

ORIGINAL RESEARCH

Noninvasive Hemodynamic Assessment of Shock Severity and Mortality Risk Prediction in the Cardiac Intensive Care Unit



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ABSTRACT

OBJECTIVES This study sought to define the 2-dimensional and Doppler echocardiographic hemodynamics associated with each Society for Cardiovascular Angiography and Interventions (SCAI) stage, and to determine their association with mortality.

BACKGROUND The SCAI shock stages classification stratifies mortality risk in cardiac intensive care unit (CICU) patients, but the echocardiographic and hemodynamic parameters that define these SCAI shock stages are unknown.

METHODS Unique CICU patients admitted from 2007 to 2015 who had a transthoracic echocardiogram within 1 day of CICU admission were included. Echocardiographic variables were evaluated as a function of SCAI shock stage. Multivariable logistic regression determined the association between echocardiographic parameters with adjusted hospital mortality.

RESULTS We included 5,453 patients with a median age of 69.3 years (interquartile range: 58.2 to 79.0 years) (37% women), and a median left ventricular ejection fraction (LVEF) of 50% (interquartile range: 35% to 61%). Higher SCAI shock stages were associated with lower LVEF and worse systemic hemodynamics. Hospital mortality was higher in patients with LVEF <40%, cardiac index <1.8 l/min/m², stroke volume index <35 ml/m², cardiac power output <0.6 W, or medial early mitral valve inflow velocity to early diastolic annular velocity (E/e') ratio >15 (particularly in SCAI shock Stages A to C). After multivariable adjustment, only stroke volume index <35 ml/m² (adjusted odds ratio: 2.0; 95% confidence interval: 1.4 to 3.0; p < 0.001) and E/e' ratio >15 (adjusted odds ratio: 1.52; 95% confidence interval: 1.04 to 2.23; p = 0.03) remained associated with higher hospital mortality.

CONCLUSIONS Noninvasive 2-dimensional and Doppler echocardiographic parameters correlate with the SCAI shock stages and improve risk stratification for hospital mortality in CICU patients. Low stroke volume index and high E/e' ratio demonstrated the strongest association with hospital mortality. (J Am Coll Cardiol Img 2021;14:321-32) © 2021 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

APACHE = Acute Physiology
and Chronic Health Evaluation

CI = cardiac index

CICU = cardiac intensive care
unit

CPI = cardiac power index

CPO = cardiac power output

CS = cardiogenic shock

E/e' = early mitral valve inflow
velocity to early diastolic
annular velocity

LV = left ventricular

LVEF = left ventricular ejection
fraction

SCAI = Society for
Cardiovascular Angiography
and Interventions

SVI = stroke volume index

TTE = transthoracic
echocardiogram

Cardiogenic shock (CS) remains associated with high mortality despite improvements in care, emphasizing the need to better define the severity and phenotypes of CS (1). The Society for Cardiovascular Angiography and Interventions (SCAI) developed a shock severity classification, which can effectively stratify hospital and post-discharge mortality risk among cardiac intensive care unit (CICU) patients, and among patients with acute myocardial infarction and CS (1-4). CICU patients with higher SCAI shock stages had worse organ dysfunction severity and greater use of critical care therapies, but the echocardiographic and hemodynamic parameters that delineate SCAI shock stages and characterize worsening CS remain undefined (2-4).

Invasive hemodynamic parameters reflecting CS severity can influence mortality risk stratification in patients with CS (5-9).

The hemodynamic variables most strongly associated with mortality in patients with CS include the cardiac index (CI), stroke volume index (SVI), cardiac power output (CPO), and cardiac power index (CPI) (5-9). Left ventricular ejection fraction (LVEF) is the primary echocardiographic parameter associated with outcomes among patients with CS (10-12). Prior studies examining the SCAI shock stages reported neither invasive hemodynamic nor echocardiographic parameters (2-4).

Noninvasive hemodynamic parameters measured by Doppler echocardiography have been shown to correlate well with invasive hemodynamic measurements without the risk inherent to an invasive procedure (13,14). Noninvasive hemodynamic assessment by Doppler echocardiography, for example, diastolic dysfunction defined by an elevated early mitral valve inflow velocity to early diastolic annular velocity (E/e') ratio, is associated with higher mortality in patients with acute myocardial infarction, heart failure, or cardiac arrest, but no prior studies have systematically evaluated echocardiographic hemodynamics in patients with CS (15-19). Therefore, we sought to describe the noninvasive echocardiographic hemodynamic parameters reflecting LV systolic and diastolic function at each SCAI shock stage in CICU patients, and to determine if those echocardiographic parameters were associated with hospital mortality as a function of SCAI shock stage. We hypothesized that echocardiographic variables would distinguish the SCAI shock stages, and that noninvasive Doppler hemodynamic variables would be associated with hospital mortality beyond the SCAI shock stages.

METHODS

STUDY POPULATION. This study was approved by the Institutional Review Board of the Mayo Clinic (IRB # 16-000722) as posing minimal risk to patients, and was performed under a waiver of informed consent. We retrospectively analyzed the index CICU admission of consecutive unique adult patients ≥ 18 years of age admitted to the CICU at Mayo Clinic Hospital St. Mary's Campus between January 1, 2007, and December 31, 2015, who had a transthoracic echocardiogram (TTE) performed within 1 day before or after CICU admission (2,3,20-23). We excluded patients who did not have available data for any of our echocardiographic variables of interest.

DATA SOURCES. We recorded demographic, vital sign, laboratory, clinical, and outcome data, as well as procedures and therapies performed during the CICU and hospital stay (2,3,20-23). The admission value of all vital signs, clinical measurements, and laboratory values was defined as either the first value recorded after CICU admission or the value recorded closest to CICU admission. Vital signs were recorded every 15 min during the first hour after CICU admission. Admission diagnoses were defined as all International Classification of Diseases-9th Revision diagnostic codes within 1 day before or after CICU admission (2,3).

TABLE 1 Formulas Used for Echocardiographic Hemodynamic Parameters, Using Data From the Time of the Echocardiogram

Echocardiographic Parameter	Formula
MAP	$[SBP + (2 \cdot DBP)] / 3$
Shock index	HR / SBP
SV	$(\pi/4) \cdot LVOT \cdot VTI \cdot (LVOT \text{ diameter})^2$
SVI	SV / BSA
CO	$SV \cdot HR$ (at time of LVOT VTI acquisition)
CI	CO / BSA
Cardiac power output	$(CO \cdot MAP) / 451$
Cardiac power index	$(CI \cdot MAP) / 451$
Systemic vascular resistance	$(MAP - RAP) / CO$
Systemic vascular resistance index	$(MAP - RAP) / CI$
LVEDP	$4.9 + (0.62 \cdot E/e' \text{ ratio})$ (25)
Left ventricular stroke work index	$0.0136 \cdot [SV \cdot (MAP - LVEDP)]$ (25)
Left ventricular stroke work index	$0.0136 \cdot [SVI \cdot (MAP - LVEDP)]$ (25)
Pressure-adjusted heart rate	$(HR \cdot RAP) / MAP$

BSA = body surface area; CI = cardiac index; CO = cardiac output; DBP = diastolic blood pressure; E/e' = early mitral valve inflow velocity to early diastolic annular velocity; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LVOT = left ventricular outflow tract; MAP = mean arterial pressure; RAP = right atrial pressure; SBP = systolic blood pressure; SV = stroke volume; SVI = stroke volume index; VTI = velocity-time integral.

