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ORIGINAL SCIENTIFIC PAPER

Influence of age and shock severity on short-term survival in patients with cardiogenic shock

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Aims Cardiogenic shock (CS) is associated with poor outcomes in older patients, but it remains unclear if this is due to higher shock severity. We sought to determine the associations between age and shock severity on mortality among patients with CS.

Methods and results Patients with a diagnosis of CS from Mayo Clinic (2007–15) and University Clinic Hamburg (2009–17) were subdivided by age. Shock severity was graded using the Society for Cardiovascular Angiography and Intervention (SCAI) shock stages. Predictors of 30-day survival were determined using Cox proportional-hazards analysis. We included 1749 patients (934 from Mayo Clinic and 815 from University Clinic Hamburg), with a mean age of 67.6 ± 14.6 years, including 33.6% females. Acute coronary syndrome was the cause of CS in 54.0%. The distribution of SCAI shock stages was 24.1%; C, 28.0%; D, 33.2%; and E, 14.8%. Older patients had similar overall shock severity, more co-morbidities, worse kidney function, and decreased use of mechanical circulatory support compared to younger patients. Overall 30-day survival was 53.3% and progressively decreased as age or SCAI shock stage increased, with a clear gradient towards lower 30-day survival as a function of increasing age and SCAI shock stage. Progressively older age groups had incrementally lower adjusted 30-day survival than patients aged <50 years.

Conclusion Older patients with CS have lower short-term survival, despite similar shock severity, with a high risk of death in older patients with more severe shock. Further research is needed to determine the optimal treatment strategies for older CS patients.

Keywords Age • Cardiogenic shock • Frailty • Survival • Shock

Introduction

Cardiogenic shock (CS) remains one of the most lethal acute cardiovascular conditions, with short-term mortality exceeding 30–40% despite contemporary therapies.[1–5] Mortality risk stratification in CS depends on the interactions between baseline patient characteristics, the severity of CS and organ failure, and the response to supportive therapy.[1,6–9] The introduction of the Society for Cardiovascular Angiography and Intervention (SCAI) CS stages classification paradigm has facilitated more consistent grading of CS severity, in order to facilitate research efforts and clinical communication between providers.[10] The SCAI shock stages system provides robust mortality risk stratification among patients with CS, and in unselected cardiac intensive care unit (CICU) patients.[11–16] Patient-specific factors, such as the occurrence of cardiac arrest, have been identified as potential risk modifiers when added to the SCAI shock stages classification, and other established risk factors can potentially augment mortality risk stratification by the SCAI shock stages.[10–12,16]

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Age is one of the most consistently identified non-modifiable risk factors for mortality in patients with CS, as well as in CICU patients.[6–9,15–28] Major randomized clinical trials of CS have uniformly shown higher mortality in older patients, despite the selected populations and standardized care in these trials.[2–5] Numerous factors may contribute to the higher mortality observed among older patients with CS, including greater co-morbidity burden, more advanced underlying cardiac disease, limited physiological reserve, and potentially higher shock severity.[29] Padkins *et al.*[16] previously reported that age and SCAI shock stage both contribute to mortality risk stratification in CICU patients, but this has not been examined in patients with CS. Despite the consistent association between age and adverse outcomes among patients with CS, prior studies have not systematically described shock severity, precluding them from exploring potential interactions between age and shock severity as determinants of outcome in CS patients. Therefore, we sought to describe the relationships between age, shock severity (as defined by the SCAI shock stages), and mortality risk in patients with CS.

Methods

This was a two-centre retrospective observational study comprising separate adult CS cohorts from Mayo Clinic (Rochester, MN, USA) and University Clinic Hamburg (Hamburg, Germany) during contiguous periods. All included patients had a diagnosis of CS based on International Classification of Diseases (ICD)-9 or ICD-10 codes (ICD-9 785.51 or ICD-10 R57.0). Prior studies have demonstrated 99.3% specificity and 98.1% positive predictive value for the ICD-9 diagnosis code for CS in administrative data.[30] Patients without haemodynamic instability or hypoperfusion (SCAI shock stage A) were excluded. This study was approved independently by the Institutional Review Board at each institution.

