Circulation: Heart Failure

ORIGINAL ARTICLE

Invasive Hemodynamic Assessment and Classification of In-Hospital Mortality Risk Among Patients With Cardiogenic Shock

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BACKGROUND: Risk stratifying patients with cardiogenic shock (CS) is a major unmet need. The recently proposed Society for Cardiovascular Angiography and Interventions (SCAI) stages as an approach to identify patients at risk for in-hospital mortality remains under investigation. We studied the utility of the SCAI stages and further explored the impact of hemodynamic congestion on clinical outcomes.

METHODS: The CS Working Group registry includes patients with CS from 8 medical centers enrolled between 2016 and 2019. Patients were classified by the maximum SCAI stage (B–E) reached during their hospital stay according to drug and device utilization. In-hospital mortality was evaluated for association with SCAI stages and hemodynamic congestion.

RESULTS: Of the 1414 patients with CS, the majority were due to decompensated heart failure (50%) or myocardial infarction (MI; 35%). In-hospital mortality was 31% for the total cohort, but higher among patients with MI (41% versus 26%, MI versus heart failure, $P<0.0001$). Risk for in-hospital mortality was associated with increasing SCAI stage (odds ratio [95% CI], 3.25 [2.63–4.02]) in both MI and heart failure cohorts. Hemodynamic data was available in 1116 (79%) patients. Elevated biventricular filling pressures were common among patients with CS, and right atrial pressure was associated with increased mortality and higher SCAI Stage.

CONCLUSIONS: Our findings support an association between the proposed SCAI staging system and in-hospital mortality among patient with heart failure and MI. We further identify that venous congestion is common and identifies patients with CS at high risk for in-hospital mortality. These findings provide may inform future management protocols and clinical studies.

Key Words: cardiogenic shock ■ heart failure ■ hemodynamics ■ hospital mortality ■ myocardial infarction ■ right atrial pressure ■ ventricular congestion

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Cardiogenic shock (CS) is a complex clinical syndrome that begins with impaired cardiac function leading to systemic hypoperfusion and results in hemodynamic, neurohormonal, and metabolic changes that progressively worsen without treatment. Despite major advances in drug and short-term mechanical circulatory support (MCS) device therapies over the past 2 decades, reported 30-day mortality due to CS remains largely unchanged, ranging between 30% and 60%.[1–4] One explanation for the broad range and inconsistent mortality over time may be that the lack of clear criteria for risk stratification of patients at the time of presentation

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WHAT IS NEW?

- Using data from the Cardiogenic Shock Working Group registry inclusive of contemporary short-term, percutaneous mechanical circulatory support devices and invasive hemodynamic data, we report a novel validation analysis showing that Society for Cardiovascular Angiography and Intervention stages directly associate with in-hospital mortality.
- We provide new insight into the distribution of short-term mechanical circulatory support use across Society for Cardiovascular Angiography and Intervention stages.
- We show that elevated right heart filling pressures (venous congestion) are common and associated with worsening shock severity and in-hospital mortality.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Our findings suggest that more clinical data inclusive of hemodynamic and metabolic variables are required to confirm the specific definitions of Society for Cardiovascular Angiography and Intervention stages for patients with cardiogenic shock due to myocardial infarction or heart failure and further identify venous congestion as an important marker of risk for in-hospital mortality.
- Future studies exploring whether a strategy of early venous decongestion improves clinical outcomes in cardiogenic shock are required.

Nonstandard Abbreviations and Acronyms

BiV	Bi-ventricular
CI	cardiac index
CO	cardiac output
CS	cardiogenic shock
CSWG	Cardiogenic Shock Working Group
HF	heart failure
MCS	mechanical circulatory support
MI	myocardial infarction
OR	odds ratio
PCI	percutaneous coronary intervention
PCWP	pulmonary capillary wedge pressure
RAP	right atrial pressure
SCAI	Society for Cardiovascular Angiography and Interventions
VT	ventricular tachycardia

obscures survival trends over time in specific subgroups, be they at low, intermediate, or high risk. This issue is further complicated by the fact that most studies involving CS focus on patients with myocardial infarction (MI).[5–7] However, the number of patients with CS in the setting of decompensated heart failure (HF) has grown, owing to exponential growth of the HF population.[8] Survival trends and risk stratification for CS have not been adequately investigated in the HF population.

The use of short-term MCS devices has also increased and device options for CS now include the intraaortic balloon pump, trans-valvular axial flow pumps (Impella; Abiomed Inc), left atrial to femoral artery pumps (TandemHeart; LivaNova Inc), venoarterial extracorporeal membrane oxygenation, and extracorporeal centrifugal flow pumps.[9,10] With an increasing number of device options for these critically ill patients, risk stratification of patients presenting with CS is now more important than ever, since clarification of mortality and hemodynamic deficits in risk subsets may inform the development of treatment algorithms and the design of registry studies and randomized controlled trials which are necessary to evaluate clinical benefits.

Recently, a proposed staging system for CS based on input from a multi-disciplinary panel of clinical experts was proposed by the Society for Coronary Angiography and Intervention (SCAI) and endorsed by 4 other American medical associations.[11] The SCAI system includes 5 classes of CS: (1) at risk for CS, (2) beginning CS, (3) classic CS, (4) deteriorating CS, and (5) extreme CS. Each stage is defined by physical exam, biochemical, and hemodynamic findings and were intentionally left as general definitions to accommodate the variability among clinical parameters available at the time of presentation. The SCAI staging system also proposes that increasing intensity of drug and device treatment over time accompanies clinical deterioration.

Two recent studies used markers of hypoperfusion and lactate levels, respectively, to define SCAI stages and showed a direct association between mortality and increasing SCAI stage. Limitations of these studies include the single-center study design, the lack of invasive hemodynamic data, and skewed distribution of short-term MCS devices in the study population.[12,13] Accordingly, additional studies are required to explore the utility of SCAI stages with contemporary real-world experience and to further determine the importance of hemodynamic parameters in risk stratifying CS patients.

To begin addressing these critical gaps in knowledge, we employed a multicenter registry of patients with CS due to decompensated HF, MI, or other causes, hospitalized at 8 medical centers in the United States. The primary objective of this study was to test whether the SCAI classification system successfully stratifies patients at risk of all-cause in-hospital mortality and to further assess associations between hemodynamic parameters at presentation with mortality.

METHODS

Data Source

The authors declare that all supporting data are available within the article and in the Data Supplement. The CS Working

Group (CSWG) is an academic research consortium of hospitals in the United States inclusive of a national registry of all-cause CS that began in 2016 with 4 initial sites across the United States contributing data on at least 100 adult refractory patients with CS annually. The registry grew to include 8 total contributing sites by 2019. The registry includes a standardized set of data elements which were defined by principal investigators from the CSWG. These include patient, procedural, and hospital characteristics. Data represent discrete CS in patient cases treated at each institution between 2016 and 2019. Patient demographic, laboratory, and hemodynamic data were collected at a single time point as close to admission as possible, before initiation of mechanical support, in the hospital records. Information about pharmacological and device therapies represented the maximum therapies provided during the hospitalization (detailed further below). CS diagnosis was physician-adjudicated at each site and was defined as a sustained episode of systolic blood pressure <90 mm Hg for at least 30 minutes and a cardiac index (CI) <2.2 L/(min·m^2) determined to be secondary to cardiac dysfunction, and the requirement for either pharmacological support (vasopressors or inotropes) or short-term MCS (ie, intraaortic balloon pump, Impella, venoarterial extracorporeal membrane oxygenation, or extracorporeal centrifugal flow pumps) at any time throughout a patient's hospitalization. Quality assurance was achieved through adjudication at each site by the respective clinical coordinators and principal investigator. In addition, values were centrally audited and screened by the CSWG research team (K.L. Thayer, S. Newman, L. Jorde, J.L. Haywood, N.M. Harwani, M. Ayouty, E. Zweck, Dr Kapur) for any discrepancies or major outliers and resolved with the submitting site.

Study Population

Between 2016 and 2019, data from 1565 individual patient hospital admissions with a diagnosis of CS were collected. Proper Institutional Review Board approval was obtained to access this data from medical records, and patient consent was not required. CS cause was reported by each site as due to MI, HF, or other. MI was defined as any primary diagnosis of either non–ST-segment–elevation MI or ST-segment–elevation MI. HF was defined as any primary diagnosis of acute on chronic HF, not otherwise related to MI. Other causes included postcardiotomy, myocarditis, or not otherwise specified CS. Patients under the age of 18 years (n=1, 0.06%) and those with unknown mortality status at the time of hospital discharge (n=150, 9.6%) were excluded leaving a study population of 1414 patients with CS from 8 hospitals for analysis.

