Concomitant use of extracorporeal membrane oxygenation and percutaneous microaxial assist device support for cardiogenic shock

Shan P. Modi, MD,[a] Yeahwa Hong, MD,[b] McKenzie M. Sicke, BE,[c] Nicholas R. Hess, MD,[d] Wyatt J. Klass, BS,[e] Luke A. Ziegler, BA,[e] Ryan M. Rivosecchi, PharmD,[f] Gavin W. Hickey, MD,[g] David J. Kaczorowski, MD,[d] and Raj Ramanan, MD[a]

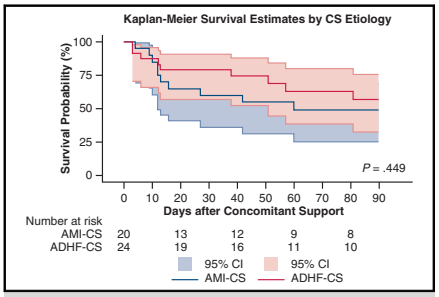
ABSTRACT

Objectives: Venoarterial extracorporeal membrane oxygenation (VA-ECMO) with concomitant percutaneous microaxial left ventricular assist device support is an emerging treatment modality for cardiogenic shock (CS). Survival outcomes by CS etiology with this support strategy have not been well described.

Methods: This study was a retrospective, single-center analysis of patients with CS due to acute myocardial infarction (AMI-CS) or decompensated heart failure (ADHF-CS) supported with VA-ECMO with concomitant percutaneous microaxial left ventricular assist device support from December 2020 to January 2023.

Results: A total of 44 patients were included (AMI-CS, n = 20, and ADHF-CS, n = 24). Patients with AMI-CS and ADHF-CS had similar survival at 90 days postdischarge ($P = .267$) with similar destinations after support ($P = .220$). Patients with AMI-CS initially supported with VA-ECMO were less likely to survive 90 days postdischarge ($P = .038$) when compared with other cohorts. Limb ischemia and acute kidney injury occurred more frequently in patients presenting with AMI-CS ($P = .013$; $P = .030$). Subanalysis of ADHF-CS patients into acute-on-chronic decompensated HF and de novo HF demonstrated no difference in survival or destination.

Conclusions: VA-ECMO with concomitant percutaneous microaxial left ventricular assist device support can be used to successfully manage patients with CS. There is no difference in survival or destination for AMI-CS and ADHF-CS with this support strategy. AMI-CS patients with initial VA-ECMO support have increased mortality in comparison to other cohorts. Future multicenter studies are required to fully analyze the differences between AMI-CS and ADHF-CS with this support strategy. (JTCVS Open 2024;17:152-61)



No survival differences exist between CS etiologies supported with VA-ECMO and pVAD.

CENTRAL MESSAGE

VA-ECMO with a percutaneous microaxial left ventricular assist device is a feasible strategy for severe CS with no difference in survival between differing CS phenotypes.

PERSPECTIVE

Limited studies analyze the concomitant use of support strategies in CS. Concomitant support may have varying survival outcomes dependent on initial support or CS etiology. Multicenter studies analyzing outcomes with differing CS phenotypes are necessary to ascertain the optimal support strategy in patients with SCAI stage D and E shock.

Cardiogenic shock (CS) is a complex syndrome associated with low cardiac output secondary to dysfunctional myocardium leading to end-organ hypoperfusion, systemic vasoconstriction, and generalized hypoxia. Early recognition with initiation of inotropic and/or mechanical support is essential in the management of CS.[1] However, the

From the Departments of [a]Critical Care Medicine, [b]Surgery, [d]Cardiothoracic Surgery, and [f]Pharmacy; [c]School of Medicine; [e]Heart and Vascular Institute; and [g]Division of Cardiology, University of Pittsburgh Medical Center, Pittsburgh, Pa.

Dr Hong is supported (T32HL160526) by the National Heart, Lung, and Blood Institute (NHLBI) and the Thoracic Surgery Foundation Resident Research Fellowship. There is no direct funding from the NHLBI related to this work.

IRB Number: 18120143 (Date of approval: April 17, 2019).

Informed Consent Statement: Informed consent was waived by our local institutional review board due to the retrospective nature of the study.

Received for publication Sept 26, 2023; revisions received Nov 21, 2023; accepted for publication Dec 11, 2023; available ahead of print Jan 12, 2024.

Address for reprints: Shan P. Modi, MD, Department of Critical Care Medicine, University of Pittsburgh Medical Center, 200 Lothrop St, Pittsburgh, PA 15213 (E-mail: shanmodi13@gmail.com).

2666-2736

https://doi.org/10.1016/j.xjon.2023.12.005

Abbreviations and Acronyms

ACDHF = acute-on-chronic decompensated heart failure
ADHF-CS = acute decompensated heart failure complicated by cardiogenic shock
AKI = acute kidney injury
AMI-CS = acute myocardial infarction complicated by cardiogenic shock
CRRT = continuous renal replacement therapy
CS = cardiogenic shock
CVVHD = continuous venovenous hemodialysis
IABP = intra-aortic balloon pump
NNT = number needed to treat
pVAD = percutaneous microaxial left ventricular assist device
SCAI = Society of Cardiovascular Angiography and Intervention
TIMI = Thrombolysis in Myocardial Infarction
VA-ECMO = venoarterial extracorporeal membrane oxygenation

outcomes of patients with CS remain poor with short-term mortality exceeding 50%, despite early coronary revascularization in the setting of acute myocardial infarction (AMI).[1,2] Over the past decade, temporary mechanical circulatory support devices have emerged as a pivotal component of CS management.[3] Among the available technologies, both venoarterial extracorporeal membrane oxygenation (VA-ECMO) and transvalvular percutaneous microaxial left ventricular assist devices (pVAD), such as the Impella (Abiomed), are increasingly employed in patients with severe CS.[2,4]