Description of Mayo Clinic Rochester cohort

Unique adult patients admitted to the CICU at Mayo Clinic Hospital St. Marys Campus between January 2007 and December 2015 with an admission ICD-9 diagnosis of CS were included; admission diagnoses were defined as all ICD-9 codes recorded within 1 day of CICU admission (including both primary and secondary diagnoses).[11–13,17,31] Demographic and clinical data from the CICU stay were extracted from the medical record using established electronic algorithms, as previously reported.[11–13,17,31] The SCAI shock stages were mapped based on the presence of hypoperfusion (SCAI shock stage C), deterioration (SCAI shock stage D), and refractory shock (SCAI shock stage E) using data from CICU admission through the first 24 h in the CICU (Supplementary material online, *Table S1A–C*), as previously described; missing data were imputed as normal for determination of SCAI shock stage.[11–13] Patients without hypoperfusion at the time of CICU admission were classified as SCAI shock stage B only if they met criteria haemodynamic instability or required vasoactive drugs (Supplementary material online, *Table S1C*); SCAI shock stage B patients not meeting these criteria were excluded. Despite different data definitions, patients in the Mayo Clinic cohort were reclassified into modified SCAI shock stages using similar criteria to the University Clinic Hamburg cohort (Supplementary material online, *Table S1B*). Due to the high prevalence of missing lactate levels in the Mayo Clinic cohort, imputation of missing lactate levels was performed (Supplementary material online, *Table S2*), and patients had the SCAI shock stages reclassified using the imputed lactate level to determine hypoperfusion.

Description of University Clinic Hamburg cohort

Adult patients from October 2009 to October 2017 with a primary ICD-9/10 diagnosis of CS confirmed on chart review were included.[14] Demographic and clinical data from the time of admission were collected in a dedicated database, as previously reported.[14] The SCAI shock stages in the Hamburg cohort were defined based on the presence of signs/symptoms of CS without hypoperfusion or vasoactive drug support (SCAI shock stage B), hypoperfusion and vasoactive drug support (SCAI shock stage C), rising serum lactate (SCAI shock stage D), and refractory cardiac arrest (SCAI shock stage E) at the time of admission (Supplementary material online, *Table S1A*).[14]

Statistical analysis

The primary outcome of interest was survival to 30 days, determined using chart review. Patients were divided into the following age groups: age <50 years, 50–59 years, 60–69 years, 70–79 years, and ≥80 years. Data are reported as mean ± standard deviation for continuous variables and *n* (%) for categorical variables. Groups were compared using Student's *t* tests for continuous variables and χ^2 tests for categorical variables. Survival to 30 days was analysed using the Kaplan–Meier analysis, with groups compared using the log-rank test. Data from the two cohorts were first analysed separately and compared to each other, and then data from the cohorts were combined for summary statistics and outcomes. Trends across age groups were analysed for each cohort separately using linear regression for continuous variables and logistic regression for categorical variables. Hazard ratio (HR) and 95% confidence interval (CI) values for 30-day mortality were generated using separate Cox proportional-hazards analysis in each cohort, before and after adjustment for relevant covariates selected *a priori*, including SCAI shock stage, age, sex, body mass index (BMI); history of hypertension, diabetes mellitus, chronic kidney disease, myocardial infarction, and stroke; admission diagnosis of acute coronary syndrome (ACS) and cardiac arrest (CA); admission values of systolic blood pressure, diastolic blood pressure, heart rate, and estimated glomerular filtration rate (eGFR); and the use of invasive mechanical ventilation, vasoactive drugs, Impella® and extracorporeal membrane oxygenator (ECMO). Two-tailed *P*-values <0.05 were considered significant. Statistical analysis performed using JMP 14.0 pro (SAS institute, Cary, NC, USA) and R version 3.5.1 (https://www.r-project.org/).

Results

Study population

The combined study cohort included 1749 total CS patients, 934 (53.4%) from Mayo Clinic and 815 (46.6%) from University Clinic Hamburg. The mean age of the combined cohort was 67.6 ± 14.6 years, and 587 (33.6%) were females (*Table 1*). The cause of CS was ACS in 945 (54.0%), 658 (69.6%) of which were ST-elevation myocardial infarction, and 599 (63.4%) underwent PCI; a total of 875 (50.0%) had a CA. Patients were critically ill (*Table 1*), with a mean lactate level of 5.2 ± 4.7 mmol/L and frequent use of supportive therapies including vasoactive drugs in 1138 (65.1%) and use of mechanical circulatory support (MCS) in 761 (43.5%). The distribution of SCAI shock stages in the combined cohort was as follows: B, 24.1%; C, 28.0%; D, 33.2%; and E, 14.8%.

