Circulation: Heart Failure

ORIGINAL ARTICLE

Clinical Characteristics and Outcomes of Patients Suffering Acute Decompensated Heart Failure Complicated by Cardiogenic Shock

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BACKGROUND: Cardiogenic shock (CS) can stem from multiple causes and portends poor prognosis. Prior studies have focused on acute myocardial infarction-CS; however, acute decompensated heart failure (ADHF)-CS accounts for most cases. We studied patients suffering ADHF-CS to identify clinical factors, early in their trajectory, associated with a higher probability of successful outcomes.

METHODS: Consecutive patients with CS were evaluated (N=1162). We studied patients who developed ADHF-CS at our hospital (N=562). Primary end point was native heart survival (NHS), defined as survival to discharge without receiving advanced HF therapies. Secondary end points were adverse events, survival, major cardiac interventions, and hospital readmissions within 1 year following index hospitalization discharge. Association of clinical data with NHS was analyzed using logistic regression.

RESULTS: Overall, 357 (63.5%) patients achieved NHS, 165 (29.2%) died, and 41 (7.3%) were discharged post advanced HF therapies. Of 398 discharged patients (70.8%), 303 (53.9%) were alive at 1 year. Patients with NHS less commonly suffered cardiac arrest, underwent intubation or pulmonary artery catheter placement, or received temporary mechanical circulatory support, had better hemodynamic and echocardiographic profiles, and had a lower vasoactive-inotropic score at shock onset. Bleeding, hemorrhagic stroke, hemolysis in patients with mechanical circulatory support, and acute kidney injury requiring renal replacement therapy were less common compared with patients who died or received advanced heart failure therapies. After multivariable adjustments, clinical variables associated with NHS likelihood included younger age, history of systemic hypertension, absence of cardiac arrest or acute kidney injury requiring renal replacement therapy, lower pulmonary capillary wedge pressure and vasoactive-inotropic score, and higher tricuspid annular plane systolic excursion at shock onset (all $P<0.05$).

CONCLUSIONS: By studying contemporary patients with ADHF-CS, we identified clinical factors that can inform clinical management and provide future research targets. Right ventricular function, renal function, pulmonary artery catheter placement, and type and timing of temporary mechanical circulatory support warrant further investigation to improve outcomes of this devastating condition.

Key Words: aftercare ■ assisted circulation ■ cardiac catheters ■ critical care ■ heart-assist devices ■ heart failure ■ shock, cardiogenic

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WHAT IS NEW?

- Comprehensive evaluation of consecutive patients developing acute decompensated heart failure-cardiogenic shock and assessment of overall and native heart survival, adverse events, major cardiac interventions, and hospital readmissions up to 1 year following index hospitalization discharge.
- Identification of clinical factors at shock onset and overall stay associated with higher probability for native heart survival.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Right ventricular and renal function and associated renal replacement therapy seem to affect outcomes in acute decompensated heart failure-cardiogenic shock and warrant further investigation.
- Pulmonary artery catheter placement and monitoring, as well as early deployment of mechanical circulatory support over escalation of pharmacotherapy, are clinical practices associated with improved outcomes and can inform the clinical management of acute decompensated heart failure-cardiogenic shock.
- Significant decline in survival and high rates of hospital readmissions within 1 year following hospital discharge for acute decompensated heart failure-cardiogenic shock suggest that longer follow-up might be warranted in this population.

Nonstandard Abbreviations and Acronyms

ADHF	acute decompensated heart failure
AKI	acute kidney injury
AMI	acute myocardial infarction
CS	cardiogenic shock
HF	heart failure
HTx	heart transplantation
IABP	intra-aortic balloon pump
LDH	lactate dehydrogenase
LV	left ventricle/left ventricular
LVAD	left ventricular assist device
MCS	mechanical circulatory support
NHS	native heart survival
OR	odds ratio
PAC	pulmonary artery catheter
PCWP	pulmonary capillary wedge pressure
pVAD	percutaneous ventricular assist device
RRT	renal replacement therapy
RV	right ventricle/right ventricular
SCAI	Society for Cardiovascular Angiography and Interventions
TAPSE	tricuspid annular plane systolic excursion
tMCS	temporary mechanical circulatory support
VAD	ventricular assist device

Cardiogenic shock (CS) is a complex and life-threatening clinical syndrome characterized by impaired cardiac function and end-organ hypoperfusion. Despite therapeutic and technological advances, CS incidence is increasing, and outcomes remain poor.[1–4] CS can be the result of multiple culprit causes with diverse underlying pathophysiology, which may affect response to treatment and subsequent outcomes. Observational studies and randomized clinical trials have primarily focused on CS related to acute myocardial infarction (AMI-CS); however, recent evidence suggests that AMI-CS represents a minority of cases currently managed in cardiovascular intensive care units.[5–7]

Acute decompensated heart failure (ADHF) is a term suggesting new or worsening symptoms and signs of dyspnea, fatigue, and edema that require urgent or emergent medical management and are consistent with underlying myocardial dysfunction.[8] In severe cases, profoundly depressed cardiac function can lead to CS (ADHF-CS). Recent studies have suggested that in-hospital mortality might be lower in ADHF-CS when compared with AMI-CS; however, many ADHF-CS patients require advanced heart failure (HF) therapies like durable left ventricular assist device (LVAD) implantation or heart transplantation (HTx).[9,10] Additionally, the chronicity of HF (acute versus acute-on-chronic) has been suggested to affect ADHF-CS patient outcomes.[3,11] Nonetheless, ADHF-CS remains an underinvestigated clinical entity, and in the absence of clinical trials in this patient population, several gaps in knowledge remain.

Observational studies to date have included patients transferred and being managed at outside facilities with a paucity of clinical information during this period and, as such, have not been well-positioned to capture the complete timeline from early symptom onset to disease progression.[9,10] In this context, we followed a cohort of patients developing ADHF-CS and being managed at a single medical institution for the length of their CS trajectory. We explored the clinical characteristics of patients at the time of CS onset and sought to identify potential associations with outcomes during index hospitalization and up to 1 year posthospital discharge. Our goal was to identify clinical factors early in the trajectory of these patients that are associated with a higher probability of a successful outcome and inform the management of patients suffering ADHF-CS.

METHODS

Data Sharing

The data and analytic methods of the study will be made available from the corresponding author upon reasonable request.

Study Population

Our study population comprised consecutive, prospectively enrolled, and retrospectively reviewed patients with CS, managed at the University of Utah Hospital from April 2015 to December 2021, and followed to December 2022. The University of Utah Hospital is a quaternary academic health care institution providing 24-7 advanced cardiovascular care including cardiovascular intensive care unit management, primary percutaneous coronary intervention and coronary artery bypass graft surgery, temporary mechanical circulatory support (tMCS) with intra-aortic balloon pump (IABP), percutaneous ventricular assist devices (pVAD; ie, Impella; Abiomed, Danvers, MA), surgically implanted ventricular assist devices (VAD; CentriMag; Abbott Laboratories, Abbott Park, IL), percutaneous arterial or venous bypass systems (veno-arterial membrane oxygenation; TandemHeart and ProtekDuo; LivaNova PLC, London, United Kingdom), and advanced HF therapies including durable LVAD implantation and HTx. The Utah Cardiac Recovery Shock Team was established in April 2015 to evaluate patients suffering CS with a standardized comprehensive multidisciplinary assessment, as described previously.[12] Patients with postcardiotomy CS or multifactorial shock etiologies (hypovolemic, vasodilatory, or septic shock preceding CS or sepsis developing within 48 hours of CS onset) were excluded. Sepsis was defined by positive blood, urine, or sputum cultures or high clinical suspicion despite negative cultures resulting in antibiotic therapy. Our study cohort comprised patients who developed ADHF-CS at the University of Utah Hospital.

Data Collection and Definitions

The study was approved by the University of Utah Institutional Review Board (IRB). Informed consent was obtained under IRB 80080 (Utah Cardiac Recovery Shock Registry), or waiver of consent was granted under IRB 72747 (Clinical Analyses in Cardiovascular Medicine). Clinical data were collected via chart review of electronic medical records and included patient demographics, baseline laboratory and hemodynamic data recorded closest to and within 8 hours of shock onset, and imaging data collected closest to and within 24 hours of shock onset. As shock onset, it was defined the first time the patient met the CS definition, as described below.

