A continuous-flow external ventricular assist device for cardiogenic shock: Evolution over 10 years

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ABSTRACT

Background: The use of percutaneous mechanical circulatory support (MCS) in the treatment of cardiogenic shock has increased. However, limitations in flow capability, ventricular unloading effect, durability, and mobility remain. We reviewed our single-center experience with continuous-flow external ventricular assist devices (VADs) to determine the role of temporary VADs for cardiogenic shock in the contemporary MCS era.

Methods: We retrospectively reviewed 252 patients who underwent continuous-flow external VAD insertion between January 2007 and December 2016. To investigate the change in indications, device configurations, and outcomes, we divided the cohort into 2 groups—2007 to 2011 (Era 1; n = 127) and 2012 to 2016 (Era 2; n = 125)—and compared early and late outcomes.

Results: Indications and device configurations changed significantly over time. The use of preoperative percutaneous MCS (53% vs 23%; $P < .01$) and use of minimally invasive VAD configurations (23% vs 6.7%; $P < .01$) were greater in Era 2 compared with Era 1. The rate of bridge to the next destinations, including myocardial recovery, transplantation, and durable VAD, was similar in the 2 groups. In-hospital mortality was significantly better in Era 2 (50% vs 37%; $P = .04$). Overall survival at 1 year was 57% in Era 2 versus 43% in Era 1 ($P = .04$).

Conclusions: Better outcomes in the recent era could be associated with the changes in practice patterns using continuous-flow external VAD in patients with refractory cardiogenic shock. (J Thorac Cardiovasc Surg 2018;156:157-65)

Minimally invasive ventricular assist system with oxygenator (Ec-VAD).

Central Message

Flexibility in the use of both percutaneous mechanical circulatory support and continuous-flow external ventricular assist devices could improve early and late outcomes in cardiogenic shock.

Perspective

Mechanical circulatory support therapy for cardiogenic shock has evolved. This study demonstrates the usefulness of continuous-flow external ventricular assist devices for patients in cardiogenic shock at a single high-volume center. The results will allow better strategy in selection and treatment for patients in cardiogenic shock.

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The use of percutaneous mechanical circulatory support (MCS) for treating acute hemodynamic decompensation and refractory cardiogenic shock has expanded rapidly.^{1,2} Various types of percutaneous MCS have been developed,

including venoarterial extracorporeal membrane oxygenation (ECMO) and the Impella system (Abiomed, Danvers, Mass), and clinical outcomes continue to improve with these new technologies.^{1,2} Nonetheless, there remain limitations, especially with regard to power, durability, requirement of special skill for insertion, and patient mobility after implantation.²

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Abbreviations and Acronyms

APTT	= activated partial thromboplastin time
BiVAD	= biventricular assist device
ECMO	= extracorporeal membrane oxygenation
Ec-VAD	= mini left ventricular assist device with extracorporeal membrane oxygenation
INTERMACS	= Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	= left ventricular assist device
MCS	= mechanical circulatory support
RVAD	= right ventricular assist device
VAD	= ventricular assist device

Because of these limitations, the role of surgical short-term MCS has remained constant. The use of the CentriMag continuous-flow external ventricular assist device (VAD; Abbott, Pleasanton, Calif) is an attractive option for treating patients in shock.³ This pump can generate 10 L/min of continuous flow at a low rotational speed of 5500 rpm. Various types of cannulas can be connected to the CentriMag system. These features facilitate easy insertion procedure, a flexible configuration, combined use with an oxygenator, midterm use, and easy postoperative maintenance.

In this report, we summarize our 10-year experience with continuous-flow external VAD to evaluate how the role of short-term surgical VAD for cardiogenic shock in the contemporary MCS era has been changing over time. The objective of the present study is to clarify the association between the outcomes of refractory cardiogenic shock and temporal institutional practice changes by era, such as shock etiologies, surgical indications, and treatment strategies, including VAD configurations.

