

# Extracorporeal Life Support for Cardiogenic Shock With Either a Percutaneous Ventricular Assist Device or an Intra-Aortic Balloon Pump

TOMOHIRO NAKAJIMA, YUKI TANAKA, IRENE FISCHER, KUNAL KOTKAR, RALPH J. DAMIANO, JR.,  
MARC R. MOON, MUHAMMAD F. MASOOD, AND AKINOBU ITOH

Extracorporeal life support (ECLS) can result in complications due to increased left ventricular (LV) afterload. The percutaneous ventricular assist device (PVAD) and intra-aortic balloon pump (IABP) are both considered to be effective means of LV unloading. This study describes the efficacy of LV unloading and related outcomes with PVAD or IABP during ECLS. From January 2010 to April 2018, all cardiogenic shock patients who underwent ECLS plus simultaneous PVAD or IABP were analyzed. Forty-nine patients received ECLS + PVAD, while 91 received ECLS + IABP. At 48 hours, mean pulmonary artery pressure was significantly reduced in both groups [34 mm Hg to 22,  $p < 0.01$ ; 32 mm Hg to 21,  $p < 0.01$ ; ECLS + PVAD and ECLS + IABP group, respectively]. The two groups had similar 30 day survival rates [19 patients (39%) vs. 35 (39%),  $p = 0.56$ ]. The ECLS + PVAD group had higher incidences of bleeding at the insertion site [11 (22%) vs. 0,  $p < 0.01$ ] and major hemolysis [9 (18%) vs. 0,  $p < 0.01$ ]. Both groups had improvement in LV end-diastolic dimension ( $61 \pm 12$  mm to  $54 \pm 12$ ,  $p = 0.03$ ;  $60 \pm 12$  mm to  $47 \pm 10$ ,  $p < 0.01$ ), and LV ejection fraction ( $16 \pm 7\%$  to  $22 \pm 10$ ,  $p < 0.01$ ;  $22 \pm 12\%$  to  $29 \pm 15$ ,  $p = 0.01$ ). Both ECLS + PVAD and ECLS + IABP effectively reduced pulmonary artery pressure and improved LV function. Bleeding at the PVAD or IABP insertion

site occurred more frequently in the ECLS + PVAD group than the ECLS + IABP group ( $p < 0.01$ ). Nine patients (18%) in the ECLS + PVAD group experienced major hemolysis, while there was no hemolysis in the ECLS + IABP group ( $p < 0.01$ ). Careful considerations are required before selecting an additional support to ECLS. *ASAIO Journal* 2021; 67:25–31.

**Key Words:** extracorporeal life support, percutaneous ventricular assist device, intra-aortic balloon pump, pulmonary artery pressure

Severe cardiogenic shock with hemodynamic derangement and end-organ hypoperfusion is a potentially fatal condition that requires immediate medical treatment or mechanical circulatory support (MCS).<sup>1</sup> Common acute cardiopulmonary support methods include veno-arterial extracorporeal life support (VA-ECLS), percutaneous ventricular assist device (PVAD; Impella, ABIO MED, Inc., Danvers, MA), intra-aortic balloon pump (IABP), and TandemHeart (Livanova PLC, London, UK).<sup>2</sup> ECLS with arterial cannulation can possibly increase LV afterload, precipitating LV distension and pulmonary edema in patients with poor cardiac function or aortic valve insufficiency.<sup>3</sup> Methods used for LV decompression during ECLS include PVAD, IABP, surgically inserted LV vent through the LV apex or atrium, and atrial septostomy.<sup>4</sup> However, the availability of comparative data is limited regarding the effectiveness of PVAD versus IABP combined with VA-ECLS. The current study investigated hemodynamic and echocardiographic data, as well as overall outcomes and complications in patients with acute cardiogenic shock treated with VA-ECLS + PVAD versus VA-ECLS + IABP.

## Materials and Methods

### Patient Population

We reviewed patients supported with ECLS from January 2010 to April 2018. From this group, patients who developed cardiogenic shock and were simultaneously supported with ECLS and PVAD (Impella 2.5, CP, or 5.0) or ECLS and IABP were enrolled. Those who received ECLS only or multiple devices but not simultaneously supported were excluded. The first instance of the concurrent use of PVAD and ECLS at our institution was in April 2012.

### Mechanical Circulatory Support Systems and Treatment Algorithm

The VA-ECLS modality was used for all patients. The ECLS circuit consisted of a centrifugal pump (CentriMag; Abbott

From the Division of Cardiothoracic Surgery, Washington University School of Medicine in St. Louis, Barnes-Jewish Hospital, St. Louis, Missouri  
Submitted for consideration October 2019; accepted for publication in revised form April 2020.

Conflict of interest: Dr. Damiano is a speaker and receives research funding from AtriCure, is a consultant for Medtronic, and is a speaker for LivaNova and Edwards. Dr. Itoh has a surgical advisory role and is a speaker honorarium for Abbott, Abiomed, and Medtronic.

