.0)	6 (20.0)	1.000
Peripheral vascular disease	1 (2.0)	0	1 (3.3)	1.000
Prior cardiac surgery	16 (32.0)	7 (35.0)	9 (30.0)	0.710
Ischemic heart disease	28 (56.0)	11 (55.0)	17 (56.6)	0.907
INTERMACS profile				0.658
Critical cardiogenic shock	2 (4.0)	1 (5.0)	1 (3.3)	1.000
Progressive decline	15 (30.0)	6 (30.0)	9 (30.0)	1.000
Stable but inotrope-dependent	30 (60.0)	13 (65.0)	17 (56.6)	0.556
Resting symptoms	3 (6.0)	0	3 (10.0)	0.265
LV ejection fraction	22.5 (18.2–26.4)	19.7 (15.6–26.7)	22.6 (19.5–26.5)	0.136
> 50%	0	0	0	-
40%–49%	0	0	0	-
30%–39%	7 (14.0)	5 (25.0)	2 (6.6)	0.100
20%–29%	25 (50.0)	8 (40.0)	17 (56.6)	0.248
< 20%	18 (36.0)	7 (35.0)	11 (36.6)	0.904
LV end-diastolic diameter, cm	6.7 (6.2–7.5)	6.6 (6.2–7.2)	6.9 (6.2–7.7)	0.504
NYHA class				
III	7 (14.0)	4 (20.0)	3 (10.0)	0.416
IV	43 (86.0)	16 (80.0)	27 (90.0)	0.416
Laboratory				
Hemoglobin, g/dL	10.7 (9.4–12.7)	10.8 (9.3–12.4)	10.7 (9.4–12.8)	1.000
White blood cell count, × 1,000/μL	7.5 (5.7–8.7)	7.1 (6.5–8.4)	7.5 (5.6–8.9)	0.937
Platelets, × 1,000/μL	152.0 (92.8–216.5)	138.5 (74.3–188.8)	161.5 (97.8–230.8)	0.221
eGFR[a], mL/min	46.8 (31.4-72.5)	36.9 (27.8-71.1)	49.3 (31.6-79.9)	0.259
Albumin, g/dL	3.5 (3.0–3.9)	3.4 (2.8–3.7)	3.8 (3.3–4.1)	0.012
ALT, μ/L	25.5 (16.8–61.3)	27.5 (18.0–112.3)	24.0 (15.0–47.3)	0.259
AST, μ/L	29.5 (21.8–61.3)	30.5 (24.0–71.8)	29.5 (19.8–61.3)	0.445
Total bilirubin, mg/dL	1.5 (0.9–2.6)	1.5 (0.9–2.5)	1.3 (0.8–2.7)	0.758
INR	1.2 (1.1–1.4)	1.3 (1.2–1.4)	1.2 (1.0–1.4)	0.145
Sodium, mmol/L	135.0 (130.0–138.0)	134.5 (131.0–137.8)	135.0 (128.0–138.0)	0.319
hsCRP, mg/L	12.6 (3.5–35.1)	34.0 (6.3–56.6)	10.9 (2.6–22.2)	0.016
NT-proBNP, pg/mL	8,459 (4,923–17,109)	10,729 (5,487–21,709)	8,179 (3,756–15,194)	0.143

Table 1. Continued

Variable	Total (n = 50)	DT (n = 20)	BTT/BTC (n = 30)	*p* value
Preoperative				
ECMO bridged	11 (22.0)	3 (15.0)	8 (26.6)	0.489
Dialysis	15 (30.0)	5 (25.0)	10 (33.3)	0.529
IABP	1 (2.0)	0	1 (3.3)	1.000
Ventilator	15 (30.0)	4 (20.0)	11 (36.6)	0.208
Hemodynamic				
Mean RA pressure, mmHg	11.0 (8.0–16.0)	11.5 (8.0–15.0)	12.0 (7.5–16.0)	0.940
Mean PA pressure, mmHg	38.0 (31.0–43.0)	37.0 (31.0–42.8)	39.0 (31.5–44.0)	0.377
Mean PWP, mmHg	26.0 (20.0–30.3)	22.5 (17.3–28.3)	28.0 (23.5–32.0)	0.053
Cardiac output, L/min	3.4 (2.7–4.0)	3.1 (2.5–3.6)	3.5 (2.8–4.2)	0.108
Medications				
ARB or ARNI	32 (64.0)	12 (60.0)	20 (66.6)	0.630
ACE inhibitor	16 (32.0)	7 (35.0)	9 (30.0)	0.710
Amiodarone	29 (58.0)	13 (65.0)	16 (53.3)	0.413
Beta blocker	27 (54.0)	10 (50.0)	17 (56.6)	0.643
Aldosterone antagonist	48 (96.0)	19 (95.0)	29 (96.6)	1.000
Ivabradine	12 (24.0)	4 (20.0)	8 (26.6)	0.740
Loop diuretics	49 (98.0)	19 (95.0)	30 (100)	0.400
Phosphodiesterase inhibitors	23 (46.0)	7 (35.0)	16 (53.3)	0.203
ICD	13 (26.0)	6 (30.0)	7 (23.3)	0.599
CRT	9 (18.0)	2 (10.0)	7 (23.3)	0.285
Device type				
HeartMate II™	17 (34.0)	7 (35.0)	10 (33.3)	0.903
HVAD™	33 (66.0)	13 (65.0)	20 (66.6)	0.903

Values are presented as median (interquartile range) or number (%).
LVAD, left ventricular assist device; DT, destination therapy; BTT/BTC, bridge to transplantation/bridge to candidacy; COPD, chronic obstructive pulmonary disease; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LV, left ventricle; NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; hsCRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal-pro hormone B-type natriuretic peptide; ECMO, Extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; RA, right atrium; PA, pulmonary artery; PWP, pulmonary wedge pressure; ARB, angiotensin II receptor blocker; ARNI, Angiotensin receptor-neprilysin inhibitor; ACE, angiotensin-converting enzyme; ICD, implantable cardioverter-defibrillator; CRT, cardiac resynchronization therapy.
[a]eGFR was calculated by Cockcroft-Gault method.

area ($p = 0.015$) and more advanced age ($p < 0.001$), which was a critical point for determining treatment strategy. As expected, patients in the DT group were associated with a higher prevalence of comorbidities. Laboratory findings were also worse in the DT group, such as lower albumin, blood urea nitrogen, and higher high-sensitivity C-reactive protein levels. Preoperative status, hemodynamic studies, echocardiographic finding, and preoperative medications were comparable between BTT/BTC and DT groups.