SCAI Classification

Patients were stratified according to the maximum SCAI classification stage reached during hospitalization to assess CS severity compared with in-hospital mortality.[11] According to the SCAI definition of stages, clinical deterioration based on persistent hypotension and hypoperfusion is the main determinant of a patient's SCAI stage and is associated with a need for intensification of treatment. Therefore, treatment escalation during hospitalization for CS was used as a proxy for persistent hypotension and hypoperfusion to retrospectively define maximum deterioration since hemo-metabolic parameters were only assessed at admission. A CSWG-adapted definition of SCAI stages was applied in our study cohort based on total use of vasopressors, inotropes, and MCS across a patient's hospital stay as follows (Figure 1): SCAI defines stage A patients as those at risk for CS and stage A was, therefore, not captured in our study population. Stage B patients are those exhibiting early symptoms not including hypoperfusion and, therefore, do not require pharmacological or mechanical support. Stage C patients are those with hypoperfusion requiring initial intervention with up to either one drug or one MCS device. Stage D patients are those whose condition deteriorates despite initial intervention, defined in our data set by the need for additional drugs or MCS treatment. Finally, stage E patients are those who have deteriorated further and require maximal support, defined in our data set as requiring at least 2 MCS devices and 2 drugs during their hospitalization. While timing of maximal vasopressor/inotrope treatment is not known in comparison to the timing of device treatment, each progression of treatment is considered a form of escalation and therefore, deterioration as defined by SCAI, so can be assessed independently when assigning maximal patient SCAI stage.

A sensitivity analysis incorporating lactate into SCAI stage definitions was performed. Stage B was defined as having a baseline lactate <2 meq/L and having received no drugs or

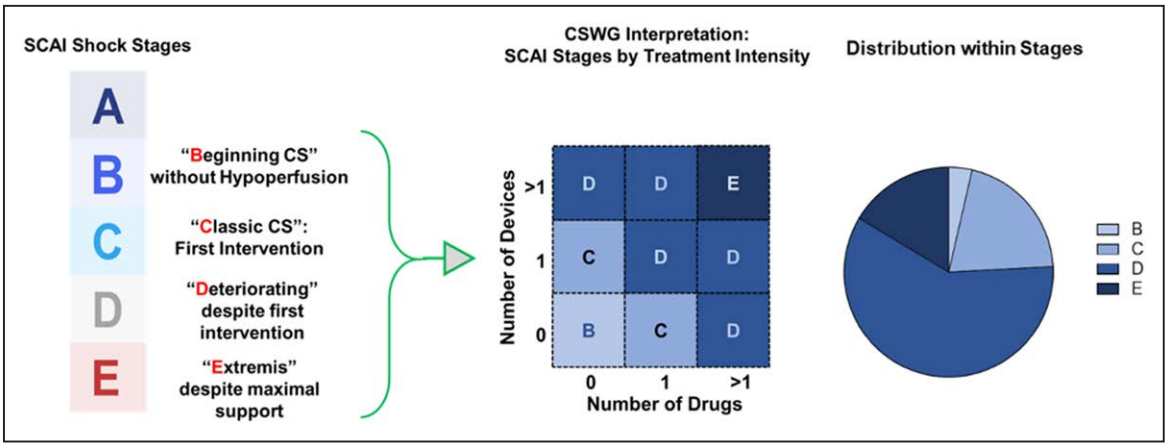

Figure 1. Definition, retrospective adjudication, and distribution of Society for Cardiovascular Angiography and Interventions (SCAI) stages within the Cardiogenic Shock Working Group (CSWG) registry.
CS indicates cardiogenic shock.

Table 1. Baseline Descriptive Statistics of CSWG Study Population by SCAI Stage

	All (N=1414)	SCAI Stage				P Value
		B (n=46)	C (n=263)	D (n=758)	E (n=212)	
	n (%)	n (%)	n (%)	n (%)	n (%)	
Nonsurvivors	431 (30.4)	0 (0)	28 (10.7)	250 (33.0)	117 (55.2)	<0.001
Male	1025 (72.5)	33 (71.7)	199 (75.7)	540 (71.2)	155 (73.1)	0.58
Shock cause						
MI	494 (34.9)	2 (4.4)	81 (30.8)	244 (32.3)	130 (61.32)	<0.001
HF	712 (50.4)	40 (87.0)	149 (56.7)	432 (57.2)	55 (25.9)	
Other	208 (14.7)	4 (8.7)	33 (12.6)	79 (10.5)	27 (12.7)	
No. of pressors/inotropes						<0.001
0	236 (16.7)	46 (100.0)	171 (65.0)	19 (2.5)	0 (0)	
1	393 (27.8)	0 (0)	92 (35.0)	301 (39.7)	0 (0)	
2+	650 (46.0)	0 (0)	0 (0)	438 (57.8)	212 (100.0)	
No. of devices						<0.001
0	224 (15.8)	46 (100.0)	92 (35.0)	61 (8.1)	0 (0)	
1	882 (62.4)	0 (0)	171 (65.0)	620 (81.8)	0 (0)	
2+	308 (21.8)	0 (0)	0 (0)	77 (10.2)	212 (100.0)	
Type of MCS						
Impella	410 (29.0)	0 (0)	38 (14.5)	186 (24.5)	137 (64.62)	<0.001
ECMO	333 (23.6)	0 (0)	12 (4.6)	127 (16.8)	154 (72.6)	<0.001
IABP	770 (54.5)	0 (0)	121 (46.0)	464 (61.2)	145 (68.4)	<0.001
Race						0.002
White	647 (45.8)	32 (69.6)	152 (57.8)	306 (40.4)	98 (46.3)	
Hispanic/Latino	31 (2.2)	1 (2.2)	9 (3.4)	13 (1.7)	3 (1.4)	
Black	31 (2.2)	0 (0)	2 (0.8)	15 (2.0)	3 (1.4)	
Asian	28 (2.0)	0 (0)	8 (3.0)	11 (1.5)	7 (3.3)	
Other	82 (5.8)	13 (28.3)	19 (7.2)	44 (5.8)	4 (1.9)	
Medical history						
HTN	681 (48.2)	12 (26.1)	118 (44.9)	380 (50.1)	115 (54.3)	<0.001
DM2	489 (34.6)	11 (23.9)	87 (33.1)	262 (34.6)	89 (42.0)	0.06
Afib/flutter	296 (20.9)	14 (30.4)	49 (18.6)	168 (22.2)	46 (21.7)	0.08
CKD (any stage)	323 (22.8)	14 (30.4)	64 (24.3)	182 (24.0)	34 (16.0)	0.24
PVD	60 (4.2)	1 (2.2)	12 (4.6)	33 (4.4)	10 (4.7)	0.55
COPD	101 (7.1)	6 (13.0)	16 (6.1)	56 (7.4)	16 (7.6)	0.55
CVA/TIA	159 (11.2)	4 (8.7)	28 (10.7)	101 (13.3)	15 (7.1)	0.01
Valvular disease	214 (15.1)	12 (26.1)	51 (24.5)	126 (25.8)	19 (15.1)	0.09
PCI	293 (20.7)	11 (23.9)	43 (21.6)	136 (29.7)	87 (44.9)	<0.001
CABG	114 (8.1)	3 (6.5)	16 (7.3)	64 (11.5)	21 (10.5)	0.29
VT	216 (15.3)	11 (23.9)	39 (18.5)	107 (20.7)	45 (32.6)	0.01
ICD	329 (23.3)	23 (50.0)	71 (34.0)	173 (33.5)	42 (30.7)	0.11
CRT	97 (6.9)	7 (15.2)	13 (6.2)	65 (12.6)	10 (7.3)	0.03

P values calculated using χ^2 test of independence or ANOVA as appropriate. Afib indicates atrial fibrillation; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRT, cathode-ray tube; CSWG, Cardiogenic Shock Working Group; CVA, cerebrovascular accident; DM2, type 2 diabetes mellitus; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HCO3, bicarbonate; HF, heart failure; HTN, hypertension; IABP, intraaortic balloon pump; ICD, implantable cardioverter defibrillator; MAP, mean arterial pressure; MCS, mechanical circulatory support; MI, myocardial infarction; PAP, pulmonary arterial pressure; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SCAI, Society for Cardiovascular Angiography and Interventions; TIA, transient ischemic attack; and VT, ventricular tachycardia.

devices throughout hospitalization; stage C was defined by a baseline lactate <5 meq/L and having received either 1 drug or 1 device; stage D patients had a baseline lactate < 5 meq/L but received >1 drug or 1 device; and stage E patients were defined by a baseline lactate of ≥5 (Figure I in the Data Supplement).