METHODS

We retrospectively reviewed our experience with continuous-flow external VAD at Columbia Presbyterian Medical Center between January 2007 and December 2016. During this period, 252 consecutive patients with various etiologies of cardiogenic shock underwent continuous-flow external VAD placement as a bridge to decision therapy. To investigate the annual changes in indications, device configurations, and outcomes, the cohort was divided into 2 equal periods by the day of continuous-flow external VAD placement: from January 1, 2007, to December 31, 2011 (Era 1; $n = 127$) and from January 1, 2012, to December 31, 2016 (Era 2; $n = 125$). Our Institutional Review Board approved this study.

Indications and Surgical Technique

All patients underwent continuous-flow external VAD as a bridge to decision therapy. Our algorithm for a bridge to decision device therapy

for cardiogenic shock has been described previously.³ A patient with cardiogenic shock is characterized by (1) systolic blood pressure <90 mmHg, a cardiac index <2.0 L/min/m², a pulmonary capillary wedge pressure >16 mmHg (or evidence of pulmonary edema in the absence of a pulmonary artery catheter), and end-organ failure, or (2) the inability to be weaned from cardiopulmonary bypass. These patients are rapidly evaluated by our multidisciplinary team. Since 2015, a “Shock Team” consisting of surgeons, cardiologists, nurse practitioners, and intensive care physicians has played a role in determining the most suitable MCS for each patient. In our institution, percutaneous MCS, such as ECMO, has gained popularity as a first rescue device over the years. As a result, continuous-flow external VAD has become a second bridge device to the final destination. Figure 1 shows the percentage of patients who were transitioned from percutaneous MCS to continuous-flow external VAD each year.

The implantation technique for conventional external VAD has been reported previously.³ We have developed several techniques for minimally invasive cannulation without cardiopulmonary bypass; the implantation technique has been described previously.⁴⁻⁶ For patients who need biventricular unloading, the femoral venous component of ECMO is integrated with a mini-LVAD to unload the right ventricle (Ec-VAD; Figure 2, B). Apical and femoral venous cannulas are connected with a Y-connector, and an oxygenator (Quadrox D; Maquet, Wayne, NJ) is spliced into the circuit. Since 2015, Ec-VAD has been our standard approach instead of BiVAD via sternotomy.

Postimplantation Device Management

Intravenous heparin is initiated at 300 U/hour once tube drainage becomes serosanguinous. Activated partial thromboplastin time (APTT) is measured every 8 hours. Heparin dose is titrated to target APTT at 60 to 80 seconds. Once the patient's condition begins to improve, as marked by acceptable hemodynamics, lactate clearance, end-organ function improvement, and stable neurologic condition, cardiac function is challenged through device weaning. The weaning protocol was reported previously.³ Weaning is generally performed in intensive care units with a Swan–Ganz catheter. In brief, with therapeutic APTT, flows are reduced to 1 L/min. Maintenance of stable hemodynamics (central venous pressure <13 mmHg, mean arterial pressure >65 mmHg, pulmonary capillary wedge pressure <18 mmHg, cardiac index >2.2 L/min/m²) ensures appropriate ventricular functions. In patients with Ec-VAD, the flow of femoral venous limb is gradually weaned to 1.5 L/min, and then the

FIGURE 1. Trend of percutaneous mechanical circulatory support use before continuous-flow external ventricular assist device implantation. MCS, Mechanical circulatory support.

FIGURE 2. A-D, Various minimally invasive external ventricular assist device configurations.

limb is temporarily clamped at bedside as a final assessment. If the above parameters are met, the venous limb and oxygenator are removed, and Ec-VAD is converted to mini-LVAD. If a patient cannot tolerate femoral venous weaning, the venous limb is switched to the jugular vein for patient mobility.⁴ According to the weaning test, the device is explanted to one of the following destinations: exchange to durable VAD, explantation if there is sufficient myocardial recovery, or explantation for heart transplantation.

Data Collection and Follow-up

Preoperative variables included age, sex, shock etiology, comorbidities including diabetes and hypertension, previous percutaneous MCS, and laboratory test results (Table 1). Intraoperative variables included the use of cardiopulmonary bypass and the configuration of the continuous-flow external VAD (Table 2). Postoperative data included duration of support, incidence of complications, and outcomes, including recovery, transition

to durable support, transplantation, and death (Table 3). Follow-up was completed in 100% of patients on January 31, 2017.