CS was defined using clinical and hemodynamic criteria as previously described,[13,14] including one of the following: (1) systolic blood pressure <90 mm Hg for >30 minutes; and (2) need for inotropes/vasopressors to maintain a systolic blood pressure >90 mm Hg, plus one of the following: (i) pulmonary capillary wedge pressure (PCWP) or left ventricular end-diastolic pressure >15 mm Hg and cardiac index <2.2 L/min·m^2, (ii) clinical or radiological signs of pulmonary edema, or (iii) impaired end-organ perfusion defined as altered mental status, cold clammy skin and extremities, or oliguria with urine output <30 mL/h.

Based on the underlying CS pathophysiology, patients were stratified into AMI or acute decompensated HF-related CS (AMI-CS and ADHF-CS, respectively).[14] AMI-CS included ST-segment elevation and non-ST-segment elevation MI, while ADHF-CS included ischemic and multiple causes of nonischemic cardiomyopathy. ADHF-CS patients were classified based on the chronicity of HF into acute or acute-on-chronic, with the latter having a prior diagnosis of HF. HF guideline-directed medical therapy at baseline was recorded for patients with chronic HF and included agents from the following 4 categories: (1) beta-blockers; (2) angiotensin receptor/neprilysin inhibitors, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blockers; (3) mineralocorticoid receptor antagonists; and (4) sodium-glucose cotransporter-2 inhibitors. CS severity by the Society for Cardiovascular Angiography and Interventions (SCAI) classification was assessed by the updated Cardiogenic Shock Working Group criteria.[15] The vasoactive-inotropic score (VIS) was calculated based on the number and dosage of inotropes and vasopressors at shock onset.[16]

We used the Society of Thoracic Surgeons Interagency Registry for Mechanically Assisted Circulatory Support definitions[17] for capturing the following adverse events: (1) neurological complications including ischemic stroke, hemorrhagic stroke, or transient ischemic attack; (2) bleeding complications including type 3 (overt bleeding accompanied by hemoglobin drop of 3 to <5 g/dL, or provided hemoglobin drop is related to bleed, or any transfusion with overt bleeding) or type 4 (infusion of ≥4 units of packed red blood cells within any 48 hours during the first 7 days post-MCS implant); (3) hemolysis defined as plasma-free hemoglobin values >20 mg/dL or serum lactate dehydrogenase (LDH) levels >2.5× the upper limit of normal, occurring >72 hours post-MCS implant; and (4) MCS device malfunction, defined as failure of one or more of the components of the MCS system, which either directly causes or could potentially induce a state of inadequate circulatory support or death. We also captured acute kidney injury (AKI) requiring renal replacement therapy (RRT) and the following vascular access site complications: surgical or transcatheter vascular repair, fasciotomy for acute compartment syndrome, or amputation.

Study End Points

Our primary end point was native heart survival (NHS), defined as survival to hospital discharge without receiving advanced HF therapies during index hospitalization (ie, LVAD implantation or HTx). Our secondary outcomes were adverse events, survival, major cardiac interventions, and hospital readmissions within 1 year following index hospitalization discharge.

Statistical Analysis

Demographics and clinical data were descriptively summarized and stratified by the outcome. Continuous variables were summarized as mean (SD), median (interquartile range), and range. Categorical variables were summarized as frequency and percentage. *P* values comparing: (1) patients discharged with a native heart versus patients who died or were discharged after receiving advanced HF therapies, and (2) patients discharged with a native heart versus discharged after receiving advanced HF therapies versus died during index hospitalization, were reported. The χ^2 or Fisher's exact test was used to compare categorical variables, and the *t* test, Wilcoxon rank-sum test, ANOVA, or Kruskal-Wallis test was used to compare continuous variables.

Association with the primary outcome (NHS) was further analyzed using logistic regression. Explanatory variables were selected based on significance in the unadjusted comparisons and prior medical literature.[3,10,18–24] Two models were

constructed. The first model included variables collected at baseline (shock onset), while the second model included clinical parameters representing overall stay and management. Multicollinearity among variables was examined using the variance inflation factor. Variables causing multicollinearity were removed from the models. Multiple imputation with chained equations as implemented in r package mice[25] was used to impute missing values. Ten imputed datasets were generated, and logistic regression modeling was applied to each. Parameter estimates and their standard errors were pooled across the 10 models. Odds ratios (OR; both univariable and multivariable) were reported with 95% CIs. Significance was determined at the P=0.05 level, and all tests were 2 sided. A Kaplan-Meier survival curve up to 1 year following index hospitalization discharge was generated. Statistical analyses were conducted in R 4.2.1.[26]

RESULTS

After excluding patients with multifactorial shock etiologies or postcardiotomy CS, 1162 patients were evaluated. Of those, 750 patients developed CS at the University of Utah Hospital, with 562 patients due to ADHF, comprising our study cohort.

Overall, 357 (63.5%) patients were discharged with a native heart, 165 (29.2%) died during index hospitalization, and 41 (7.3%) were discharged after receiving advanced HF therapies. Demographics and baseline clinical characteristics according to in-hospital outcome are presented in Table 1 and Table S1, while HF chronicity and underlying cause are presented in Table S2.

Comparison of Patients With NHS Versus Surviving Post Advanced HF Therapies or Death

Patients with NHS stayed longer in the hospital (12 [7, 19] versus 8 [3, 22] days; P<0.001), and at shock onset had lower CS severity as evidenced by SCAI stage, compared with patients who died or survived after receiving advanced HF therapies. Patients with NHS less commonly suffered cardiac arrest (12.6% versus 25.9%; P<0.001), underwent intubation (40.9% versus 70.7%; P<0.001), or underwent pulmonary artery catheter (PAC) placement (40.9% versus 53.2%; P=0.005), were less likely to be nonsmokers (45.5% versus 59.5%; P<0.001), while they more commonly had a history of systemic hypertension (68.1% versus 57.6%; P=0.013).

Patients with NHS compared with those who died or survived postadvanced HF therapies, had similar rates of acute versus acute-on-chronic HF, were less likely to have ICM as the underlying cause of ADHF, more commonly underwent intravenous diuresis (36.1 versus 27.3%, P=0.032) at shock onset, and had significant differences in terms of the underlying cause of NICM.

In terms of CS therapies, patients with NHS less commonly received temporary mechanical circulatory support (tMCS; 11.8% versus 30.7%; P<0.001), including IABP (3.6 versus 11.2%, P<0.001), pVAD (3.6% versus 12.7%; P<0.001), or temporary surgical RVAD (0% versus 3.4%; P<0.001), and had a lower VIS (5 [2, 11] versus 13 [6, 23]; P<0.001), at shock onset.

Regarding hemodynamic assessment at shock onset, patients with NHS had an overall better profile compared with patients who died during index hospitalization or survived after receiving advanced HF therapies. Patients with NHS had a lower right ventricular (RV) diastolic pressure (9 [4, 13] versus 10 [7, 14]; P=0.019) and PCWP (22±9 versus 25±10 mm Hg; P=0.002), with mean right atrial pressure, pulmonary artery pressures, as well as cardiac output and index measurements being comparable.

Laboratory assessment at shock onset was comparable between patients with NHS versus death or survival post advanced HF therapies, except higher hemoglobin (12.9±2.9 versus 12.3±2.9 g/dL; P=0.014), lower troponin I (0.09 [0.04, 0.29] versus 0.16 [0.05, 0.82] ng/mL, P=0.002), lower LDH (407 [271, 577] versus 477 [334, 696] mg/dL; P=0.029), and lower fraction of inspired oxygen (40 [21, 100]% versus 60 [21, 100]%; P=0.004), in patients with NHS.

Last, echocardiographic assessment at shock onset was comparable except a higher tricuspid annular plane systolic excursion (TAPSE; 15 [12, 19] versus 14 [10, 16] mm; P=0.027) in patients with NHS compared with patients who died or survived after receiving advanced HF therapies.