Disclosure: The authors have no conflicts of interest to report.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML and PDF versions of this article on the journal's Web site ([www.asaiojournal.com](http://www.asaiojournal.com)).

The Institutional Review Board of Washington University School of Medicine approved this study on the 14<sup>th</sup> of September 2014 and the 5<sup>th</sup> of March 2016 (approval numbers: 201409140 and 201603057).

Correspondence: Akinobu Itoh, Washington University School of Medicine, Barnes-Jewish Hospital, 660 South Euclid Avenue, Campus Box 8234, St. Louis, MO 63110, Email: [akinobuitoh@wustl.edu](mailto:akinobuitoh@wustl.edu); Twitter: @tomojima1129122.

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DOI: 10.1097/MAT.0000000000001192

Laboratory, Lake Bluff, IL) and an adult microporous membrane oxygenator. Central ECLS was conducted via cannulation of the ascending aorta and right atrium or femoral vein, whereas peripheral ECLS was administered through the femoral artery and vein cannulation with 15 or 17 Fr for female and 15–19 Fr for male with 6 Fr sheath insertion to the ipsilateral superficial femoral artery. Multistage percutaneous venous cannulas, size 21 or 25 Fr were inserted percutaneously to the femoral vein. The PVAD was percutaneously inserted into the common femoral artery directly, or through a sewn vascular graft to the axillary artery or the common femoral artery. The IABP was inserted into the common femoral artery under ultrasound guiding by the modified Seldinger technique. For those patients who underwent ECLS insertion, the mean arterial pressure was maintained lower than 80 in order to facilitate the LV ejection and the aortic valve opening. A mild to moderate dose of epinephrine or dobutamine was also used to enhance the LV ejection with the target arterial pulsatility over 20 mm Hg. IV heparin drip was utilized with the target prothrombin time between 50 and 90 seconds if there were no signs of bleeding. Once VA ECLS was established, TTE or TEE was utilized to rule out the presence of spontaneous echo contrast (smoke sign), which was a trigger to place an additional venting method, such as IABP or PVAD based on the availability and attending physicians' discretion. If the femoral artery was accessible, Impella 2.5 or CP was utilized. If not, Impella 5.0 was surgically inserted through the right axillary artery graft. Heparin dose in the purge solution was reduced to half dose, quarter dose, or none if necessary. Central ECLS was utilized in postcardiotomy cases where there was failure to wean the cardiopulmonary bypass after IABP support. Patients who had their circulatory support initiated with PVAD or IABP underwent peripheral VA-ECLS insertion for severe cardiogenic shock and metabolic derangement.

#### Outcome Variables

The primary outcome was hemodynamic improvement indicated by pulmonary artery pressure (PAP) and central venous pressure (CVP). Secondary outcomes were MCS decannulation, transition to a ventricular assist device (LVAD) or heart transplant, and vascular complications during combined support. In addition, survival to 30 days after combined support initiation was analyzed. Complications included limb ischemia or bleeding requiring surgical repair at the PVAD or IABP insertion, major hemolysis, gastrointestinal bleeding, cerebral stroke, acute kidney injury (AKI), and in-hospital dialysis. Significant bleeding was defined as bleeding requiring transfusion of packed red blood cells or reoperation after support initiation.<sup>5</sup> Major hemolysis was defined as a serum lactate dehydrogenase level of greater than 1,000 U/L with the gross appearance of hemolyzed blood samples.<sup>6</sup> Systolic PAP, diastolic PAP, mean PAP, and CVP were analyzed. The cardiac index, ECLS flow, and PVAD flow were reported. The pH, levels of lactate, total bilirubin, lactate dehydrogenase, and creatinine were recorded to assess LV unloading and end-organ perfusion. These hemodynamic and laboratory values were obtained at the following time-points: immediately before the initiation of combined support, and 48 hours and 30 days after the initiation of combined support. Echocardiogram data were collected 1) before combined support and 2) the last echocardiogram assessment either before weaning or withdrawal of ECLS.

#### Statistical Analysis

Continuous variables were reported as mean  $\pm$  standard deviation if normally distributed, and as median (interquartile range) if non-normally distributed. Normality was examined by means of both Shapiro–Wilk and Kolmogorov–Smirnov tests. Continuous variables were compared using the paired t-test if normally distributed, and the Wilcoxon signed rank test if non-normally distributed. Categorical variables were compared with the  $\chi^2$  test. All statistical tests were two-sided, with alpha set at 0.05 for statistical significance. All statistical analyses were conducted using SPSS (version 25.0, IBM, Armonk, NY) and R software, version 3.3.3. For the supplemental data (see Figures and Tables, Supplemental Digital Content 1, <http://links.lww.com/ASAIO/A503>), we performed propensity score matching by choosing the covariates based on the comparison between the original groups and also their clinical relevance. The selected variables were: age, body mass index, smoking, COPD, nonischemic cardiomyopathy, postcardiotomy shock, left ventricular ejection fraction, and central ECLS. We performed a one-to-one propensity score–matched analysis using nearest-neighbor matching within a caliper of 0.25 standard deviation of the logit of the propensity score. We examined balance in baseline variables using standardized differences, where more than 25.0% was regarded as imbalanced.