Statistical Analysis

Statistical analyses were performed using R version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables are expressed as frequencies and percentages and compared using Fisher's exact test. Continuous variables are expressed as median with interquartile range and compared using the Mann-Whitney *U* test. Kaplan-Meier curves were used to represent survival and were compared using the log-rank test. Univariable and multivariable Cox regression analyses were performed to identify factors significantly associated with hazard of death after external VAD implantation. A stepwise selection algorithm was used for multivariable model building to minimize the Akaike information criterion. Missing variables were replaced by multiple imputation with predictive mean matching. For all analyses, a *P* value <.05 was considered statistically significant.

TABLE 1. Baseline characteristics

Characteristic	Era 1	Era 2	P value
Number of patients	127	125	
Age, y, median (IQR)	56.0 (45.0-63.0)	58.0 (47.0-65.0)	.436
Body mass index, kg/m ² , median (IQR)	27.0 (23.6-32.2)	27.4 (24.7-31.3)	.421
Body surface area, m ² , median (IQR)	1.97 (1.80-2.12)	1.97 (1.81-2.12)	.793
Female, n (%)	40 (31.5)	41 (32.8)	.931
Hypertension, n (%)	65 (51.2)	70 (56.0)	.452
Diabetes mellitus, n (%)	39 (30.7)	44 (35.2)	.503
Hyperlipidemia, n (%)	48 (37.8)	49 (47.2)	.161
Previous stroke, n (%)	6 (4.7)	12 (9.6)	.149
Previous myocardial infarction, n (%)	42 (33.1)	34 (27.2)	.338
Etiology of shock, n (%)			.190
Acute myocardial infarction	32 (25.2)	36 (28.8)	
Postcardiotomy shock	31 (24.4)	24 (19.2)	
Acute decompensated chronic heart failure	29 (22.8)	30 (24.0)	
Graft failure after heart transplantation	20 (15.8)	12 (9.6)	
RV failure after durable LVAD insertion	6 (4.7)	16 (12.8)	
Myocarditis	6 (4.7)	6 (4.8)	
Others	3 (2.4)	1 (0.8)	
Preoperative IABP, n (%)	67 (52.8)	55 (44.0)	.234
Preoperative percutaneous MCS, n (%)	29 (22.8)	66 (52.8)	<.001
ECMO	22	41	
Impella	4	6	
ECMO and Impella	2	18	
TandemHeart	1	1	
Preoperative ventilator support, n (%)	81 (63.8)	85 (68.0)	.508
Preoperative CVVH, n (%)	22 (17.3)	15 (12.1)	.287
Total protein, g/dL, median (IQR)	5.4 (4.7-6.3)	5.5 (4.6-6.4)	.626
Albumin-g/dL, median (IQR)	3.1 (2.7-3.6)	3.0 (2.6-3.5)	.248
Blood urea nitrogen, mg/dL, median (IQR)	25.0 (19.0-37.0)	29.0 (17.0-42.0)	.463
Creatinine, mg/dL, median (IQR)	1.4 (1.1-1.8)	1.5 (1.1-2.3)	.326
WBC, ×1000/mL, median (IQR)	12.6 (8.4-17.3)	12.6 (8.5-17.7)	.948
Hemoglobin, g/dL, median (IQR)	10.2 (9.1-12.2)	10.2 (9.0-12.3)	.890
Hematocrit, %, median (IQR)	30.2 (26.5-36.1)	28.7 (25.1-32.9)	.089
Platelets, ×1000/mL, median (IQR)	159.0 (101.5-210.0)	144.0 (79.0-215.0)	.479
Total bilirubin, mg/dL, median (IQR)	1.6 (0.9-3.0)	1.2 (0.8-2.2)	.055
Direct bilirubin, mg/dL, median (IQR)	0.5 (0.3-1.6)	0.4 (0.2-1.0)	.073
AST, U/L, median (IQR)	99.0 (42.0-367.0)	81.0 (33.0-281.0)	.196
ALT, U/L, median (IQR)	53.0 (24.5-161.0)	45.0 (20.0-128.0)	.409
PT-INR, median (IQR)	1.4 (1.2-1.8)	1.3 (1.2-1.6)	.042
Lactate, mmol/L, median (IQR)	2.9 (1.4-7.2)	1.8 (1.4-2.7)	<.001

IQR, Interquartile range; RV, right ventricle; LVAD, left ventricular assist device; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; ECMO, extracorporeal membrane oxygenation; CVVH, continuous veno-venous hemofiltration; WBC, white blood cell; AST, aspartate transaminase; ALT, alanine transaminase; PT-INR, prothrombin time international normalized ratio.