Comparison of Patients With NHS Versus Surviving Post Advanced HF Therapies Versus Death

Comparison of patients with NHS versus those surviving after advanced HF therapies versus dying during index CS hospitalization revealed the following. Of 41 patients surviving to discharge after receiving advanced HF therapies, 21 (51.2%) received a durable LVAD, 18 (43.9%) underwent HTx, and 2 (4.9%) received both. Patients surviving after advanced HF therapies versus NHS versus death were younger (53±15 versus 59±16 versus 60±16 years; P=0.025), had a longer length of stay (31 [21, 44] versus 12 [7, 19] versus 6 [2, 13] days; P<0.001), and at shock onset had higher SCAI stage. Patients who received advanced HF therapies versus NHS versus death less commonly suffered cardiac arrest (0% versus 12.6% versus 32.3%; P<0.001), and more commonly underwent intubation (70.7% versus 40.9% versus 70.7%; P<0.001), or PAC placement (92.7% versus 40.9% versus 43.3%; P<0.001).

Patients surviving post advanced HF therapies versus NHS versus death more commonly had acute-on-chronic

Table 1. Baseline Clinical Characteristics in Patients Stratified by In-Hospital Outcome

Variable	Native heart survival (N=357)	Survival post advanced HF therapies or death (N=205)	*P* value†	Survival post advanced HF therapies (N=41)	Death (N=164)	*P* value‡
Demographics						
Age, mean (SD)	59 (16)	59 (16)	0.94§	53 (15)	60 (16)	0.025‖
Sex						
Female	122 (34.2%)	64 (31.2%)	0.47¶	7 (17.1%)	57 (34.8%)	0.08¶
Male	235 (65.8%)	141 (68.8%)	…	34 (82.9%)	107 (65.2%)	…
Race						
White	288 (81.6%)	162 (81.8%)	0.92#	29 (72.5%)	133 (84.2%)	0.38**
Black/African American	13 (3.7%)	7 (3.5%)	…	4 (10.0%)	3 (1.9%)	…
American Indian/Alaska Native	10 (2.8%)	5 (2.5%)	…	0 (0.0%)	5 (3.2%)	…
Native Hawaiian/Other Pacific Islander	8 (2.3%)	2 (1.0%)	…	1 (2.5%)	1 (0.6%)	…
Asian	6 (1.7%)	3 (1.5%)	…	1 (2.5%)	2 (1.3%)	…
Other	28 (7.9%)	19 (9.6%)	…	5 (12.5%)	14 (8.9%)	…
Ethnicity						
Hispanic/Latino	30 (8.7%)	24 (12.6%)	0.15¶	7 (17.5%)	17 (11.3%)	0.17#
Not Hispanic/Latino	316 (91.3%)	167 (87.4%)	…	33 (82.5%)	134 (88.7%)	…
Body mass index, kg/m^2, mean (SD)	30 (25, 34)	28 (24, 34)	0.10††	27 (23, 31)	29 (24, 35)	0.11‡‡
Transfer from outside hospital	124 (34.7%)	78 (38.0%)	0.43¶	12 (29.3%)	66 (40.2%)	0.31¶
Cardiogenic shock management and treatment						
Hospital length of stay, d, median (IQR)	12 (7, 19)	8 (3, 22)	<0.001††	31 (21, 44)	6 (2, 13)	<0.001‡‡
SCAI-CSWG stage at shock onset						
B	43 (12.1%)	4 (2.0%)	<0.001¶	0 (0%)	4 (2.4%)	<0.001**
C	121 (34.0%)	33 (16.1%)	…	0 (0%)	33 (20.1%)	…
D	89 (25.0%)	30 (14.6%)	…	1 (2.4%)	29 (17.7%)	…
E	103 (28.9%)	138 (67.3%)	…	40 (97.6%)	98 (59.8%)	…
Chronicity of disease						
Acute heart failure	137 (38.4%)	86 (42.0%)	0.40¶	1 (2.4%)	85 (51.8%)	<0.001¶
Acute-on-chronic heart failure	220 (61.6%)	119 (58.0%)	…	40 (97.6%)	79 (48.2%)	…
Heart transplantation	0 (0%)	20 (9.8%)	<0.001¶	20 (48.8%)	0 (0%)	<0.001#
Durable LVAD implantation	0 (0%)	25 (12.2%)	<0.001¶	23 (56.1%)	2 (1.2%)	<0.001#
Temporary MCS	42 (11.8%)	63 (30.7%)	<0.001¶	29 (70.7%)	34 (20.7%)	<0.001¶
Time to 1st temporary MCS, min, median (IQR)*	286 (93, 1809)	478 (118, 4972)	0.27§§	2481 (612, 8504)	140 (102, 478)	0.001‡‡
IABP	13 (3.6%)	23 (11.2%)	<0.001¶	17 (41.5%)	6 (3.7%)	<0.001#
IABP access site*						
Axillary	0 (0%)	2 (8.7%)	0.39#	2 (11.8%)	0 (0%)	0.44#
Femoral	13 (100%)	19 (82.6%)	…	13 (76.5%)	6 (100%)	…
Femoral, axillary	0 (0%)	2 (8.7%)	…	2 (11.8%)	0 (0%)	…
Impella	13 (3.6%)	26 (12.7%)	<0.001¶	12 (29.3%)	14 (8.5%)	<0.001#
Impella type*						
2.5	2 (15.0%)	1 (3.8%)	0.54#	0 (0%)	1 (7.1%)	0.33#
CP	11 (85.0%)	18 (69.2%)	…	7 (58.3%)	11 (78.6%)	…
RP	0 (0%)	2 (7.7%)	…	1 (8.3%)	1 (7.1%)	…
5.0	0 (0%)	1 (3.8%)	…	1 (8.3%)	0 (0%)	…
5.5	0 (0%)	2 (7.7%)	…	2 (16.6%)	0 (0%)	…
Multiple Impella devices	0 (0%)	2 (7.7%)	…	1 (8.3%)	1 (7.1%)	…
VA-ECMO	20 (5.6%)	20 (9.8%)	0.07¶	4 (9.8%)	16 (9.8%)	0.16#

(*Continued*)