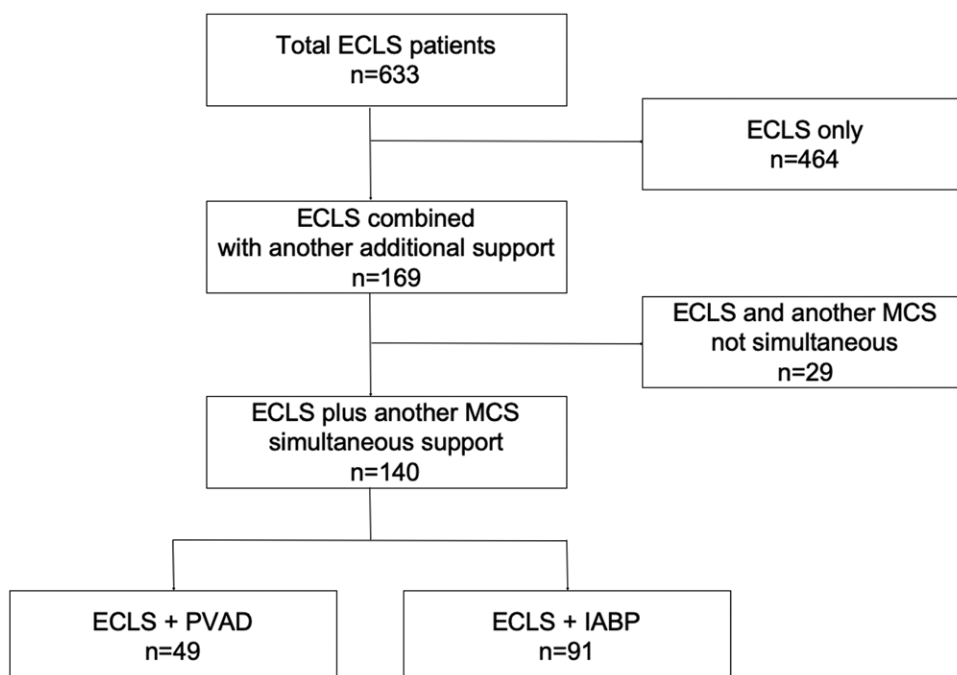
#### Results

During the study period, a total of 49 patients were simultaneously supported by ECLS and PVAD (ECLS + PVAD group), while 91 were simultaneously supported by ECLS and IABP (ECLS + IABP group) (**Figure 1**). Demographics and baseline characteristics were reported in **Table 1**.

The indications for MCS are reported in **Table 2**. Compared with the ECLS + PVAD group, the ECLS + IABP group had a greater incidence of postcardiotomy shock ( $p = 0.01$ ), post-heart transplant graft dysfunction ( $p = 0.01$ ) and a lower incidence of postpartum cardiomyopathy ( $p = 0.04$ ). In the ECLS + PVAD group, 10 patients (20%) received the Impella 2.5, 27 (55%) received the Impella CP, and 12 (24%) received the Impella 5.0. In the ECLS + IABP group, 12 patients (13%) received a 34 ml IABP, 55 (60%) received a 40 ml IABP, and 24 (26%) received a 50 ml IABP.

The device selection algorithm is summarized in **Figure 2**. The first mechanical support was initiated as follows: PVAD in 32 patients, ECLS in 23 patients, and IABP in 85 patients. All of the 32 patients supported by PVAD first received ECLS and 17 of the ECLS first patients received PVAD (ECLS + PVAD,  $n = 49$ ). All of the IABP first patients received ECLS, and six of the ECLS first patients underwent IABP insertion subsequently (ECLS + IABP,  $n = 91$ ). For in-hospital patients ( $n = 91$ ), combined support was established within 6 hours after initiation of the first mechanical support. For 49 patients, the first MCS was inserted at an outside hospital before the transfer to our hospital; they then received an additional MCS within 24 hours.

Hemodynamic data are summarized in **Table 3** and **Figure 3**. Compared with the mean PAP before the initiation of support, the mean PAP after 48 hours was significantly reduced in the ECLS + PVAD group ( $p < 0.01$ ) and the ECLS + IABP group ( $p < 0.01$ ). The systolic PAP, diastolic PAP, and CVP significantly changed from before the initiation of support to 48 hours after



**Figure 1.** Flow diagram of the patient selection algorithm. Patients with ECLS only or nonsimultaneous ECLS and another MCS were excluded. ECLS, extracorporeal life support; PVAD, percutaneous ventricular assist device; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support.

support initiation. PVAD flow was  $2.5 \pm 0.9$  L/min in the ECLS + PVAD group. There were significant improvements in the pH level after 48 hours of MCS both in the ECLS + PVAD group ( $p < 0.01$ ) and the ECLS + IABP group ( $p < 0.01$ ). The serum lactate level was also reduced significantly in both groups after 48 hours of MCS ( $p < 0.01$ ). There were no significant differences between the two groups with respect to the pH and lactate level at each data point, before, or 48 hours of support.