SEVERITY OF ILLNESS SCORES. The Acute Physiology and Chronic Health Evaluation (APACHE)-III score, APACHE-IV predicted hospital mortality, and Sequential Organ Failure Assessment score were automatically calculated with data from the first 24 h of CICU admission using previously validated electronic algorithms (20-22). The Charlson Comorbidity Index and individual comorbidities were extracted from the medical record using a previously validated electronic algorithm (24).

ECHOCARDIOGRAPHIC DATA. The Mayo Clinic Echocardiography Database was queried, and data were extracted from the TTE performed closest to CICU admission, including vital signs at the time of TTE (Supplemental Table 1). Echocardiographic variables of interest included LVEF, CI, SVI, CPO, and medial E/e' ratio (Table 1). One best LVEF value for each patient was determined using a hierarchical approach: volumetric LVEF calculated using Simpson's biplane method was preferred, followed by monoplane volumetric approach, followed by linear methods, and finally by visual estimation if these other methods were unavailable; the specific method of LVEF measurement could not be determined. The E/e' ratio was used to estimate LV end-diastolic pressure for calculation of LV stroke work index (Table 1) (25). Right atrial pressure was either recorded at the time of TTE (if measured invasively) or estimated based on inferior vena cava size and collapsibility (26). We defined LVEF <40%, SVI <35 ml/m², CI <1.8 l/min/m², CPO <0.6 W, and E/e' ratio >15 as abnormal (9,11,12,16-18,27,28).

DEFINITION OF SCAI SHOCK STAGES. We defined hypotension or tachycardia, hypoperfusion, deterioration, and refractory shock using data from CICU admission through the first 24 h in the CICU (Supplemental Table 2) (2,3). We mapped the 5 SCAI shock stages with increasing severity (A through E) using combinations of these variables (Supplemental Table 3) (1-3). Late deterioration was defined as an increasing number or dose of vasopressors after 24 h, independent of the initial SCAI shock stage (2,3).

STATISTICAL ANALYSIS. Hospital mortality was determined using electronic review of health records. Variables of interest were compared across the SCAI shock stages. Categorical variables are reported as number and percentage and the Pearson chi-square test was used to compare groups; trends across the SCAI shock stages were determined using logistic regression. Continuous variables are reported as median (interquartile range [i.e., first and third

TABLE 2 Baseline Characteristics, Comorbidities, Admission Diagnoses, and Therapies of Included and Excluded Patients (i.e., Final Study Population vs. Patients in the Database Who Did Not Meet Study Inclusion Criteria)

	Included Patients (n = 5,453)	Excluded Patients (n = 4,551)	p Value
Demographics and outcomes			
Age, yrs	69.3 (58.2-79.0)	68.8 (57.2-78.8)	0.06
Female	2,001 (36.7)	1,745 (38.3)	0.09
White	5,037 (92.4)	4,199 (92.3)	0.84
CICU length of stay, days	1.9 (1.0-3.0)	1.5 (0.9-2.7)	<0.001
Hospital length of stay, days	4.5 (2.8-8.4)	4.6 (2.5-9.7)	0.63
CICU mortality	293 (5.4)	277 (6.1)	0.13
Hospital mortality	449 (8.2)	459 (10.1)	0.001
Comorbidities			
Charlson Comorbidity Index	1 (0-3)	2 (0-4)	<0.001
History of MI	1,052 (19.3)	928 (20.4)	0.16
History of HF	863 (15.9)	1,090 (24.0)	<0.001
History of CKD	974 (17.9)	1,057 (23.3)	<0.001
Prior dialysis	291 (5.3)	280 (6.2)	0.08
Admission diagnoses*			
Acute coronary syndrome	2,956 (54.8)	1,311 (29.1)	<0.001
Heart failure	2,551 (47.3)	2,013 (44.7)	0.009
Cardiac arrest	727 (13.5)	466 (10.3)	<0.001
Respiratory failure	1,280 (23.7)	799 (17.7)	<0.001
Sepsis	369 (6.8)	236 (5.2)	<0.001
Procedures and therapies			
Vasoactives first 24 h	1,109 (20.3)	1,102 (24.2)	<0.001
Vasoactives first 24 h	0 (0-0)	0 (0-0)	<0.001
Peak VIS first 24 h	0 (0-0)	0 (0-0)	<0.001
Peak NEE first 24 h	0 (0-0)	0 (0-0)	0.56
Invasive ventilator first 24 h	845 (15.5)	553 (12.2)	<0.001
Dialysis in CICU	231 (4.2)	256 (5.6)	0.001
IABP in CICU	544 (10.0)	321 (7.0)	<0.001
PAC in CICU	324 (5.9)	397 (8.7)	<0.001
Coronary angiogram	3,331 (61.1)	1,953 (42.9)	<0.001
PCI	2,140 (39.2)	1,287 (28.3)	<0.001
RBC transfusion	659 (12.1)	514 (11.3)	0.22
In-hospital CPR	164 (3.0)	149 (3.3)	0.41
Severity of illness			
APACHE-III score	59 (44-74)	57 (44-72)	0.001
APACHE-IV predicted hospital mortality, %	9.7 (3.9-21.9)	8.7 (3.7-20.5)	0.003
Day 1 SOFA score	2 (1-5)	2 (1-5)	0.27
SCAI shock stage			0.06
A	2,460 (45.1)	2,142 (47.1)	
B	1,623 (29.8)	1,375 (30.2)	
C	887 (16.3)	688 (15.1)	
D	428 (7.8)	304 (6.7)	
E	55 (1.0)	42 (0.9)	
Late deterioration	382 (7.0)	326 (7.2)	0.76

Values are median (interquartile range) or n (%). The p value is for the chi-square test (categorical variables) or Wilcoxon test (continuous variables) comparing included and excluded patients. *Admission diagnoses are not mutually exclusive.

ACS = acute coronary syndrome; APACHE = Acute Physiology and Chronic Health Evaluation; CICU = cardiac intensive care unit; CKD = chronic kidney disease; CPR = cardiopulmonary resuscitation; HF = heart failure; IABP = intra-aortic balloon pump; MI = myocardial infarction; NEE = norepinephrine-equivalent dose; PAC = pulmonary artery catheter; PCI = percutaneous coronary intervention; RBC = red blood cell; SCAI = Society for Cardiovascular Angiography and Interventions; SOFA = Sequential Organ Failure Assessment; VIS = Vasoactive-Inotropic Score.