Table 1. Continued

Variable	Native heart survival (N=357)	Survival post advanced HF therapies or death (N=205)	*P* value†	Survival post advanced HF therapies (N=41)	Death (N=164)	*P* value‡
VA-ECMO venting*						
IABP	0 (0%)	1 (5.0%)	1.00#	1 (25.0%)	0 (0%)	0.040#
Impella	4 (20.0%)	4 (20.0%)	…	2 (50.0%)	2 (12.0%)	…
No	16 (80.0%)	15 (75.0%)	…	1 (25.0%)	14 (88.0%)	…
Temporary surgical RVAD	0 (0%)	7 (3.4%)	<0.001#	5 (12.2%)	2 (1.2%)	<0.001#
ProtekDuo	0 (0%)	1 (0.5%)	0.36#	0 (0%)	1 (0.6%)	0.36#
Cardiac arrest	45 (12.6%)	53 (25.9%)	<0.001¶	0 (0%)	53 (32.3%)	<0.001¶
In-hospital*	27 (60.0%)	29 (54.7%)	0.60¶	0 (NaN%)	29 (54.7%)	0.68#
In-hospital-Initial shockable rhythm*	5 (18.5%)	7 (24.1%)	0.61¶	0 (NaN%)	7 (24.1%)	0.75#
Out-of-hospital*	19 (42.2%)	26 (50.0%)	0.44¶	0 (NaN%)	26 (50.0%)	0.54#
Out-of-hospital-Initial shockable rhythm*	14 (77.8%)	16 (61.5%)	0.26¶	0 (NaN%)	16 (64.0%)	0.33#
Pulmonary artery catheter placement	146 (40.9%)	109 (53.2%)	0.005¶	38 (92.7%)	71 (43.3%)	<0.001¶
Intubation	146 (40.9%)	145 (70.7%)	<0.001¶	29 (70.7%)	116 (70.7%)	<0.001¶
Inotropes/vasopressors at shock onset	291 (81.5%)	197 (96.1%)	<0.001¶	41 (100%)	156 (95.1%)	<0.001¶
Inotrope/vasopressors number, median (IQR)	1 (1, 2)	3 (2, 4)	<0.001††	4 (4, 5)	2.5 (1, 3)	<0.001‡‡
Vasoactive-inotropic score, median (IQR)	5 (2, 11)	13 (6, 23)	<0.001††	15 (12, 19)	13 (5, 30)	<0.001‡‡
Intravenous diuresis before shock onset	129 (36.1%)	56 (27.3%)	0.032¶	12 (29.3%)	44 (26.8%)	0.10¶
Multiple intravenous diuretic agents*	7 (5.4%)	8 (14.3%)	0.07#	1 (8.3%)	7 (15.9%)	0.07#
Medical history						
Hypertension	243 (68.1%)	117 (57.6%)	0.013¶	21 (51.2%)	96 (59.3%)	0.029¶
Diabetes	103 (28.9%)	64 (31.4%)	0.53¶	10 (24.4%)	54 (33.1%)	0.45¶
Smoking						
Current smoker	70 (19.7%)	15 (7.5%)	<0.001¶	0 (0%)	15 (9.4%)	<0.001¶
Former smoker	124 (34.8%)	66 (33.0%)	…	17 (41.5%)	49 (30.8%)	…
Non-smoker	162 (45.5%)	119 (59.5%)	…	24 (58.5%)	95 (59.7%)	…
Hyperlipidemia	140 (39.2%)	89 (43.8%)	0.28¶	18 (43.9%)	71 (43.8%)	0.56¶
Chronic kidney disease stage III–V	53 (14.8%)	37 (18.2%)	0.30¶	6 (14.6%)	31 (19.1%)	0.45¶
Dialysis*	10 (18.9%)	6 (18.2%)	0.84¶	1 (16.7%)	5 (18.5%)	1.00#
Coronary artery disease	118 (33.1%)	69 (34.0%)	0.82¶	15 (36.6%)	54 (33.3%)	0.90¶
Prior coronary artery bypass graft surgery*	35 (29.7%)	26 (38.8%)	0.23¶	6 (40.0%)	20 (39.2%)	0.47#
Prior percutaneous coronary intervention*	55 (46.6%)	35 (52.2%)	0.59¶	8 (53.3%)	27 (51.9%)	0.84¶
Prior myocardial infarction	76 (21.3%)	46 (22.7%)	0.71¶	11 (26.8%)	35 (21.6%)	0.72¶
Chronic heart failure	220 (61.6%)	119 (58.0%)	0.40¶	40 (97.6%)	79 (48.2%)	<0.001¶
Heart failure cause*						
ICM	65 (29.5%)	42 (35.3%)	0.009¶	11 (27.5%)	31 (39.2%)	0.021#
NICM	135 (61.4%)	76 (63.9%)	…	29 (72.5%)	47 (59.5%)	…
Combined ICM/NICM	20 (9.1%)	1 (0.8%)	…	0 (0%)	1 (1.3%)	…
Reduced LV ejection fraction (<50%)*	184 (83.6%)	100 (84.0%)	0.92¶	38 (95.0%)	62 (78.5%)	0.07¶
New York Heart Association class*						
I	3 (1.5%)	3 (2.8%)	0.32#	0 (0%)	3 (4.4%)	0.38#
II	30 (14.9%)	15 (14.0%)	…	5 (12.8%)	10 (14.7%)	…
III	136 (67.7%)	64 (59.8%)	…	23 (59.0%)	41 (60.3%)	…
IV	32 (15.9%)	25 (23.4%)	…	11 (28.2%)	14 (20.6%)	…
GDMT agents number at presentation*						
0	45 (20.5%)	28 (23.5%)	0.12#	7 (17.5%)	21 (26.6%)	0.14**
1	72 (32.7%)	25 (21.0%)	…	6 (15.0%)	19 (24.1%)	…
2	63 (28.6%)	44 (37.0%)	…	16 (40.0%)	28 (35.4%)	…
3	37 (16.8%)	22 (18.5%)	…	11 (27.5%)	11 (13.9%)	…
4	3 (1.4%)	0 (0%)	…	0 (0%)	0 (0%)	…

(*Continued*)

Table 1. Continued

Variable	Native heart survival (N=357)	Survival post advanced HF therapies or death (N=205)	*P* value†	Survival post advanced HF therapies (N=41)	Death (N=164)	*P* value‡
Valvular heart disease	52 (14.6%)	34 (16.8%)	0.48¶	7 (17.1%)	27 (16.8%)	0.77¶
Prior valve replacement/repair*	21 (6.1%)	16 (8.2%)	0.37¶	3 (7.3%)	13 (8.4%)	0.58#
Hemodynamics at shock onset						
Mean right atrial pressure, mm Hg, median (IQR)	12 (7, 18)	12 (8, 18)	0.80††	12 (7, 18)	12 (8, 18)	0.94‡‡
RV systolic pressure, mm Hg, median (IQR)	47 (36, 56)	50 (40, 59)	0.16††	50 (40, 54)	52 (40, 62)	0.24‡‡
RV diastolic pressure, mm Hg, median (IQR)	9 (4, 13)	10 (7, 14)	0.019††	10 (7, 13)	11 (7, 15)	0.046‡‡
Pulmonary capillary wedge pressure, mm Hg, mean (SD)	22 (9)	25 (10)	0.002§	27 (11)	25 (9)	0.009‖
Cardiac index by Fick, L/min·m^2, median (IQR)	1.8 (1.4, 2.3)	1.7 (1.3, 2.3)	0.40††	1.7 (1.3, 1.9)	1.7 (1.3, 2.4)	0.27‡‡
Cardiac index by thermodilution, L/min·m^2, median (IQR)	1.9 (1.4, 2.5)	1.8 (1.4, 2.5)	0.40††	1.7 (1.4, 2.5)	1.9 (1.4, 2.4)	0.66‡‡
Systemic vascular resistance, dynes×s/cm^5, median (IQR)	1339 (930, 1778)	1255 (939, 1902)	0.71††	1270 (1039, 1792)	1251 (921, 1951)	0.82‡‡
Pulmonary vascular resistance index, Wood units/m^2, median (IQR)	499 (300, 767)	462 (288, 772)	0.84††	411 (251, 690)	486 (341, 823)	0.32‡‡
Laboratory assessment at shock onset						
Hemoglobin, g/dL, mean (SD)	12.9 (2.9)	12.3 (2.9)	0.014§	12.6 (3.1)	12.2 (2.9)	0.033‖
Creatinine, mg/dL, median (IQR)	1.5 (1.1, 2.1)	1.5 (1.1, 2.3)	0.73††	1.3 (1.0, 1.6)	1.6 (1.1, 2.5)	0.055‡‡
Aspartate transaminase, mg/dL, median (IQR)	43 (24, 154)	58 (27, 212)	0.16††	26 (19, 40)	75 (32, 259)	<0.001‡‡
Alanine transaminase, mg/dL, median (IQR)	41 (21, 156)	48 (21, 156)	0.63††	22 (16, 54)	62 (27, 181)	<0.001‡‡
Total bilirubin, mg/dL, median (IQR)	1.2 (0.7, 2.1)	1.2 (0.6, 2.2)	0.74††	1.3 (0.9, 1.8)	1.2 (0.6, 2.3)	0.80‡‡
B-type natriuretic peptide, pg/mL, median (IQR)	1131 (531, 2524)	1762 (692, 2613)	0.06††	1891 (912, 2940)	1575 (646, 2370)	0.11‡‡
Lactate, mg/dL, median (IQR)	2.1 (1.3, 3.9)	2.6 (1.3, 5.8)	0.08††	1.4 (1.0, 2.8)	2.8 (1.4, 6.9)	<0.001‡‡
Troponin I, ng/mL, median (IQR)	0.09 (0.04, 0.29)	0.16 (0.05, 0.82)	0.002††	0.05 (0.02, 0.08)	0.20 (0.06, 1.00)	<0.001‡‡
Lactate dehydrogenase, IU/L, median (IQR)	407 (271, 577)	477 (334, 696)	0.029††	372 (298, 492)	610 (429, 893)	<0.001‡‡
pH, median (IQR)	7.4 (7.3, 7.4)	7.4 (7.2, 7.4)	0.13††	7.4 (7.4, 7.4)	7.3 (7.2, 7.4)	<0.001‡‡
Bicarbonate, mmol/L, mean (SD)	22 (6)	21 (6)	0.13§	23 (5)	20 (6)	0.010‖
Echocardiographic assessment at shock onset						
LV ejection fraction, %, median (IQR)	28 (17, 52)	28 (16, 56)	0.99††	16 (15, 24)	32 (20, 59)	<0.001‡‡
LV end-diastolic diameter, cm, median (IQR)	5.3 (4.7, 6.3)	5.2 (4.3, 6.2)	0.30††	6.3 (5.4, 7.2)	4.9 (4.1, 5.8)	<0.001‡‡
RV systolic function						
Hyperdynamic/normal/low normal/mildly decreased	158 (62.9%)	75 (54.3%)	0.10¶	18 (52.9%)	57 (54.8%)	0.25¶
Moderately/severely decreased	93 (37.1%)	63 (45.7%)	…	16 (47.1%)	47 (45.2%)	…
Tricuspid annular plane systolic excursion, mm, median (IQR)	15 (12, 19)	14 (10, 16)	0.027††	14 (10.0, 16)	14 (11, 17)	0.08‡‡