We performed a comparison of baseline characteristics according to sex (Supplementary Table 3) and implantation period (pre- vs. post-reimbursement) (Supplementary Table 4). Women had a significantly smaller body surface area, lower cardiac output, lower sodium, and higher N-terminal-pro hormone B-type natriuretic peptide (NT-proBNP) levels compared to men. Due to a small body surface area,

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Table 2. Cause of death after LVAD implantation (n = 11)

Cause of death	No. (%)
Hemorrhagic stroke	3 (27.3)
VAD-related infection	1 (9.1)
Right heart failure	1 (9.1)
Cancer	1 (9.1)
Other chronic illness	1 (9.1)
Sudden unexplained death	2 (18.2)
Suicide	1 (9.1)
Trauma or accident	1 (9.1)

LVAD, left ventricular assist device; VAD, ventricular assist device.

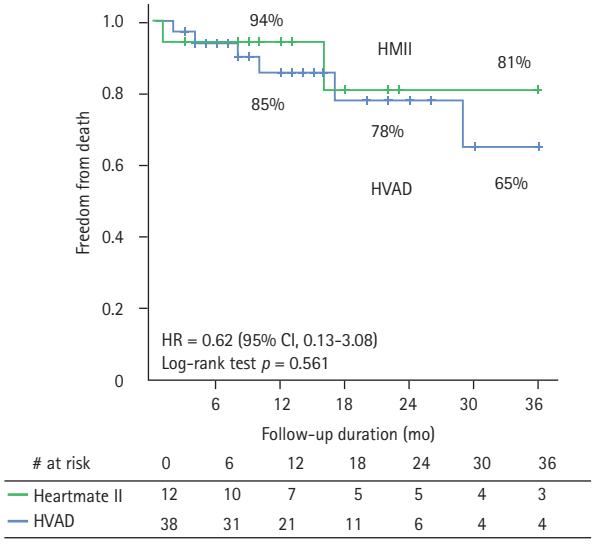

Figure 2. Overall survival stratified by implanted device. Survivals were similar between devices. Hazard ratios (HR) and 95% confidence intervals (CI) are shown for mortality with HeartMate II (HMII) compared to HeartWare Ventricular Assist Device (HVAD).

all women underwent HVAD implantation, while 55% of men had implanted HVAD. In our cohort, 23 (46%) patients underwent LVAD implantation at the pre-reimbursement period. Compared to patients after reimbursement, those who received LVAD before reimbursement were significantly older, and had a lower mean pulmonary wedge pressure. More patients evaluated at NYHA class III underwent LVAD implantation in the pre-reimbursement period when compared to the post-reimbursement period.

All-cause mortality and adverse outcomes

There was no in-hospital mortality after LVAD implantation in the initial 50 LVAD patient cohort. The median hospital stay after implantation was 44 days (IQR, 28 to 66). A total of 11 patients died during follow-up. The causes of mortality are described in Table 2. The most common cause was hemorrhagic stroke (n = 3, 27%).

Overall survival stratified by implanted device is depicted in Fig. 2. There was no significant difference in overall survival according to device type, even when grouped by intention of implantation (Fig. 3). Of the 30 patients who underwent LVAD as BTT/BTC, 22 (73.3%) underwent HTx in a median of 10 months (IQR, 7 to 14). Estimates for receiving HTx were 46% at 12 months and 80% at 24 months. In the DT group, the median survival time was 22 months (IQR, 13 to 37).

Fig. 4 summarizes the benefit and risk of LVAD implanted patients at the first year of LVAD implantation. The most common adverse event during the first year was major bleeding (44%) and stroke (28%), followed by VAD-associated infection (28%). Among major bleeding events, gastrointestinal (GI) bleeding was the most common, followed by surgical site bleeding. Supplementary Table 5 shows comparisons of hemocompatibility-associated adverse events between HeartMate II (n = 17, 34%) vs. HVAD (n = 33, 66%) devices. Similar to previous studies, patients implanted with the HeartMate II device had similar rates of stroke or bleeding compared with those with the HVAD device (Supplementary Table 5). Among ventricular assist device (VAD)-associated infections, VAD-specific infection (18%) was the most common. There was one case of device malfunction due to alleged pump failure, which resulted in device exchange. RHF after surgery occurred in 22% of patients, one-third of which required right ventricular assist device (RVAD) insertion (8%).

Rehospitalizations

A total of 38 (76%) and 42 (84%) patients experienced rehospitalization within the first year of LVAD implantation and during follow-up, respectively. The most common cause of rehospitalization was GI bleeding. Time to rehospitalization or rehospitalization rates did not differ between the groups receiving HeartMate II versus HVAD or for patients with DT or BTT/BTC designations (Supplementary Table 6).