The use of VA-ECMO has grown exponentially over the past decade in the United States, especially in the setting of CS secondary to AMI.[5] Peripheral VA-ECMO is able to provide full circulatory support, although the retrograde nature of the blood flow toward the heart leads to increased left ventricular afterload and wall stress.[6] In the setting of severely impaired left ventricular contractility, the left ventricle may become pressurized with increased end-diastolic volume causing increased myocardial oxygen demand.[7] Furthermore, overall coronary perfusion may become compromised due to high diastolic ventricular pressures.[8] The incidence of left ventricular overload from VA-ECMO varies widely, but the previously reported rate is as high as 70%.[8,9] With emerging evidence suggesting adverse consequences of left ventricular overload, the topic of left ventricular unloading strategies is an area of active investigation.[9]

Of the various available strategies, the concomitant use of pVAD support to unload the left ventricle in patients supported with VA-ECMO has been increasingly utilized. Prior studies evaluating the influence of this support strategy in patients with CS have collectively demonstrated favorable outcomes.[10,11] Many of these prior studies were limited to partial flow, peripherally inserted pVADs, such as the Impella 2.5 and CP, with shorter support duration.[12] Therefore, the influence of larger microaxillary pumps with flow support to 6.2 L, such as the Impella 5.5, for longer support duration is rather limited. In this study, we aim to evaluate CS patients with VA-ECMO with concomitant pVAD support with Impella CP or Impella 5.5 and stratify outcomes by CS etiology.

MATERIALS AND METHODS

This single-center, retrospective cohort study was approved by the local institutional review board (#18120143; approved: April 17, 2019) at the University of Pittsburgh Medical Center, and performed in accordance with the principles set forth by the Declaration of Helsinki. This study was completed at the University of Pittsburgh Presbyterian Hospital, an academic tertiary center in the University of Pittsburgh Medical Center Health System. The need for informed consent was waived by our local institutional review board due to the retrospective nature of the study.

Study Population

Patients were identified through internal review of an internal ECMO and Impella database between December 2020 and January 2023. Adult patients (aged 18 years or older) who received simultaneous pVAD support with an Impella CP or Impella 5.5 axial flow pump and VA-ECMO were included in the study. These devices are currently the only percutaneous microaxial flow pumps approved in both the United States and Europe. All devices discussed in this article are of this brand. The Impella CP and 5.5 models can provide hemodynamic support with flows up to 3.5 and 6.2 L/minute, respectively. Patients with postcardiotomy shock were excluded. Systemic anticoagulation with bivalirudin was provided to all patients in concordance with protocol at the study center. Bivalirudin was utilized as the primary anticoagulant because patients at our study center receiving bivalirudin for system anticoagulation experienced a decreased number of ECMO-related thrombotic events and required less blood administration for both venovenous- and VA-ECMO in comparison to heparin.[13,14] All patients received at least 24 hours of concomitant support to be included in the analysis.

Determination of concomitant support for patients declining from CS was made collectively by adjudication via a diverse, multidisciplinary physician team of a cardiothoracic intensivist, cardiothoracic surgeon, and an advanced heart failure cardiologist. For patients transferred from outside hospitals, a cardiogenic shock conference call would be initiated before transfer with the abovementioned specialties to determine the initial mechanical support strategy, if not already initiated, and if any further interventions needed to be performed before transfer to our institution. Our cardiogenic shock team preferentially utilized pVAD support rather than intra-aortic balloon pump (IABP) support for severe cardiogenic shock due to its ability to decrease left ventricular end-diastolic pressure, left ventricular end-systolic volume, and left ventricular end-diastolic volume to a higher magnitude in comparison to IABP.[15] In addition, patients with severe cardiogenic shock would often have significantly decreased pulsatility, which would reduce the efficiency of IABP given its function as a counterpulsation device. Furthermore, given the ability to provide 6.2 L/minute of flow, pVADs were preferred for concomitant support as it allowed for a sufficient stepdown strategy when VA-ECMO support was no longer necessary. Axillary placement of these devices was preferred to allow for improved mobility of patients when compared with patients with IABP or femorally inserted pVADs.

Study Variables

All baseline demographic and laboratory variables were obtained via the internal ECMO and Impella database and cross-referenced with review of the electronic medical record. Patients with VA-ECMO with concomitant pVAD support were classified by CS etiology, including CS secondary to AMI or CS secondary to acute decompensated heart failure (ADHF-CS). Society of Cardiovascular Angiography and Intervention (SCAI) stages are reported from initial patient presentation as defined by the SCAI consensus statement.[16]

Clinical End Points

Primary outcomes assessed were 90-day survival and destination after concomitant support stratified by CS etiology and support strategy. Destinations included death, bridge to recovery, bridge to LVAD, and bridge to heart transplant. Secondary outcomes included length of stay and complications during support, including bleeding per Thrombolysis in Myocardial Infarction (TIMI) score criteria, limb ischemia requiring surgical intervention, deep vein thrombosis or pulmonary embolism, ischemic and hemorrhagic cerebrovascular accidents, infection, acute kidney injury (AKI), necessity for continuous renal replacement therapy (CRRT) or continuous venovenous hemodialysis (CVVHD), and Impella pump thrombosis. Primary and secondary outcomes were also assessed by acute heart failure etiology (de novo heart failure vs acute-on-chronic decompensated heart failure [ACDHF]).

Statistical Analysis

Data are presented as frequency (percentage) for categorical variables, mean ± SD for Gaussian continuous variables and median (interquartile range) for non-Gaussian continuous variables. Pearson χ^2 test was utilized for categorical comparisons with Fisher exact test utilized for group sizes with a $n \leq 5$. Post hoc analysis via Pearson adjusted residuals were utilized to delineate associations in significant categorical comparisons. Student *t* test was employed for parametric continuous variables with Wilcoxon rank sum (Mann-Whitney *U*) test employed for nonparametric variables. Shapiro-Wilk test was applied to all continuous variables to assess for normality. Kaplan-Meier survival estimate curves were calculated with freedom from mortality and assessed by 2-sided log-rank test. Time-to-event analysis was censored for patients that received a heart transplant or durable left ventricular assist device for the duration of this study. Analyses were performed via Stata SE version 17.0 (StataCorp).