Table 1 Baseline characteristics of Mayo Clinic and Hamburg cardiogenic shock patients, and the combined cohort

	Combined cardiogenic shock cohort (*n* = 1749)	Mayo Clinic CICU cardiogenic shock cohort (*n* = 934)	Hamburg cardiogenic shock cohort (*N* = 815)	*P* value (Mayo Clinic vs. Hamburg)
Demographics				
Age	67.6 ± 14.6	67.7 ± 14.0	67.4 ± 15.2	NS
<50 years	206 (11.8%)	111 (11.9%)	95 (11.7%)	
50–59 years	273 (15.6%)	132 (14.1%)	141 (17.3%)	
60–69 years	403 (23.0%)	243 (26.0%)	160 (19.6%)	
70–79 years	486 (27.8%)	257 (27.5%)	229 (28.1%)	
80+ years	381 (21.8%)	191 (20.4%)	190 (23.3%)	
Female sex	587 (33.6%)	350 (37.5%)	237 (29.1%)	<0.001
Body mass index (kg/m^2)	28.2 ± 6.2	29.5 ± 6.7	26.3 ± 4.7	<0.001
Co-morbidities				
Hypertension	716 (41.1%)	320 (34.3%)	396 (48.9%)	<0.001
Diabetes mellitus	476 (27.4%)	266 (28.6%)	210 (26.0%)	NS
Chronic kidney disease	321 (18.4%)	187 (20.1%)	134 (16.6%)	0.002
Prior myocardial infarction	379 (21.8%)	181 (19.4%)	198 (24.5%)	0.01
Prior stroke	184 (10.6%)	110 (11.8%)	74 (9.1%)	0.07
Admission diagnoses				
Acute coronary syndrome	945 (54.0%)	556 (59.5%)	389 (47.7%)	<0.001
% STEMI	658 (69.6%)	373 (67.1%)	285 (73.3%)	0.04
% PCI	599 (63.4%)	268 (48.2%)	331 (85.1%)	<0.001
Cardiac arrest	875 (50.0%)	371 (39.7%)	504 (61.9%)	<0.001
Admission vital signs and laboratory values				
Systolic blood pressure (mmHg)	107.8 ± 31.7	109.5 ± 28.1	105.7 ± 35.3	0.01
Diastolic blood pressure (mmHg)	63.5 ± 21.2	64.7 ± 19.3	62.1 ± 23.2	0.01
Mean blood pressure (mmHg)	77.6 ± 23.1	78.5 ± 20.7	76.6 ± 25.6	0.09
Heart rate (b.p.m.)	91.3 ± 28.5	92.8 ± 24.3	89.4 ± 32.7	0.01
Tachycardia (heart rate >100 BPM)	599 (35.2%)	339 (36.5%)	260 (33.5%)	0.05
Shock index[a]	0.91 ± 0.41	0.89 ± 0.30	0.93 ± 0.51	0.05
TIMI risk index[b]	42.8 ± 27.3	42.0 ± 21.7	43.7 ± 32.8	NS
Lactate (mmol/L)	5.2 ± 4.7	4.1 ± 3.7	6.1 ± 5.1	<0.001
pH	7.27 ± 0.16	7.30 ± 0.12	7.25 ± 0.19	<0.001
eGFR (mL/min, CKD-EPI)	51.2 ± 26.9	56.4 ± 28.3	45.0 ± 23.7	<0.001
eGFR >60 mL/min	530 (31.3%)	350 (28.8%)	180 (22.7%)	
eGFR 30–60 mL/min	758 (44.7%)	368 (40.8%)	390 (49.2%)	
eGFR <30 mL/min	406 (24.0%)	183 (20.3%)	223 (28.1%)	
AST (IU/mL)	495.6 ± 1490.4	449.1 ± 1368.0	538.3 ± 1594.4	NS
Troponin T (mcg/dL)[c]	1.8 ± 3.8	2.3 ± 4.6	1.4 ± 2.7	<0.001
LVEF				NS
>50%	281 (19.1%)	165 (22.1%)	116 (18.0%)	
40–50%	331 (22.5%)	122 (16.3%)	109 (16.9%)	
<40%	861 (58.5%)	460 (61.6%)	421 (65.2%)	
Support therapies				
Invasive mechanical ventilator at admission	974 (55.7%)	399 (42.7%)	575 (70.9%)	<0.001
Vasoactive drugs at admission	1138 (65.1%)	421 (45.1%)	717 (88.3%)	<0.001
Any MCS	761 (43.5%)	399 (42.7%)	362 (44.4%)	NS
IABP	363 (20.8%)	363 (38.9%)	0 (0%)	<0.001
Impella®	149 (8.5%)	9 (1.0%)	140 (17.2%)	<0.001
ECMO	270 (15.4%)	47 (5.0%)	223 (27.4%)	<0.001