Although patient numbers were limited regarding cardiac function analysis (Table 3, ECLS + PVAD  $n = 40$ , ECLS + IABP  $n = 70$ ), improvement of left ventricular ejection fraction (LVEF) and also reduction in left ventricular end-diastolic diameter (LVEDd) and

left ventricular end-systolic diameter (LVESd) were similarly observed after 48 hours of combined MCS in both groups.

Table 4 summarizes the outcomes and complications. The two groups had similar rates of survival to 30 days ( $p = 0.56$ ). Survival to hospital discharge was observed in 39% of the ECLS + PVAD group and 30% of the ECLS + IABP group ( $p = 0.25$ ).

**Table 1. Demographics and Baseline Characteristics**

Variables	ECLS + PVAD $n = 49$ (%)	ECLS + IABP $n = 91$ (%)	$p$ Values
Age, years	$52.1 \pm 13.9$	$56.7 \pm 12.3$	0.06
Male	33 (67)	64 (70)	0.71
Body mass index, kg/m <sup>2</sup>	$28.7 \pm 6.1$	$31.0 \pm 6.0$	0.04
Body surface area, m <sup>2</sup>	$2.1 \pm 0.3$	$2.0 \pm 0.2$	0.45
Preexisting cardiac disease			
Systemic hypertension	11 (22)	27 (30)	0.43
Diabetes mellitus	14 (29)	21 (23)	0.54
Hyperlipidemia	10 (20)	20 (22)	0.51
Smoking	17 (35)	11 (12)	< 0.01
Coronary artery disease	25 (51)	51 (56)	0.60
Peripheral artery disease	4 (8)	4 (4)	0.45
Chronic obstructive pulmonary disease	1 (2)	10 (11)	0.10
Past cardiothoracic intervention	21 (43)	42 (46)	0.73

Values are presented as mean  $\pm$  standard deviation or n (%).

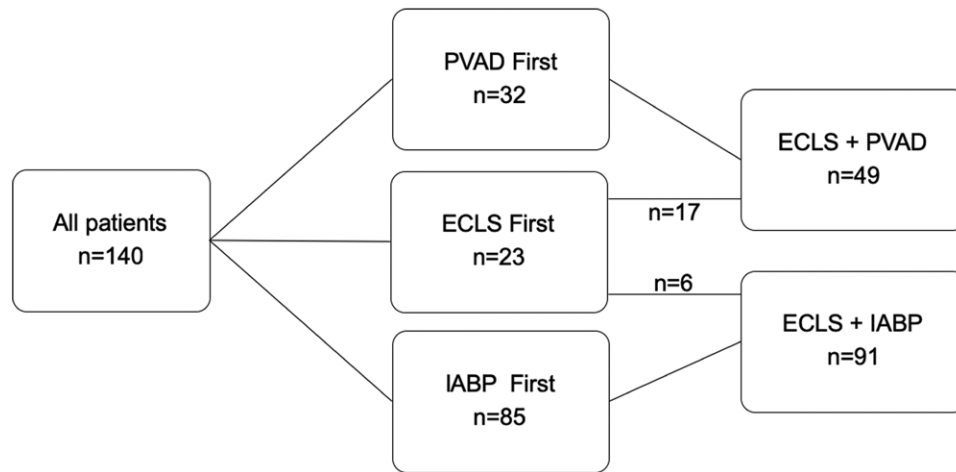
ECLS, extracorporeal life support; PVAD, percutaneous ventricular assist device; IABP, intra-aortic balloon pump.

**Table 2. Clinical and Procedural Characteristics Variables**

Variables	ECLS + PVAD $n = 49$ (%)	ECLS + IABP $n = 91$ (%)	$p$ Value
Indication for circulatory support			
Acute myocardial infarction	16 (33)	28 (31)	0.85
Ischemic cardiomyopathy	7 (14)	9 (10)	0.58
Nonischemic cardiomyopathy	18 (37)	21 (23)	0.11
Postcardiotomy shock	1 (2)	16 (18)	0.01
Post-heart transplant graft dysfunction	0	11 (12)	0.01
Postpartum cardiomyopathy	3 (6)	0	0.04
Others	4 (8)	6 (7)	0.74
Pre-ECLS cardiac function			
LV ejection fraction, %	$16 \pm 8$	$27 \pm 15$	< 0.01
LV end-diastolic diameter, mm	$59 \pm 11$	$57 \pm 12$	0.38
LV end-systolic diameter, mm	$54 \pm 14$	$47 \pm 14$	0.07
Central ECLS	7 (14)	62 (68)	< 0.01
Impella PVAD model			
2.5	10 (20)	-	-
CP	27 (55)	-	-
5.0	12 (24)	-	-
IABP	-	91 (100)	-

Values are presented as mean  $\pm$  standard deviation or n (%).

ECLS, extracorporeal life support; PVAD, percutaneous ventricular assist device; IABP, intra-aortic balloon pump; LV, left ventricle.