TABLE 3 Baseline Characteristics, Comorbidities, Admission Diagnoses and Therapies of Patients According to SCAI Shock Stages

	With Data (%)	Stage A (n = 2,460)	Stage B (n = 1,623)	Stage C (n = 887)	Stage D (n = 428)	Stage E (n = 55)	p Value
Demographics							
Age, yrs	100	68.2 (57.8–78.6)	68.3 (57.1–77.9)	72.5 (61.0–81.9)	70.0 (60.2–79.0)	72.5 (55.9–76.7)	<0.001
Female	100	805 (32.7)	657 (40.5)	360 (40.6)	164 (38.3)	17 (27.3)	<0.001
White	100	2,293 (93.2)	1,506 (92.8)	803 (90.5)	388 (90.6)	47 (85.4)	0.001
CICU length of stay, days	100	1.7 (1.0–2.6)	1.9 (1.0–3.2)	1.9 (1.0–3.2)	3.4 (1.6–6.5)	1.1 (0.5–3.8)	<0.001
Hospital length of stay, days	100	3.8 (2.5–6.5)	5.1 (3.0–9.6)	5.2 (2.9–9.4)	8.6 (3.9–14.6)	3.2 (1.0–11.2)	<0.001
CICU mortality	100	31 (1.3)	44 (2.7)	59 (6.6)	130 (30.4)	29 (52.7)	<0.001
Hospital mortality	100	69 (2.8)	89 (5.5)	92 (10.4)	164 (38.3)	35 (63.6)	<0.001
Comorbidities							
Charlson Comorbidity Index	99.8	1 (0–3)	2 (0–4)	2 (0–4)	2 (1–4)	1 (0–3)	<0.001
History of MI	99.8	474 (19.3)	303 (18.7)	174 (19.7)	93 (21.7)	8 (14.6)	0.57
History of HF	99.8	312 (12.7)	275 (17.0)	158 (17.9)	109 (25.5)	9 (16.4)	<0.001
History of CKD	99.8	360 (14.7)	278 (17.2)	207 (23.4)	118 (27.6)	11 (20.0)	<0.001
Prior dialysis	100	61 (2.5)	62 (3.8)	95 (10.7)	64 (15.0)	9 (16.4)	<0.001
Admission ICD-9 diagnoses*							
ACS	98.9	1,438 (59.2)	819 (50.8)	454 (51.9)	217 (51.1)	28 (51.8)	<0.001
HF	98.9	884 (36.4)	861 (53.4)	456 (52.1)	314 (73.9)	36 (66.7)	<0.001
Cardiac arrest	98.9	202 (8.3)	185 (11.5)	126 (14.4)	185 (43.5)	29 (53.7)	<0.001
Respiratory failure	98.9	293 (12.1)	418 (25.9)	227 (25.9)	304 (71.5)	38 (70.4)	<0.001
Sepsis	98.9	58 (2.4)	126 (7.8)	64 (7.3)	100 (23.5)	21 (38.9)	<0.001
Therapies and procedures							
Vasoactives first 24 h	100	219 (8.9)	389 (24.0)	49 (5.5)	398 (93.0)	54 (98.2)	<0.001
Vasoactives first 24 h	100	0 (0–0)	0 (0–0)	0 (0–0)	2 (1–3)	3 (2–4)	<0.001
Peak VIS first 24 h	99.1	0 (0.0–0.0)	0 (0.0–0.0)	0 (0.0–0.0)	13 (5.0–35.0)	52.8 (19.7–120.0)	<0.001
Peak NEE first 24 h	100	0 (0.00–0.00)	0 (0.00–0.00)	0 (0.00–0.00)	0.10 (0.03–0.32)	0.57 (0.19–1.15)	<0.001
Invasive ventilator first 24 h	100	151 (6.1)	241 (14.8)	134 (15.1)	274 (64.0)	45 (81.8)	<0.001
Dialysis in CICU	100	45 (1.8)	60 (3.7)	33 (3.7)	78 (18.2)	15 (27.3)	<0.001
IABP in CICU	100	140 (5.7)	207 (12.8)	50 (5.6)	120 (28.0)	27 (49.1)	<0.001
PAC in CICU	100	68 (2.8)	108 (6.6)	30 (3.4)	100 (23.4)	18 (32.7)	<0.001
Coronary angiogram	100	1,642 (66.8)	934 (57.6)	484 (54.6)	243 (56.8)	28 (50.9)	<0.001
PCI	100	1,134 (46.1)	581 (35.8)	269 (30.3)	139 (32.5)	17 (30.9)	<0.001
RBC transfusion	100	175 (7.1)	212 (13.1)	100 (11.3)	152 (35.5)	20 (36.4)	<0.001
In-hospital CPR	99.7	34 (1.4)	35 (2.2)	27 (3.0)	55 (12.8)	13 (23.6)	<0.001
Severity of illness							
APACHE-III score	100	51.0 (38.2–63.0)	60.0 (48.0–73.0)	68.0 (53.0–82.0)	96.0 (78.0–117.8)	119.0 (93.0–144.0)	<0.001
APACHE-IV predicted hospital mortality, %	100	5.9 (2.5–12.6)	10.6 (4.9–21.1)	14.4 (6.7–29.5)	52.0 (26.6–75.3)	72.5 (47.9–88.1)	<0.001
Day 1 SOFA score	100	2 (1–3)	3 (1–5)	4 (2–6)	10 (7–12)	12 (9–15)	<0.001
Late deterioration	100	86 (3.5)	87 (5.4)	72 (8.1)	127 (29.7)	10 (18.2)	<0.001

Values are median (interquartile range) or n (%). The p value is for linear regression (continuous variables) or logistic regression (categorical variables) across SCAI shock stages. *Admission diagnoses are not mutually exclusive and sum to >100%.

Abbreviations as in Table 2.

quartiles)], and the Wilcoxon rank sum test was used to compare groups; trends across the SCAI shock stages were determined using linear regression. Logistic regression was used to determine the association between dichotomized echocardiographic variables of interest and hospital mortality before and after adjusting for age, sex, Charlson Comorbidity Index, APACHE-IV predicted mortality, SCAI shock stage, and late deterioration; admission diagnoses of acute coronary syndrome, heart failure, and cardiac arrest; and the use of vasoactive medications, intra-

aortic balloon pump, coronary angiography, percutaneous coronary intervention, dialysis, in-hospital cardiopulmonary resuscitation, pulmonary artery catheter, red blood cell transfusion, and invasive mechanical ventilation. Multivariable models were generated for each echocardiographic variable of interest individually, and then all significant echocardiographic variables of interest were included in a final multivariable model; only patients with complete data were included in the multivariable analysis. Two-tailed p values <0.05 were considered