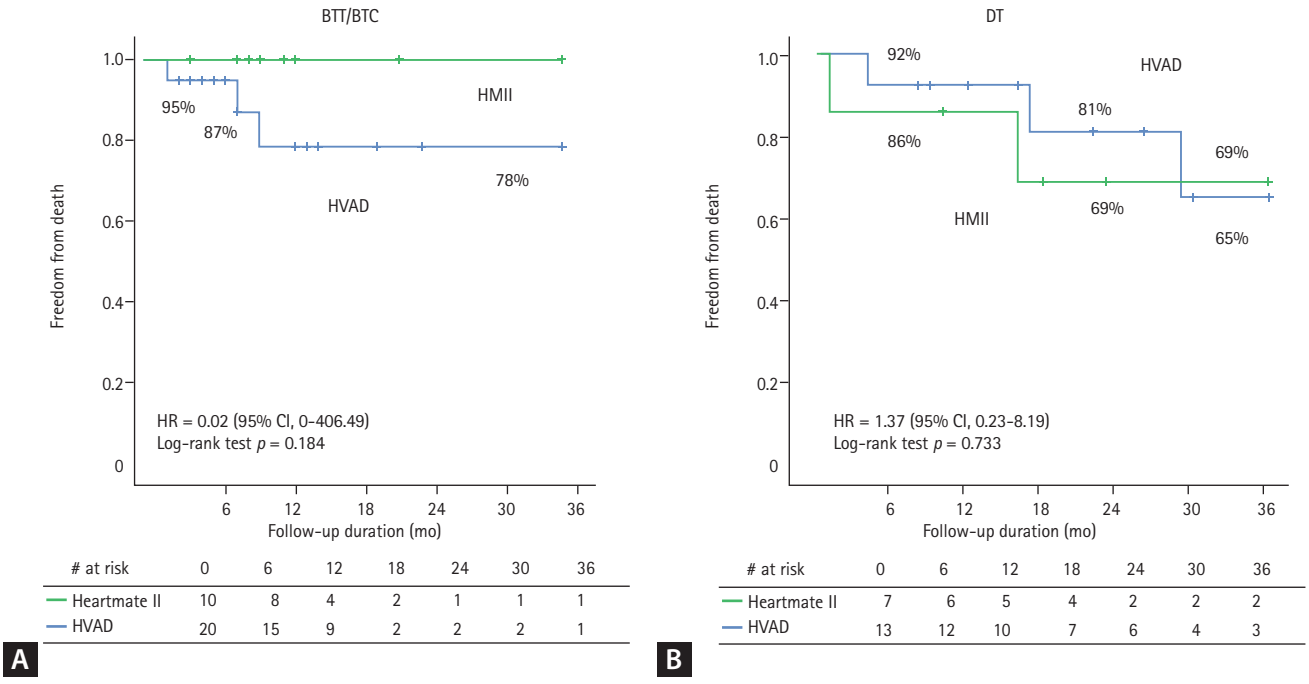

Figure 3. Overall survival for bridge to transplantation (BTT) and destination therapy (DT) patients stratified by implanted device. In both (A) BTT/bridge to candidacy (BTC) and (B) DT patients, survivals were similar between devices. HMII, HeartMate II; HVAD, HeartWare Ventricular Assist Device.

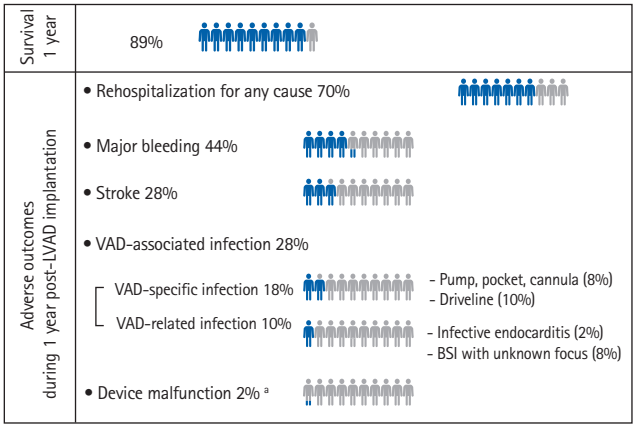

Figure 4. Survival and adverse outcomes at 1 year after left ventricular assist device (LVAD) implantation. Overall survival and predefined adverse outcomes at 1 year are shown. VAD, ventricular assist device; BSI, blood stream infection. [a]A case of pump failure.

Subgroup clinical outcome analysis stratified by sex

Supplementary Table 7 describes clinical outcomes after LVAD implantation according to sex. All-cause mortality (Supplementary Fig. 1) and adverse events after LVAD implantation was similar in both sexes, but a significantly higher RHF was noted after surgery in women.

Subgroup clinical outcome analysis stratified by LVAD implant period (pre- vs. post-reimbursement)

Supplementary Table 8 describes the clinical outcomes after LVAD implantation according LVAD implantation periods (pre- vs. post reimbursement period). Patients who had underwent LVAD implantation in the pre-reimbursement period had a higher rate of RHF after surgery. However, all-cause mortality was similar between groups (Supplementary Fig. 2).

DISCUSSION

In this article, we summarized clinical outcomes of the initial 50 cases of cf-LVAD implantation from a single center for the first time in Korea. Survival of all LVAD patients was 89% at 1 year. In BTT/BTC patients, survival was 86% in 1 and 2 years post LVAD implantation. In DT patients, survival was 90 and 77% in 1 and 2 years post LVAD implantation,

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respectively. The most common cause of death was hemorrhagic stroke and 76% patients experienced rehospitalization during the first year after being discharged with LVAD implantation. The most common adverse event during the first year was major bleeding.

In our cohort, 94% patients were in the INTERMACS profile range of 1 to 3. According to the recent IMACS registry, 85% of implants were in patients in INTERMACS profile 1 to 3 [27], which reflects the lack of sufficient endorsement by clinicians in ambulatory HF patients considering the burden of adverse events. In our cohort, 44% of patients received LVAD as DT. In the IMACS registry, 70% patients underwent LVAD as DT [28]. With improvement of durability, safety profile, and outcomes, patients undergoing LVAD implantation as DT are increasing due to limited donors for HTx and an increasing number of end-staged HF patients. In our center, we are also experiencing increasing LVAD implantation as DT cases, amounting to a similar number to that of our BTT cases.

Implantation of cf-LVAD is a safe and effective treatment strategy for patients with end-stage HF who are refractory to medical therapy. In the United States, survival among all CF-VAD patients is currently 81% and 70% at 1 and 2 years post LVAD implantation, respectively [29]. In our cohort, survival showed similar results: 89% and 79% at 1 and 2 years post LVAD implantation, respectively. Survival rates were similar in BTT/BTC and DT patients. In the DT population, despite the advanced age and higher comorbidities that contraindicate them for HT, long-term outcomes were still satisfactory with 77% overall survival at 2 years, which is similar to the outcomes of recent IMACS registry [27]. In our cohort, survival without disabling stroke or reoperation of DT patients was 64% at 2 years (Supplementary Fig. 3), while in previously reported data from HVAD and HeartMate II trials, 46% to 59% of patients were able to achieve survival without disabling stroke or reoperation at 2 years [30-32]. In this analysis, patients were implanted with either HeartMate II or HVAD devices. Results from Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3 (MOMENTUM 3) demonstrated superiority of the HeartMate 3 device compared with HeartMate II, including a significant reduction in disabling stroke and hemocompatibility-associated adverse events, such as pump thrombosis, stroke of any type or severity, and nonsurgical bleeding [33]. The HeartMate 3 cohort recently achieved a 79% rate of survival without disabling stroke or reoperation at 2 years, owing to a significantly reduced stroke and pump thrombosis burden. With the recent approval of the HeartMate 3 device in Korea, outcomes are expected to improve as well in Korea.

Consistent with the previous IMACS registry, the most common cause of death from our cohort was hemorrhagic stroke [27]. Stroke incidence were similar between HeartMate II and HVAD (32.1% vs. 31.8%). This is consistent with the early results from The HeartWare Ventricular Assist System as Destination Therapy of Advanced Heart Failure (ENDURANCE II) trial reporting similar stroke rates between HVAD and HeartMate II devices, as long as blood pressure is well controlled [34]. Major bleeding was the most common adverse event in the first year of LVAD implantation and GI bleeding was the most common bleeding event, consistent with previous reports. Among VAD-associated infections (n = 14), superficial driveline infection was the most common focus (n = 4, 28.6%). A significant proportion of patients (76%) experienced rehospitalization at the first year after LVAD implantation. This was comparable to readmission rates in other registries, which were reported to be approximately 55% to 81% [35-37]. In our cohort, the most common cause of readmission was GI bleeding (n = 4, 9.5%). High rates of rehospitalization remain to be profound clinical and economic considerations in LVAD patients, which is expected to be improved with HeartMate 3.