TABLE 2. Intraoperative variables

Variable	Era 1	Era 2	P value
Total device runs (n = 268), n	135	133	
Use of cardiopulmonary bypass, n (%)	63 (46.7)	67 (50.4)	.625
VAD flow, L/min, median (IQR)	5.5 (4.9-6.3)	5.8 (5.0-6.4)	.155
VAD configuration, n (%)			<.001
LVAD	10 (7.4)	9 (6.8)	
RVAD	39 (28.9)	24 (18.1)	
BiVAD	86 (63.7)	74 (55.6)	
Ec-VAD	0 (0)	26 (19.6)	
Minimally invasive approach, n (%)	9 (6.7)	31 (23.3)	<.001
Cannulation, n (%)			
LVAD inflow, n (%)			<.001
Left ventricle apex	48 (49.5)	94 (87.9)	
Left atrium	37 (38.1)	13 (12.2)	
Left ventricle through left atrium	11 (11.3)	0 (0.0)	
Other	1 (1.03)	0 (0.0)	
LVAD outflow, n (%)			.003
Aorta	90 (92.8)	83 (77.6)	
Axillary artery	7 (7.22)	24 (22.4)	
RVAD inflow, n (%)			<.001
Right atrium	119 (95.2)	92 (74.8)	
Right ventricle	1 (0.8)	4 (3.3)	
Right atrium through femoral vein	5 (4.0)	27 (21.6)	
RVAD outflow, n (%)			.234
Pulmonary artery	120 (96.0)	94 (95.9)	
Pulmonary artery through jugular vein	5 (4.0)	2 (2.0)	
Other	0 (0)	2 (2.0)	

VAD, Ventricular assist device; IQR, interquartile range; LVAD, left ventricular assist device; RVAD, right ventricular assist device; BiVAD, biventricular assist device; Ec-VAD, ventricular assist device integrated with extracorporeal membrane oxygenation.

RESULTS

Baseline Characteristics

A total of 252 patients received continuous-flow external VAD support, with a total of 268 device runs. Baseline data for Eras 1 and 2 are summarized in Table 1. Patients in Era 2 had a significantly higher rate of preoperative use of percutaneous MCS. ECMO was the most predominant percutaneous MCS used in both eras. Serum lactate level was significantly lower in Era 2 patients. Other laboratory variables were similar in the 2 groups.

Intraoperative Variables

Table 2 summarizes the intraoperative outcomes among 268 device runs. The cardiopulmonary bypass was used similarly in both groups. BiVAD was the most common configuration in both eras, whereas Ec-VAD was used

only in Era 2. A minimally invasive approach was more frequently used in Era 2. Accordingly, the cannulation strategy changed significantly over time. The majority of patients in Era 2 (88%) received apical cannulation as an LVAD inflow. Peripheral cannulation, such as axillary arterial or femoral venous cannulation, was more frequently used as LVAD outflow and RVAD inflow in Era 2.

Early Clinical Outcomes

In the entire cohort, 67 patients (27%) died during device support (median, 18 days; interquartile range, 10-33). Eighty-six patients (34%) could wean from device support after adequate recovery of ventricular function. Thirty-one (12%) were bridged to heart transplantation, and 54 (21%) were transitioned to a durable VAD. In entire cohort, 30-day mortality was 27%. During the index hospitalization, 109 in-hospital deaths (43%) occurred.