TABLE 4 Echocardiographic Findings of Patients According to SCAI Shock Stages

	With Data	Stage A (n = 460)	Stage B (n = 1,623)	Stage C (n = 887)	Stage D (n = 428)	Stage E (n = 55)	p Value
Timing and vital signs at TTE							
TTE on day of admission	5,453	1,118 (45.4)	880 (54.2)	440 (49.6)	258 (60.3)	38 (69.1)	<0.001
Systolic BP, mm Hg	5,203	120 (108-134)	110 (98-125)	115 (101-133)	103 (91-117)	94.5 (79.8-107.5)	<0.001
Diastolic BP, mm Hg	5,198	66 (58-75)	62 (53-73)	64 (54-73)	58 (50-69)	56 (45-65)	<0.001
Mean BP, mm Hg	5,198	84.3 (76.3-93.3)	78.3 (69.3-89.3)	81.3 (71.7-92.0)	73.3 (65.3-84.0)	69.5 (57.8-78.2)	<0.001
Pulse pressure, mm Hg	5,198	53 (42.0-66.0)	46 (36.0-58.0)	51 (39.0-65.0)	44 (33.5-58.0)	38 (28.8-41.0)	<0.001
Heart rate	5,080	69 (60.0-78.0)	81 (69.0-98.0)	76 (65.0-90.0)	83 (71.0-99.8)	95 (77.0-107.5)	<0.001
Shock index	5,013	0.57 (0.48-0.68)	0.74 (0.60-0.90)	0.66 (0.54-0.83)	0.83 (0.64-1.01)	0.96 (0.76-1.19)	<0.001
Atrial fibrillation	4,881	179 (8.0)	286 (19.6)	116 (14.5)	67 (19.3)	10 (22.2)	<0.001
Left ventricular systolic function							
LVEF, %	5,375	54 (40.0-61.0)	48 (32.0-60.0)	50 (33.8-61.0)	35 (23.0-53.0)	30 (20.0-45.0)	<0.001
LVEF <40%	5,375	536 (22.1)	588 (36.7)	288 (33.1)	239 (56.5)	30 (54.6)	<0.001
Wall motion score index	3,372	1.6 (1.3-2.0)	1.8 (1.4-2.2)	1.8 (1.4-2.2)	2.2 (1.7-2.6)	2.2 (1.6-2.6)	<0.001
Lateral mitral s', cm/s	2,928	7.0 (6.0-9.0)	7.0 (6.0-9.0)	7.0 (5.0-8.0)	6.0 (5.0-9.0)	5.5 (4.8-7.2)	0.006
LVOT peak velocity; m/s	4,566	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	0.9 (0.8-1.1)	0.9 (0.8-1.0)	<0.001
LVOT VTI, cm	4,565	21.0 (18.0-23.7)	18.5 (15.0-22.0)	19.0 (16.0-22.8)	16.0 (13.0-19.6)	14.0 (11.5-16.6)	<0.001
SV, ml	4,525	83.0 (69.0-98.0)	72.0 (57.0-87.0)	75.0 (60.0-90.0)	62.0 (46.0-79.0)	51.5 (40.2-68.5)	<0.001
SVI, ml/m ²	4,478	42 (36-49)	37 (30-45)	39 (31-46)	33 (24-40)	26 (21-33)	<0.001
SVI <35 ml/m ²	4,478	411 (19.3)	544 (41.4)	263 (36.4)	161 (57.1)	25 (86.2)	<0.001
LVS _W , g*min	3,666	80.2 (62.6-100.5)	63.5 (48.2-84.2)	67.7 (50.9-85.4)	50.7 (37.5-63.5)	31.9 (28.8-49.5)	<0.001
LVS _W I, g*min/m ²	3,635	40.6 (33.0-49.4)	32.7 (25.6-42.3)	35.4 (27.1-44.4)	26.0 (19.3-32.3)	16.5 (13.8-18.1)	<0.001
Systemic hemodynamics							
CO, l/min	4,468	5.5 (4.7-6.6)	5.6 (4.6-6.8)	5.4 (4.4-6.5)	4.8 (3.9-6.1)	4.2 (3.2-5.4)	<0.001
CI, l/min/m ²	4,432	2.8 (2.5-3.3)	2.9 (2.4-3.4)	2.8 (2.4-3.3)	2.5 (2.0-3.2)	2.1 (1.7-2.8)	0.001
CI <1.8 l/min/m ²	4,432	80 (3.8)	70 (5.4)	56 (7.8)	51 (18.3)	8 (26.7)	<0.001
CPO, W	4,388	1.04 (0.85-1.27)	0.98 (0.77-1.24)	0.99 (0.76-1.24)	0.79 (0.62-1.06)	0.63 (0.49-0.89)	<0.001
CPO <0.6 W	4,388	96 (4.6)	114 (8.9)	88 (12.3)	59 (21.3)	15 (46.9)	<0.001
CPI, W/m ²	4,355	0.53 (0.44-0.63)	0.50 (0.41-0.62)	0.52 (0.40-0.64)	0.40 (0.32-0.53)	0.33 (0.27-0.40)	<0.001
SVR, dyne/s/cm ⁵	3,957	1,105 (899-1,338)	986 (779-1,247)	1,063 (852-1,336)	1,008 (781-1,319)	983 (626-1,362)	0.03
SVR <800 dyne/s/cm ⁵	3,957	235 (12.6)	314 (26.9)	123 (18.7)	66 (26.8)	9 (32.1)	<0.001
SVR index, dyne/s/cm ⁵ /m ²	3,929	2,148 (1,800-2,598)	1,915 (1,517-2,382)	2,026 (1,624-2,536)	1,989 (1,494-2,567)	2,023 (1,282-2,535)	<0.001
Estimated RAP, mm Hg	4,527	5 (5-10)	10 (5-14)	10 (5-14)	14 (10-20)	14 (10-20)	<0.001
Pressure-adjusted heart rate	4,276	4.9 (3.8-0.1)	9.7 (5.2-15.3)	8.6 (4.9-13.7)	14.9 (9.8-20.8)	17.6 (14.1-27.7)	<0.001
Left ventricular diastolic function							
Mitral E velocity, cm/s	4,158	0.8 (0.6-1.0)	0.8 (0.7-1.1)	0.8 (0.6-1.0)	0.8 (0.6-1.1)	0.7 (0.6-0.9)	<0.001
Mitral E/A ratio	3,404	1.0 (0.8-1.3)	1.1 (0.8-1.5)	1.0 (0.7-1.5)	1.0 (0.7-1.6)	1 (0.8-1.8)	0.003
Mitral e' velocity, cm/s	4,147	6 (5-7)	6 (4-8)	5 (4-7)	5 (4-6)	5 (4-6)	<0.001
Mitral E/e' ratio	3,953	12.5 (10.0-18.0)	13.8 (10.0-20.0)	15.0 (10.0-20.0)	16.0 (11.6-23.3)	15.0 (11.3-22.3)	<0.001
Mitral E/e' ratio <15	3,953	676 (34.0)	460 (41.6)	287 (46.1)	115 (53.0)	10 (50.0)	<0.001