Notably, women were unlikely to receive LVAD compared to men and baseline NT-proBNP was significantly higher than men at the time of LVAD implantation. Due to smaller body size, all women underwent HVAD implantation. Women experienced significantly more RHF after LVAD implantation. LVAD implantation at relatively more severe HF in women, as well as smaller chamber size may increase risk of RHF in women due to increased vulnerability to pressure changes with the LVAD.

Limitations

This study is the result of a small number of patients from a single center and carries the innate limitations of observational data. The small number of patients in our study limited statistically significant multivariable analysis. However, our results are meaningful considering this registry data reports early experience from a leading center in Korea. Our data could be used to help make decisions for end-stage HF patients and their physician, especially in the era where

LVAD implantation as DT is increasing worldwide. As the number of LVAD cases are rapidly increasing, our results could contribute to increasing evidence of clinical benefit from LVAD implantation in Korea. A multi-center national LVAD registry is strongly needed to provide information for quality control/improvement after LVAD implantation and to provide prognostic information for long term clinical outcome of LVAD patients in Korea.

KEY MESSAGE

1. This is the first domestic report on 50 cases of continuous flow left ventricular assist device (cf-LVAD) implantations from a single center in Korea.
2. With creditable survival and adverse event rates, our results support the use of LVAD for bridge to transplantation and destination therapy.
3. With the newer generation LVAD and a dedicated team approach, clinical outcomes of LVAD for end-stage heart failure could be improved.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Table 1. Criteria for LVAD implantation in Korea

Indications	1. Bridge to transplantation (BTT) in end-stage heart failure patient registered as a heart transplantation candidate 2. End-stage heart failure patient ineligible for heart transplantation and has severe symptoms > 2 months despite medication including beta blockers or mechanical circulatory devices such as IABP and ECMO, and fulfills one or more of the following: a. LVEF < 25% or equivalent evidence of ventricular dysfunction with peak VO_2 < 12 mL/kg/min (14 mL/kg/min in case of beta blocker intolerance) or an equivalent exercise test result b. Unable to discontinue intravenous inotropes c. Progressive renal or hepatic dysfunction caused by heart failure (PCWP ≥ 20 mmHg and either systolic blood pressure ≤ 90 mmHg or cardiac index ≤ 2.0 L/min/m^2)
Contraindications	Contraindications for each case are debated by the official expert panels. 1. End-stage renal disease receiving permanent dialysis therapy 2. Irreversible organ dysfunction of the kidneys, liver, or lung 3. Severe brain damage 4. Sepsis 5. Contraindication to long-term anticoagulation 6. Comorbidity limiting life expectancy such as advanced cancer

LVAD, left ventricular assist device; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; LVEF, left ventricular ejection fraction; VO_2, oxygen consumption; PCWP, pulmonary capillary wedge pressure.

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Supplementary Table 2. Definitions of comorbidities and adverse outcomes [17-26]

	Definition
Comorbidities	
Ischemic heart disease	Significant coronary artery disease, defined as the presence of any epicardial coronary vessels with ≥ 75% stenosis or any history of myocardial infarction or coronary revascularization, accompanied by depressed myocardial contractility
Severe diabetes mellitus	Type 2 diabetes mellitus with hemoglobin A1c ≥ 8.0% or requiring insulin therapy
Chronic renal disease	Kidney damage or glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 for 3 months or more, irrespective of cause
Chronic lung disease	Chronic respiratory symptoms with persistent airflow limitation confirmed by spirometry (post-bronchodilator forced expiratory volume in 1 second [FEV1]/forced vital capacity [FVC] ratio < 0.70)
Peripheral arterial disease	Hypoperfusion symptoms and signs of the lower extremities such as claudication or ischemic wound, accompanied by an ankle-brachial index (ABI) ≤ 0.9 or vascular imaging (e.g., Doppler ultrasonography or invasive and noninvasive angiography)
Major stroke	An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage and persists ≥ 24 hours or until death Ischemic stroke: An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction Hemorrhagic stroke: Rapidly developing clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma, ventricular system, or subarachnoid space
Major adverse events	
Major bleeding	An episode of suspected internal or external bleeding that results in one or more of the following: (a) Death, (b) Reoperation, (c) Hospitalization, (d) Transfusion of red blood cells as follows: If transfusion is selected, then apply the following rules: During first 7 days post-implant: • ≥ 50 kg: ≥ 4U packed red blood cells (PRBC) within any 24-hour period during first 7 days post-implant • < 50 kg: ≥ 20 cc/kg PRBC within any 24-hour period during the first 7 days post-implant After 7 days post-implant*: • Any transfusion of PRBC after 7 days following implant with the investigator recording the number of units given (record number of units given per 24-hour period) Major bleeding: Bleeding occurring > 7 days after implant, events requiring 2 units of packed red blood cells within a 24-hour period, and death from bleeding Note: Hemorrhagic stroke is considered a neurological event and not as a separate bleeding event *Any transfusion of ≥ 2 U PRBC after 7 days following implant will be considered a serious bleed
Cardiac arrhythmia	Any documented arrhythmia that results in clinical compromise (e.g., diminished VAD flow, oliguria, pre-syncope, or syncope) that requires hospitalization or occurs during a hospital stay
Device thrombosis	Device thrombosis is an event in which the pump or its conduits contain a thrombus that results in or could potentially induce circulatory failure Suspected device thrombus is an event in which clinical or mechanical circulatory support device (MCSD) parameters suggest thrombus on the blood contacting components of the pump, cannulae, or grafts. Signs and symptoms should include at least 2 of the 3 following criteria: presence of hemolysis, worsening heart failure or inability to decompress the left ventricle, abnormal pump parameters Confirmed device thrombus is an event in which thrombus is confirmed by sponsor-returned product analysis to be found within the blood contacting surfaces of device inflow cannula or outflow conduit or grafts
Hemolysis	A plasma-free hemoglobin value that is greater than 40 mg/dL, concomitant with a rise in serum LDH above three times the upper limit of normal, in association with clinical signs associated with hemolysis (e.g., anemia, low hematocrit, hyperbilirubinemia) occurring after the first 72 hours post-implant