**Figure 2.** Mechanical circulatory support device selection algorithm. Out of 49 patients in the ECLS + PVAD group, 32 patients had PVAD first and 17 patients had ECLS first. Out of 91 patients in the ECLS + IABP group, 85 patients had IABP first, and six patients had ECLS first.

**Table 3.** Hemodynamic and Laboratory Data Before, After 48 Hours of Support, and Before Weaning

Variables	ECLS + PVAD, n = 49 (%)			ECLS + IABP, n = 91 (%)		
	Before combined support	48 Hours	p Value	Before combined support	48 Hours	p Value
SPAP, mm Hg	47 ± 10	30 ± 8	< 0.01	46 ± 14	28 ± 9	< 0.01
DPAP, mm Hg	29 ± 8	19 ± 6	< 0.01	25 ± 8	18 ± 7	< 0.01
MPAP, mm Hg	34 ± 7	22 ± 7	< 0.01	32 ± 10	21 ± 7	< 0.01
CVP, mm Hg	14 ± 6	10 ± 5	< 0.01	17 ± 6	13 ± 5	< 0.01
C.I., L/min/m <sup>2</sup>	1.3 ± 0.6	...	-	1.8 ± 0.8	-	-
ECLS flow, L/min	-	4.3 ± 1.1	-	-	4.9 ± 1.5	-
PVAD flow, L/min	-	2.5 ± 0.9	-	-	-	-
Laboratory values						
Ph	7.3 ± 0.2	7.4 ± 0.1	< 0.01	7.3 ± 0.1	7.4 ± 0.1	< 0.01
Lactate, mmol/L	8.1 (4.1–11.5)	2 (1.5–3.5)	0.04	7.9 (3.5–12.5)	2.3 (1.8–3.6)	0.01
Total bilirubin, mg/dL	1.5 (0.7–2.7)	3.3 (1.4–6.2)	0.07	1.5 (0.8–2.7)	2.7 (1.2–5.0)	< 0.01
LDH, U/L	884 (469–2,586)	1,118(796–1889)	0.03	404 (327–634)	828 (573–152)	0.02
Creatine, mg/dL	1.7 ± 0.8	1.8 ± 0.9	0.60	1.9 ± 1.2	1.8 ± 1.1	0.54
	ECLS + PVAD, n = 40 (%)			ECLS + IABP, n = 70 (%)		
Cardiac Function Data Before Combined Support and Before Weaning	Before Combined Support	Before Weaning	p Value	Before Combined Support	Before Weaning	p Value
LV ejection fraction, %	16 ± 7	22 ± 10	< 0.01	22 ± 12	29 ± 15	0.01
LV end-diastolic diameter, mm	61 ± 12	54 ± 12	0.03	60 ± 12	47 ± 10	< 0.01
LV end-systolic diameter, mm	55 ± 13	46 ± 12	< 0.01	52 ± 13	37 ± 12	< 0.01

Values are presented as mean ± standard deviation, median (interquartile range) or n (%).

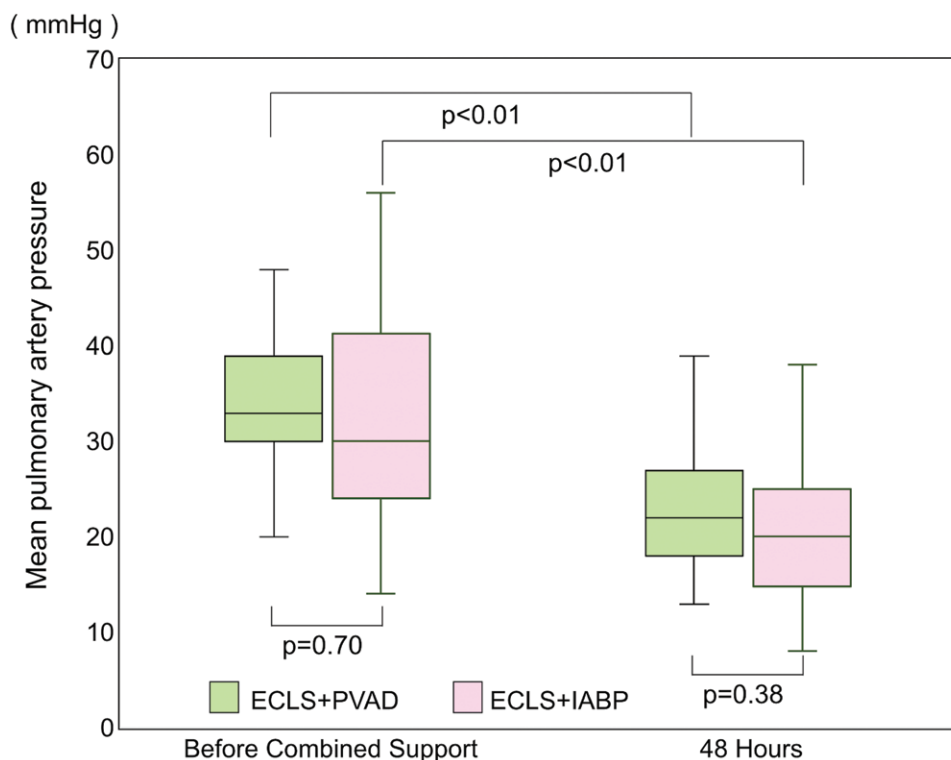
ECLS, extracorporeal life support; PVAD, percutaneous ventricular assist device; IABP, intra-aortic balloon pump; SPAP, systolic pulmonary artery pressure; DPAP, diastolic pulmonary artery pressure; MPAP, mean pulmonary artery pressure; CVP, central venous pressure; C.I., cardiac index; LDH, lactate dehydrogenase; LV, left ventricle.