RESULTS

Baseline Characteristics

Forty-five patients with CS and concomitant VA-ECMO and pVAD support were identified in our registry with 1 patient with postcardiotomy shock excluded. Twenty patients (45.5%) sustained CS secondary to AMI. Baseline characteristics are summarized in Table 1. Patients who presented with AMI-CS were more likely to be diabetic (AMI-CS: 70.0%, ADHF-CS: 25.0%; $P = .003$) and have a prior history of coronary artery disease (AMI-CS: 85.0%, ADHF-CS: 33.3%; $P = .001$). In addition, patients that presented with AMI-CS were more likely to have coronary intervention during their admission (AMI-CS: 90.0%, ADHF-CS: 12.5%; $P < .001$). Of the 18 patients with AMI-CS, 4/18 received surgical revascularization with coronary artery bypass grafting and 14 out of 18 received percutaneous coronary intervention with culprit-only revascularization.

In a subanalysis stratifying patients with ADHF-CS into ACDHF and de novo HF, 12 patients (50.0%) presented with de novo acute HF (Table 2). Patients with ACDHF were more likely to be older (ACHDF: 57.8 ± 10.4, de novo HF: 41.4 ± 14.6; $P = .044$) and male (ACHDF: 91.7%, de novo HF: 25.0%; $P = .001$). Patients with ACDHF were more likely to have hypertension (ACDHF: 66.7%, de novo HF: 25.0%; $P = .041$) and chronic kidney disease (ACDHF: 50.0%, de novo HF: 0.0%; $P = .005$).

Clinical End Points

The overall 90-day postdischarge survival with concomitant VA-ECMO and pVAD support was 54.6% (Table 3). There was no significant difference in 90-day postdischarge survival among patients with AMI-CS and ADHF-CS (AMI-CS: 45.0%, ADHF-CS: 62.5%; $P = .335$) (Figure 1). However, patients with AMI-CS and initial VA-ECMO had lower survival at 90 days postdischarge than other cohorts (AMI-CS with initial VA-ECMO: 10.0%; $P = .038$). In the ADHF-CS cohort (Table 4), no significant difference in 90-day postdischarge survival was detected between each subgroup (ACDHF: 41.7%, de novo HF: 83.3%; $P = .057$) and there was no difference in survival by initial support strategy ($P = .296$).

In our study population, 36.4% of patients recovered with only VA-ECMO with concomitant pVAD support, whereas 11.4% of patients were bridged to left ventricular assist device support and another 11.4% of patients were bridged to heart transplant. Although more patients with ADHF-CS were bridged to advanced therapies (left ventricular assist device or heart transplant), there was no significant difference in destination between AMI-CS and ADHF-CS cohorts ($P = .220$) (Figure 2). Among patients with ADHF-CS, there was no significant difference in destination between subgroups despite a larger proportion of patients with de novo HF who recovered without transition to advanced therapies (ACDHF: 25.0%, de novo HF: 50%; $P = .515$).

The overall median length of stay for all patients was 31 days with no significant differences between CS subtypes. Patients with AMI-CS were more likely to sustain limb ischemia (AMI-CS: 40%, ADHF-CS: 8.3%; $P = .013$) and AKI (AMI-CS: 100.0%, ADHF-CS: 79.2%; $P = .030$). For ADHF-CS subgroups, patients with ACDHF had a higher proportion of patients requiring CRRT (ACDHF: 58.3%, de novo HF: 16.7%; $P = .035$), whereas a larger proportion of patients with de novo HF experienced minor TIMI bleeding (ACDHF: 33.3%, de novo HF: 75.0%; $P = .041$).

DISCUSSION

The aim of this study was to stratify survival outcomes among patients supported with VA-ECMO with concomitant pVAD support and describe the interaction between

TABLE 1. Baseline characteristics by cardiogenic shock (CS) etiology

Variable	All (n = 44)	AMI-CS (n = 20)	ADHF-CS (n = 24)	*P* value
Patient demographic				
Male	27 (61.4)	13 (65.0)	14 (58.3)	.651
Age (y)	51.8 ± 13.0	54.5 ± 9.9	49.6 ± 14.9	.224
Race				.160
White	35 (79.5)	15 (75.0)	20 (83.3)	
Black	2 (4.5)	0 (0)	2 (8.3)	
Not specified	7 (16.0)	5 (25.0)	2 (8.3)	
DCI	44.2 ± 26.7	49.2 ± 27.1	40.0 ± 26.3	.264
Transfer	36 (81.8)	17 (85.0)	19 (79.2)	.617
SCAI stage before MCS				.557
C	8 (18.2)	4 (20.0)	4 (16.7)	
D	17 (38.6)	6 (30.0)	11 (45.8)	
E	19 (43.2)	10 (50.0)	9 (37.4)	
Comorbidities				
HTN	23 (52.3)	12 (60.0)	11 (45.8)	.349
DM	20 (45.5)	14 (70.0)	6 (25.0)	**.003**
CKD	8 (18.2)	2 (10.0)	6 (25.0)	.199
CAD	25 (56.8)	17 (85.0)	8 (33.3)	**.001**
CVA/TIA	2 (4.6)	1 (5.0)	1 (4.2)	.895
DVT/PE	1 (2.3)	0 (0.0)	1 (4.2)	.356
Atrial fibrillation	3 (6.8)	1 (5.0)	2 (8.3)	.662
PAD	2 (4.6)	0 (0.0)	2 (8.3)	.186
COPD	3 (6.8)	1 (5.0)	2 (8.3)	.662
Coronary intervention and mechanical support				
Impella* type				.908
Impella CP	15 (34.1)	7 (35.0)	8 (33.3)	
Impella 5.5	29 (65.9)	13 (65.0)	16 (66.7)	
Days to Impella* placement	1 (0-3)	1 (0-2.5)	1.5 (0-5.5)	.177
Days of Impella* support	11 (6.0-22.5)	11.5 (7.0-29.5)	11 (6.0-15.5)	.555
Initial VA-ECMO support	21 (47.7)	11 (55)	10 (41.7)	.378
Coronary intervention	21 (47.7)	18 (90.0)	3 (12.5)	<**.001**
Labs before support				
Lowest pH	7.30 (7.22-7.36)	7.30 (7.20-7.34)	7.33 (7.22-7.40)	.317
Highest lactate (mmol/L)	4.3 (2.1-9.6)	9.1 (2.75-11.5)	3.3 (1.9-7.1)	.113
Lowest hemoglobin (g/dL)	10.6 ± 2.9	10.2 ± 3.1	11.0 ± 2.8	.380
Lowest platelets (10^9/L)	151 (99-237)	166.5 (95-261)	136 (102-216)	.671
Highest creatinine (mg/dL)	1.5 (1.1-2.4)	1.6 (1.2-2.7)	1.4 (1.1-2.4)	.629
Highest total bilirubin (mg/dL)	1.4 (0.6-2.4)	1.1 (0.7-1.5)	1.4 (0.6-2.6)	.398