Supplementary Table 2. Continued

	Definition
Hepatic dysfunction	An increase in any two of the following hepatic laboratory values (total bilirubin, aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) to a level greater than three times the upper limit of normal for the hospital, beyond 14 days post-implant (or if hepatic dysfunction is the primary cause of death)
Major infection	A clinical infection accompanied by pain, fever, drainage and/or leukocytosis that is treated by anti-microbial agents (non-prophylactic). A positive culture from the infected site or organ should be present unless strong clinical evidence indicates the need for treatment despite negative cultures. The general categories of infection are listed below: Localized non-device infection: Infection localized to any organ system or region without evidence of systemic involvement, ascertained by standard clinical methods and either associated with evidence of bacterial, viral, fungal or protozoal infection, and/or requiring empirical treatment Percutaneous site, driveline and/or pocket infection: A positive culture from the skin and/or tissue surrounding the drive line or from the tissue surrounding the external housing of a pump implanted within the body, coupled with the need to treat with antimicrobial therapy, when there is clinical evidence of infection such as pain, fever, drainage, or leukocytosis. Internal pump component, inflow or outflow tract infection: Infection of blood-contacting surfaces of the LVAD documented by positive site culture (Sepsis: Evidence of systemic involvement by infection, manifested by positive blood cultures and/or hypotension) ISHLT standardization of definition of infection in LVAD patients [26] VAD-specific infections: Infections that are specific to patients with VADs, are related to the device hardware, and do not occur in non-VAD patients; for example, pump and cannula infections, pocket infections, and percutaneous driveline infections VAD-related infections: Infections that can also occur in patients who do not have VADs; however, there may be unique considerations in patients with VADs with respect to making the correct diagnosis or determining the cause-and-effect relationship (e.g., mediastinitis and IE) Non-VAD infections: Infections essentially not affected by the presence of the VAD, and are unlikely related to the VAD presence but are included to encourage comprehensive and comparable data recording of all infections in this patient population to facilitate multi-center review
Neurologic dysfunction	Transient ischemic attack: As an acute transient neurological deficit conforming anatomically to arterial distribution cerebral ischemia, which resolves in < 24 hours and is associated with no infarction on brain imaging (head CT performed > 24 hours after symptom onset; or MRI) Ischemic stroke: A new acute neurologic deficit of any duration associated with acute infarction on imaging corresponding anatomically to the clinical deficit, or a clinically covert ischemic stroke seen by surveillance imaging, without clinical findings of stroke or at the time of event recognition. Hemorrhagic stroke: A new acute neurologic deficit attributable to intracranial hemorrhage (ICH), or a clinically covert ICH seen by surveillance imaging, without clinical findings of ICH at the time of event recognition Encephalopathy: Acute new encephalopathy due to hypoxic-ischemic injury (HIE), or other causes, manifest as clinically evident signs or symptoms, or subclinical electrographic seizures found by complete neurological diagnostic evaluation to be attributable to acute global or focal hypoxic, or ischemic brain injury not meeting one of ischemic stroke or ICH events as defined above Seizure of any kind
Renal dysfunction	Acute renal dysfunction: Abnormal kidney function requiring dialysis (including hemofiltration) in subjects who did not require this procedure prior to implant, or a rise in serum creatinine of greater than 3 times baseline or greater than 5 mg/dL sustained for over 48 hours Chronic renal dysfunction: An increase in serum creatinine of 2 mg/dL or greater above baseline, or requirement for hemodialysis sustained for at least 90 days
Respiratory failure	Impairment of respiratory function requiring reintubation, tracheostomy or (the inability to discontinue ventilatory support within 6 days (144 hours) post-VAD implant. This excludes intubation for reoperation or temporary intubation for diagnostic or therapeutic procedures

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Supplementary Table 2. Continued

	Definition
Right heart failure	Symptoms and signs of persistent right ventricular dysfunction requiring RVAD implantation, or requiring inhaled nitric oxide or inotropic therapy for a duration of more than 1 week at any time after LVAD implantation
Device malfunction	Either directly causes or could potentially induce a state of inadequate circulatory support (low cardiac output state) or death. A failure that was iatrogenic or recipient-induced will be classified as an iatrogenic/recipient-induced failure Device failure should be classified according to which components fails as follows: Pump failure (blood contacting components of pump and any motor or other pump actuating mechanism that is housed with the blood contacting components). In the special situation of pump thrombosis, thrombus is documented to be present within the device or its conduits that result in or could potentially induce circulatory failure Non-pump failure (e.g., external pneumatic drive unit, electric power supply unit, batteries, controller, interconnect cable, compliance chamber)

VAD, ventricular assist device; LDH, lactate dehydrogenase; LVAD, left ventricular assist device; ISHLT, International Society for Heart and Lung Transplantation; IE, lactate dehydrogenase; CT, computed tomography; MRI, magnetic resonance imaging; RVAD, right ventricular assist device.