Early clinical outcomes in the 2 groups are compared in Table 3. The median duration of support was significantly longer in Era 2 (20 vs 15 days; $P = .016$). Eighty-eight patients (70%) in Era 2 reached the next destination (myocardial recovery in 45 [36%], device exchange to a durable VAD in 31 [25%], and heart transplantation in 12 [9.6%]), compared with 83 patients (65%) in Era 1 (myocardial recovery in 41 [32%], device exchange to a durable VAD in 23 [18%], and heart transplantation in 19 [15%]; $P = .42$). In-hospital mortality was significantly better in Era 2 compared with Era 1 (37% vs 50%; $P = .042$). Incidences of stroke, bleeding, and sepsis/bacteremia during support were similar in the 2 groups.

Figure 3 compares in-hospital mortality according to shock etiology in the 2 groups. Mortality was highest in patients with postcardiotomy shock in both eras. There was a statistically significant tendency toward reduced mortality over time in patients with acute myocardial infarction (44% in Era 1 vs 25% in Era 2; $P = .085$) and those with myocarditis (50% in Era 1 vs 0% in Era 2; $P = .091$).

Late Clinical Outcomes and Risk Factors for Overall Mortality

The 1-year overall survival in the 2 eras is compared in groups Figure 4, A. The 1-year survival rate was significantly better in Era 2 (43% vs 57%; $P = .043$). Because the patients with isolated RVADs had different etiologies than the patients with other external VADs, we stratified the entire cohort by isolated RVAD or not (Figure 4, B). The 1-year survival rates in both the isolated RVAD cohort and the entire cohort without isolated RVAD were better in Era 2, albeit not significantly so (isolated RVAD: 43% vs 61%, $P = .227$; all but isolated RVAD: 43% vs 56%, $P = .106$). In the entire cohort, 121 patients (48%) died during the 1-year follow-up period. Cox proportional hazard analysis in the entire cohort was performed to elucidate the risk factors for overall death (Table 4). In this analysis,

TABLE 3. Early outcomes

Outcome	Era 1	Era 2	P value
Number of patients	127	125	
Days of support, median (IQR)	15 (8-28)	20 (12-39)	.016
Death on device, n (%)	37 (29.1)	30 (24.0)	.394
Recovery (weaned off device), n (%)	41 (32.3)	45 (36.0)	.596
Heart transplant, n (%)	19 (15.0)	12 (9.60)	.250
Durable LVAD, n (%)	23 (18.1)	31 (24.8)	.221
Others, n (%)	6 (4.7)	7 (5.6)	.784
Morbidity during support, n (%)			
Stroke	20 (15.7)	21 (16.8)	.956
Major and minor bleeding	95 (74.8)	86 (68.8)	.358
Sepsis/bacteremia	19 (15.0)	21 (16.8)	.820

IQR, Interquartile range; LVAD, left ventricular assist device.

older age, female sex, and higher preoperative serum lactate, total bilirubin, and creatinine concentrations were identified as independent risk factors.

DISCUSSION

A major finding of this study is that treatment of patients with cardiogenic shock using continuous-flow external VAD has evolved, and significantly better early and late outcomes were seen in Era 2. These better outcomes in the more recent era could be related to various practical changes in our institution over the 10-year study period.

Mortality in patients with cardiogenic shock remains high. There is growing interest in MCS therapy to improve outcomes.^{1,2} Recent advances in technology now enable treatment of shock patients with various percutaneous MCS devices. Comparison of baseline demographic data for the 2 eras (Table 1 and Figure 1) clearly represent current trends in MCS therapy for cardiogenic shock. Patients

with greater acuity and severity tend to be treated with percutaneous MCS. In our program, we prefer to use venoarterial ECMO because of easy insertion and the ability to provide high-flow circulatory support.^{3,7} Our multivariable analysis showed that end-organ failure as well as rising lactate levels had significant impacts on worse midterm survival. This finding suggests that restoring tissue perfusion before end-organ dysfunction is a key aspect of MCS therapy for these patients. One challenge is the time-sensitive nature of this illness. In that sense, ECMO is the fastest way to stabilize a patient and prevent end-organ failure, because it can be implanted even at bedside. In fact, patients in Era 2 had significantly lower lactate levels compared with those in Era 1. However, traditional femoral veno-arterial ECMO is limited by adverse hemodynamics due to increases in afterload with left ventricular loading rather than unloading. Other major limitations of femoral veno-arterial ECMO include the patient's immobility and the durability of the configuration, especially when combined with other percutaneous MCS devices, such as the Impella, for ventricular unloading.⁸ Moreover, veno-arterial ECMO requires the use of an oxygenator in its circuit, which may be associated with platelet consumption and clotting issues.⁹ Other percutaneous MCSs also have inherent limitations.²