The causes of death were similar in the two groups. The main cause of death was cardiac, which occurred in 35% of the ECLS + PVAD group vs. 38% of the ECLS + IABP group ( $p = 0.67$ ). The duration of MCS utilization was as follows: the ECLS + PVAD group had 4.4 days with Impella 2.5, 7.8 days with Impella CP, and 6.2 days with Impella 5.0 with 6.1 days of ECLS use.

The incidence of death during MCS support was 47% in both groups. Myocardial recovery was similar (33%) for both the ECLS + PVAD and ECLS + IABP groups, which allowed for MCS decannulation without LVAD support; transition to LVAD occurred in 20% and 16% of the ECLS + PVAD and ECLS + IABP

groups, respectively, while transition to heart transplant occurred in 0% and 3%, respectively.

Five patients developed limb ischemia due to the PVAD insertion, while three patients developed limb ischemia due to the IABP insertion ( $p = 0.09$ ). Bleeding at the PVAD or IABP insertion site occurred more frequently in the ECLS + PVAD group than the ECLS + IABP group ( $p < 0.01$ ). Nine patients (18%) in the ECLS + PVAD group experienced major hemolysis with combined MCS (three patients with Impella 2.5, five with Impella CP, and none with Impella 5.0), while there was no major hemolysis in the ECLS + IABP group ( $p < 0.01$ ). The two groups had similar incidences of gastrointestinal



**Figure 3.** Box-and-whisker plots of mean pulmonary artery pressure measured before initiation of combined support with ECLS + PVAD (green) or ECLS + IABP (pink) and after 48 hours of support. In both groups, mean pulmonary artery pressure was significantly reduced after 48 hours of combined support ( $p < 0.01$ ). The horizontal line in the middle of each box indicates the median; the top and bottom borders of the box mark the 75th and 25th percentiles, respectively; the whiskers mark the minimum and maximum values. [full color online](#)

bleeding, cerebral stroke, acute kidney injury, and in-hospital dialysis.

*Propensity score matched group comparison* (see Figures and Tables, Supplemental Digital Content 1, <http://links.lww.com/ASAIO/A503>): Propensity score matching was performed in a 1:1 ratio, resulting in 24 patients in the ECLS + PVAD group and 24 in the ECLS + IABP group. The patient selection algorithm is illustrated in Figure E1. Figures E2 and E3 illustrate the standardized mean differences before and after propensity score matching. Results for the propensity score-matched patients are reported in Tables E2 and E3.

### Discussion

The primary findings of our study were that both PVAD and IABP similarly reduced PAP and LV diameter when used in combination with VA-ECLS. ECLS + PVAD and ECLS + IABP resulted in similar survival rates, but the ECLS + PVAD group had more complications related to bleeding and major hemolysis than the ECLS + IABP group. To the best of our knowledge, the current study is the first to compare PVAD *versus* IABP with concomitant ECLS.

The use of ECLS may increase the afterload of the LV,<sup>2,7</sup> which exacerbates pulmonary edema and leads to worse outcomes.<sup>8</sup> Thus, various LV venting strategies have been developed. Tschöpe *et al.* reported that the increased afterload and filling pressures can be offset by combining ECLS with a PVAD, but did not clearly describe precise cardiac echo data, complications, or clinical outcomes.<sup>9</sup> Werdan *et al.* reported that IABP achieved less LV unloading than PVAD without ECLS.<sup>10</sup>

Nuding and Werdan reported significantly lower 28 day and in-hospital mortality rates with IABP/VA-ECLS than with VA-ECLS alone, with a significant difference in survival.<sup>11</sup> However, limited data are available related to PVAD utilization with ECLS compared to IABP. Our study focused on which device had the best impact on LV unloading when used simultaneously with ECLS regardless of MCS order (ECLS first or PVAD/IABP first). We observed a significant reduction in the PAP and CVP after 48 hours of ECLS + PVAD and ECLS + IABP support, suggesting that both ECLS + PVAD and ECLS + IABP achieved similar reductions in ECLS-related pulmonary edema and LV dimension. The incidence of leg ischemia also tended to be greater in the ECLS + PVAD group than the ECLS + IABP group, but this difference did not reach statistical significance. The current study also found that there were significantly more bleeding events requiring surgical repair at the insertion site in the ECLS + PVAD group than the ECLS + IABP group. Currently, the Impella 2.5 and CP devices need 12 and 14 Fr sheaths for the insertion and repositioning of the catheter in the groin, while an IABP requires a sheath size of 7.5 to 8 Fr. This sheath size difference between devices may particularly affect patients with cardiogenic shock who are on inotropic and vasopressor support, have vascular calcifications, or anticoagulation-related coagulopathy or device displacement.<sup>12</sup> To address the issue of bleeding from the insertion site, the design of the repositioning sheath was modified in late 2018. While this sheath modification should help reduce bleeding, it is unclear whether it will reduce the occurrence of lower extremity ischemia. As lower-extremity ischemia leads to detrimental outcomes,<sup>13</sup> early recognition is important and requires