Values are presented as mean ± SD, n (%), or median (interquartile range). The bolded numbers are *P*-values that are <.05. *AMI*, Acute myocardial infarction; *ADHF*, acute decompensated heart failure; *DCI*, Distressed Communities' Index; *SCAI*, Society of Cardiovascular Angiography and Intervention; *MCS*, mechanical circulatory support; *HTN*, hypertension; *DM*, diabetes mellitus; *CKD*, chronic kidney disease; *CAD*, coronary artery disease; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *DVT*, deep vein thrombosis; *PE*, pulmonary embolism; *PAD*, peripheral artery disease; *COPD*, chronic obstructive pulmonary disease; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation. *Abiomed.

CS etiology and initial support strategy in regard to survival and destination. The overall 90-day postdischarge survival of all patients with CS was 54.6%, illustrating the vulnerability of the CS population despite maximal cardiac support. This support strategy was employed in a severely ill cohort of patients with CS in this study, in which patients with AMI-CS with initial VA-ECMO support had a significant higher mortality than other cohorts. There was no difference in 90-day survival or destination between the AMI-CS and ADHF-CS cohorts and stratification of the ADHF-CS cohort into ACDHF and de novo HF groups did not reveal a significant difference in survival or destination.

AMI-CS and ADHF-CS are 2 distinct phenotypes of CS with differing pathophysiology.[17] Patients with AMI-CS undergo an abrupt reduction in functional myocardium requiring an extensive period of ventricular remodeling and are heavily dependent on revascularization for rescue of viable myocardium.[18] The pathophysiology of ADHF-CS is

TABLE 2. Baseline characteristics: Acute-on-chronic decompensated heart failure (ACDHF) versus de novo HF

Variable	ACDHF (n = 12)	De novo HF (n = 12)	*P* value
Patient demographics			
Age (y)	57.8 ± 10.4	41.4 ± 14.6	**.044**
Male	11 (91.7)	3 (25.0)	**.001**
SCAI stage			.381
C	1 (8.3)	3 (25.0)	
D	7 (58.3)	4 (33.3)	
E	4 (33.3)	5 (41.7)	
Impella* type			1.000
CP	4 (33.3)	4 (33.3)	
5.5	8 (66.7)	8 (66.7)	
Initial support strategy			
Impella*	9 (75.0)	5 (41.7)	.098
VA-ECMO	3 (25.0)	7 (58.3)	
Days to Impella* placement	1.5 (0.5-9)	1.5 (0-3)	.394
Days of Impella* support	10.5 (4-26)	11 (6.5-15.5)	.750
Comorbidity			
HTN	8 (66.7)	3 (25.0)	**.041**
DM	3 (25.0)	3 (25.0)	1.000
CKD	6 (50.0)	0 (0.0)	**.005**
CAD	7 (58.3)	1 (8.3)	.009
CVA/TIA	1 (8.3)	0 (0.0)	.307
DVT/PE	1 (8.3)	0 (0.0)	.307
Atrial fibrillation	2 (16.7)	0 (0.0)	.140
PAD	2 (16.7)	0 (0.0)	.140
COPD	1 (8.3)	1 (8.3)	1.000
Labs before support			
Lowest pH	7.34 (7.26-7.43)	7.3 (7.14-7.37)	.267
Highest lactate (mmol/L)	3.9 (2.4-4.8)	2.4 (1.5-10.3)	.689
Lowest hemoglobin (g/dL)	10.3 (9.0-12.3)	12.1 (7.8-13.6)	.817
Lowest platelets (10^9/L)	136.0 (111.5-189.5)	142 (93.5-238.0)	.954
Highest creatinine (mg/dL)	1.9 (1.1-2.5)	1.3 (0.9-2.4)	.285
Highest total bilirubin (mg/dL)	1.4 (0.7-3.1)	0.7 (0.6-2.4)	.372

Values are presented as mean ± SD, n (%), or median (interquartile range). The bolded numbers are *P*-values that are <.05. *SCAI*, Society of Cardiovascular Angiography and Intervention; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *HTN*, hypertension; *DM*, diabetes mellitus; *CKD*, chronic kidney disease; *CAD*, coronary artery disease; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *DVT*, deep vein thrombosis; *PE*, pulmonary embolism; *PAD*, peripheral artery disease; *COPD*, chronic obstructive pulmonary disease. *Abiomed.

incompletely understood and has been attributed to multiple factors, including prior comorbidities, prior myocardial damage from previous ischemic insults or inflammatory processes such as myocarditis, and neurohormonal activation states influencing arterial and venous vascular tone.[19] Limited evidence exists regarding the differing mortality between these 2 cohorts; however, a recent single-center study by Sinha and colleagues[17] demonstrated that patients with ADHF-CS have a lower 1-year mortality compared with patients with AMI-CS. This difference was attributed to patients with ADHF-CS possessing a higher tolerance of lower cardiac output states due to development of chronic compensation, although this is only applicable to patients with ACDHF rather than patients presenting with de novo HF.[17,20,21]