Supplementary Table 3. Baseline characteristics by sex

Variable	Women (n = 12)	Men (n = 38)	*p* value
Clinical			
Age, yr	70.0 (60.5–77.0)	66.5 (57.8–73.0)	0.333
Body mass index, kg/m^2	23.0 (21.7–24.3)	23.0 (20.9–24.9)	0.884
Body surface area, m^2	1.5 (1.4–1.6)	1.8 (1.7–1.9)	< 0.001
Severe diabetes mellitus	3 (25.0)	12 (31.5)	1.000
Chronic renal disease	7 (58.3)	15 (39.4)	0.492
Prior cardiac surgery	2 (16.6)	14 (36.8)	0.292
Ischemic heart disease	6 (50.0)	22 (57.8)	0.631
INTERMACS profile			
Critical cardiogenic shock	0	2 (5.2)	1.000
Progressive decline	4 (33.3)	11 (28.9)	1.000
Stable but inotrope-dependent	8 (66.6)	22 (57.8)	0.740
Resting symptoms	0	3 (7.8)	1.000
LV ejection fraction	20.9 (14.7–27.2)	22.5 (19.2–26.0)	0.401
> 50%	0	0	-
40%–49%	0	0	-
30%–39%	2 (16.6)	5 (13.1)	1.000
20%–29%	7 (58.3)	18 (47.3)	0.508
< 20%	3 (25.0)	15 (39.4)	0.497
LV end-diastolic diameter, cm	6.6 (5.8–7.7)	6.9 (6.2–7.5)	0.417
NYHA class			
III	3 (25.0)	4 (10.5)	0.337
IV	9 (75.0)	34 (89.4)	0.337
Laboratory			
Hemoglobin, g/dL	10.9 (9.6–12.4)	10.3 (9.2–12.8)	0.682
White blood cell count, × 1,000/μL	7.6 (6.7–8.5)	7.3 (5.5–9.1)	0.606
Platelets, × 1,000/μL	197.5 (93.3–235.8)	145.0 (91.5–200.3)	0.499
Blood urea nitrogen, mg/dL	17.3 (14.3–29.1)	24.1 (16.8–47.0)	0.180
Creatinine, mg/dL	1.1 (0.9–1.8)	1.4 (0.9–1.8)	0.683
Albumin, g/dL	3.6 (3.0–4.0)	3.5 (3.0–3.9)	0.977
ALT, μ/L	21.0 (15.8–27.5)	29.5 (16.8–77.3)	0.125
AST, μ/L	27.0 (20.3–29.8)	34.0 (21.8–74.5)	0.270
Total bilirubin, mg/dL	1.5 (0.8–2.8)	1.5 (0.9–2.5)	0.820
INR	1.2 (1.1–1.5)	1.2 (1.1–1.4)	0.514
Sodium, mmol/L	130.5 (128.0–136.3)	135.0 (131.8–139.0)	0.040
hsCRP, mg/L	20.0 (2.8–42.1)	11.7 (4.5–34.2)	0.716
NT-proBNP, pg/mL	17,244 (11,755–35,000)	7,563 (4,255–12,958)	0.002
Preoperative			
ECMO bridged	1 (8.3)	10 (26.3)	0.257
Dialysis	3 (25.0)	12 (31.5)	1.000
IABP	0	1 (2.6)	1.000
Ventilator	2 (16.6)	13 (34.2)	0.304

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Supplementary Table 3. Continued

Variable	Women (n = 12)	Men (n = 38)	*p* value
Hemodynamic			
Mean RA pressure, mmHg	9.0 (4.0–15.0)	12.5 (8.0–16.5)	0.151
Mean PA pressure, mmHg	38.0 (29.0–43.0)	38.5 (31.8–43.3)	0.384
Mean PWP, mmHg	21.0 (16.0–29.0)	27.0 (22.5–31.5)	0.163
Cardiac output, L/min	2.7 (2.5–3.4)	3.5 (2.8–4.2)	0.010
Medications			
ARB or ARNI	9 (75.0)	23 (60.5)	0.497
ACE inhibitor	7 (58.3)	9 (23.6)	0.036
Amiodarone	4 (33.3)	25 (65.7)	0.047
Beta blocker	7 (58.3)	20 (52.6)	0.730
Aldosterone antagonist	12 (100)	36 (94.7)	1.000
Ivabradine	4 (33.3)	8 (21.0)	0.448
Loop diuretics	12 (100)	37 (97.3)	1.000
Phosphodiesterase inhibitors	7 (58.3)	16 (42.1)	0.325
ICD	3 (25.0)	10 (26.3)	1.000
CRT	4 (33.3)	5 (13.1)	0.191
Implant strategy			
BTT/BTC	6 (50.0)	24 (63.2)	0.506
DT	6 (50)	14 (36.8)	0.506
Device type			
Heartmate II™	0	17 (44.7)	0.004
HVAD™	12 (100)	21 (55.2)	0.004

Values are presented as median (interquartile range) or number (%).
INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LV, left ventricle; NYHA, New York Heart Association; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; hsCRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal-pro hormone B-type natriuretic peptide; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; RA, right atrium; PA, pulmonary artery; PWP, pulmonary wedge pressure; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; ACE, angiotensin-converting enzyme; ICD, implantable cardioverter-defibrillator; CRT, cardiac resynchronization therapy; BTT/BTC, bridge to transplantation/bridge to candidacy; DT, destination therapy; HVAD, HeartWare Ventricular Assist Device.

Supplementary Table 4. Baseline characteristics of patients before and after reimbursement

Variable	Pre-reimbursement period[a] (n = 23)	Post-reimbursement period[a] (n = 27)	*p* value
Clinical			
Age, yr	71.0 (64.0–77.0)	63.0 (54.0–72.0)	0.036
Male sex	22.9 (21.2–24.4)	23.6 (21.7–24.8)	0.750
Body mass index, kg/m^2	1.7 (1.6–1.9)	1.7 (1.6–1.9)	0.480
Body surface area, m^2	1.6 ± 0.1	1.7 ± 0.1	0.397
Severe diabetes mellitus	9 (39.1)	6 (22.2)	0.193
Chronic renal disease	9 (39.1)	13 (48.1)	0.662
Prior cardiac surgery	10 (43.4)	6 (22.2)	0.108
Ischemic heart disease	14 (60.8)	14 (51.8)	0.522
INTERMACS profile			
Critical cardiogenic shock	2 (8.6)	0	0.207
Progressive decline	7 (30.4)	8 (29.6)	0.951
Stable but inotrope-dependent	14 (60.8)	16 (59.2)	0.908
Resting symptoms	0	3 (11.1)	0.240
LV ejection fraction	22.5 (19.7–27.0)	22.5 (15.0–26.0)	0.225
> 50%	0	0	-
40%–49%	0	0	-
30%–39%	4 (17.3)	3 (11.1)	0.689
20%–29%	12 (52.1)	13 (48.1)	0.777
< 20%	7 (30.4)	11 (40.7)	0.449
LV end-diastolic diameter, cm	6.9 (5.9–7.7)	6.6 (6.3–7.4)	0.368
NYHA class			
III	6 (26.0)	1 (3.7)	0.039
IV	17 (73.9)	26 (96.2)	0.039
Laboratory			
Hemoglobin, g/dL	10.1 (9.4–11.9)	11.8 (9.2–13.3)	0.164
White blood cell count, × 1,000/μL	6.8 (5.2–8.7)	7.8 (6.4–8.9)	0.754
Platelets, × 1,000/μL	119.0 (93.0–197.0)	160.0 (90.0–229.0)	0.373
Blood urea nitrogen, mg/dL	29.3 (17.3–53.4)	17.7 (15.2–30.1)	0.075
Creatinine, mg/dL	1.4 (0.9–2.0)	1.2 (0.9–1.6)	0.496
Albumin, g/dL	3.4 (2.9–3.9)	3.6 (3.3–4.0)	0.221
ALT, μ/L	21.0 (16.0–48.0)	28.0 (17.0–90.0)	0.447
AST, μ/L	28.0 (24.0–61.0)	30.0 (21.0–62.0)	0.838
Total bilirubin, mg/dL	1.4 (0.9–2.8)	1.5 (0.8–2.2)	0.612
INR	1.3 (1.2–1.4)	1.2 (1.0–1.4)	0.087
Sodium, mmol/L	135.0 (132.0–138.0)	134.0 (130.0–138.0)	0.317
hsCRP, mg/L	30.6 (3.5–49.3)	11.7 (3.1–22.3)	0.216
NT-proBNP, pg/mL	9,314 (4,681–22,066)	8,435 (5,358–14,769)	0.540
Preoperative			
ECMO bridged	7 (30.4)	4 (14.8)	0.184