CSWG indicates Cardiogenic Shock Working Group; GDMT, guideline-directed medical therapy; HF, heart failure; IABP, intra-aortic balloon pump; ICM, ischemic cardiomyopathy; IQR, interquartile range; LV, left ventricular; LVAD, left ventricular assist device; MCS, mechanical circulatory support; NaN, not a number; NICM, nonischemic cardiomyopathy; RV, right ventricular; RVAD, right ventricular assist device; SCAI, Society for Cardiovascular Angiography & Interventions; and VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

*Only applies if previous question is yes.

†Native heart survival vs survival postadvanced HF therapies or death.

‡Native heart survival vs survival postadvanced HF therapies vs death.

§*t* test.

‖ANOVA.

¶χ^2 test.

#Fisher exact test.

**χ^2 test by Montecarlo simulation.

††Wilcoxon rank-sum test.

‡‡Kruskal-Wallis test.

§§Exact Wilcoxon rank-sum test.

HF (97.6% versus 61.6% versus 48.2%; *P*<0.001), ICM as the cause of ADHF (26.8 versus 21.3 versus 26.2; *P*=0.023), and they had significant differences in terms of the underlying cause of NICM, with higher rates of idiopathic or nonspecific cause (60.0% versus 21.3% versus 28.6%; *P*<0.001), among others.

In terms of CS therapies, patients surviving after receiving advanced HF therapies versus death versus NHS more commonly received tMCS (70.7% versus 20.7% versus 11.8%; *P*<0.001), CS onset to tMCS implementation time was longer (2481 [612, 5804] versus 140 [102, 478] versus 286 [93, 1809] minutes; *P*=0.001), and more commonly received IABP (41.5% versus 3.7% versus 3.6%; *P*<0.001), pVAD (29.3% versus 8.5% versus 3.6%; *P*<0.001), and temporary surgical RVAD (12.2% versus 1.2% versus 0%; *P*<0.001), while at shock onset, had higher VIS (15 [12, 19] versus 13 [5, 30] versus 5 [2, 11]; *P*<0.001).

Regarding hemodynamic assessment at shock onset, patients who survived post advanced HF therapies versus died during index hospitalization versus NHS had a higher PCWP (27±11 versus 25±9 versus 22±9 mm Hg; *P*=0.009) and RV diastolic pressure (10 [7, 13] versus 11 [7, 15] versus 9 [4, 13]; *P*=0.046), with the remaining variables being comparable.

Overall, laboratory assessment at shock onset revealed that patients surviving post advanced HF therapies had better and patients who died worse systemic perfusion and end-organ function, compared with patients who survived with native heart. In patients who survived after advanced HF therapies versus NHS versus died, the following differences were identified: hemoglobin (12.6±3.1 versus 12.9±2.9 versus 12.2±2.9 g/dL; *P*=0.033), aspartate transaminase (26 [19, 40] versus 43 [24, 154] versus 75 [32, 259] mg/dL; *P*<0.001), alanine transaminase (22 [16, 54] versus 41 [21, 156] versus 62 [27, 181] mg/dL; *P*<0.001), lactate (1.4 [1.0, 2.8] versus 2.1 [1.3, 3.9] versus 2.8 [1.4, 6.9] mg/dL; *P*<0.001), LDH (372 [298, 492] versus 407 [271, 577] versus 610 [429, 893]), and bicarbonate (23±5 versus 22±6 versus 20±6 mEq/L; *P*=0.010).

Last, echocardiographic assessment at shock onset revealed that patients surviving after advanced HF therapies versus death versus NHS had worse LV structure and function (LV ejection fraction, 16 [15, 24]% versus 32 [20, 59]% versus 28 [17, 52]%; *P*<0.001; LV end-diastolic diameter, 6.3 [5.4, 7.2] versus 4.9 [4.1, 5.8] versus 5.3 [4.7, 6.3] cm; *P*<0.001), and worse mitral valvular function (moderate/severe mitral regurgitation, 32.4% versus 11.8% versus 17.4%; *P*=0.023).

Adverse Events During Index Hospitalization

Adverse event rates during index CS hospitalization are presented in Table 2. Bleeding complications were more common in patients surviving after advanced HF therapies compared with patients with NHS or who died during index hospitalization. Neurological complications, hemolysis in patients receiving MCS, and AKI requiring RRT were more common in patients who died versus patients who survived with native heart or post advanced HF therapies. Vascular complications and

Table 2. Adverse Event Rates During Index Hospitalization

Variable	Native heart survival (n=357)	Survival post advanced HF therapies or death (n=205)	*P* value*	Survival post advanced HF therapies (n=41)	Death (n=164)	*P* value†
Bleeding complications	71 (19.6%)	57 (27.8%)	**0.031‡**	25 (61.0%)	32 (19.5%)	**<0.001‡**
Type 3 bleeding	71 (19.6%)	57 (27.8%)	**0.031‡**	25 (61.0%)	32 (19.5%)	**<0.001‡**
Type 4 bleeding (only MCS patients)	14 (33.3%)	16 (22.5%)	0.26‡	7 (18.9%)	9 (26.5%)	0.39‡
Vascular complications	14 (3.9%)	5 (2.4%)	0.35‡	1 (2.4%)	4 (2.4%)	0.80§
Vascular repair	12 (3.4%)	3 (1.5%)	0.18‡	1 (2.4%)	2 (1.2%)	0.34§
Amputation	2 (0.6%)	0 (0%)	0.54§	0 (0%)	0 (0%)	1.00§
Fasciotomy	2 (0.6%)	3 (1.5%)	0.36§	0 (0%)	3 (1.8%)	0.33§
Neurological complications	22 (6.2%)	20 (9.8%)	0.12‡	1 (2.4%)	19 (11.6%)	**0.046§**
Ischemic stroke	20 (5.6%)	14 (6.8%)	0.56‡	0 (0%)	14 (8.5%)	0.10§
Hemorrhagic stroke	2 (0.6%)	7 (3.4%)	**0.014§**	0 (0%)	7 (4.3%)	**0.010§**
Transient ischemic attack	1 (0.3%)	2 (1.0%)	0.30§	1 (2.4%)	1 (0.6%)	0.14§
Hemolysis (only MCS patients)	3 (7.1%)	16 (22.5%)	**0.039‡**	6 (16.2%)	10 (29.4%)	**0.039‡**
Acute kidney injury requiring renal replacement therapy	24 (6.7%)	39 (19.0%)	**<0.001‡**	5 (12.2%)	34 (20.7%)	**<0.001§**
Device malfunction (only MCS patients)	0 (0%)	1 (1.4%)	1.00§	1 (2.7%)	0 (0%)	0.63§

Values in bold indicate statistical significance at the *P*<0.05 level.
HF indicates heart failure; and MCS, mechanical circulatory support.
*Native heart survival vs survival postadvanced HF therapies or death.
†Native heart survival vs survival postadvanced HF therapies vs death.
‡χ^2 test.
§Fisher exact test.

device malfunction rates in patients receiving MCS were comparable.