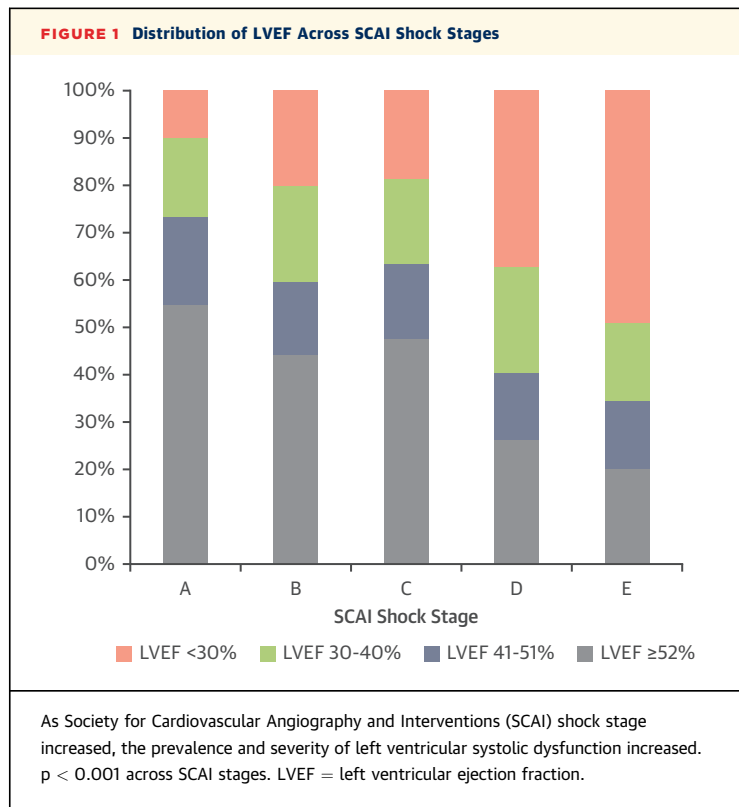
Values are n (%) or median (interquartile range). The p value is for linear regression (continuous variables) or logistic regression (categorical variables) across SCAI shock stages.
BP = blood pressure; CPI = cardiac power index; CPO = cardiac power output; LVEF = left ventricular ejection fraction; LVS_W = left ventricular stroke work; LVS_WI = left ventricular stroke work index; SCAI = Society for Cardiovascular Angiography and Interventions; SVR = systemic vascular resistance; TTE = transthoracic echocardiogram; other abbreviations as in Table 1.

statistically significant. Statistical analyses were performed using JMP Pro version 14.1.0 (SAS Institute, Cary, North Carolina).

RESULTS

STUDY POPULATION. Out of 10,004 potentially eligible unique CICU patient admissions, 4,098 were excluded because of lack of appropriate TTE (1,616 without a TTE and 2,482 with a TTE more than 1 day before or after CICU admission), leaving 5,906

patients with an appropriately timed TTE; we excluded another 453 patients who did not have available data for any of the echocardiographic variables of interest, leaving 5,453 patients in the final study population (Supplemental Figure 1) (2,20-23) TTE was performed on the day of CICU admission in 50.1% of patients, the day before in 3.9%, and the day after in 46.0%. Patients who were included in the final study population differed from excluded patients (Table 2), with higher illness severity, fewer comorbidities, lower hospital



mortality, and a different distribution of admission diagnoses (particularly, a higher prevalence of acute coronary syndrome).

The median age of the population was 69.3 years (interquartile range: 58.2 to 79.0 years), and 36.7% were women. Admission diagnoses included acute coronary syndrome in 54.8%, heart failure in 47.3%, sepsis in 6.8%, and cardiac arrest in 13.5%. Admission SCAI shock stages were as follows: Stage A, 45.1%; Stage B, 29.7%; Stage C, 16.3%; Stage D, 7.8%; Stage E, 1.0%; and late deterioration occurred in 7.0%. There were significant differences in most variables of interest across the SCAI shock stages (Table 3), with higher illness severity, greater use of critical care therapies, and a different distribution of comorbidities and admission diagnoses at higher SCAI shock stages.

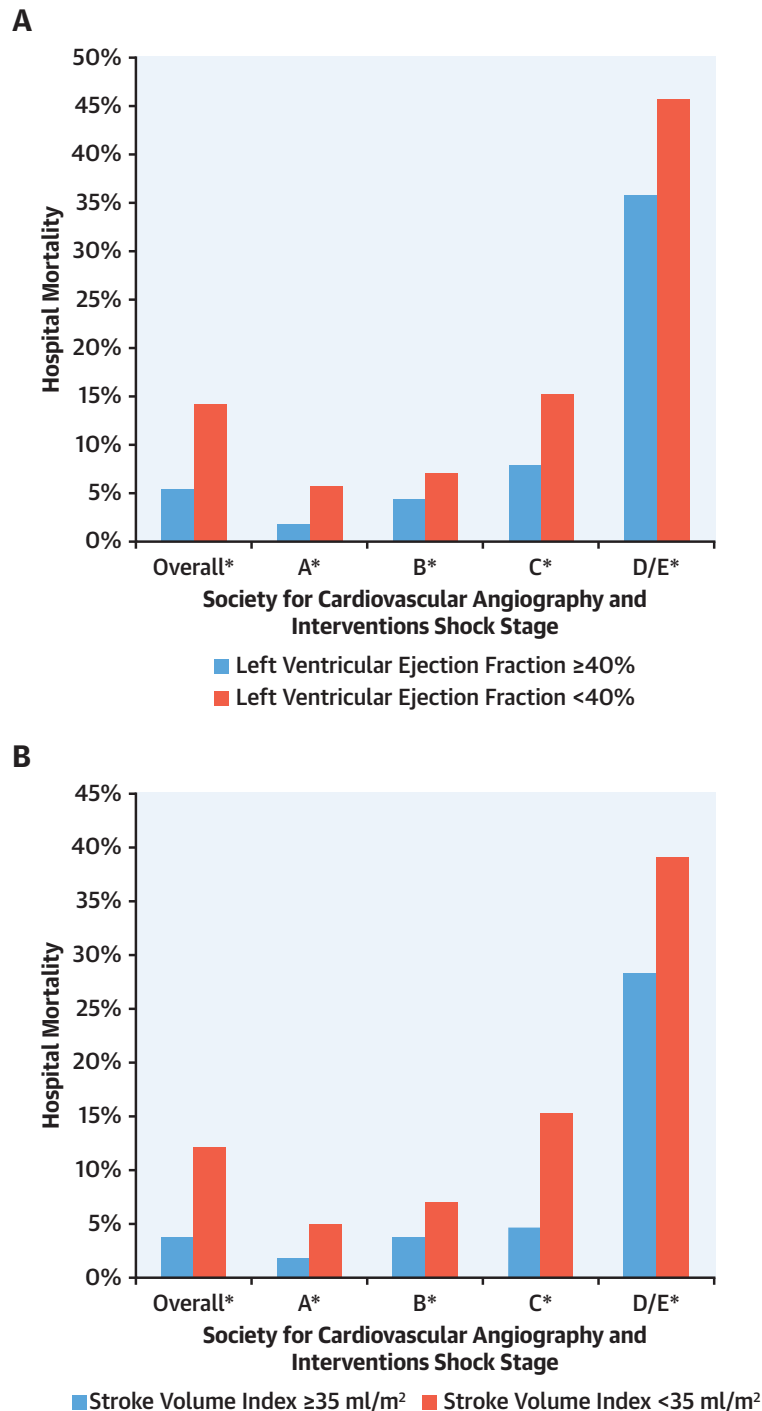
ECHOCARDIOGRAPHIC FINDINGS. All of the TTE parameters we evaluated differed across the SCAI stages (Table 4). Overall, we observed trends toward lower LV systolic function, worse systemic hemodynamics, and higher LV filling pressures with rising SCAI shock stage, particularly in SCAI Stages D and E (Table 4). The median LVEF of the study population was 50% (interquartile range: 35% to 61%), and 31.3% of patients had LVEF <40%. The LVEF decreased as a function of rising SCAI shock stage, with a