**Table 4. In-hospital Outcomes and Complications**

Variables	ECLS + PVAD n = 49 (%)	ECLS + IABP n = 91 (%)	p value
Survival 30 days	19 (39)	35 (39)	0.56
Survival to discharge	19 (39)	27 (30)	0.25
Cause of death			
Cardiac death	17 (35)	36 (38)	0.67
Multiple system organ failure	3 (6)	13 (14)	0.06
Bleeding	2 (4)	2 (2)	0.95
Sepsis	3 (6)	1 (1)	0.09
Anoxic cerebral event	4 (8)	12 (13)	0.60
MCS duration, days	7 (3–12)	8 (4–13)	0.24
MCS decannulation	26 (53)	48 (53)	0.97
Length of hospital stay	17 (6–54)	23 (9–45)	0.80
Next destination			
Death on MCS	23 (47)	43 (47)	0.97
Myocardial recovery	16 (33)	30 (33)	0.97
Transition to ventricular assist device	10 (20)	15 (16)	0.56
Transition to heart transplant	0	3 (3)	0.20
Complications			
Limb ischemia caused by PVAD or IABP	5 (10)	3 (3)	0.09
Bleeding caused by PVAD or IABP	11 (22)	0	< 0.01
Major hemolysis	9 (18)	0	< 0.01
Gastrointestinal bleeding	5 (10)	7 (8)	0.75
Cerebral stroke	2 (4)	1 (1)	0.30
Acute kidney injury	36 (74)	60 (66)	0.28
In-hospital dialysis	28 (57)	56 (62)	0.72

Values are presented as n (%) or median (interquartile range).

ECLS, extracorporeal life support; PVAD, percutaneous ventricular assist device; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support.

prompt treatment with a distal limb perfusion cannula<sup>14</sup> or removal of PVAD. The PVAD carries a risk of hemolysis,<sup>15</sup> especially the Impella CP and 2.5 devices with higher RPM setups. In the current study, major hemolysis occurred in 18% of the ECLS + PVAD group, but none in the ECLS + IABP group. This rate of major hemolysis in the ECLS + PVAD group was acceptable in this very sick patient population, but it must be noted that the PVAD RPM setup was reduced to P2–P5 when it was used with ECLS due to the reduction in pulmonary circulatory volume with VA-ECLS. The introduction of MCS resulted in significant improvements in pH and serum lactate in both groups, indicating adequate perfusion. However, the serum total bilirubin and creatinine did not significantly decrease within 48 hours in either group. This was because it may take longer than 48 hours for serum total bilirubin and creatinine to change after improvement of hemodynamics.<sup>16</sup>

The 30 day survival rates in the current study were similar in both groups: 36% in the ECLS + PVAD group and 33% in the ECLS + IABP group. The overall survival in this group of severely deteriorated cardiogenic shock patients treated with ECLS + PVAD or IABP was not superior compared to previously published data.<sup>1,10,17</sup>

These results imply that we need a careful consideration on the LV venting strategy depending on how patients are initially treated with mechanical assist devices.<sup>18</sup> When a patient is already placed on PVAD or IABP and then undergoes VA-ECLS, the PVAD or IABP may not need to be changed. When a patient is supported by only VA-ECLS, then spontaneous echo contrast

is seen despite all the effort for the best VA-ECLS management, either PVAD or IABP can be a choice. Considering the fact that PVAD is a direct LV venting, this could be the first choice with a careful attention to the risk of complications, such as leg ischemia, insertion site bleeding, or major hemolysis, in those institutions which are familiar with the insertion process. Other methods, such as LV apex surgical venting and intra-atrial septostomy are potential surrogates for the LV unloading.

### Limitations

This study has several limitations. The LV unloading method was selected by multiple physicians during the 9 year study period and was not randomized. This could introduce selection bias. Although propensity score matching was conducted in the supplemental analysis, the PAP, cardiac echo data, and outcomes were similar before and after propensity score matching. In these analyses, we focused on the differences in LV unloading by PVAD *versus* IABP; therefore, the degree of LV unloading with preload reduction by ECLS only was not assessed. The two groups differed regarding the incidences of central and peripheral ECLS, and the indication for MCS; these intergroup differences were mainly due to the nature of the support systems and the initial MCS situation. Furthermore, the order of device introduction varied depending on the case and location; some cases experienced cardiogenic shock at an outside hospital and underwent insertion of an IABP alone, immediately followed by transfer to our hospital for further treatment. Multiple providers were involved in the decision-making process of which MCS to be initiated and added. Finally, the current study was retrospective and had a small sample; however, this is one of the largest series of patients receiving simultaneous support with PVAD or IABP plus ECLS.