Survival, Major Cardiac Interventions, and Hospital Readmissions Within 1 Year Following Index Hospitalization Discharge

Of 562 patients developing ADHF-CS, 398 (70.7%) survived index CS hospitalization, 365 (64.9%) were alive 30 days post discharge, and 303 (53.9%) were alive 1 year post discharge (Table 3), with the Kaplan-Meier mortality curve presented in Figure 1. Of 562 patients, 30 (5.3%) underwent LVAD implantation, 23 (4.1%) HTx, 49 (8.7%) cardioverter-defibrillator implantation or cardiac resynchronization therapy, 24 (4.3%) revascularization, and 20 (3.6%) valve repair or replacement by 1 year post index hospitalization discharge (Table 3). Of 398 patients surviving to index hospitalization discharge, 204 (51.3%) had at least one readmission for all reasons and 110 (27.6%) 1 HF-related readmission by 1 year post discharge (Table 3).

Table 3. Survival, Major Cardiac Interventions, and Hospital Readmissions Within 1 Year Following Index Hospitalization Discharge

Outcomes	N (%)
Survival	All patients (n=562)
Survival to hospital discharge	398 (70.8%)
Survival 30 d post hospital discharge	365 (64.9%)
Survival 1 y post hospital discharge	303 (53.9%)
Major cardiac interventions	All patients (n=562)
Durable LVAD implantation	30 (5.3%)
Temporary surgical RVAD implantation	9 (1.6%)
Heart transplantation	23 (4.1%)
ICD/CRT implantation	49 (8.7%)
Revascularization	24 (4.3%)
Percutaneous coronary intervention*	21 (87.5%)
Coronary artery bypass graft surgery*	3 (12.5%)
Valve repair/replacement	20 (3.6%)
Surgical*	12 (60.0%)
Mitral valve†	5 (41.7%)
Aortic valve†	3 (25.0%)
Multiple valves†	3 (25.0%)
Tricuspid valve†	1 (8.3%)
Percutaneous*	8 (40.0%)
Aortic valve†	5 (62.5%)
Mitral valve†	2 (25.0%)
Pulmonic valve†	1 (12.5%)
Hospital readmissions	Survivors to hospital discharge (n=398)
All-reason readmissions	204 (51.3%)
Recurrent all-reason readmissions*	131 (64.2%)
Heart failure-related readmissions	110 (27.6%)
Recurrent heart failure-related readmissions*	49 (44.5%)

CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; LVAD, left ventricular assist device; and RVAD, right ventricular assist device.

*Only applies if previous question is yes.

†Only applies if valve repair/replacement is surgical or percutaneous.

Clinical Characteristics at Shock Onset Associated With Higher Likelihood of NHS

Univariable logistic regression applied to all available clinical variables is presented in Table S3. Demographics, medical and social history, and laboratory, hemodynamic, and imaging data collected at shock onset were considered for inclusion in a multivariable model assessing the likelihood for NHS (Table 4; multivariable model 1). The following clinical variables were statistically significantly associated with NHS likelihood after multivariable adjustments: history of hypertension (OR, 1.53 [1.00–2.32]; P=0.049), cardiac arrest (OR, 0.56 [0.31–1.00]; P=0.050), VIS (OR, 0.98 [0.96–0.99]; P<0.001), PCWP (OR, 0.97 [0.93–1.00]; P=0.049), and TAPSE (OR, 1.06 [1.01–1.12]; P=0.017) at shock onset.

Clinical Characteristics During the Shock Hospitalization Associated With Higher Likelihood of NHS

On top of clinical characteristics at shock onset, we evaluated clinical variables pertaining to the entire index CS hospitalization, which were added to multivariable model 1 (discussed above). The same set of clinical variables were statistically significantly associated with NHS likelihood, with the removal of PCWP and the addition of age per 10 years increase (OR, 0.86 [0.75–0.99] P=0.041) and AKI requiring RRT (OR, 0.33 [0.17–0.61]; P<0.001; Table 4; multivariable model 2).

DISCUSSION

CS is a clinical syndrome with high morbidity and mortality, result of various culprit etiologies. Advances in CS management, including MCS therapy and specialized care models, aim to improve early identification, timing and type of treatment, and escalation of care.[4,12,27–32] Despite progress, prognosis remains poor, with the incidence of CS rising.[1–4] Since CS can result from various causes, patients may differ in clinical presentation, response to therapy, and outcomes. While traditionally studied in the context of AMI (AMI-CS), recent evidence indicates that non-AMI-CS cases are more common in cardiovascular intensive care units, leading to increased interest in investigating non-AMI causes,[5–7] prompting increased interest in investigating CS arising from causes other than AMI.[3,9,10,33]

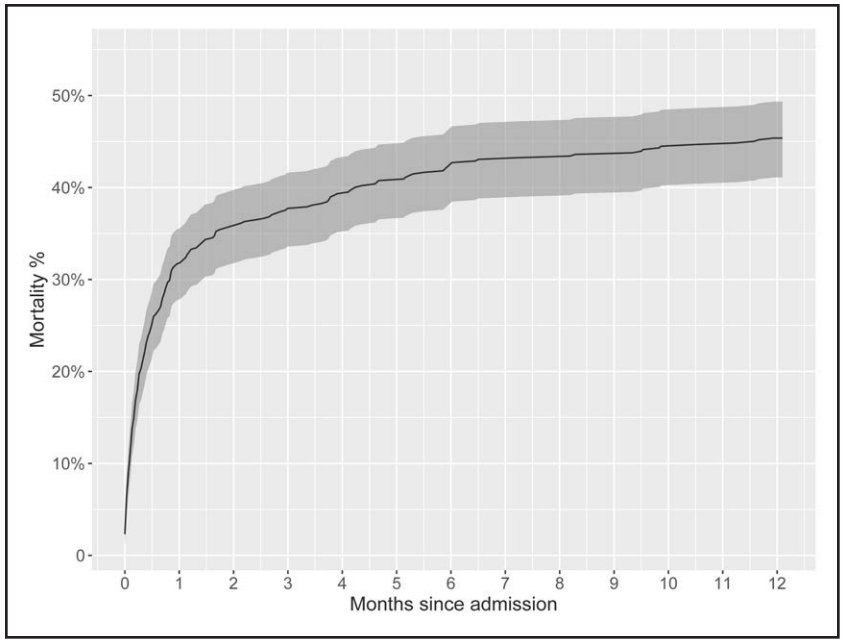

Figure 1. Kaplan-Meier overall mortality curve up to 1 year following index hospitalization admission.

In this context, we studied patients developing ADHF-CS and being managed at our quaternary academic health care institution throughout their CS trajectory. Prior studies have included patients initially managed at outside facilities. While studying this external cohort is important, paucity of clinical information during the outside facility stay may hinder our ability to capture the complete timeline from early symptom onset.[3,9,10] The diversity in capabilities and clinical practices at different centers can influence outcomes and potentially skew study results. Additionally, previous studies employing multicenter registries are limited by nonhomogeneity in clinical protocols and practices and a lack of data granularity.[3,6,9] Therefore, our study focused on patients who developed ADHF-CS while at our hospital. We explored the clinical characteristics of patients at the time of CS onset and sought to identify potential associations with NHS (ie, index hospitalization discharge without the need of advanced HF therapies) as well as survival up to 1 year post index hospitalization discharge. Our aim was to identify clinical factors early in the disease trajectory that might be linked to a higher likelihood of a successful outcome.