distribution skewed toward lower LVEF values and an increasing prevalence of patients with LVEF <40% (Figures 1 and 2A). Noninvasive hemodynamic parameters reflecting forward flow all decreased with rising SCAI shock stage (Figure 2B), with an increase in the proportion of patients with low SVI <35 ml/m², low CI <1.8 l/min/m², and low CPO <0.6 W at higher SCAI shock stages (Table 4). The medial E/e' ratio increased at higher SCAI shock stages, and the proportion of patients with E/e' ratio >15 increased (Table 4). Markers of LV systolic and diastolic function, including LVEF and hemodynamic variables, were similar between patients with SCAI shock Stages B and C (Figure 2, Table 4). LV stroke work index strongly decreased across SCAI shock stages, with a modest decrease in systemic vascular resistance index (Supplemental Figure 2).

HOSPITAL MORTALITY. A total of 8.2% of patients died in the hospital, including 5.4% of patients who died in the CICU. Patients with LVEF <40%, SVI <35 ml/m², CI <1.8 l/min/m², CPO <0.6 W, or E/e' ratio >15 had higher crude hospital mortality (Central Illustration, Supplemental Figures 3 to 5). After multivariable adjustment considering each echocardiographic variable individually, LVEF <40%, SVI <35 ml/m², CPO <0.6 W, and E/e' ratio >15 remained associated with higher hospital mortality (Table 5), while CI <1.8 l/min/m² was not ($p = 0.37$). SVI <35 ml/m² (adjusted odds ratio: 2.03; 95% confidence interval: 1.37 to 3.00; $p < 0.001$) remained strongly associated with higher hospital mortality after LVEF <40%, CPO <0.6 W, and E/e' ratio >15 were included in the multivariable model (Table 5). E/e' ratio >15 also remained associated with higher hospital mortality (adjusted odds ratio: 1.52; 95% confidence interval: 1.04 to 2.23; $p = 0.03$), while LVEF <40% and CPO <0.6 W were no longer significantly associated with hospital mortality (both $p > 0.05$).

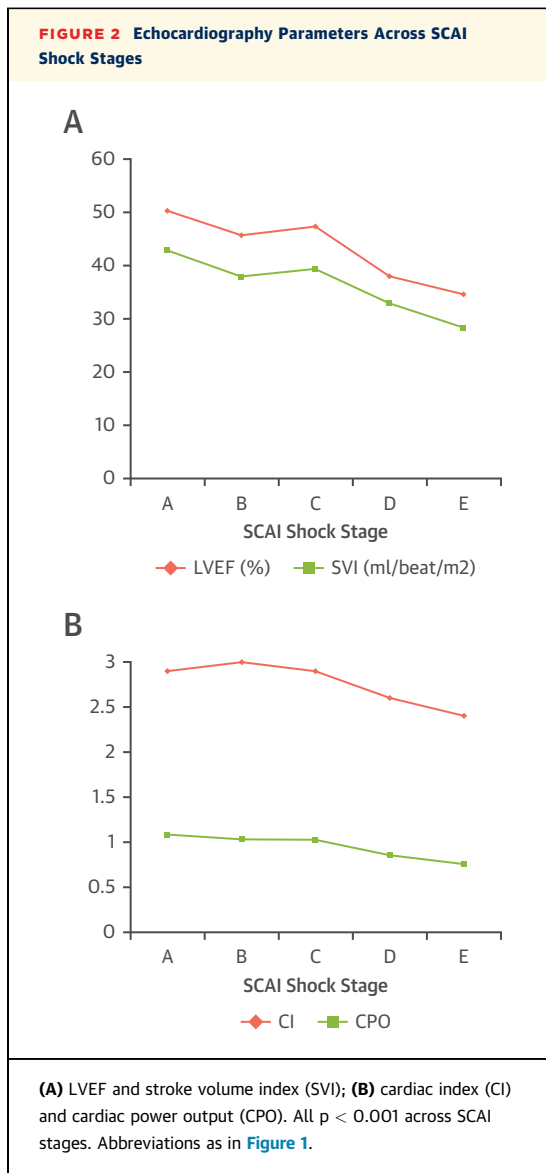
Both CICU and hospital mortality rose with each higher SCAI shock stage (Table 3). Patients with low LVEF, CI, SVI, and CPO and high E/e' ratio had higher hospital mortality in SCAI shock Stages A through C (Central Illustration, Supplemental Figures 3 to 5). When all patients with shock (i.e., SCAI shock stages C, D, and E) were grouped together, low LVEF, CI, SVI, and CPO and high E/e' ratio were all associated with significantly higher unadjusted hospital mortality (all $p < 0.001$). None of the echocardiographic variables of interest were associated with unadjusted hospital mortality in SCAI shock Stage E, and only LVEF <40% was associated with higher hospital mortality in Stage D; when patients with SCAI Stages D and E were grouped together, both LVEF <40% and

CENTRAL ILLUSTRATION Hospital Mortality as a Function of SCAI Shock Stage in Patients With Preserved Versus Reduced LVEF and Stroke Volume Index



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Hospital mortality in patients with and without (A) low left ventricular ejection fraction $< 40\%$ or (B) stroke volume index < 35 ml/m² in the overall population and as a function of Society for Cardiovascular Angiography and Interventions shock stage. Society for Cardiovascular Angiography and Interventions shock Stages D and E are grouped due to the low number of patients. * $p < 0.05$ between groups.



SVI <35 ml/m² were associated with higher hospital mortality ($p < 0.05$) ([Central Illustration](#)). After multivariable adjustment when considered individually in each SCAI shock stage ([Table 6](#)), LVEF $<40\%$, CPO <0.6 W, and SVI <35 ml/m² were associated with higher hospital mortality in SCAI shock Stage A, CPO <0.6 W was associated with higher hospital mortality in SCAI shock Stage B, and LVEF $<40\%$ and SVI <35 ml/m² were associated with higher hospital mortality in SCAI shock Stage C and SCAI shock Stages D and E (all $p < 0.05$).

Patients in SCAI shock Stage A with low LVEF, CI, SVI, and CPO or high E/e' ratio had hospital mortality that was equivalent to patients in SCAI shock Stage B without these TTE abnormalities. Likewise, patients

in SCAI Shock Stage B with each of these TTE abnormalities had hospital mortality that was equivalent to patients in SCAI shock Stage C without these TTE abnormalities. Patients in SCAI shock Stage C with each of these TTE abnormalities had mortality that was significantly higher than patients in SCAI shock Stage C without these TTE abnormalities (all $p < 0.05$), but hospital mortality was significantly lower than patients in SCAI shock Stage D without these TTE abnormalities (all $p < 0.05$). Among patients with available data for all of the TTE variables of interest, addition of these TTE variables to the SCAI shock stages improved discrimination for hospital mortality (C-statistic 0.807 vs. 0.736; $p < 0.001$ by DeLong test). Addition of the TTE variables of interest to the multivariable model modestly increased improved discrimination for hospital mortality (C-statistic 0.921 vs. 0.908; $p = 0.01$ by DeLong test), although this difference was only significant in SCAI shock Stage B ($p = 0.009$ by DeLong test) ([Supplemental Table 4](#)).