The lack of significant difference in survival and destination to advanced therapies in our study between the ADHF-CS cohort and AMI-CS cohort is multifactorial. Despite their differing pathophysiology, approximately 80% of the patients in this study presented with SCAI stage D or E shock, suggesting that end-organ damage had already occurred before full cardiac support with this support strategy. This is supported by almost 90% of all-comers in CS presenting with AKI before full support. These findings contrast with the prior study by Sinha and colleagues[17] in which only 10% of all-comers with CS received VA-ECMO and concomitant pVAD support and 50% of patients presented with SCAI stage C shock. Although there was a trend toward increased survival in the ADHF-CS cohort at 90 days (ADHF-CS: 62.5%, AMI-CS: 50%,

TABLE 3. Primary and secondary outcomes by cardiogenic shock (CS) etiology

Variable	All (n = 44)	AMI-CS (n = 20)	ADHF-CS (n = 24)	*P* value
Primary outcome				
Destination				.220
Death	18 (40.9)	11 (55.0)	7 (29.2)	
Bridge to recovery	16 (36.4)	7 (35.0)	9 (37.5)	
Bridge to LVAD	5 (11.4)	1 (5.0)	4 (16.7)	
Bridge to transplant	5 (11.4)	1 (5.0)	4 (16.7)	
90-d survival post-ECpella*	25 (56.8)	10 (50.0)	15 (62.5)	.449
Survival to discharge	25 (56.8)	9 (45.0)	16 (66.7)	.231
90-d survival postdischarge	24 (54.6)	9 (45.0)	15 (62.5)	.335
90-d survival by initial support				
VA-ECMO		2 (10.0)†	7 (29.2)	**.038**
Impella*		7 (35.0)	8 (33.4)	
Secondary outcome				
LOS (d)	31 (14.5-47)	29.5 (14.5-48.5)	35.5 (14.5-47)	.176
Limb ischemia	10 (22.7)	8 (40.0)	2 (8.3)	**.013**
DVT/PE	11 (25)	5 (25.0)	6 (25.0)	1.000
CVA	7 (15.9)	4 (20.0)	3 (12.5)	.516
Ischemic	6 (13.6)	3 (15.0)	3 (12.5)	
Hemorrhagic	1 (2.3)	1 (5.0)	0 (0.0)	
Major TIMI bleeding	5 (11.4)	2 (10.0)	3 (12.5)	.795
Minor TIMI bleeding	23 (52.3)	10 (22.7)	11 (29.6)	.783
Infection	26 (59)	12 (27.3)	14 (31.8)	.911
AKI	39 (88.6)	20 (100.0)	19 (79.2)	**.030**
CRRT/CVVHD	15 (34.1)	6 (30.0)	9 (37.5)	.601
Pump thrombosis	1 (2.3)	0 (0.0)	1 (4.2)	.356

Values are presented as n (%) or median (interquartile range). The bolded numbers are *P*-values that are <.05. *AMI*, Acute myocardial infarction; *ADHF*, acute decompensated heart failure; *LVAD*, left ventricular assist device; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *LOS*, length of stay; *DVT*, deep vein thrombosis; *PE*, pulmonary embolism; *CVA*, cardiovascular accident; *TIMI*, Thrombolysis in Myocardial Infarction; *AKI*, acute kidney injury; *CRRT*, continuous renal replacement therapy; *CVVHD*, continuous venovenous hemodialysis. *Abiomed. †$P < .05$ by adjusted residuals.

number needed to treat [NNT]: 8.0), durable left ventricular assist device implantation (ADHF-CS: 16.7%, AMI-CS: 5%, NNT: 8.5), and heart transplant (ADHF-CS: 16.7%, AMI-CS: 5%, NNT: 8.5), the lack of significant differences may be attributed to the study being underpowered to detect true differences, if they exist. As the use of VA-ECMO and concomitant pVAD support continues to increase for refractory CS, further research with larger sample sizes is needed to delineate survival and destination differences between these 2 cohorts.

Patients with AMI-CS with initial VA-ECMO support had significantly higher mortality within 90 days relative to other cohorts. A recent meta-analysis by Batchelor and colleagues[22] demonstrated that patients with AMI-CS (n = 7093) that were treated with Impella support rather than VA-ECMO support had reduced short- and medium-term mortality, which was attributed to the initial increased afterload with VA-ECMO limiting myocardial recovery. Although the median for Impella placement after VA-ECMO support was 1 day, recent studies have shown that left ventricular venting via pVADs before 12 hours of support is associated with reduced short-term mortality.[22-24] Therefore, this initial increase in afterload to the left ventricle may have limited initial myocardial recovery and resulted in additional complications that influenced mortality and eventual destination despite the majority of patients with AMI-CS receiving coronary intervention. All 4 patients who received coronary artery bypass grafting and 2 patients who received culprit-only percutaneous coronary intervention had VA-ECMO support with concomitant pVAD support before coronary intervention with no difference in survival in comparison to patients with AMI-CS who received full support after coronary intervention. Further studies are required to determine whether or not this support strategy before coronary intervention in SCAI stage D or E shock leads to improved outcomes in AMI-CS because most studies have only compared the use of 1 device rather than the combination.[22]

Regarding secondary outcomes, patients with AMI-CS were more likely to sustain limb ischemia requiring surgical intervention and all patients with AMI-CS sustained AKI during their hospital admission. These outcomes are likely secondary to lack of compensatory mechanisms to lower cardiac output states that have been demonstrated in