We have reported the use of external VAD using the CentriMag pump to treat patients in cardiogenic shock.³⁻⁶ Our present results further solidify the role of this approach as a second bridge to decision tool in the contemporary percutaneous MCS era. It can overcome the drawbacks of percutaneous MCS by providing flexible configurations, a direct ventricular unloading effect, and prolonged circulatory support with ambulatory rehabilitation. External VAD, which is essentially a left-heart bypass, also allows for earlier weaning off the oxygenator compared with a veno-arterial ECMO configuration.

For patients with predominant left ventricular failure, the question always rises of whether to place a durable LVAD from percutaneous MCS without a second bridge by CentriMag support. However, all shock patients do not necessarily need a durable LVAD, as our present results show. Furthermore, the outcomes of durable LVAD implantation are known to be poor in patients with Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile I.¹⁰ A recent study found a significantly high 90-day mortality of 39% in patients with INTERMACS profile I.¹¹ We previously reported a favorable bridge to a durable LVAD outcome with 18% in-hospital mortality in INTERMACS I patients.¹⁰ Our patients seemed to be an extremely high-risk cohort. We believe that a bridging strategy using an external VAD is more rational for elucidating appropriate candidates for durable LVAD, optimizing patients, and determining an appropriate goal for each patient

FIGURE 3. Comparison of in-hospital mortality stratified by etiology of shock. ADHF, Acute decompensated heart failure; AMI, acute myocardial infarction; PCS, postcardiotomy shock; PGD, primary graft dysfunction; RVF, right ventricular failure; LVAD, left ventricular assist device.

FIGURE 4. A, Comparison of overall survival in Eras 1 and 2. B, Comparison of overall survival in Eras 1 and 2, stratified by isolated RVAD or not. RVAD, Right ventricular assist device.

(ie, recovery, transplantation, or durable LVAD) in this high-risk cohort.

The conventional approach to implanting the CentriMag system requires sternotomy and generally cardiopulmonary bypass use, which limit its applications and may be contraindicated in patients with severe coagulopathy or other relative contraindications to sternotomy.³ To overcome these

drawbacks, we have developed minimally invasive cannulation techniques,^{4,6} and in 2015, Ec-VAD (Figure 2, B) became our standard transition configuration between peripheral ECMO and durable LVAD.⁴ Major benefits of our Ec-VAD approach are in preventing left ventricular distension, perfusing oxygenated blood from the upper body, unloading both the right and left ventricles efficiently (ECMO may increase LV afterload), mobilizing the patient, removing the oxygenator sooner, and preventing adhesion. Regarding the last point, in patients with conventional Bi-VAD, we often encountered dense adhesions around the cannula, which certainly increased the surgical complexity when we converted to durable VAD. We found that sparing the sternum greatly facilitates subsequent durable LVAD surgery. For RV failures after durable LVAD implantation, percutaneous RVAD is a more attractive approach, because the majority are temporal phenomena.^{12,13}

We found significantly improved in-hospital mortality over time, which also seems to affect better midterm outcomes. A certain degree of reduced mortality was observed predominantly in patients with acute myocardial infarction and myocarditis. We speculate that invisible but important factors attributed are change of our conception with regard to MCS therapy to cardiogenic shock and improvement of patient management. After the Intra-Aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial conferred no benefit of IABP in acute myocardial infarction and cardiogenic shock,¹⁴ we have adopted aggressive MCS therapy to cardiogenic shock. Furthermore, to streamline care for these critically ill patients, our center established a multidisciplinary Shock Team for patients with acute cardiogenic shock.¹⁵ We believe this team approach greatly facilitates timely support with both percutaneous and surgical MCSs to avoid the consequences of circulatory collapse.