DISCUSSION

This is the first study to examine the prevalence and prognostic importance of abnormal hemodynamic parameters assessed by 2-dimensional and Doppler echocardiography in a large cohort of CICU patients stratified by shock severity. We demonstrated clear trends toward decreasing LV systolic and diastolic function in patients with increasing shock severity, as represented by rising SCAI shock Stage from C to E. Differences in echocardiographic variables between patients with SCAI shock Stage B (pre-shock) and SCAI shock Stage C (classic shock) were modest, implying that the success or failure of intrinsic compensatory responses and initial supportive therapies may be a greater determinant of progression from pre-shock to shock than hemodynamics. Patients with a low LVEF, SVI, CI, or CPO or a high E/e' ratio had higher hospital mortality, particularly at lower SCAI shock stages; patients in SCAI shock Stages A or B with abnormal values of these TTE variables had mortality equivalent to patients in the next higher SCAI shock stage without these TTE abnormalities. Each of these echocardiographic parameters was associated with higher hospital mortality among patients with shock (i.e., SCAI shock Stages C, D, and E together). A low SVI (<35 ml/m²) was associated with 2-fold higher odds of adjusted hospital mortality, emphasizing the importance of measuring LVOT-based hemodynamic parameters in CICU patients. An elevated medial E/e' ratio >15 was associated with 50% higher odds of adjusted hospital

mortality, highlighting the importance of diastolic function as a determinant of outcomes. The addition of TTE data improved mortality risk stratification beyond the SCAI shock stages alone.

This study highlights the utility of 2-dimensional and Doppler echocardiographic hemodynamic assessment for stratification of shock severity and hospital mortality in CICU patients with or at risk for shock. The association between echocardiographic variables and clinical outcomes across the spectrum shock severity demonstrates the importance of a comprehensive 2-dimensional and Doppler hemodynamic TTE in CICU patients. Early noninvasive echocardiographic hemodynamic assessment may be particularly helpful for risk stratification of patients with pre-shock (SCAI shock Stage B) or early shock (SCAI Stage C). As cardiac ultrasound becomes increasingly integrated into contemporary critical care practice, it is crucial that echocardiographic assessments performed in the CICU extend beyond simple visual assessment of LV function and incorporate Doppler measurements of hemodynamic parameters that provide prognostic information (14).

Prior studies of echocardiography in CS have focused on standard measures of LV function, particularly LVEF (10). Lower LVEF has been associated with higher mortality among patients with CS, as it was in our CICU population (10-12). Some studies used LVEF cutoff values lower than our cutoff <40% to stratify mortality risk, but our results did not change materially when our abnormal LVEF cutoff was changed to <50% or <30% (10). Despite its association with outcomes in patients with cardiovascular disease, LVEF remains an imperfect assessment of cardiac performance in critically ill patients that can be affected by cardiac loading conditions, vasoactive medications, LV remodeling, and systemic physiologic factors (29). A normal LVEF does not guarantee the presence of a normal stroke volume or cardiac output, as exemplified by the syndrome of paradoxical low flow despite normal LVEF that has been associated with higher mortality in patients with aortic stenosis (27). Our finding that SVI but not LVEF was independently associated with hospital mortality demonstrates the primacy of flow indices over LVEF when assessing hemodynamic status.

Low values of invasively measured SVI, CI, and CPO reflecting poor forward flow have been associated with higher mortality in patients with CS (5-8). Low CPO and CPI are associated with worse outcomes in patients with CS and among unselected CICU patients, and measurement of CPO has been advocated in CS care protocols (5-7,9,28,30). Low CPO measured by TTE was associated with higher adjusted hospital

TABLE 5 Associations of Selected Echocardiographic Variables With Hospital Mortality on Multivariate Logistic Regression, When Entered Into the Model Individually or in Combination With Other Significant Echocardiographic Predictors

	Echocardiographic Variable Individually		With Other Echocardiographic Variables	
	Adjusted OR (95% Confidence Interval)	p Value	Adjusted OR (95% Confidence Interval)	p Value
LVEF <40%	1.611 (1.230-2.111)	<0.001	1.287 (0.855-1.938)	0.23
CI <1.8 l/min/m ²	1.217 (0.789-1.877)	0.37	—*	—*
CPO <0.6 W	1.859 (1.291-2.678)	<0.001	1.504 (0.939-2.408)	0.09
SVI <35 ml/m ²	2.144 (1.594-2.883)	<0.001	2.030 (1.372-3.004)	<0.001
Medial E/e' ratio >15	1.542 (1.088-2.186)	0.01	1.519 (1.036-2.228)	0.03

*CI was not included in the model with other echocardiographic variables because it was not significant when entered into the model alone.
OR = odds ratio; other abbreviations as in Tables 1 and 4.

mortality in our CICU patients, but this association weakened after adjusting for other echocardiographic variables. Our data demonstrate the feasibility of noninvasive measurement of CPO, SVI, and CI using Doppler echocardiography in CICU patients and suggest that Doppler echocardiographic measurement could be used for risk stratification in this population.

Unexpectedly, CI was not associated with adjusted hospital mortality, despite prior studies demonstrating the prognostic importance of invasively measured CI in CS (6-8). In contrast, we found that low SVI remained strongly associated with higher adjusted hospital mortality, even when adjusting for other echocardiographic variables. Mele et al. (19) similarly reported a strong association between low SVI (<30 ml/m²) by TTE and higher mortality in 258 hospitalized heart failure patients, while CI measured by TTE was not associated with mortality. SVI was among the strongest hemodynamic correlates of mortality in a recent multicenter study of patients with CS, although SVI was not as strongly associated as CPI or CI (7). Patients may compensate for low SVI by increasing their heart rate to maintain adequate CI, making SVI a more direct marker of LV performance than CI; alternatively, TTE directly measures SVI on beat-to-beat basis, whereas CI per minute must be extrapolated using heart rate, contributing to potential inaccuracy (19). The observed CI values were higher than expected in this CICU cohort in which approximately 80% of shock is classified as cardiogenic. Mixed vasodilatory shock states could have contributed to this observation, as suggested by the increasing prevalence of sepsis and a low systemic vascular resistance (<800 dyne/s/cm⁵) from SCAI shock Stages C to E. Furthermore, vasoactive medications are titrated in CICU patients with the goal of normalizing CI and blood pressure, potentially diluting the associations between CI and CPO with mortality.