Table 2. Baseline Descriptive Statistics of CSWG Study Population by SCAI Stage

	All (N=1414)			SCAI Stage												
				B (n=46)			C (n=263)			D (n=758)			E (n=212)			
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	*P* Value
Demographic																
Age	1412	59.9	14.8	46	54.6	16.0	263	60.5	15.2	758	60.5	14.6	212	57.6	13.6	0.004
Weight, kg	1138	85.3	22.6	46	87.0	20.2	231	87.4	22.2	589	83.7	23.6	155	86.1	19.9	0.15
Metabolic																
AST	788	459.4	1492.6	37	32.0	19.9	124	153.5	547.8	424	355.6	1168.9	174	1023.4	2446.2	<0.001
BUN	1026	32.4	20.5	46	28.6	16.6	196	29.8	19.9	538	33.6	21.2	199	33.2	20.9	0.08
Lactate	676	4.4	4.2	1	1.4	0	62	4.2	4.0	401	3.7	3.8	165	5.9	4.9	<0.001
HCO3	836	22.1	5.4	44	25.7	3.0	159	23.8	4.8	444	22.0	5.3	170	20.0	5.9	<0.001
Serum creatinine	1295	1.8	1.1	46	1.3	0.4	248	1.5	0.8	739	1.8	1.2	203	1.9	1.1	<0.001
pH	577	7.3	0.2	2	7.4	0.1	51	7.3	0.1	312	7.3	0.1	168	7.3	0.1	0.18
Hemodynamic																
Admission EF, %	771	24.9	15.5	1	65.0	0	126	28.1	16.5	490	24.2	15.0	111	24.1	17.1	0.005
RAP	1037	14.2	6.9	44	8.8	6.2	177	12.9	6.7	619	14.3	6.9	165	16.2	6.3	<0.001
PCWP	847	24.5	8.9	45	16.5	7.3	177	24.3	8.3	473	25.2	8.8	131	24.6	9.2	<0.001
Mean PAP	904	32.8	9.8	44	27.0	11.3	178	33.3	9.5	646	33.5	9.6	169	30.8	9.4	<0.001
CO	1062	3.8	2.4	45	3.8	0.7	188	3.5	1.2	651	3.8	2.4	153	4.4	3.6	0.003
CPO	999	0.6	0.4	45	0.6	0.1	178	0.6	0.3	607	0.6	0.4	146	0.7	0.6	0.44
Heart rate	1248	92.0	22.7	46	75.2	12.8	234	85.9	19.7	685	93.8	22.2	193	97.3	24.8	<0.001
Cardiac index	1071	1.9	0.6	45	1.9	0.3	191	1.8	0.5	659	1.9	0.6	151	1.9	0.6	0.09
MAP	1230	74.5	14.7	46	71.8	7.5	250	80.3	15.7	724	74.4	14.3	205	67.8	12.9	<0.001

P values calculated using χ^2 test of independence or ANOVA as appropriate. AST indicates aspartate aminotransferase; BUN, blood urea nitrogen; CABG, coronary artery bypass grafting; CO, cardiac output; CPO, cardiac power output; CSWG, Cardiogenic Shock Working Group; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HCO3, bicarbonate; MAP, mean arterial pressure; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; RAP, right arterial pressure; and SCAI, Society for Cardiovascular Angiography and Interventions.

Hemodynamic Congestion and Clinical Outcomes

Hemodynamic associations with mortality and their distribution across SCAI stages were evaluated according to 4 specific profiles of congestion. Pulmonary capillary wedge pressure (PCWP) was considered elevated at ≥18 mm Hg and right atrial pressure (RAP) was considered elevated when ≥12 mm Hg. Values of RAP and PCWP in excess of these upper limits were used to stratify patients into 1 of the following 4 congestion profiles: right-ventricular (RV) (elevated RAP) congestion, left-ventricular (LV) (elevated PCWP) congestion, bi-sided (BiV, both RAP and PCWP elevated) congestion, or euvolemic (EuV, both RAP and PCWP below cutoff values).

Statistical Analyses

The primary outcome of interest was all-cause, in-hospital mortality; all mortality outcomes analyzed in this report refer exclusively to in-hospital mortality. Secondary analyses explored descriptive statistics comparing characteristics and outcomes of SCAI stages and congestion profiles (as described above). All analyses were performed on an all-cause CS cohort, an MI CS subcohort, and an HF-CS subcohort. Univariate logistic regression models were used to estimate odds and 95% CIs of mortality in association with SCAI stages and congestion profile. Multivariate analyses were then performed, adjusting by significant comorbidities, to assess the independent associations of SCAI, congestion profile, and shock cause. Descriptive statistics for categorical variables were reported as percentages and compared by χ^2 tests, and continuous variables were reported as means with standard deviations and were compared using *t* tests or ANOVA as appropriate to report *P* values with a significance level of α=0.05.

RESULTS

Patient Characteristics

Data from a total of 1414 patient hospitalizations for CS were analyzed. Patient characteristics are summarized in Table 1. Mean CI in the total cohort and across each SCAI subcohort ranged between 1.8 and 1.9 L/(min·m^2). The majority of the study population was male and White. From the total population, the primary cause of CS was identified as HF in 50.4% (n=712), MI in 34.9% (n=494), and other causes in 14.71% (n=208). Stage B, C, and D patients were also more commonly HF patients while stage E was primarily patients with MI. While short-term MCS devices were

Table 3. Baseline Descriptive Statistics of the CSWG Study Population by Shock Cause

	Overall (N=1414)		Shock Cause				
			MI (N=494)		HF (N=712)		
	n	%	n	%	n	%	*P* Value
SCAI stage							<0.001
B	1	0.1	0	0	1	0.34	
C	232	16.4	75	26.0	139	47.9	
D	220	15.6	114	39.6	85	29.3	
E	192	13.6	99	34.4	65	22.4	
No. of pressors/inotropes							<0.001
0	236	16.7	86	18.8	119	17.6	
1	393	27.8	115	25.2	241	35.7	
2+	650	46.0	256	56.0	316	46.8	
No. of MCS devices							<0.001
0	224	15.8	21	4.3	161	22.6	
1	882	62.4	294	59.5	465	65.3	
2+	308	21.8	179	36.2	86	12.1	
Type of MCS							
Impella	410	29.0	210	42.5	148	20.8	<0.001
ECMO	333	23.6	169	43.2	106	14.9	<0.001
IABP	770	54.5	292	59.1	382	53.7	0.06
Gender							0.005
Female	387	27.4	153	31.0	169	23.7	
Male	1025	72.5	340	68.8	543	76.3	
Race							<0.001
White	647	45.8	175	35.4	321	45.1	
Hispanic/Latino	31	2.2	16	3.2	7	1.0	
Asian	31	2.2	18	3.6	4	0.6	
Black	28	2.0	8	1.6	13	1.8	
Other	82	5.8	15	3.0	55	7.7	
Medical history							
HTN	681	48.2	321	65.0	276	38.8	<0.001
DM	489	34.6	220	44.5	222	31.2	<0.001
Afib/flutter	296	20.9	37	7.5	227	31.9	<0.001
CKD (any stage)	323	22.8	84	17.0	207	29.1	<0.001
PVD	60	4.2	27	5.5	22	3.1	0.0177
COPD	101	7.1	27	5.5	62	8.7	0.0028
CVA/TIA	159	11.2	60	12.1	88	12.4	0.2023
Valvular disease	214	15.1	24	4.9	154	21.6	<0.001
PCI	293	20.7	160	32.4	101	14.2	<0.001
CABG	114	8.1	40	8.1	60	8.4	0.0135
VT	216	15.3	37	7.5	154	21.6	<0.001
ICD	329	23.3	15	3.0	287	40.3	<0.001
CRT	97	6.9	10	2.0	86	12.1	<0.001

P values calculated using χ^2 test of independence or *t* test as appropriate. Afib indicates atrial fibrillation; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRT, cathode-ray tube; CSWG, Cardiogenic Shock Working Group; CVA, cerebrovascular accident; DM, diabetes mellitus; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HCO3, bicarbonate; HF, heart failure; HTN, hypertension; IABP, intraaortic balloon pump; ICD, implantable cardioverter defibrillator; MCS, mechanical circulatory support; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SCAI, Society for Cardiovascular Angiography and Interventions; TIA, transient ischemic attack; and VT, ventricular tachycardia.