Continued

Table 1 *Continued*

	Combined cardiogenic shock cohort ($n = 1749$)	Mayo Clinic CICU cardiogenic shock cohort ($n = 934$)	Hamburg cardiogenic shock cohort ($N = 815$)	*P* value (Mayo Clinic vs. Hamburg)
SCAI shock stage				
B	422 (24.1%)	387 (41.4%)	35 (4.3%)	<0.001
C	489 (28.0%)	120 (12.8%)	369 (45.3%)	
D	580 (33.2%)	354 (37.9%)	226 (27.7%)	
E	258 (14.8%)	73 (7.8%)	185 (22.7%)	
Outcomes				
30-day survival	932 (53.3%)	579 (62.0%)	353 (43.3%)	<0.001

Data are presented as mean ± standard deviation for continuous variables and *n* (%) for categorical variables. *P* value is for the comparison of the Mayo Clinic and Hamburg cohorts using Student's *t* test for continuous variables and χ^2 test for categorical variables. *P* values >0.1 are reported as non-significant (NS). The following variables had >10% missingness: BMI (Hamburg), lactate/pH (Mayo Clinic), AST/LVEF/troponin T (both cohorts).

CKD-EPI, Chronic Kidney Disease Epidemiology study; ECMO, extracorporeal membrane oxygenator; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

[a]Shock index is defined as heart rate/systolic blood pressure, and values >1 are considered elevated.

[b]The TIMI risk index was calculated as age^2 * shock index Ref.[32]

[c]Troponin T values were determined using different assays. Mayo Clinic used a fourth-generation assay during the study period, and Hamburg used a fifth-generation (high-sensitivity) assay.

Comparison of Mayo Clinic and University Clinic Hamburg cohorts

Both cohorts had a similar age ($P = 0.67$), although the Mayo Clinic cohort had a higher prevalence of female patients (*Table 1*). More patients from the Mayo Clinic cohort had acute coronary syndrome, while cardiac arrest was more common in the University Clinic Hamburg cohort; among patients with acute coronary syndromes, those in the University Clinic Hamburg cohort were more likely to undergo PCI. Overall illness severity was higher among the University Clinic Hamburg cohort, including a distribution skewed towards higher SCAI shock stage (*Table 1*). The University Clinic Hamburg cohort had greater use of supportive therapies, including vasoactive drugs. The intra-aortic balloon pump (IABP) was the primary MCS device used in the Mayo Clinic cohort, while extracorporeal membrane oxygenation (ECMO) was the primary MCS device used in the University Clinic Hamburg cohort (*Table 1*).

Characteristics according to age groups

The majority (72.6%) of patients was aged ≥60 years, and the largest age group was age 70–79 years (Supplementary material online, *Table S3*). Older patients were more often females, had more comorbidities, and were more likely to have acute coronary syndrome. Older patients had worse kidney function but similar markers of liver and myocardial injury. Older patients were less likely to receive MCS, while use of other supportive therapies was similar. Similar trends across age groups were observed in the Mayo Clinic and University Clinic Hamburg cohorts (Supplementary material online, *Tables S4* and *S5*). The distribution of SCAI shock stages differed across age groups ($P < 0.001$; Supplementary material online, *Figure S1*) with a higher prevalence of SCAI shock stage C/D and a lower prevalence of SCAI shock stage B/E in older age groups. The distribution of SCAI shock stages did not differ substantially across age groups in the Mayo Clinic cohort ($P = 0.67$; Supplementary material online, *Table S4*), although there was significant variation in the University Clinic Hamburg cohort ($P < 0.001$; Supplementary material online, *Table S5*).

Analysis of 30-day survival

A total of 932 patients died during the study period, yielding an overall combined 30-day survival rate of 53.3% that was similar for patients who did and did not receive MCS (54.9% vs. 52.0%, $P = 0.23$). The 30-day survival was higher in the Mayo Clinic cohort than the University Clinic Hamburg cohort (62.0% versus 43.3%, $P = <0.001$) in the overall cohort and this finding was consistent as a function of SCAI shock stage and among patients who did and did not receive MCS. There were clear trends towards lower 30-day survival with increasing age observed in the Mayo Clinic cohort, the University Clinic Hamburg cohort, and the combined cohort (*Figure 1*). Expectedly, 30-day survival decreased with increasing SCAI shock stage in both cohorts (Supplementary material online, *Figure S2A*). In the combined cohort, 30-day survival decreased with increasing age in patients who did and did not receive MCS, although this relationship appeared steeper among patients not receiving MCS (Supplementary material online, *Figure S2B*). There were graded relationships between age and 30-day survival in each SCAI shock stage, and between SCAI shock stage and 30-day survival in each age group in the combined cohort (*Figure 2*); similar findings were observed in each individual cohort (Supplementary material online, *Figure S3A* and *B*).