TABLE 6 Associations of Selected Echocardiographic Variables With Hospital Mortality After Multivariate Logistic Regression, as a Function of SCAI Shock Stage

	SCAI Stage A	SCAI Stage B	SCAI Stage C	SCAI Stage D/E
LVEF <40%	2.06 (1.10-3.86)*	0.97 (0.56-1.68)	1.87 (1.01-3.47)*	1.82 (1.14-2.93)*
CI <1.8 l/min/m ²	1.57 (0.52-4.68)	1.39 (0.53-3.64)	1.01 (0.38-2.65)	1.14 (0.58-2.22)
CPO <0.6 W	3.18 (1.34-7.55)*	2.61 (1.30-5.24)*	1.80 (0.82-3.95)	1.09 (0.57-2.08)
SVI <35 ml/m ²	2.35 (1.20-4.63)*	1.59 (0.89-2.83)	3.81 (1.90-7.66)*	1.88 (1.05-3.36)*
Medial E/e' ratio >15	0.87 (0.43-1.79)	1.93 (0.92-4.03)	1.35 (0.63-2.88)	1.81 (0.89-3.66)

Values are adjusted odds ratio (95% confidence interval). Each echocardiographic variable was added to the multivariate logistic regression model individually. Owing to a lower number of patients, Stages D and E were analyzed together. *p < 0.05.

SCAI, Society for Cardiovascular Angiography and Intervention; abbreviations as in Tables 1 and 4.

The prognostic relevance of LV diastolic function has not been systematically examined in patients with CS, but markers of LV diastolic dysfunction have been consistently associated with adverse outcomes in acutely ill cardiac patients. An elevated E/e' ratio is associated with higher mortality among patients with acute myocardial infarction, and E/e' ratio was more strongly associated with mortality than echocardiographic markers of LV systolic function (17,18). Among patients resuscitated from cardiac arrest, an elevated E/e' ratio was the strongest echocardiographic correlate of mortality, while LVEF was not associated (15,16). We observed that an elevated E/e' ratio remained associated with higher hospital mortality after adjustment for echocardiographic markers of LV systolic function, highlighting the importance of LV diastolic function in critical illness. As a measure of diastolic dysfunction, the E/e' ratio correlates with LV filling pressures (pulmonary capillary wedge pressure and LV end-diastolic pressure) (16,17,25). An elevated LV end-diastolic pressure has been associated with higher mortality in patients with acute myocardial infarction (31,32). Pulmonary capillary wedge pressure was associated with mortality in patients with CS in 1 study on univariable analysis but not on multivariable analysis (7). We could not determine whether the association between an elevated E/e' ratio and mortality was mediated through elevated LV filling pressures or myocardial diastolic dysfunction per se.

This study provides novel data about the hemodynamic abnormalities across the shock severity spectrum and highlights the value of Doppler echocardiography for risk stratification. Echocardiographic hemodynamic variables appeared more useful for mortality risk stratification in patients without severe shock (i.e., SCAI shock Stages A to C), and echocardiography provided less robust risk stratification in patients with severe or refractory shock (SCAI Shock Stages D and E). The expectedly

higher prevalence of hemodynamic abnormalities likely weakened the prognostic value of echocardiography in the smaller subgroup of patients with more severe shock. Hemodynamic variables may be less important for determining outcomes once severe or refractory shock has developed and among patients with cardiac arrest and brain injury, and markers of LV systolic function and forward flow may be less relevant in patients with a mixed or vasodilatory shock phenotype as we observed in patients with higher shock severity. We found that hemodynamic Doppler echocardiography were more relevant for risk stratification in patients with pre-shock and early shock whose outcomes may be more directly influenced by hemodynamic abnormalities that could be amenable to early therapeutic interventions.

STUDY LIMITATIONS. This unselected CICU cohort is a lower-risk population than that represented in most published studies of CS, which have more closely resembled our SCAI shock Stage D or E patients than our SCAI shock Stage C patients (4-9,11,12,28,29). Not all patients in the CICU database had available TTE data, and not all TTEs had all available variables reported, leading to potential selection bias. We only included data from formal TTEs, which were read by a staff cardiologist and entered into the database. We did not over-read individual TTE images in order to demonstrate the pragmatic utility of TTE assessment for mortality risk stratification in clinical practice, recognizing that measurement variability could have affected our results. We were unable to ascertain whether patients were mechanically ventilated or on vasoactive drugs at the time of echocardiography, nor could we determine the effects of underlying valvular heart disease or anemia on hemodynamic variables. Echocardiographic data reflect a single time point in a patient's course, and may not capture the inherent variability and changing nature of hemodynamics in shock. Simultaneous echocardiographic and invasive hemodynamic measurements were not available, so

we could not validate the accuracy of the measured echocardiographic hemodynamic variables with the gold standard of invasive hemodynamic assessment (14).

CONCLUSIONS

Noninvasive hemodynamic parameters based on 2-dimensional and Doppler echocardiography correlate with increasing shock severity based on the SCAI shock stages classification, and improve mortality risk stratification by the SCAI shock stages. Deteriorating and refractory shock were associated with progressively worse LV function, while pre-shock and mild shock had similar hemodynamic parameters. Hemodynamic variables known to be associated with mortality in patients with CS were associated with mortality when measured noninvasively using Doppler echocardiography, with a low SVI or elevated E/e' ratio remaining associated with higher hospital mortality after multivariable adjustment. In addition to characterizing the echocardiographic and hemodynamic abnormalities seen at each SCAI shock stage, this study highlights the incremental value of noninvasive hemodynamic assessment for mortality risk stratification among CICU patients. Our findings support the more extensive use of echocardiography with integrated Doppler indices for evaluation and management of CICU patients, and demonstrate the added value that easily obtained Doppler measurements provide in prognostic assessment. Further studies will be needed to determine the extent to which noninvasive echocardiographic measurements correlate with and complement invasive hemodynamic measurements, in order to determine which patients may benefit from each method of hemodynamic assessment.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Noninvasive hemodynamic parameters obtained using Doppler echocardiography can be used to characterize each of the SCAI shock stages, and to provide mortality risk stratification for CICU patients at each SCAI shock stages. Although LVEF <40% and CPO <0.6 W were associated with higher hospital mortality, SVI <35 ml/m² and the medial E/e' ratio >15 were strongly associated with hospital mortality.

COMPETENCY IN PATIENT CARE AND PROCEDURAL

SKILLS: Doppler echocardiography remains an important diagnostic and prognostic tool in CICU patients, allowing identification of high-risk patients across the spectrum of shock severity. Patients with less severe shock appeared to have the most robust risk stratification by Doppler echocardiography, allowing identification of higher-risk patients within this overall lower-risk cohort.

TRANSLATIONAL OUTLOOK 1: The easily obtained Doppler echocardiographic parameters examined in this retrospective study will need to be validated in prospective studies using a systematic approach to echocardiographic assessment in patients with CS.

TRANSLATIONAL OUTLOOK 2: Future clinical trials in CS populations should consistently report the hemodynamic and echocardiographic variables examined in this study, to better elucidate the factors contributing to greater shock severity and worse outcomes.

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KEY WORDS cardiac intensive care unit, cardiogenic shock, Doppler, echocardiography, hemodynamics, left ventricular ejection fraction, mortality, shock

APPENDIX For supplemental tables and figures, please see the online version of this paper.