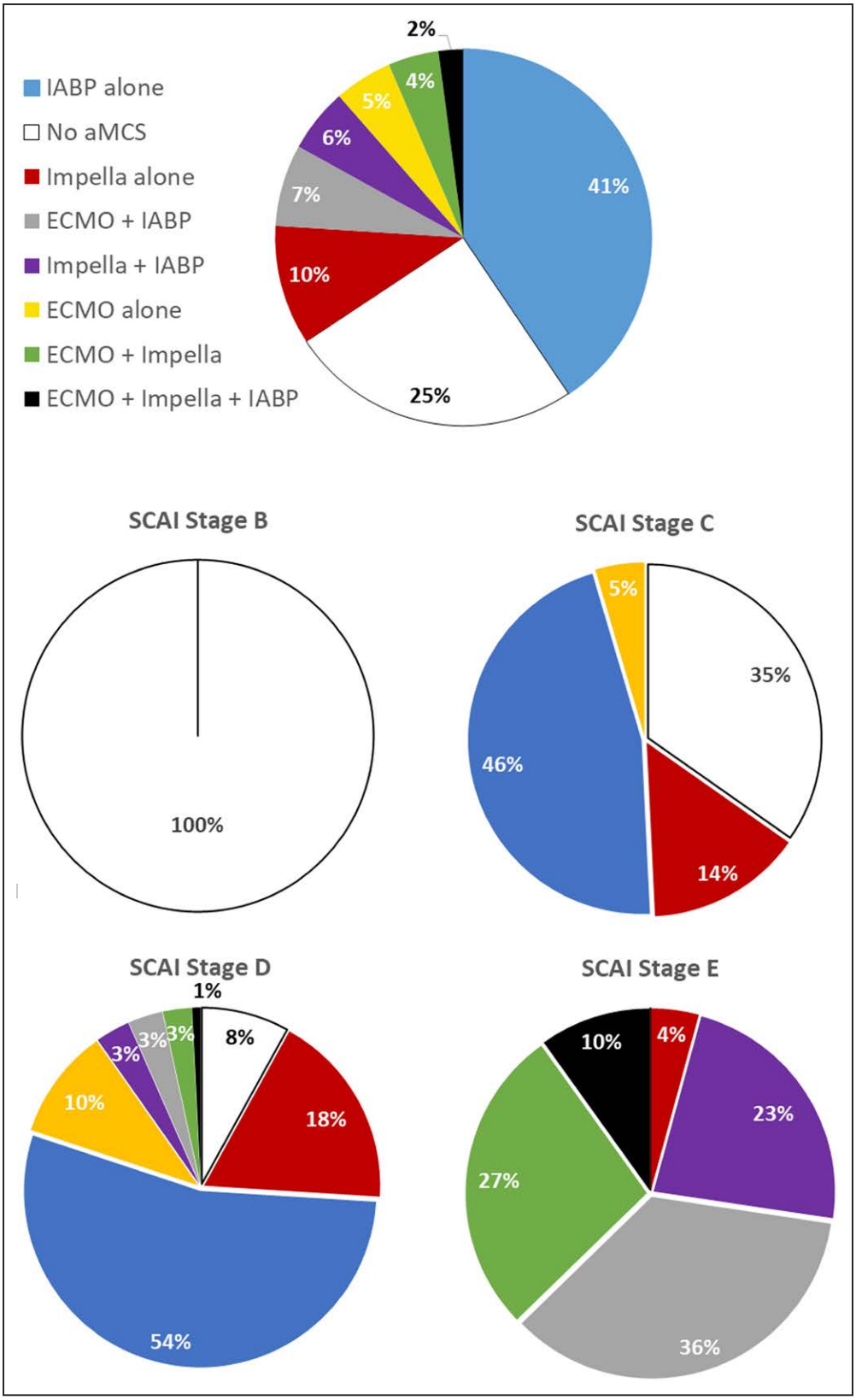

Figure 2. Device usage among Cardiogenic Shock Working Group (CSWG) patients with available hemodynamic data among the entire study cohort and each Society for Cardiovascular Angiography and Interventions (SCAI) stage.
aMCS indicates acute mechanical circulatory support; ECMO, extracorporeal membrane oxygenation; and IABP, intraaortic balloon pump.

Table 4. Baseline Descriptive Statistics of the CSWG Study Population by Shock Cause

	Overall (N=1414)			Shock Cause						*P* Value
				MI (N=494)			HF (N=712)			
	n	Mean	SD	n	Mean	SD	n	Mean	SD	
Demographic										
Age	1412	59.9	14.8	493	64.9	12.8	712	57.9	14.1	<0.001
Weight (kg)	1138	85.3	22.6	403	83.2	19.5	534	86.5	24.6	0.027
Metabolic										
AST	788	459.4	1492.6	345	448.5	1066.3	328	441.4	1805.2	0.950
BUN	1026	32.4	20.5	416	28.3	17.8	456	37.7	22.6	<0.001
Lactate	676	4.4	4.2	292	4.7	4.1	307	3.8	4.1	0.011
HCO3	836	22.1	5.4	367	20.2	4.9	330	24.3	5.3	<0.001
Serum creatinine	1295	1.8	1.1	448	1.7	1.2	687	1.9	1.1	0.003
pH	577	7.3	0.2	306	7.3	0.2	179	7.3	0.1	<0.001
Hemodynamic										
Admission EF	771	24.9	15.5	260	30.9	15.9	429	20.2	12.4	<0.001
RAP	1037	14.2	6.9	303	14.6	6.5	626	14.0	7.2	0.176
PCWP	847	24.5	8.9	271	24.2	9.2	486	24.8	8.8	0.354
Mean PAP	904	32.8	9.8	257	30.2	9.0	549	34.4	9.8	<0.001
Cardiac output	1062	3.8	2.4	329	3.8	2.1	630	3.8	2.4	0.826
CPO	999	0.6	0.4	314	0.6	0.4	584	0.6	0.4	0.638
Heart rate	1248	92.0	22.7	407	91.2	23.0	660	92.2	22.1	0.474
Cardiac index	1071	1.9	0.6	335	1.9	0.6	635	1.8	0.6	0.096
MAP	1230	74.5	14.7	433	74.9	16.9	628	74.0	12.7	0.483

P values calculated using χ^2 test of independence or *t* test as appropriate. AST indicates aspartate aminotransferase; BUN, blood urea nitrogen; CPO, cardiac power output; CSWG, Cardiogenic Shock Working Group; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HCO3, bicarbonate; HF, heart failure; MAP, mean arterial pressure; MI, myocardial infarction; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; and RAP, right arterial pressure.

broadly represented in different treatment combinations among the overall study (Figure 2) cohort, intraaortic balloon pump was the most commonly used device in the overall cohort (n=770, 54.5%). This was also the case in stage C (n=121, 46.0%) and D (n=464, 61.2%) and ECMO devices were the most commonly used devices in stage E patients (n=154, 72.6%). Prior percutaneous coronary intervention (PCI), hypertension, elevated AST, elevated lactate, and elevated filling pressures were also more common among stage E patients. Characteristics of shock cause sub-cohorts are presented in Table 2. Compared with patients with HF-CS, patients with MI were older with higher lactate and lower serum creatinine levels. Additionally, left-sided ejection fraction was higher among patients with MI, and mean pulmonary arterial pressure was lower. No differences in cardiac filling pressures, cardiac output (CO), mean arterial pressure, or heart rate were noted between the HF and MI cohorts. Characteristics of congestion sub-cohorts are presented in Table 3.

In-Hospital Outcomes

In-hospital mortality in the study cohort was 30.5%. In-hospital mortality was higher among patients with MI (39.5%) than HF patients (25.3%; *P*<0.0001; Table 4). Overall, survivors were younger and exhibited lower prevalence of arterial hypertension, type 2 diabetes mellitus, and prior coronary artery bypass grafting compared with nonsurvivors (Table 4). Clinical variables stratified by survivorship among patients with MI and HF are shown in Tables I and II in the Data Supplement. MI survivors were less likely to receive ventricular assist devices or heart transplant compared with HF survivors (Figure II in the Data Supplement).

Association of SCAI Stages With Outcomes

Patients with known drug and device data (n=1279) were classified into SCAI stages based on the number of drug and device treatments (Figure 1). Increasing drug or device treatment was directly associated with in-hospital mortality (Figure III in the Data Supplement, Table 4). All stage B patients survived to hospital discharge. Thereafter, each increased stage was associated with an increased risk of in-hospital mortality (Figure 3). Compared with SCAI stage C, stage D had 4.1 (95% CI, 2.7–6.3) times the odds of in-hospital mortality while stage E had 10.3 (95% CI, 6.4–16.6) times the odds of in-hospital mortality. Additionally, stage D had less than

Table 5. Baseline Characteristics of CSWG Study Population by Congestion Profile

	Congestion Profile								
	Euvolemic		Left Ventricular		Right Ventricular		Biventricular		
	n	%	n	%	n	%	n	%	*P* Value
Mortality	24	16.9	35	18.8	23	34.9	143	36.9	<0.001
Shock cause									0.01
MI	39	27.5	45	24.2	29	43.9	111	28.6	
HF	88	62.0	120	64.5	25	37.9	238	61.5	
Other	15	10.6	21	11.3	12	18.2	38	9.8	
SCAI stage									0.06
B	1	2.4	0	0	0	0	0	0	
C	14	33.3	29	43.9	9	22.0	75	35.9	
D	17	40.5	23	34.9	14	34.2	71	34.0	
E	10	23.8	14	21.2	18	43.9	63	30.1	
No. of pressors/inotropes									<0.001
0	40	29.0	25	13.6	7	10.8	60	15.9	
1	49	35.5	75	40.8	19	29.2	116	30.7	
2+	49	35.5	84	45.7	39	60.0	202	53.4	
No. of devices									<0.001
0	64	45.1	50	26.9	10	15.2	60	15.5	
1	56	39.4	104	55.9	30	45.5	233	60.1	
2+	22	15.5	32	17.2	26	39.4	95	24.5	
Device type									
Impella	29	20.4	48	25.8	24	36.4	116	30.0	0.06
ECMO	19	13.4	25	13.4	22	33.3	89	22.9	<0.001
IABP	52	36.6	96	51.6	36	54.6	223	57.5	<0.001
Male	99	69.7	141	75.8	45	68.2	267	68.8	0.35
Race									0.10
White	79	71.8	105	80.8	38	84.4	183	77.2	
Hispanic/Latino	1	0.9	1	0.8	2	4.4	10	4.2	
Black	4	3.6	3	2.3	1	2.2	8	3.4	
Asian	3	2.7	1	0.8	2	4.4	9	3.8	
Other	23	20.9	20	15.4	2	4.4	27	11.4	
Medical history									
HTN	59	43.1	76	43.7	32	50.8	180	51.9	0.35
DM2	41	29.1	57	30.7	22	33.9	141	36.4	0.33
Afib/flutter	33	27.1	51	33.3	18	33.3	123	40.2	0.07
CKD (any stage)	36	26.9	45	26.6	11	18.3	104	30.6	0.24
PVD	6	4.6	6	3.7	5	8.6	20	6.4	0.44
COPD	12	8.8	12	6.9	3	4.8	40	11.1	0.23
CVA/TIA	22	16.1	28	16.2	6	9.5	52	14.4	0.60
Valvular disease	25	21.2	39	26.5	16	29.6	75	26.3	0.61
PCI	25	20.8	43	29.5	23	42.6	71	25.7	0.02
CABG	9	6.8	13	8.2	8	13.8	32	10.4	0.39
VT	36	29.5	41	26.6	15	27.8	71	23.1	0.54
ICD	54	44.3	77	50.0	11	20.0	116	37.9	<0.001
CRT	16	13.1	18	11.7	1	1.8	36	11.8	0.14

P values calculated using χ^2 test of independence or ANOVA as appropriate. Afib indicates atrial fibrillation; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRT, cathode-ray tube; CSWG, Cardiogenic Shock Working Group; CVA, cerebrovascular accident; DM2, type 2 diabetes mellitus; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HCO3, bicarbonate; HF, heart failure; HTN, hypertension; IABP, intraaortic balloon pump; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SCAI, Society for Cardiovascular Angiography and Interventions; TIA, transient ischemic attack; and VT, ventricular tachycardia.