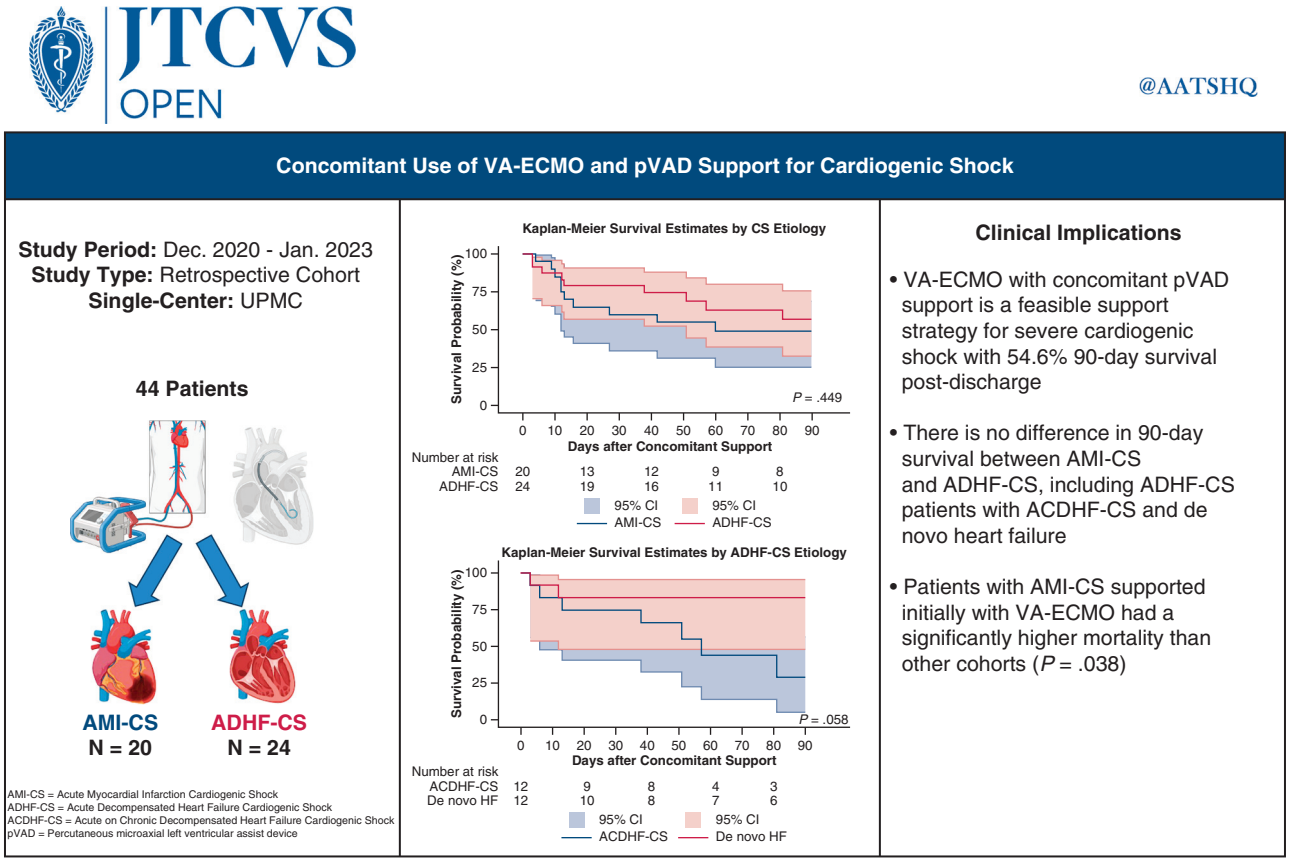


FIGURE 1. Cardiogenic shock (*CS*) etiology does not affect 90-day survival. A total of 62.5% (n = 16) of patients with acute decompensated heart failure (*ADHF*) CS survived after 90 days after venoarterial extracorporeal membrane oxygenation with concomitant percutaneous microaxial left ventricular assist device support compared with 45% (n = 9) of patients with acute myocardial infarction complicated by CS ($P = .449$). In a subanalysis of ADHF-CS, 41.7% (n = 5) of patients with ADHF-CS survived after 90 days postsupport compared with 83.3% (n = 10) of patients with de novo heart failure ($P = .058$). *VA-ECMO*, Venoarterial extracorporeal membrane oxygenation; *pVAD*, percutaneous microaxial left ventricular assist device; *AMI*, acute myocardial infarction. Illustration created with BioRender.com.

patients with ADHF-CS due to long-term adaptation to left ventricle dilation and higher filling pressures.[16,21,25] In addition, despite 0% of patients with AMI-CS having a prior diagnosis of peripheral artery disease, we suspect this is potentially due to underdiagnosis and these patients likely had higher burden of atherosclerosis leading to a higher incidence of limb ischemia in this cohort. Furthermore, 10% of patients with AMI-CS were unable to get coronary intervention due to significant shock despite concomitant support, which likely exacerbated these complications. Lastly, 5 patients with AMI-CS had femoral-placed microaxillary left ventricular assist devices (Impella CP) in comparison to 2 patients in ADHF-CS group that experienced limb ischemia. Limb ischemia has been a known complication this device, and in combination with the abovementioned comorbidities in the AMI-CS cohort, likely led to an increased propensity towards limb ischemia.[26] The use of bilateral distal perfusion catheters in patients with concomitant VA-ECMO and femoral microaxillary pumps have been shown to be feasible and can potentially lead to less limb ischemia in this cohort.[27]

In the subanalysis of patients with ADHF-CS, patients with de novo HF had similar survival and destination to advanced therapies compared with patients with ACDHF despite being younger and having fewer comorbidities. Although patients with de novo HF trended toward increased survival at 90 days postdischarge (de novo HF: 83.3%, ACDHF: 41.7%, NNT: 2.4%), the lack of significant difference may be attributed to the study being underpowered to detect true differences, if they exist. Patients with ACDHF have been hypothesized to have physiologic adaptations that preserve stroke volume with lower left ventricular ejection fraction and have even been shown to have different myosin structure in diaphragmatic muscles to assist oxidative capacity.[21] These compensatory mechanisms have led to patients with ACDHF having similar and even lower short-term mortality rates than those with de novo HF in large retrospective studies.[21,28] Although patients with de novo HF supported

TABLE 4. Primary and secondary outcomes: Acute-on-chronic decompensated heart failure (ACDHF) versus de novo HF