### Conclusion

This study demonstrated that both PVAD and IABP similarly and effectively provided the pulmonary artery pressure reduction with ECLS, resulting in similar survival rates but higher bleeding complications with PVAD. These findings suggest that PVAD or IABP can be continued with careful ECLS management when these are placed before VA ECLS. When additional LV unloading is required during ECLS, either IABP or PVAD can be utilized. However, a careful consideration is needed to avoid device-related complications. Further studies are necessary to determine whether these devices improve the outcomes and survival of patients receiving ECLS.

### Acknowledgement

The authors thank the Heart Failure Research Group at Washington University School of Medicine and the Barnes and Jewish Hospital Shock Team for the patient data and helpful discussions.

### References

- van Diepen S, Katz JN, Albert NM, *et al*; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline: Contemporary management of cardiogenic shock: A scientific statement from the American Heart Association. *Circulation* 136: e232–e268, 2017.

2. Atkinson TM, Ohman EM, O'Neill WW, Rab T, Cigarroa JE: A practical approach to mechanical circulatory support in patients undergoing percutaneous coronary intervention an interventional perspective. *JACC Cardiovasc Interv* 9: 871–883, 2016.
3. Uriel N, Sayer G, Annamalai S, Kapur NK, Burkhoff D: Mechanical unloading in heart failure. *J Am Coll Cardiol* 72: 569–580, 2018.
4. Donker DW, Brodie D, Henriques JPS, Broomé M: Left ventricular unloading during veno-arterial ECMO: A simulation study. *ASAIO J* 65: 11–20, 2019.
5. Takayama H, Landes E, Truby L, et al: Feasibility of smaller arterial cannulas in venoarterial extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg* 149: 1428–1433, 2015.
6. Pieri M, Contri R, Winterton D, et al: The contemporary role of Impella in a comprehensive mechanical circulatory support program: A single institutional experience. *BMC Cardiovasc Disord* 15: 126, 2015.
7. Napp LC, Kühn C, Hoepfer MM, et al: Cannulation strategies for percutaneous extracorporeal membrane oxygenation in adults. *Clin Res Cardiol* 105: 283–296, 2016.
8. Van Linthout S, Tschöpe C: Inflammation – Cause or consequence of heart failure or both? *Curr Hear Fail Rep* 14: 251–265, 2017.
9. Tschöpe C, Van Linthout S, Klein O, et al: Mechanical unloading by fulminant myocarditis: LV-IMPELLA, ECMELLA, BI-PELLA, and PROPELLA concepts. *J Cardiovasc Transl Res* 12: 116–123, 2019.
10. Werdan K, Gielen S, Ebelt H, Hochman JS: Mechanical circulatory support in cardiogenic shock. *Eur Heart J* 35: 156–167, 2014.
11. Nuding S, Werdan K: IABP plus ECMO-Is one and one more than two? *J Thorac Dis* 9: 961–964, 2017.
12. Patel SM, Lipinski J, Al-Kindi SG, et al: Simultaneous venoarterial extracorporeal membrane oxygenation and percutaneous left ventricular decompression therapy with Impella is associated with improved outcomes in refractory cardiogenic shock. *ASAIO J* 65: 21–28, 2019.
13. Lamb KM, DiMuzio PJ, Johnson A, et al: Arterial protocol including prophylactic distal perfusion catheter decreases limb ischemia complications in patients undergoing extracorporeal membrane oxygenation. *J Vasc Surg* 65: 1074–1079, 2017.
14. Jin Jang W, Hyun Cho Y, Kyu Park T, et al: Fluoroscopy-guided simultaneous distal perfusion as a preventive strategy of limb ischemia in patients undergoing extracorporeal membrane oxygenation. *Ann Intensive Care* 8: 101, 2018.
15. Slaughter MS: Hematologic effects of continuous flow left ventricular assist devices. *J Cardiovasc Transl Res* 3: 618–624, 2010.
16. Ko WJ, Lin CY, Chen RJ, Wang SS, Lin FY, Chen YS: Extracorporeal membrane oxygenation support for adult postcardiotomy cardiogenic shock. *Ann Thorac Surg* 73: 538–545, 2002.
17. Tepper S, Garcia MB, Fischer I, et al: Clinical outcomes and reduced pulmonary artery pressure with intra-aortic balloon pump during central extracorporeal life support. *ASAIO J* 65: 173–179, 2019.
18. Al-Fares AA, Randhawa VK, Englesakis M, et al: Circulation: Heart failure optimal strategy and timing of left ventricular venting during veno-arterial extracorporeal life support for adults in cardiogenic shock a systematic review and meta-analysis. *Circ Hear Fail* 12: e006486, 2019.