Table 6. Baseline Characteristics of CSWG Study Population by Congestion Profile

	Congestion Profile								
	Euvolemic		Left Ventricular		Right Ventricular		Biventricular		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P* Value
Demographic									
Age	56.5	15.4	57.6	15.4	60.6	14.9	59.4	14.7	0.11
Weight, kg	81.6	20.1	82.5	20.3	83.2	22.8	87.1	22.1	0.03
Metabolic									
AST	452.3	1552.6	340.2	1067.9	860.9	3070.4	447.0	1447.0	0.29
BUN	28.3	15.7	31.2	19.2	32.2	22.1	37.6	22.8	<0.001
Lactate	3.6	3.3	3.7	4.5	5.1	3.4	4.7	3.4	0.13
HCO3	23.7	4.9	23.9	5.2	20.0	5.5	22.2	5.7	<0.001
Serum creatinine	1.6	0.8	1.5	1.0	1.8	1.5	1.9	1.2	0.002
pH	7.3	0.1	7.4	0.1	7.3	0.1	7.3	0.1	<0.001
Hemodynamic									
EF, %	22.6	12.2	24.0	16.8	25.2	16.8	23.5	15.2	0.85
RAP	6.7	3.1	8.7	2.9	16.7	3.5	19.2	5.1	<0.001
PCWP	13.2	3.9	25.6	5.3	15.8	2.4	29.3	7.4	<0.001
Mean PAP	23.3	6.8	33.6	6.9	25.8	8.3	37.3	9.0	<0.001
Cardiac output	4.0	1.6	3.6	0.9	4.2	2.9	3.9	3.3	0.40
CPO	0.6	0.3	0.6	0.2	0.7	0.5	0.6	0.5	0.57
Heart rate	83.8	19.0	90.2	19.2	91.6	23.9	93.8	21.4	<0.001
Cardiac index	2.0	0.5	1.9	0.5	1.9	0.6	1.8	0.6	<0.001
Mean arterial pressure	73.2	13.6	74.7	13.6	71.9	19.1	73.7	13.1	0.53

P values calculated using χ^2 test of independence or ANOVA as appropriate. AST indicates aspartate aminotransferase; BUN, blood urea nitrogen; CPO, cardiac power output; CSWG, Cardiogenic Shock Working Group; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HCO3, bicarbonate; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; and RAP, right arterial pressure.

half the odds of in-hospital mortality of stage E (odds ratio [OR], 0.4 [95% CI, 0.29–0.55]). This was also true among the MI cohort with mortality ORs of 3.9 (95% CI, 2.0–7.6) and 8.1 (95% CI, 4.0–16.3) among stage D and E patients, respectively, compared with stage C patients and an OR of 0.49 (95% CI, 0.32–0.75) among stage D patients compared with those in stage E. The same trend was also observed in patients with HF. HF stage D and E patients had ORs of 3.5 (95% CI, 2.0–6.1) and 10.0 (95% CI, 4.7–21.0) compared with stage C patients and stage D patients had 0.35× the odds of mortality (95% CI, 0.20–0.61) compared with stage E patients.

Lactate and drug and device data were available in 645 patients and were used to perform a sensitivity analysis of SCAI staging incorporating lactate levels. Of these 645 patients, 1 patient (0.1%) was classified as stage B, 232 (35.9%) were stage C, 220 (34.1%) were stage D, and 192 (29.8%) were stage E. This distribution differed significantly from the entire study cohort using only drug and device escalation. However, a similar trend in mortality was observed in this sensitivity analysis with 0% mortality in stage B, 32.3% in stage C, 48.6% in stage D, and 57.3% in stage E (Figure I in the Data Supplement).

Association of Congestion Profiles With Outcomes

We next explored the impact of hemodynamic congestion on mortality. Pulmonary artery catheters were used to collect any hemodynamic data in 79% of the total study population (n=1116) with both RAP and PCWP assessed in 55% of the total population (n=781). Mean CI was 1.9±0.6 across the study population. A positive correlation between RAP and PCWP (R^2=0.26, *P*<0.001) was observed in these patients. Using these data, we grouped patients with CS into one of 4 congestion profiles as defined above (Figure 4). BiV congestion (ie, elevated right and left heart filling pressures) was most commonly observed (50%, n=390). Both BiV and right-sided congestion profiles were associated with the highest in-hospital mortality among the total cohort and among either MI or HF subgroups (Figure 5). Stage B patients were comprised mainly of euvolemic

patients. The frequency of BiV congestion increased with increased SCAI stage among the entire cohort and in the MI and HF subgroups (Figure 5).

Multivariate Analyses

To better understand the relationship between SCAI stages, shock cause, and hemodynamics with in-hospital mortality, we ran several multivariate analyses. In the entire study cohort, after adjusting for shock cause, congestion profile, and other comorbidities (hypertension, age, type 2 diabetes mellitus, prior PCI, and ventricular tachycardia [VT]), we found that SCAI stages were still a significant predictor of mortality with stage D and E patients having aORs of 11.8 (95% CI, 4.6–30.5) and 21.3 (95% CI, 7.7–59.0), respectively, compared with stage C patients and stage D patients having an adjusted odds ratio (aOR) of 0.6 (95% CI, 0.3–0.9) compared with stage E patients. After adjustment, shock cause was not a significant independent predictor of mortality while biventricular congestion remained a signifcant independent predictor of mortality compared with left ventricular congestion or no congestion (BiV versus LV aOR, 2.4 [95% CI, 1.4–3.7]; BiV versus euvolemic aOR, 2.1 [95% CI, 1.1–4.0]). Additionally, after adjusting for SCAI stage in a separate multivariable model, RAP remained a significant predictor of mortality (OR, 1.06 [95% CI, 1.03–1.08]).

DISCUSSION

Using a large, multicenter registry inclusive of invasive hemodynamics and contemporary short-term MCS strategies, we identified that the proposed SCAI staging system is associated with in-hospital mortality among patients with CS due to HF and MI. Compared with HF, patients with MI have higher mortality, but MI survivors have a greater likelihood of recovery to discharge, with few patients bridging to durable ventricular assist devices or orthotopic heart transplantation. Given the availability of hemodynamic data, we confirmed a low mean CI in the study population and observed a high prevalence of both right- and left-sided (biventricular) congestion in the study population. Worsening congestion was associated with both increasing SCAI stages and in-hospital mortality. These findings address critical gaps in our understanding of CS by confirming not only that SCAI stages identify patients at risk for in-hospital mortality in a population that reflects contemporary clinical practice, but also that basic hemodynamic data may be used to further stratify risk among patients with CS.

We assigned SCAI stages based on the consensus statement parameters focused on treatment intensity, defined by the number of drug and device therapies used during admission for CS (Figure 1). Drug or device escalation were each directly associated with in-hospital mortality. This observation is particularly important given the broad range of short-term MCS devices included in the analysis and supports the need for future prospective studies exploring the utility of device-based CS algorithms. Progression from one SCAI classification to the next represents a deteriorating clinical course of CS as indicated by increasing intensity of medical and device-based therapies to stabilize a critically ill patient, ultimately ending with use of all resources at hand in stage E. Therefore, we employed a matrix of drug and device escalation and identified that SCAI stages are directly associated with in-hospital mortality.

To validate our method of assigning SCAI stages, a sensitivity analysis incorporating lactate levels was performed. While a different distribution of patients across SCAI stages was observed, the relationship between SCAI stage and mortality remained unchanged (Figure I in the Data Supplement). Patient characteristics for this alternate definition of SCAI stages are displayed in Table III in the Data Supplement. Since lactate levels are not uniformly collected, these observations suggest that stratifying patients based on maximal drug or device utilization may be a reasonable approach to defining SCAI stages for the purpose of data analysis. Clinically, a more uniform definition for SCAI stages is needed, and prospective registries should incorporate lactate levels in addition to measures of hypotension, hypoperfusion, and drug/device utilization.

Recent reports exploring the utility of SCAI stages have employed different definitions for each stage. Jentzer et al[12] defined SCAI stages based on clinical indices of hypotension and hypoperfusion with inclusion of a change in lactate from admission to maximal value recorded as a marker of deterioration. This group showed a correlation with in-hospital mortality in a single-center database that largely focused on intraaortic balloon pump use with minimal exposure to other short-term MCS devices. Schrage et al[13] defined SCAI stages based primarily on lactate levels. This single-center study also identified a correlation between SCAI stages and in-hospital mortality. Neither study included invasive hemodynamic data. Our findings now employ a multicenter registry inclusive of contemporary short-term MCS devices and provide new information derived from invasive hemodynamic data that support our distinct approach to assigning SCAI stages.