Our study's key findings are presented in Figure 2. Factors associated with a higher likelihood of NHS included medical and social history (prior history of systemic hypertension, current smoking), CS severity and management (lower SCAI-Cardiogenic Shock Working Group stage and VIS at shock onset, tMCS deployment overall, and more specifically IABP, pVAD, or temporary surgical RVAD, delayed tMCS implementation, PAC placement, cardiac arrest, intubation, intravenous diuresis before shock onset), and complications (bleeding, hemorrhagic stroke, hemolysis in MCS patients, and AKI requiring RRT). Additionally, at shock onset, variables favoring a higher likelihood of NHS included hemodynamic data (lower RV diastolic pressure, PCWP, and cardiac index), laboratory data (higher hemoglobin and pH, and lower lactate, troponin I, LDH, and fraction of inspired oxygen), and imaging data (higher TAPSE).

Comparing patients with NHS to those who survived after advanced HF therapies or died, we found that patients who survived after advanced HF therapies or died were generally more critically ill than NHS patients. They had higher SCAI stages, higher VIS and PCWP at shock onset, more frequent cardiac arrest and intubation rates, and more frequent tMCS use than NHS patients. Notably, survivors after advanced HF therapies were typically younger, more likely to have acute-on-chronic HF, less commonly suffered cardiac arrest, had a longer time from CS onset to tMCS deployment, and received IABP, pVAD, or temporary surgical RVAD more often, along with PAC placement. They were also less likely to be current smokers, which might relate to eligibility for advanced HF therapies. At shock onset, they had higher PCWP, lower aspartate transaminase, alanine transaminase, blood glucose, lactate, troponin I, LDH, and fraction of inspired oxygen levels, higher pH and bicarbonate values, but markedly lower LV ejection fraction and higher LV end-diastolic diameter compared with patients achieving NHS or those who died during CS hospitalization.

After multivariable adjustments, factors significantly associated with a higher likelihood of NHS included younger age, history of systemic hypertension, absence of cardiac arrest, lower VIS and PCWP, higher TAPSE at shock onset, and absence of AKI requiring RRT. Our findings are consistent with previous research on CS survival.[3,10,18–24,34] Some of these factors, like age and hypertension history, are nonmodifiable patient demographics and medical history. Others, such as inotrope/vasopressor use, PCWP and TAPSE at shock onset, cardiac arrest,

Table 4. Multivariable Assessment of Clinical Characteristics Associated with the Likelihood of Native Heart Survival

	Univariable analysis		Multivariable model 1		Multivariable model 2	
Variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Clinical variables at shock onset						
Age (per 10 y)	1.00 (0.89, 1.11)	0.94	0.91 (0.80, 1.04)	0.16	0.86 (0.75, 0.99)	**0.041**
Body mass index (per 5 kg/m^2)	1.09 (0.98, 1.22)	0.11	1.10 (0.96, 1.27)	0.16	1.11 (0.96, 1.29)	0.17
History of systemic hypertension (yes vs no)	1.57 (1.10, 2.23)	**0.014**	1.53 (1.00, 2.32)	**0.049**	1.79 (1.15, 2.79)	**0.011**
Chronic kidney disease stage III–V (yes vs no)	0.79 (0.50, 1.25)	0.31	0.66 (0.39, 1.11)	0.12	0.80 (0.46, 1.41)	0.45
New York Heart Association class (III/IV vs no heart failure or class <III)	1.12 (0.79, 1.59)	0.52	0.92 (0.46, 1.82)	0.81	0.98 (0.48, 2.02)	0.97
Chronicity of disease (acute-on-chronic vs acute)	1.16 (0.82, 1.65)	0.40	1.03 (0.50, 2.13)	0.93	0.98 (0.46, 2.09)	0.97
Cardiac arrest (yes vs no)	0.41 (0.27, 0.64)	**<0.001**	0.56 (0.31, 1.00)	**0.050**	0.53 (0.29, 0.96)	**0.038**
Intravenous diuresis before shock onset	1.51 (1.03, 2.19)	**0.033**	1.43 (0.93, 2.20)	0.10	1.49 (0.95, 2.34)	0.08
Vasoactive-inotropic score at shock onset	0.97 (0.96, 0.98)	**<0.001**	0.98 (0.96, 0.99)	**<0.001**	0.98 (0.97, 0.99)	**0.002**
RV diastolic pressure, mm Hg	0.99 (0.95, 1.02)	0.52	0.98 (0.94, 1.03)	0.45	1.00 (0.96, 1.05)	0.89
Pulmonary capillary wedge pressure, mm Hg	0.97 (0.95, 1.00)	0.07	0.97 (0.93, 1.00)	**0.049**	0.97 (0.93, 1.00)	0.10
Cardiac index by Fick, L/min·m^2	0.86 (0.75, 0.97)	**0.017**	0.90 (0.74, 1.10)	0.31	0.85 (0.69, 1.05)	0.13
Systemic vascular resistance, dynes×s/cm^5	1.35 (0.96, 1.90)	0.09	1.06 (0.66, 1.71)	0.80	1.07 (0.65, 1.76)	0.80
Hemoglobin, g/dL	1.07 (1.01, 1.14)	**0.018**	1.05 (0.98, 1.13)	0.14	1.04 (0.96, 1.12)	0.36
Lactate, mg/dL	0.92 (0.87, 0.96)	**<0.001**	1.00 (0.93, 1.08)	0.92	1.00 (0.92, 1.08)	0.99
Bicarbonate, mmol/L	1.03 (1.00, 1.06)	0.06	1.00 (0.95, 1.04)	0.83	0.99 (0.95, 1.03)	0.68
Tricuspid annular plane systolic excursion, mm	1.05 (1.01, 1.10)	**0.029**	1.06 (1.01, 1.12)	**0.017**	1.06 (1.01, 1.12)	**0.036**
Clinical variables associated with overall management during shock hospitalization						
Temporary MCS (yes vs no)*	0.35 (0.22, 0.57)	**<0.001**	…	…	0.59 (0.33, 1.06)	0.08
Time from shock onset to first temporary MCS, min*	1.00 (0.99, 1.00)	0.19	…	…	1.00 (0.99, 1.00)	0.10
Pulmonary artery catheter placement (yes vs no)	0.61 (0.43, 0.86)	**0.005**	…	…	0.60 (0.36, 1.00)	0.051
Acute kidney injury requiring renal replacement therapy (yes vs no)	0.31 (0.18, 0.53)	**<0.001**	…	…	0.33 (0.17, 0.61)	**<0.001**

Values in bold indicate statistical significance at the *P*<0.05 level.
LV indicates left ventricular; MCS, mechanical circulatory support; OR, odds ratio; and RV, right ventricular.
*Temporary MCS (yes vs no) and time from shock onset to first temporary MCS (min) is considered 1 variable, with the reference level being "no temporary MCS."

and AKI requiring RRT, reflect the severity of disease and could be targeted for intervention.

Although in-hospital mortality might be lower in ADHF-CS compared with AMI-CS, many ADHF-CS patients require advanced HF therapies such as durable LVAD or HTx.[9,10] In our study, 41 of 562 (7.3%) patients with ADHF-CS underwent these therapies. Survival rates decreased significantly post discharge, from 70.8% during index CS hospitalization to 64.9% at 30 days and 53.9% at 1 year post discharge. Moreover, of 398 patients surviving to hospital discharge, 51.3% had at least 1 all-reason and 27.6% at least 1 HF-related readmission by 1 year. This highlights the need for extended follow-up for this patient group, as survival during index CS hospitalization might be better compared with AMI-CS; however, morbidity and mortality are considerable following hospital discharge.

In ADHF-CS, the acuity of cardiac dysfunction has been suggested to affect patient outcomes.[3,11] Patients with a history of HF (acute-on-chronic HF) may have developed compensatory cardiac remodeling, potentially affecting presentation and response to therapy. Simultaneously, chronic disease and neurohormonal adaptations might adversely affect various organ systems (vascular, hepatic, renal, and so on), with potential implications in prognosis and outcomes. In our study, chronicity of disease did not affect NHS likelihood. However, we found that acute HF was more common in patients who died (51.8%) compared with those who achieved NHS (38.4%), and it was sparse in patients undergoing advanced HF therapies (2.4%).