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Supplementary Table 4. Continued

Variable	Pre-reimbursement period[a] (n = 23)	Post-reimbursement period[a] (n = 27)	*p* value
Dialysis	7 (30.4)	8 (29.6)	0.951
IABP	1 (4.3)	0	0.460
Ventilator	7 (30.4)	8 (29.6)	0.951
Hemodynamic			
Mean RA pressure, mmHg	14.0 (4.5–15.5)	11.5 (8.0–16.0)	0.513
Mean PA pressure, mmHg	34.0 (29.0–41.0)	40.5 (32.0–43.8)	0.111
Mean PWP, mmHg	24.0 (17.0–28.5)	28.5 (23.3–32.5)	0.042
Cardiac output, L/min	3.4 (2.9–4.3)	3.0 (2.5–3.6)	0.189
Medications			
ARB or ARNI	14 (60.8)	18 (66.6)	0.670
ACE inhibitor	7 (30.4)	9 (33.3)	0.827
Amiodarone	12 (52.1)	17 (62.9)	0.441
Beta blocker	12 (52.1)	15 (55.5)	0.811
Aldosterone antagonist	22 (95.6)	26 (96.2)	1.000
Ivabradine	0	12 (44.4)	0.000
Loop diuretics	22 (95.6)	27 (100)	0.460
Phosphodiesterase inhibitors	11 (47.8)	12 (44.4)	0.811
ICD	8 (34.7)	5 (18.5)	0.191
CRT	2 (8.6)	7 (25.9)	0.152
Implant strategy			
BTT/BTC	12 (52.2)	18 (66.7)	0.297
DT	11 (47.8)	9 (33.3)	0.297
Device type			
Heartmate II™	6 (26.0)	11 (40.7)	0.276
HVAD™	17 (73.9)	16 (59.2)	0.276

Values are presented as median (interquartile range), mean ± standard deviation, or number (%).
INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LV, left ventricle; NYHA, New York Heart Association; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; hsCRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal-pro hormone B-type natriuretic peptide; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; RA, right atrium; PA, pulmonary artery; PWP, pulmonary wedge pressure; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; ACE, angiotensin-converting enzyme; ICD, implantable cardioverter-defibrillator; CRT, cardiac resynchronization therapy; BTT/BTC, bridge to transplantation/bridge to candidacy; DT, destination therapy; HVAD, HeartWare Ventricular Assist Device.
[a]The national insurance commenced reimbursement for pre-approved cases since October, 2018.

Supplementary Table 5. Hemocompatibility-associated adverse events compared between HeartMate II vs. HVAD devices

Adverse event	Total (n = 50)	HeartMate II (n = 17)	HVAD (n = 33)	*p* value
Suspected or confirmed pump thrombosis				
All patients (n = 50)	2 (4.0)	2 (11.8)	0	0.111
BTT/BTC (n = 30)	2 (6.7)	2 (20.0)	0	0.103
DT (n = 20)	0	0	0	-
Any stroke				
All patients (n = 50)	16 (32.0)	4 (23.5)	12 (36.4)	0.357
BTT/BTC (n = 30)	9 (30.0)	2 (20.0)	7 (35.0)	0.675
DT (n = 20)	7 (35.0)	2 (28.6)	5 (38.5)	1.000
Ischemic stroke				
All patients (n = 50)	8 (16.0)	2 (11.8)	6 (18.2)	0.699
BTT/BTC (n = 30)	4 (13.3)	1 (10.0)	3 (15.0)	1.000
DT (n = 20)	4 (20.0)	1 (14.3)	3 (23.1)	1.000
Hemorrhagic stroke				
All patients (n = 50)	9 (18.0)	3 (17.6)	6 (18.2)	1.000
BTT/BTC (n = 30)	5 (16.7)	1 (10.0)	4 (20.0)	0.640
DT (n = 20)	4 (20.0)	2 (28.6)	2 (15.4)	0.587
Major bleeding				
All patients (n = 50)	26 (52.0)	9 (52.9)	17 (51.5)	0.924
BTT/BTC (n = 30)	17 (56.7)	5 (50.0)	12 (60.0)	0.705
DT (n = 20)	9 (45.0)	4 (57.1)	5 (38.5)	0.642
Bleeding requiring surgery				
All patients (n = 50)	7 (14.0)	4 (23.5)	3 (9.1)	0.210
BTT/BTC (n = 30)	4 (13.3)	2 (20.0)	2 (10.0)	0.584
DT (n = 20)	3 (15.0)	2 (28.6)	1 (7.7)	0.270
Gastrointestinal bleeding				
All patients (n = 50)	13 (26.0)	3 (17.6)	10 (30.3)	0.499
BTT/BTC (n = 30)	5 (23.3)	1 (10.0)	6 (30.0)	0.372
DT (n = 20)	6 (30.0)	2 (28.6)	4 (30.8)	1.000

Values are presented as number (%).
HVAD, HeartWare Ventricular Assist Device; BTT/BTC, bridge to transplantation/bridge to candidacy; DT, destination therapy.

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Supplementary Table 6. Rehospitalizations

	HeartMate II	HVAD	*p* value
BTT/BTC (n = 30)	10	20	
Time to rehospitalization, day	38 (17–241)	29 (8–390)	0.488
Rehospitalization within 1 year	9 (90.0)	13 (65.0)	0.210
DT (n = 20)	7	13	
Time to rehospitalization, day	30 (28–53)	65 (39–246)	0.570
Rehospitalization within 1 year	5 (71.4)	11 (84.6)	0.587

Values are presented as median (interquartile range) or number (%).
HVAD, HeartWare Ventricular Assist Device; BTT/BTC, bridge to transplantation/bridge to candidacy; DT, destination therapy.