We observed 0% mortality in SCAI stage B patients, who represent patients with early-stage shock. Since our report evaluated maximal SCAI stage during a patient's hospitalization, these patients did not progress into CS and a low mortality rate may be expected and is consistent with prior reports.[12,13] Furthermore, in our sensitivity analysis incorporating lactate levels, SCAI stage B patients continued to have the lowest mortality rate of 0%. More study of this unique population of preshock patients is required.

Table 7. Differences Between Survivors and Nonsurvivors in the Overall CSWG Study Cohort

	Mortality				
	Survivors (n=938)		Nonsurvivors (n=431)		
	n	%	n	%	*P* Value
SCAI stage					<0.001
B	1	0.3	0	0	
C	157	44.5	75	25.7	
D	113	32.0	107	36.6	
E	82	23.2	110	37.7	
No. of pressors/inotropes					<0.001
0	206	23.3	30	7.6	
1	305	34.5	88	22.3	
2+	373	42.2	277	70.1	
No. of MCS devices					<0.001
0	197	20.0	27	6.3	
1	631	64.2	251	58.2	
2+	155	15.8	153	35.5	
Types of MCS					
Impella	218	22.2	192	44.6	<0.001
ECMO	168	17.1	165	38.3	<0.001
IABP	560	57.0	210	48.7	0.004
Cause					<0.001
MI	299	30.4	195	45.2	
HF	532	54.1	180	41.8	
Gender					0.236
Female	260	26.5	127	29.5	
Male	722	73.5	303	70.3	
Race					0.259
White	460	46.8	187	43.4	
Hispanic/Latino	20	2.0	11	2.6	
Asian	24	2.4	7	1.6	
Black	18	1.8	10	2.3	
Other	66	6.7	16	3.7	
Medical history					
HTN	426	43.3	255	59.2	<0.001
Diabetes mellitus	310	31.5	179	41.5	<0.001
Afib/flutter	207	21.1	89	20.6	0.462
CKD (any stage)	218	22.2	105	24.4	0.339
PVD	37	3.8	23	5.3	0.040
COPD	68	6.9	33	7.7	0.883
CVA/TIA	109	11.1	50	11.6	0.682
Valvular disease	161	16.4	53	12.3	0.296
PCI	187	19.0	106	24.6	0.040
CABG	59	6.0	55	12.8	<0.001
VT	143	14.5	73	16.9	0.049
ICD	250	25.4	79	18.3	0.020
CRT	69	7.0	28	6.5	0.985

P values calculated using χ^2 test of independence or *t* test as appropriate. Afib indicates atrial fibrillation; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRT, cathode-ray tube; CSWG, Cardiogenic Shock Working Group; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HF, heart failure; HTN, hypertension; IABP, intraaortic balloon pump; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SCAI, Society for Cardiovascular Angiography and Interventions; TIA, transient ischemic attack; and VT, ventricular tachycardia.

Table 8. Differences Between Survivors and Nonsurvivors in the Overall CSWG Study Cohort

	Mortality						
	Survivors (n=938)			Nonsurvivors (n=431)			
	n	Mean	SD	n	Mean	SD	*P* Value
Demographic							
Age	982	58.3	15.0	430	63.6	13.5	<0.001
Weight, kg	803	85.3	22.8	335	85.2	22.1	0.970
Metabolic							
AST	526	364.1	1324.0	262	650.8	1771.0	0.011
BUN	703	30.3	18.7	323	37.0	23.3	<0.001
Lactate	377	3.6	3.4	299	5.4	4.9	<0.001
HCO3	576	23.2	5.2	260	19.8	5.3	<0.001
Serum creatinine	907	1.7	1.0	388	2.0	1.3	<0.001
pH	336	7.3	0.1	241	7.3	0.2	<0.001
Hemodynamic							
Admission EF	522	24.6	15.2	249	25.7	16.1	0.335
RAP	747	13.2	6.5	290	16.6	7.4	<0.001
PCWP	595	24.0	8.9	252	25.6	8.8	0.018
Mean PAP	665	32.8	9.8	239	32.9	10.0	0.899
Cardiac output	747	3.7	2.0	315	4.1	3.2	<0.001
CPO	704	0.6	0.4	295	0.6	0.5	0.381
Heart rate	894	91.0	22.3	354	94.6	23.5	0.012
Cardiac index	760	1.8	0.6	311	1.9	0.7	0.120
MAP	849	76.3	14.2	381	70.6	15.2	<0.001

P values calculated using χ^2 test of independence or *t* test as appropriate. AST indicates aspartate aminotransferase; BUN, blood urea nitrogen; CPO, cardiac power output; CSWG, Cardiogenic Shock Working Group; EF, ejection fraction; HCO3, bicarbonate; MAP, mean arterial pressure; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; and RAP, right arterial pressure.

Accordingly, our findings strengthen the proposed SCAI classification structure by (1) providing contemporary evidence that treatment escalation may be an objective means of defining deterioration irrespective of the cause of CS, (2) enabling future analyses to evaluate both escalation and de-escalation of therapies, and (3) informing the development of future registry and randomized clinical trials where different CS strategies can be tested in patient populations with similar expected outcomes.

A unique aspect of the CSWG Registry is the availability of invasive hemodynamic data for analysis. Across survivors and nonsurvivors, cardiac filling pressures were elevated and CO, CI and cardiac power output (CPO) were low. Nonsurvivors had higher filling pressures and no significant difference in CPO or CI compared with survivors. CPO and CI were also not significantly changed across SCAI stages, but CO was paradoxically higher among stage E patients and among nonsurvivors. This may reflect variability in how CO is calculated (ie, Fick or thermodilution method) and the impact of maximal drug

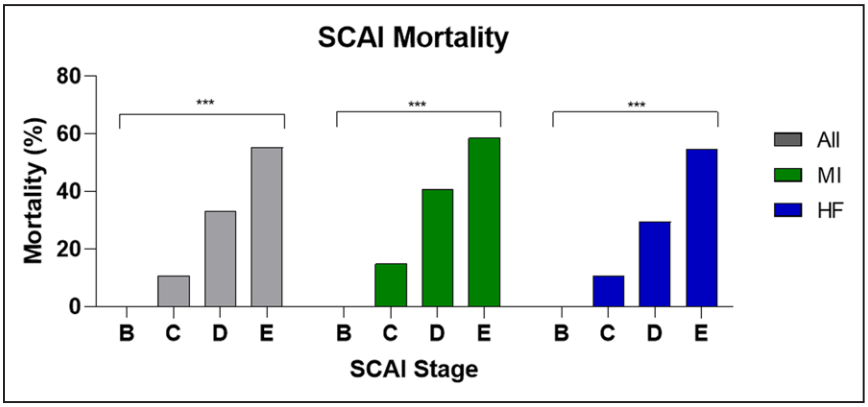

Figure 3. In-hospital mortality by Society for Cardiovascular Angiography and Interventions (SCAI) stage among different causes of shock.
HF indicates heart failure; and MI, myocardial infarction. ***$P \leq 0.001$.

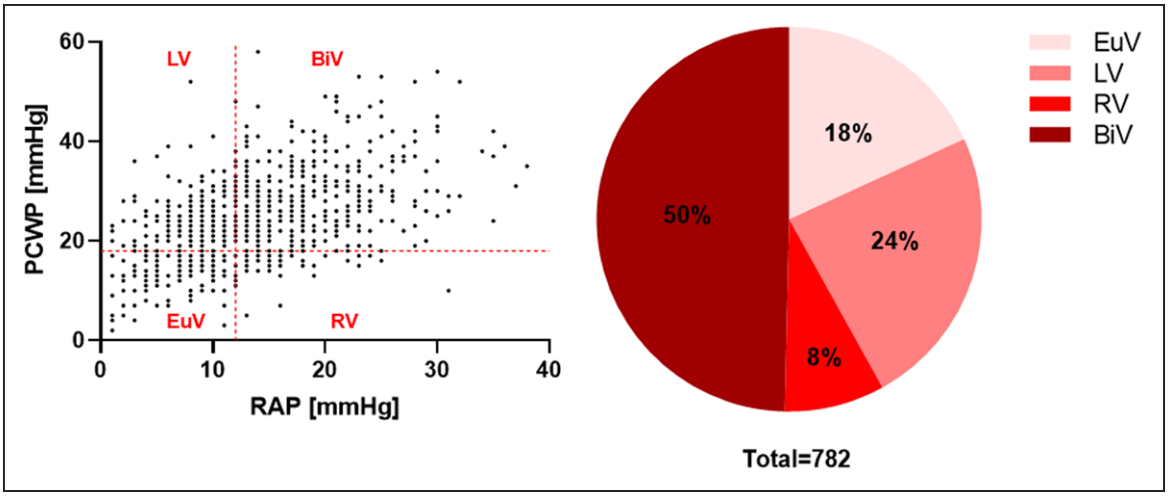

Figure 4. Adjudication and distribution of congestion profiles among the Cardiogenic Shock Working Group (CSWG) study population with available hemodynamic data.
BiV indicates bi-ventricular; EuV, euvolemic; LV, left-ventricular; PCWP, pulmonary capillary wedge pressure; RAP, right arterial pressure; and RV, right-ventricular.