Finally, it is noteworthy that the effect of era was not independently associated with the risk of death after continuous-flow external VAD implantation, after adjusting

TABLE 4. Cox regression analysis for hazard of death

Variable	HR	95% CI lower	95% CI upper	P value
Univariable analysis				
Year of procedure	0.940	0.882	1.001	.055
Age	1.022	1.008	1.037	.002
Female sex	1.325	0.935	1.878	.114
Body mass index	1.002	0.977	1.028	.868
Minimally invasive	0.860	0.516	1.432	.562
Acute myocardial infarction	0.824	0.556	1.219	.332
Total bilirubin	1.037	1.009	1.066	.008
Creatinine	1.061	0.993	1.134	.079
Lactate	1.055	1.015	1.097	.006
Ventilator support	1.103	0.775	1.571	.587
Multivariable analysis				
Year of procedure	—	—	—	—
Age	1.031	1.016	1.046	<.001
Female sex	1.608	1.121	2.306	.009
Body mass index	—	—	—	—
Minimally invasive	—	—	—	—
Acute myocardial infarction	—	—	—	—
Total bilirubin	1.041	1.012	1.071	.005
Creatinine	1.086	1.018	1.159	.012
Lactate	1.072	1.030	1.116	<.001
Ventilator support	—	—	—	—

Mean $\pm$ standard deviation for total bilirubin, creatinine, and lactate: total bilirubin, 3.0 ± 4.9 ; creatinine, 1.8 ± 2.3 ; lactate, 3.9 ± 3.9 . HR, Hazard ratio; CI, confidence interval.

for other covariates such as total bilirubin, creatinine, and lactate levels (Table 4). Given that the major baseline differences between the 2 eras were in percutaneous MCS, organ function, and lactate (Table 1), we believe it reasonable to stabilize organ functions and tissue perfusion with percutaneous MCS before continuous-flow external VAD implantation. Though there was no clear time point when we switched our strategy, the present study supports our current treatment approach.

This study has several limitations, starting with its design as a retrospective analysis of a single-center experience. Second, because of the nature of single-center studies, the outcomes described here are based on our practice in terms of patient selection, surgery, and management, and our findings might not be applicable to other centers. Third, the analysis between groups was a historical comparison, and so residual bias by unmeasured confounders might still exist. However, because the primary aim of this study was to elucidate the association between temporal changes of practice patterns and improving the outcomes of continuous-flow external VAD implantation, potential historical bias is an inevitable aspect of this study.

In conclusion, the early and late outcomes of continuous-flow external VAD implantation for refractory cardiogenic shock were significantly improved in Era 2. These dramatic improvements may be related to our institutional changes in treatment strategies. In the contemporary MCS era, flexibility in the use of both percutaneous MCS and temporary VAD as the situation demands is necessary to treat this seriously ill patient population.

Webcast

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Conflict of Interest Statement

Dr Naka has received consulting fees from Abbott. All other authors have nothing to disclose with regard to commercial support.

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Discussion

Dr Stephan W. Schueler (Newcastle upon Tyne, United Kingdom). Dr Takeda, thank you very much for providing me with the manuscript and it was a delight to read this. I would like to congratulate you and your colleagues from Columbia for their contribution in the field of acute mechanical circulatory support. Your group has repeatedly demonstrated that for undoubtedly the sickest group of patients it is possible to achieve reasonable results with continuous technical and strategical refinements.

Today you have presented your comprehensive 10-year review with external ventricular assist devices in patients with cardiogenic shock with a detailed reflection on various

cannulation techniques and surgical approaches in a wide range of cardiogenic shock scenarios. You have shown how to improve early and midterm outcomes and how to reduce adverse events, thus paving a way for future developments in this field.

Within this new framework you have been able to treat significantly more sicker patients, ie, a high number of INTERMACS +1 patients, as opposed to in the first era, which is very remarkable. In addition, in more than 50% of the patients, or era 2 percutaneous, VA-ECMO was necessary prior to external implant in order to facilitate hemodynamic stability, again, an indication to us that within this era you have treated a sicker group of patients altogether.