Supplementary Table 7. Clinical outcomes stratified by sex

Variable	Women (n = 12)	Men (n = 38)	*p* value
All-cause mortality during follow-up	5 (41.7)	6 (15.8)	0.105
Stroke	6 (50.0)	10 (26.3)	0.163
Driveline infection	1 (8.3)	7 (18.4)	0.661
Gastrointestinal bleeding	6 (50.0)	7 (18.4)	0.055
Major bleeding	8 (66.6)	18 (47.3)	0.243
Postop bleeding control surgery	2 (16.6)	5 (13.1)	1.000
Device malfunction	0	1 (2.6)	1.000
Postoperative RHF	6 (50.0)	5 (13.1)	0.014
Inotropic weaning failure	5 (41.6)	3 (7.8)	0.014
Inotropic restart or multidrug	2 (16.6)	2 (5.2)	0.240
RVAD insertion	2 (16.6)	2 (5.2)	0.240

Values are presented as number (%).
RHF, right heart failure; RVAD, right ventricular assist device.

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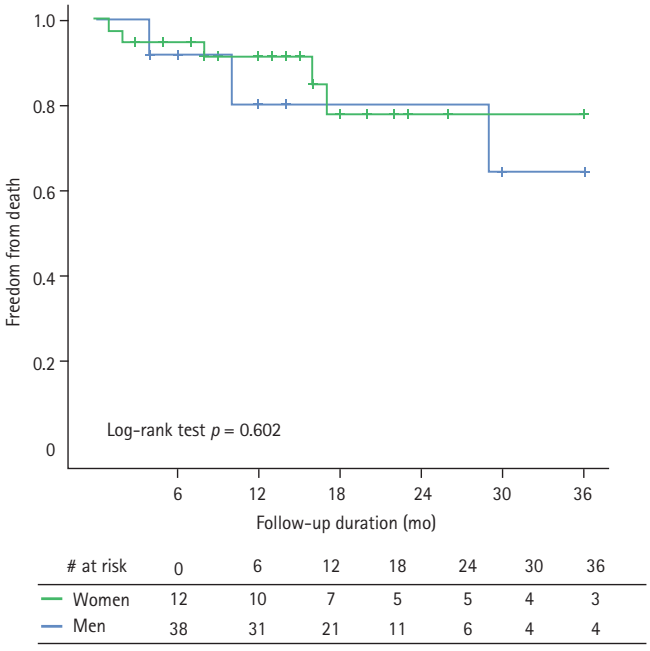
Supplementary Table 8. Clinical outcomes stratified by LVAD implantation periods

Variable	Pre-reimbursement period[a] (n = 23)	Post-reimbursement period[a] (n = 27)	*p* value
All-cause mortality during follow-up	7 (30.4)	4 (14.8)	0.184
Stroke	9 (39.1)	7 (25.9)	0.318
Driveline infection	6 (26.0)	3 (11.1)	0.270
Gastrointestinal bleeding	8 (34.7)	5 (18.5)	0.191
Major bleeding	14 (60.8)	13 (48.1)	0.368
Postop bleeding control surgery	4 (17.3)	3 (11.1)	0.689
Device malfunction	0	1 (3.7)	1.000
Postoperative RHF	8 (34.7)	3 (11.1)	0.044
Inotropic weaning failure	7 (30.4)	1 (3.7)	0.017
Inotropic restart or multidrug	1 (4.3)	3 (11.1)	0.614
RVAD insertion	4 (17.3)	0	0.038

Values are presented as number (%).
LVAD, left ventricular assist device; RHF, right heart failure; RVAD, right ventricular assist device.
[a]The national insurance commenced reimbursement for pre-approved cases since October, 2018.



# at risk	0	6	12	18	24	30	36
Women	12	10	7	5	5	4	3
Men	38	31	21	11	6	4	4

Supplementary Figure 1. Three-year survival stratified by sex. Overall survival up to 3 years were similar between men and women.

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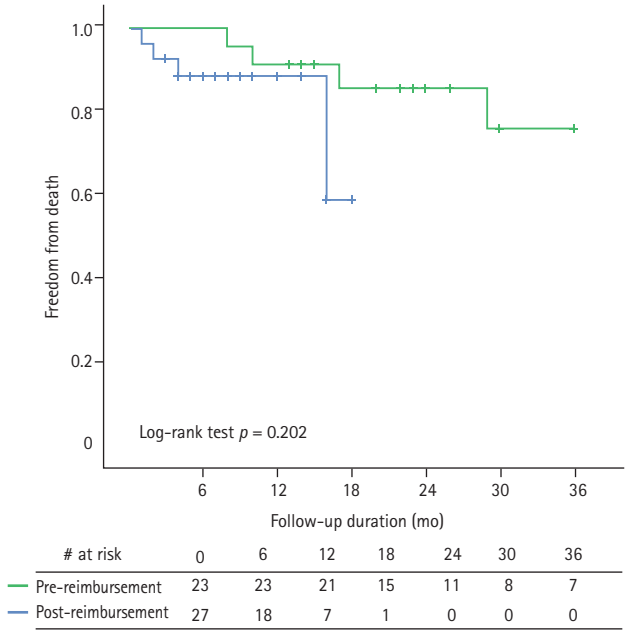
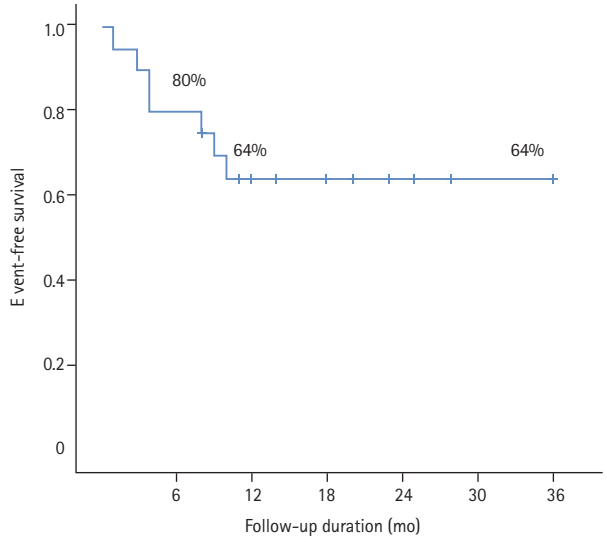


Supplementary Figure 2. Three-year survival before and after reimbursement. Overall survival up to 3 years were similar before and after reimbursement. The national insurance commenced reimbursement for pre-approved cases since October, 2018.



Months	0	6	12	18	24	30	36
# at risk	20	16	11	9	6	4	4

Supplementary Figure 3. Survival free from disabling stroke, reoperation or death in destination therapy patients. Event-free survival up to 3 years. Estimated survival rates are given at 6, 12, and 36 months.

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