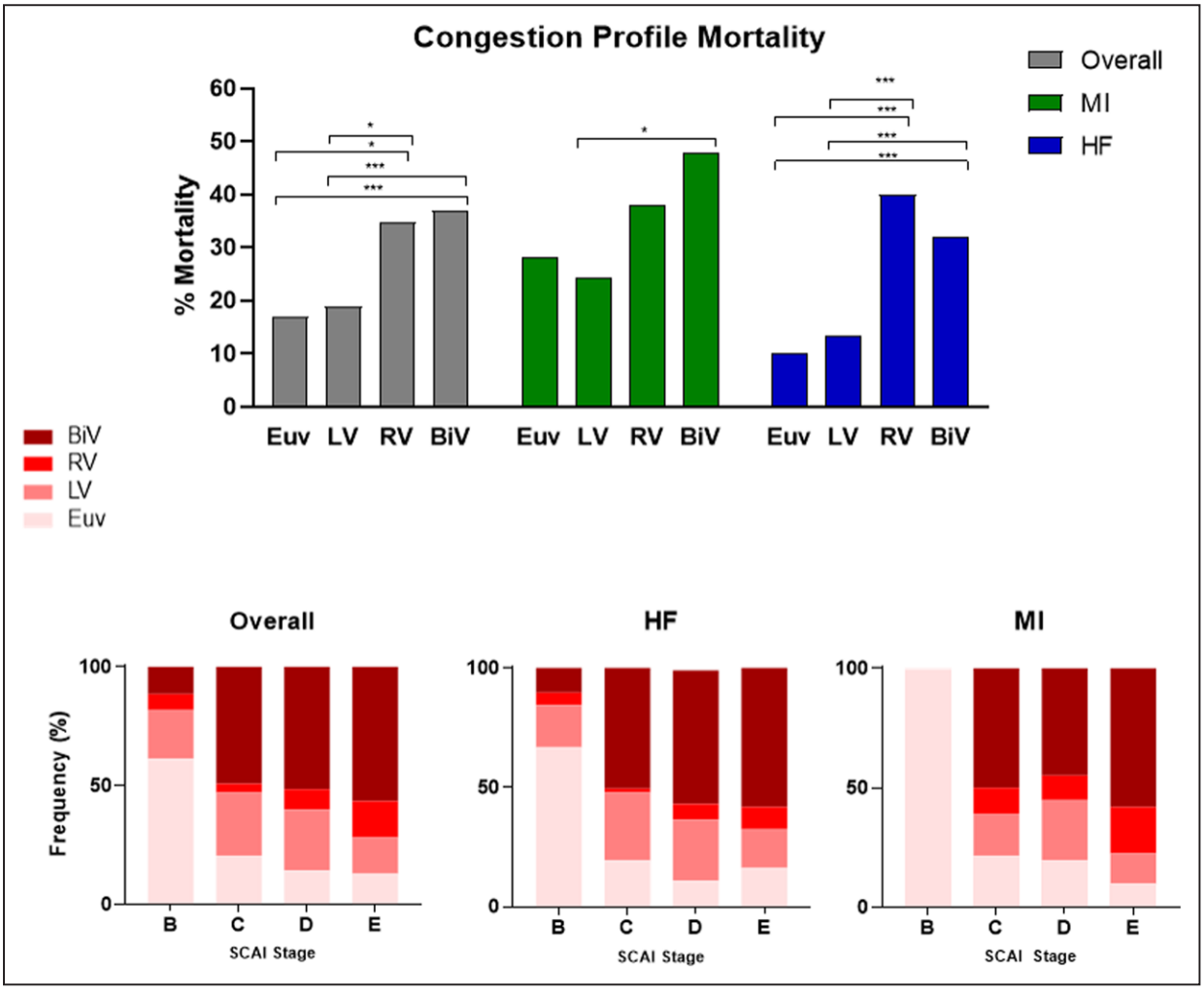

Figure 5. Congestion profiles as indicators of mortality and cardiogenic shock severity.
A, Comparisons of mortality across congestion profiles among the overall, myocardial infarction (MI), and heart failure (HF) study cohorts. Comparisons adjusted by Bonferroni. **B**. Distribution of congestion profiles across Society for Cardiovascular Angiography and Interventions (SCAI) stages. BiV indicates bi-ventricular; EuV, euvolemic; LV, left-ventricular; and RV, right-ventricular. *P<0.05, ***P<0.001.

and device treatment to increase CO in sicker patients (ie, stage E). Furthermore, CPO has been validated primarily in MI populations[14] but is less well understood in HF populations, where low CO does not always correlate with low mean arterial pressure. The SHOCK trial also did not include multiple short-term MCS approaches. Our data suggest that CPO requires further validation in MI and HF shock populations treated with contemporary short-term MCS devices.

In contrast to CO measurements, cardiac filling pressures were consistently elevated across all shock cohorts. Both RAP and PCWP were significantly higher among nonsurvivors and increased across SCAI stages. We further characterized the impact of cardiac filling pressures on clinical outcomes by defining congestive profiles based on RAP and PCWP. In-hospital mortality was highest among patients with biventricular or right ventricular congestive profiles. Furthermore, the distribution of congestive profiles across SCAI stages suggests that sicker patients are more likely to have biventricular congestion. These findings suggest that venous congestion is potentially an important determinant of clinical outcomes and may be explained by the fact that venous congestion is associated with worsening renal function and congestive hepatopathy,[15,16] which may exacerbate metabolic derangement. Prior reports have also illustrated the association between venous congestion and poor outcomes in HF and MI.[17] These observations suggest that approaches to decongest patients with CS may improve clinical outcomes.

We further observed that the presence of biventricular congestion was associated with worsening kidney and liver function and elevated lactate levels compared with other congestive profiles. These data are also consistent with studies suggesting that the presence of right HF in the setting of CS is associated with increased mortality.[18] Recent data from prospective shock registries using congestive profiles as part of a treatment strategy algorithm showed improvement in mortality due to acute MI and CS.[19,20] These findings suggest that CS algorithms that include an assessment of congestive profile may lead to improved outcomes by identifying and managing patients with venous congestion before metabolic failure worsens.

Limitations

The retrospective nature of the registry limits the ability to account for missing data elements, is subject to clinical and selection bias, and further limits our ability to adjust for metabolic and hemodynamic indicators of prognosis. Since the exact timing of data collection cannot be ascertained, it would be inappropriate to assess these measures as confounders relative to each other. A limitation of the current analysis is the lack of detail regarding drug dosage, sequence of device application, and timing of therapy as well as specific vasopressors or inotropes used. Future studies specifically looking at drug and device escalation across a patient's hospitalization for CS are required. Furthermore, information about cardiac arrest was not available for analysis. However, even without serial data available, maximal escalation of treatment serves a reasonable marker of overall clinical deterioration. Though, this approach prevents drawing inferences about treatment strategies at each SCAI stage and may be influenced by other factors including institutional availability of devices, physician preference, variations in shock treatment algorithms, and other clinical or anatomic limitations to drug or device implementation. For these reasons, an additional sensitivity analysis incorporating baseline lactate levels into the SCAI staging scheme was performed. As hemodynamic data in this study were assessed after index hospital admission, data was most likely acquired after initiation of drug or device therapy in the case of transfer patients. Future studies involving a more granular retrospective data set or prospective studies are required to put these findings into context.

Conclusions

In this large, multicenter analysis of a national registry, we provide new insight into the characteristics, contemporary treatment strategies, and predictors of in-hospital mortality among patients with all-cause CS or CS due to MI or HF. We provide real-world validation of the SCAI staging scheme as an approach to identify patients with CS at risk of in-hospital mortality. We also identified venous congestion as a critical marker of risk, thus potentially identifying an important target of therapy for patients with CS. Future prospective studies are required to confirm the long-term prognostic significance of these findings.

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Circulation: Heart Failure

EDITORIAL

Understanding Cardiogenic Shock Severity and Mortality Risk Assessment

Jacob C. Jentzer, MD

Cardiogenic shock (CS) represents the most extreme form of cardiac compromise, where inadequate cardiac output compromises tissue and organ perfusion.[1,2] Short-term mortality for patients with CS remains >30%, highlighting a persistent unmet need for improved treatment strategies to decrease mortality.[1,3,4] A major challenge in caring for patients with CS is that the initial hemodynamic problem can deteriorate into a downward spiral of progressive hypoperfusion, organ dysfunction, and shock driven by accumulated metabolic derangements.[1] Therapeutic interventions targeting different components of this hemodynamic-metabolic shock cascade presumably will have varying efficacy depending on the phase of shock when they are instituted. Targeting hemodynamics during the metabolic phase of shock may not improve outcomes, explaining why clinical trials of mechanical circulatory support (MCS) devices have not demonstrated reductions in mortality compared with medical therapy.[1,3,4]

See Article by Thayer et al

Mortality risk in patients with CS depends on numerous factors, including shock severity and response to therapy, the magnitude and reversibility of organ dysfunction, patient characteristics, and complicating factors, such as brain injury from cardiac arrest.[1,2] The risk of dying can differ dramatically between individual patients with CS based on their clinical profile, but standard severity-of-illness scores do not perform well for mortality risk stratification in CS populations.[5] Risk scores have been developed to improve mortality risk stratification for patients with CS, but these primarily include nonmodifiable risk factors, with few relevant markers of shock severity.[6,7] Comprehensive assessment of shock severity incorporates hemodynamic parameters, the magnitude of hypoperfusion, the need for supportive therapies, and the response to initial therapy (Figure).[2,6–8]

Until recently, there was no universal system for grading CS severity, preventing researchers from comparing CS study populations and determining whether the efficacy of therapeutic interventions varies as a function of shock severity.[2] The Society for Cardiovascular Angiography and Intervention (SCAI) developed a consensus-driven CS classification system, dividing CS into 5 stages of increasing severity including preshock (stage B) and 3 CS stages of increasing severity (stages C–E; Table).[2] The SCAI shock stages paradigm was designed to be flexible, without rigid definitions of each stage, to allow easy applicability at bedside with the goal of facilitating communication between providers and streamlining clinical decision-making. Implicit in the SCAI shock stages classification is the concept that clinical outcomes and the efficacy of certain therapeutic interventions will vary as a function of the severity of CS.