Surprisingly, though, which didn't come out in your tables, is that you still had a high application of intra-aortic balloon pumps, which you might want to comment on a little bit later. The spectrum of underlying pathologies leading to cardiogenic shock has not really changed over time significantly, and it comprises the typical range of very sick patients who are referred to most tertiary centers and university hospitals around the world. Despite an increase of the number of sicker patients, you have been able to improve your outcomes, and you have demonstrated this very nicely. Within these different patient groups, the post-cardiotomy group still seems to have the highest early mortality. The acute MI-related failure patients seem to show a trend towards improved survival as opposed to the past. Your long-term survival has also significantly improved, up to 57% at one year in the era 2 respectively, and obviously you have identified a few independent risk factors.

I have the following questions in sequential order. Number one, what is your algorithm for the assessment for patients with questionable neurological status or those who are referred under CPR condition?

Dr Koji Takeda (New York, NY). For percutaneous devices we have a very low threshold to insert such as ECMO, VA-ECMO. So we do ECPR. If questionable, if we believe the patient has stroke or has hemorrhagic something, we don't put that patient on ECMO.

Dr Schueler. And the same if you have, let's say, outside referrals where you have a questionable downtime?

Dr Takeda. We always ask, but it is always questionable, the answer, so in that case we just wait.

Dr Schueler. Second question. What is your concept of transitioning from external support to a more durable LVAD, particularly if you are not able to wean the RVAD element of your support circuit? I am particularly interested in the timing of this.

Dr Takeda. We stabilize the patient as much as possible with CentriMag. We let the patient walk, patient eat, we

won't see the end-organ recovery first, and then off the vent, and then we consider switch to CentriMag, to durable LVAD.

Dr Schueler. But if you still struggle on the RV side, what are you going to do then?

Dr Takeda. We reported last year at the meeting bridge from CentriMag to durable LVAD. As we reported, there is a very high incidence of RV failure.

Dr Schueler. So what do you do with those patients?

Dr Takeda. We switch to a durable LVAD. There is no actual good RVAD. So we keep the CentriMag RVAD.

Dr Schueler. So you put an LVAD in on the left side and you leave the CentriMag system on the right, and then you are aiming for?

Dr Takeda. Recovery, hopefully, but outcomes are not great, actually.

Dr Schueler. So you are kind of aiming for recovery from RV failure? How do you mobilize these patients, how do you get them through this period of recovery after LVAD implant plus leaving the CentriMag in on the right?

Dr Takeda. That's why we came up with this minimally invasive approach. We used to do a BIVAD with open chest, put the full cannula into the heart, and we found very, very tough adhesions around the cannula when we reopened the chest. That's why we save the sternum. Right now we don't open the sternum to support a biventricular patient. We just do a mini thoracotomy and axillary cannulation with femoral venous cannulation.

Dr Schueler. So how do they walk with a femoral venous cannula, because you said they walk?

Dr Takeda. No, no. Let me finish. So once patient comes out from deep shock status, in more than 90% of cases we can come off the femoral venous cannula, RVAD component. Then we switch to closed ECMO component from mini LVAD axillary configuration, and then patient can walk.

If a patient cannot wean from their femoral venous cannula, we switch to neck. We have a project with your cannula right now.

Dr Schueler. I have one more question. Concerning your various techniques, you could argue that you might as well stay on percutaneous support if there is no problem and avoid the move to an external LVAD and convert from the percutaneous ECMO system directly to a durable device, a philosophy some centers would favor, including myself. In other words, why not refine the percutaneous techniques in the future, which would potentially save you an additional third procedure?

Dr Takeda. I totally agree. The improvement in outcome is driven by technology. So if we have a more durable, powerful percutaneous device, this field is going to be a percutaneous device field. That is what I believe.

Dr Schueler. Thank you very much again, congratulations, and thank you for having me as a discussant.

FIGURE E1. Trend of continuous-flow external ventricular assist device over a 10-year periods. Minimally indicates minimally invasive approach. Ec-VAD indicates minimally invasive ventricular assist device implantation with venous cannula from extracorporeal membrane oxygenation support (Figure 2, B). *Ec-VAD*, Ventricular assist device integrated with extracorporeal membrane oxygenation.