Variable	ACDHF (n = 12)	De novo HF (n = 12)	*P* value
Primary outcome			
Destination			.515
Death	5 (41.7)	2 (16.7)	
Bridge to recovery	3 (25.0)	6 (50.0)	
Bridge to LVAD	2 (16.7)	2 (16.7)	
Bridge to transplant	2 (16.7)	2 (16.7)	
90-d survival post-ECpella*	5 (41.7)	10 (83.3)	.058
Survival to discharge	6 (50.0)	10 (83.3)	.126
90-d survival postdischarge	5 (41.7)	10 (83.3)	.058
90-d survival by initial support			.296
VA-ECMO	1 (8.3)	6 (50.0)	
Impella*	4(33.3)	4 (33.3)	
Secondary outcome			
LOS (d)	44.5 (17.5-49)	28 (12-39)	.174
Limb ischemia	1 (8.3)	1 (8.3)	1.000
DVT/PE	1 (8.3)	5 (41.7)	.059
CVA			.537
Ischemic	1 (8.3)	2 (16.7)	
Hemorrhagic	0 (0.0)	0 (0.0)	
Major TIMI bleeding	1 (8.3)	2 (16.7)	.537
Minor TIMI bleeding	4 (33.3)	9 (75.0)	**.041**
Infection	8 (66.7)	6 (50.0)	.408
AKI	10 (83.3)	9 (75.0)	.615
CRRT/CVVHD	7 (58.3)	2 (16.7)	**.035**
Pump thrombosis	1 (8.3)	0 (0.0)	.307

Values are presented as n (%) or median (interquartile range). The bolded numbers are *P*-values that are <.05. *LVAD*, Left ventricular assist device; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *LOS*, length of stay; *DVT*, deep vein thrombosis; *PE*, pulmonary embolism; *CVA*, cardiovascular accident; *TIMI*, Thrombolysis in Myocardial Infarction; *AKI*, acute kidney injury; *CRRT*, continuous renal replacement therapy; *CVVHD*, continuous venovenous hemodialysis. *Abiomed.

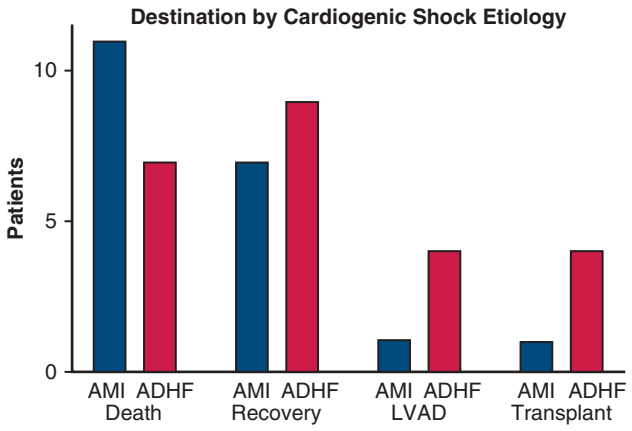


FIGURE 2. Destination does not vary with cardiogenic shock (*CS*) etiology. Despite a higher proportion of patients with acute myocardial infarction (*AMI*) CS who died while on venoarterial extracorporeal membrane oxygenation with concomitant percutaneous microaxial left ventricular assist device support (55%; n = 11) compared with patients with acute decompensated heart failure (*ADHF*) complicated by CS (29%; n = 7), there was no statistical significance in destination between the 2 cohorts (*P* = .220). *LVAD*, Left ventricular assist device.

on VA-ECMO with concomitant pVAD support trended toward higher survival at 90 days postdischarge, further studies with larger sample sizes in these groups are required to minimize the potential of Type II error in this cohort.

Patients with ACDHF were more likely to require continuous venovenous hemodialysis (CVVHD) or CRRT, whereas patients with de novo HF had higher TIMI minor bleeding events. The greater progression to CVVHD/CRRT in the ACDHF group was likely secondary to a higher proportion of patients with chronic kidney disease before VA-ECMO with concomitant pVAD support. Given that TIMI score criteria for minor bleeding is based off hemoglobin level $\geq$3 g/dL, it is unclear if patients with de novo HF had higher bleeding events or initially had hemodilution from greater volume resuscitation due to initial undifferentiated shock, which warrants further investigation.

Limitations

Despite this study's strengths in evaluating VA-ECMO with concomitant pVAD support across AMI-CS and ADHF-CS, there are several limitations that should be

acknowledged. To begin, given that the use of VA-ECMO with concomitant pVAD support is often limited to a subset of patients with CS who are extremely ill, the low sample size of each cohort may have contributed to the study being underpowered to detect true differences between each group. Despite similar SCAI staging between AMI-CS cohorts and ADHF-CS cohorts, patients with AMI-CS with initial VA-ECMO support were potentially more ill on presentation, necessitating emergency placement on VA-ECMO as the initial support strategy and therefore influencing their overall survival in this study. The duration of chronic HF before presentation is unknown in the ACDHF cohort, and varying chronicity of HF is a factor not accounted for in survival analysis of this study. Our study also had a higher proportion of White men, influencing the generalizability to the greater CS population. Lastly, given that the study is retrospective, nonrandomized and only involves a single-center, the study is subject to potential selection bias and subject to center-specific practice patterns in CS management. Future multicenter, randomized, adequately powered, prospective studies are necessary to validate our results and analyze all associations related to VA-ECMO with concomitant pVAD support for different phenotypes of CS.

CONCLUSIONS

VA-ECMO with concomitant pVAD support is a feasible support strategy for both AMI-CS and ADHF-CS with no difference in survival rates or destination. Patients with AMI-CS and initial VA-ECMO support tend to have worse survival outcomes at 90 days compared with patients with AMI-CS initially supported with an Impella device. Patients with AMI-CS are more prone to sustaining AKI and limb ischemia requiring surgical intervention as complications of support. No survival or destination differences are noted between patients with ACDHF and de novo HF, although patients with ACDHF are more likely require CRRT/CVVHD. Future large, multicenter studies are required to fully discern the differences between CS phenotypes with this support strategy.