Single-center retrospective studies using research definitions of the SCAI shock stages have demonstrated an incremental increase in mortality risk with rising severity of CS.[9,11,13,14] The SCAI shock stages were first examined in 10 004 Mayo Clinic cardiac intensive care unit patients, using a combination of vital signs, laboratory data, vasopressor doses and use of MCS during the

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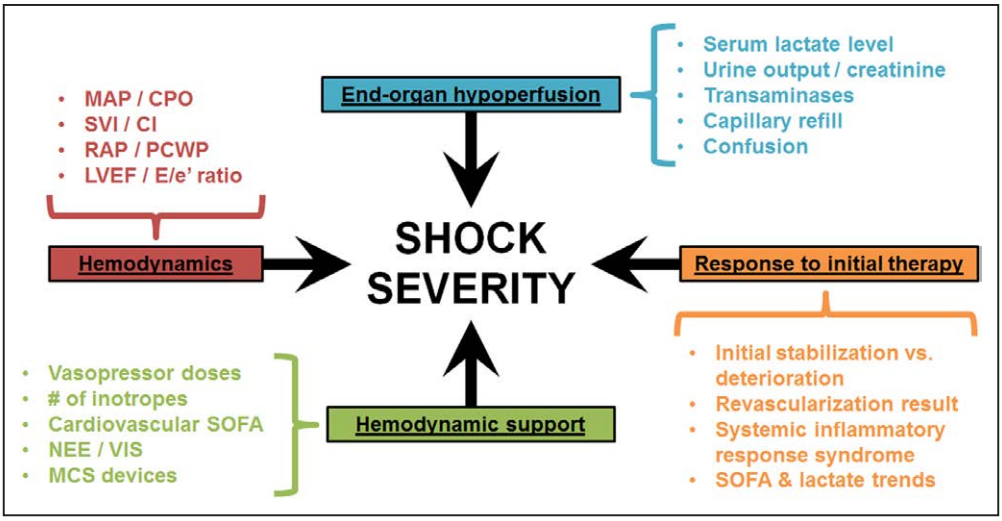

Figure. Parameters included in the assessment of shock severity for patients with cardiogenic shock.[1,2,5–10]
CI indicates cardiac index; CPO, cardiac power output; LVEF, left ventricular ejection fraction; MAP, mean arterial pressure; MCS, mechanical circulatory support; NEE, norepinephrine equivalents; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; SOFA, Sequential Organ Failure Assessment; SVI, stroke volume index; and VIS, Vasoactive-Inotropic Score.

first 24 hours after admission (Table).[9] This SCAI shock stages classification demonstrated substantial mortality discrimination across subgroups, even after adjusting for standard measures of illness severity. The presence and type of cardiac arrest further augmented mortality risk at each SCAI shock stage, and SCAI shock stage at the time of admission predicted post-discharge mortality among hospital survivors.[13,14] Schrage et al[11] reported similar findings using different SCAI shock stage definitions (Table) in a population of patients with CS or large myocardial infarction.

In this issue of *Circulation: Heart Failure*, Thayer et al[12] from the CS working group report a new, simplified research definition of the SCAI shock stages using 1414 contemporary patients with CS from 8 centers, 35% of whom had CS due to myocardial infarction, and 50% of whom had CS due to heart failure (HF). The maximum SCAI shock stage during hospitalization was defined based on the degree of hemodynamic support required in terms of the number of vasopressors and MCS devices used (Table); most patients were classified as SCAI shock stage D. Congruent with prior studies of SCAI shock stages and mortality, a stepwise increase in hospital mortality was observed with higher SCAI shock stages even after adjustment for relevant clinical variables. This new simplified SCAI shock stages definition can easily be applied at the bedside, as well as in registries and administrative databases, allowing more widespread use than prior definitions that incorporate numerous data points. The major drawback of defining shock severity using the degree of hemodynamic support is the inability to draw conclusions regarding the variable impact of different treatment strategies as a function of CS severity, and this approach may potentially oversimplify the relationship between vasopressor requirements and outcomes.[10]

This study highlights the important differences between patients with CS due to myocardial infarction versus HF and underscores the prevalence of CS due to nonischemic causes, a growing CS subpopulation for which we have few evidence-based therapies.[1] Patients

Table. Definitions of SCAI Shock Stages Used in Clinical Research Studies[2,9,11,12]

SCAI Shock Stage	SCAI Definition[2]	Mayo Clinic[9]	Hamburg[11]	CS Working Group[12]
A (at risk)	Acute cardiac disease without hemodynamic instability	No hemodynamic instability or hypoperfusion	Hemodynamically stable large myocardial infarction	Not applicable
B (beginning)	Hemodynamic instability without hypoperfusion	Hemodynamic instability without hypoperfusion	No hypoperfusion or vasoactive support	No vasopressors or MCS
C (classic)	Hypoperfusion requiring intervention	Hypoperfusion (elevated lactate or acute kidney injury)	Hypoperfusion or vasoactive support	One vasopressor or MCS device (either)
D (deteriorating)	Deterioration despite initial therapy	Deterioration (rising vasopressor requirements or lactate)	Rising lactate at 6 h	Need for >1 vasopressor or MCS device or both vasopressors and MCS
E (extremis)	Actual or impending circulatory collapse	Refractory shock (very high lactate or vasopressor requirements)	Prolonged cardiac arrest or ongoing cardiopulmonary resuscitation	Need for >1 vasopressor and >1 MCS device (both)

CS indicates cardiogenic shock; MCS, mechanical circulatory support; and SCAI, Society for Cardiovascular Angiography and Intervention.

with myocardial infarction had higher SCAI shock stage despite similar hemodynamics and higher left ventricular ejection fraction and were less likely to require advanced HF therapies.[12] As in prior studies, patients with CS with ACS had higher crude hospital mortality, but this difference dissipated after adjustment for SCAI shock stage.[6] Although patients with CS due to myocardial infarction are sicker and are more likely to die overall, they hold the prospect of myocardial recovery after revascularization unlike other patients with CS who often require cardiac replacement therapies.

Most notably, Thayer et al[12] provide a wealth of data regarding the hemodynamic correlates of CS severity in the 1116 patients with invasive hemodynamic data from a pulmonary artery catheter. As SCAI shock stage increased, the mean values of cardiac index and cardiac power output did not differ substantially. By contrast, cardiac filling pressures (particularly the right atrial pressure) increased with rising SCAI shock stage, reflecting worsening biventricular congestion and associated organ dysfunction as CS severity increased. Biventricular congestion and elevated right atrial pressure were associated with increased hospital mortality risk after adjustment for SCAI shock stage, whereas cardiac index and cardiac power output were not. This underscores the important relationship between right ventricular dysfunction and congestion with higher shock severity, organ failure, and adverse outcomes.[8] Lala et al[15] previously reported that right ventricular dysfunction and congestion were common among patients with CS, but the association between right ventricular dysfunction with higher mortality was not statistically significant. Insofar as severe CS appears to be primarily a biventricular disease, it may not be surprising that MCS devices targeting the left ventricle have not improved survival in clinical trials.[3,4]

To move forward in our study of CS, we need to recognize and embrace the heterogeneity of patients with CS, whereas clinical trials typically consider all patients as alike. Although certain therapies may not be effective when applied across mixed CS populations, they may still be useful in selected patients depending on their shock severity, hemodynamic phenotype, cause, risk profile, or phase during the disease course.[1] Understanding these clinically relevant nuances is the key to developing a personalized-medicine approach for patients with CS that matches the level and type of hemodynamic support to the level and type of hemodynamic compromise, particularly for MCS devices that provide a range of cardiac output augmentation.[1,3]

Employing the SCAI shock stages paradigm in clinical practice is the crucial first step in this process and can facilitate triage-and-transfer protocols to ensure that patients with CS are managed at a center that can provide the level of support they require.[1,2] Only by speaking a common language regarding CS severity can we develop tailored CS therapies targeting shock severity itself as opposed to mortality risk. With our increasingly sophisticated electronic medical record systems, the SCAI shock stages can be classified real-time in an automated fashion, allowing an escalating treatment strategy to be implemented as the severity of CS increases. Future observational studies of CS should consistently report SCAI shock stage using transparent definitions that are congruent with prior studies, and ideally, clinical trials should stratify randomization and report outcomes by SCAI shock stage to permit risk-treatment inferences. This strategy may be our only hope for establishing effective treatment strategies and successfully developing novel therapies for CS across the spectrum of shock severity.

ARTICLE INFORMATION

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Disclosures

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