The utility of continuous hemodynamic monitoring with PAC in CS patients has been debated.[35] Early trials in other patient populations did not reveal a benefit,[36,37] but recent CS studies suggested improved in-hospital survival with PAC monitoring.[24] In our study, PAC placement appeared to be associated with a lower likelihood of NHS, but this was not the case after multivariable adjustments, although statistical significance was approached (*P*=0.051). Higher utilization of PAC in critically ill patients could be a confounding factor. Notably, in our study, 92.7% of patients requiring advanced HF therapies had PAC placement, while the rates were comparable in patients who died compared with those achieving NHS (43.3% and 40.9%). This suggests that

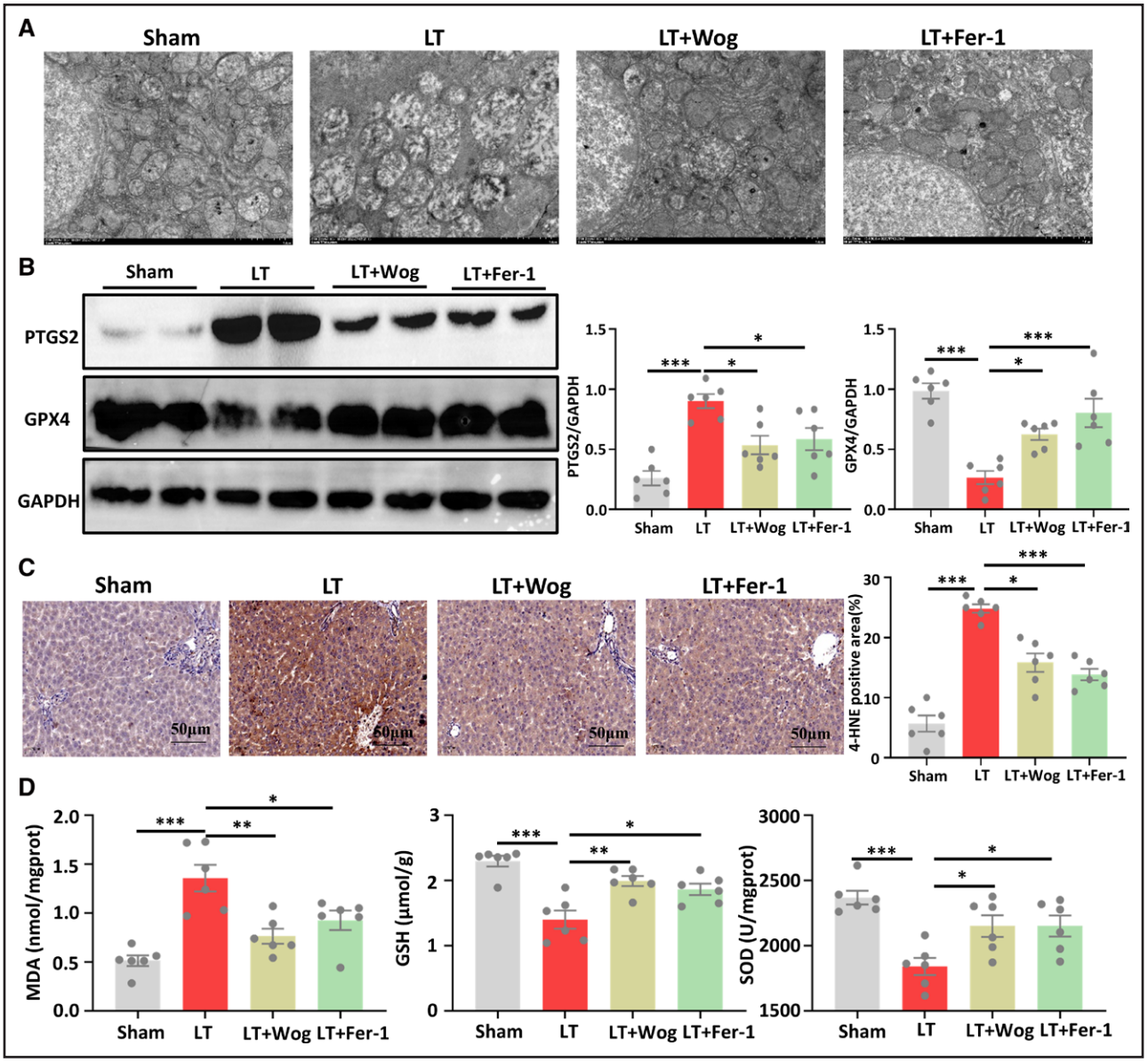

Figure 2. Clinical characteristics and outcomes of patients suffering acute decompensated heart failure complicated by cardiogenic shock.

ADHF indicates acute decompensated heart failure; AKI, acute kidney injury; CS, cardiogenic shock; HF, heart failure; MCS, mechanical circulatory support; PCWP, pulmonary capillary wedge pressure; RRT, renal replacement therapy; TAPSE, tricuspid annular plane systolic excursion; and VIS, Vasoactive Inotropic Score.

the decision to use advanced HF therapies may have influenced our findings.

Previous studies have shown that RV dysfunction affects CS patient outcomes, with RV hemodynamic derangements linked to lower survival in both AMI and ADHF cases.[38] Our study corroborates these findings, with patients achieving NHS having better RV function (lower RV diastolic pressure and higher TAPSE) compared with those who died or survived post advanced HF therapies. Importantly, higher TAPSE was associated with a higher likelihood of NHS after multivariable adjustments, highlighting the importance of RV function in assessing and treating ADHF-CS patients.

Last, early identification of CS and implementation of MCS have been suggested to affect outcomes.[12,31,32,39–41] In a study of 287 patients suffering AMI-CS, deployment of a pVAD within 1.25 hours from shock onset improved in-hospital survival.[40] Another study involving AMI-CS and ADHF-CS patients showed that delaying MCS was associated with higher mortality risk.[31] In our study, a longer time from shock onset to tMCS deployment was associated with a lower likelihood of NHS; however, this was not evident after multivariable adjustments, with the timing of tMCS not reaching statistical significance. At the same time, escalation of pharmacological CS treatment at shock onset was independently associated with

lower NHS likelihood. This suggests that early tMCS deployment, instead of escalating inotrope/vasopressor agents, should be further explored in managing ADHF-CS patients.

Limitations

Besides the prospective enrollment of patients, the retrospective chart review makes our study prone to inherent limitations of observational studies, including unmeasured confounding and selection bias. The relatively small sample size and focus on patients developing CS and being managed at our institution might limit the generalizability of our findings. We focused on patients developing shock at our hospital due to the paucity of clinical information during an outside facility stay, hindering our ability to capture the complete timeline from early symptom onset and variations in clinical practices that might affect our findings. Most patients in our study were male (66.9%) and white (81.7%), which limits generalizability to women and nonwhite races. Despite the use of a commonly and widely used definition for CS, defining the exact onset of shock is challenging. Also, patients suffering ADHF-CS comprise a group of patients with heterogeneous underlying pathologies and potentially divergent disease trajectories and responses to treatment. Last, patients ineligible for advanced HF therapies have been included, which might have impacted our findings.

Conclusions

We studied a contemporary cohort of consecutive patients with ADHF-CS and identified clinical factors associated with a higher likelihood of a successful outcome (NHS). Some are related to patient demographics and medical history and are not actionable (age and history of systemic hypertension), while others reflect disease severity (VIS, PCWP, and TAPSE at shock onset, cardiac arrest, and AKI requiring RRT) and could inform the management of patients suffering ADHF-CS. Noteworthy observations in our study are the significant decline in survival rates and high rates of readmissions following index CS hospitalization discharge, suggesting that longer follow-up for this patient cohort might be warranted. RV function might be a key clinical factor to be considered when assessing patients suffering ADHF-CS, while the utility of PAC monitoring should be further assessed. Lastly, given the increasing utilization of tMCS in the management of CS patients, earlier tMCS deployment as opposed to escalation of inotrope/vasopressor agents might be a clinical approach to be further investigated in the management of patients suffering ADHF-CS.

ARTICLE INFORMATION

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Disclosures

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Supplemental Material

Tables S1–S3

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