Conflict of Interest Statement

Dr Kaczorowski has received consultant and speaking fees from Medtronic and Abiomed and has an intellectual property interest in ECMOTek LLC. Dr Hickey has received speaking fees from Abiomed. Mr Klass receives consultant fees from Boston Scientific. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK, et al. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e232-68.
2. Wayangankar SA, Bangalore S, McCoy LA, Jneid H, Latif F, Karrowni W, et al. Temporal trends and outcomes of patients undergoing percutaneous coronary interventions for cardiogenic shock in the setting of acute myocardial infarction: a report from the CathPCI Registry. *JACC Cardiovasc Interv*. 2016;9:341-51.
3. Adams KF, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J*. 2005;149:209-16.
4. Shah M, Patnaik S, Patel B, Ram P, Garg L, Agarwal M, et al. Trends in mechanical circulatory support use and hospital mortality among patients with acute myocardial infarction and non-infarction related cardiogenic shock in the United States. *Clin Res Cardiol*. 2018;107:287-303.
5. Vallabhajosyula S, Prasad A, Bell MR, Sandhu GS, Eleid MF, Dunlay SM, et al. Extracorporeal membrane oxygenation use in acute myocardial infarction in the United States, 2000 to 2014. *Circ Heart Fail*. 2019;12:e005929.
6. Dickstein ML. The starling relationship and veno-arterial ECMO: ventricular distension explained. *ASAIO J*. 2018;64:497-501.
7. Donker DW, Brodie D, Henriques JPS, Broomé M. Left ventricular unloading during veno-arterial ECMO: a review of percutaneous and surgical unloading interventions. *Perfusion*. 2019;34:98-105.
8. Belohlavek J, Hunziker P, Donker DW. Left ventricular unloading and the role of ECpella. *Eur Heart J Suppl*. 2021;23(Suppl A):A27-34.
9. Truby LK, Takeda K, Mauro C, Yuzefpolskaya M, Garan AR, Kirtane AJ, et al. Incidence and implications of left ventricular distention during venoarterial extracorporeal membrane oxygenation support. *ASAIO J*. 2017;63:257-65.
10. Pappalardo F, Schulte C, Pieri M, Schrage B, Contri R, Soeffker G, et al. Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock. *Eur J Heart Fail*. 2017;19:404-12.
11. Patel SM, Lipinski J, Al-Kindi SG, Patel T, Saric P, Li J, 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*. 2019;65:21.
12. Grajeda Silvestri ER, Pino JE, Donath E, Torres P, Chait R, Ghumman W. Impella to unload the left ventricle in patients undergoing venoarterial extracorporeal membrane oxygenation for cardiogenic shock: a systematic review and meta-analysis. *J Card Surg*. 2020;35:1237-42.
13. Rivosecchi RM, Arakelians AR, Ryan J, Murray H, Ramanan R, Gomez H, et al. Comparison of anticoagulation strategies in patients requiring venovenous extracorporeal membrane oxygenation: heparin versus bivalirudin. *Crit Care Med*. 2021;49:1129-36.
14. Uricchio MN, Ramanan R, Esper SA, Murray H, Kaczorowski DJ, D'Aloiso B, et al. Bivalirudin versus unfractionated heparin in patients with cardiogenic shock requiring venoarterial extracorporeal membrane oxygenation. *ASAIO J*. 2023;69:107.
15. De Lazzari B, Capoccia M, Badagliacca R, Bozkurt S, De Lazzari C. IABP versus Impella support in cardiogenic shock: "In Silico" study. *J Cardiovasc Dev Dis*. 2023;10:140.
16. Baran DA, Grines CL, Bailey S, Burkhoff D, Hall SA, Henry TD, et al. SCAI Clinical Expert Consensus Statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Catheter Cardiovasc Interv*. 2019;94:29-37.
17. Sinha SS, Rosner CM, Tehrani BN, Maini A, Truesdell AG, Lee SB, et al. Cardiogenic shock from heart failure versus acute myocardial infarction: clinical characteristics, hospital course, and 1-year outcomes. *Circ Heart Fail*. 2022;15:e009279.
18. Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, et al. Early revascularization improves long-term survival for cardiogenic shock complicating acute myocardial infarction. *JAMA*. 2006;295:2511-5.
19. Garza MA, Wason EA, Zhang JQ. Cardiac remodeling and physical training post myocardial infarction. *World J Cardiol*. 2015;7:52-64.
20. Njoroge JN, Teerlink JR. Pathophysiology and therapeutic approaches to acute decompensated heart failure. *Circ Res*. 2021;128:1468-86.

21. Hummel A, Empen K, Dörr M, Felix SB. De novo acute heart failure and acutely decompensated chronic heart failure. *Dtsch Arztebl Int*. 2015;112:298-310.
22. Batchelor RJ, Wheelahan A, Zheng WC, Stub D, Yang Y, Chan W. Impella versus venoarterial extracorporeal membrane oxygenation for acute myocardial infarction cardiogenic shock: a systematic review and meta-analysis. *J Clin Med*. 2022; 11:3955.
23. Upadhrasta S, Museedi A, Thannoun T, Chaanine AH, Le Jemtel TH. Early mechanical circulatory support for cardiogenic shock. *Cardiol Rev*. 2023;31:215-8.
24. Al-Fares AA, Randhawa VK, Englesakis M, McDonald MA, Nagpal AD, Estep JD, et al. 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 Heart Fail*. 2019;12:e006486.
25. Bhatt AS, Berg DD, Bohula EA, Alviar CL, Baird-Zars VM, Barnett CF, et al. De novo vs acute-on-chronic presentations of heart failure-related cardiogenic shock: insights from the Critical Care Cardiology Trials Network Registry. *J Cardiac Fail*. 2021;27:1073-81.
26. Abaunza M, Kabbani LS, Nypaver T, Greenbaum A, Balraj P, Qureshi S, et al. Incidence and prognosis of vascular complications after percutaneous placement of left ventricular assist device. *J Vasc Surg*. 2015;62:417-23.
27. McDermott L, Cook G, Park J, Yang Q, Hirose H. Save the leg: utilization of distal perfusion catheter with Impella CP® may prevent morbidity of limb. Accessed October 29, 2023. https://www.cureus.com/articles/116346-save-the-leg-utilization-of-distal-perfusion-catheter-with-impella-cp-may-prevent-morbidity-of-limb
28. Younis A, Mulla W, Goldkorn R, Klempfner R, Peled Y, Arad M, et al. Differences in mortality of new-onset (de-novo) acute heart failure versus acute decompensated chronic heart failure. *Am J Cardiol*. 2019;124:554-9.

Key Words: VA-ECMO, cardiogenic, shock, AMI-CS, ADHF-CS, pVAD