On Cox proportional-hazards analysis in both cohorts (*Table 2*), older age was strongly associated with higher adjusted 30-day mortality (adjusted HR per 10 years 1.39 in the Mayo Clinic cohort and 1.31 in the University Clinic Hamburg cohort, both $P < 0.001$). Each higher SCAI shock stage was associated with 1.5-fold higher adjusted 30-day mortality in each cohort (*Table 2*). Age and SCAI shock stage were the only two variables that were significantly associated with adjusted 30-day mortality in both cohorts (*Table 2*) and were among the most

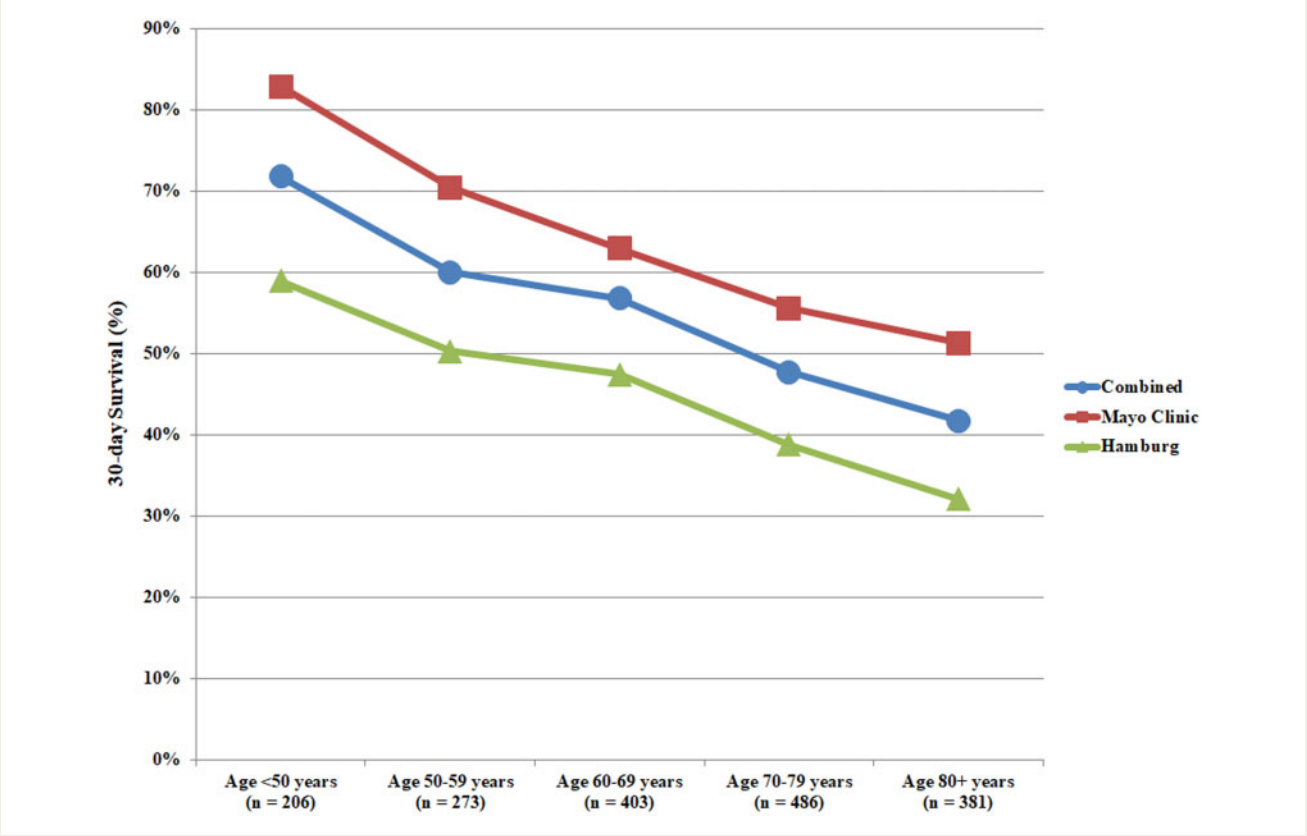

Figure 1 Crude 30-day survival as a function of age group in the combined cohort, the Mayo Clinic cohort and the University Clinic Hamburg cohort.

significant predictors of adjusted 30-day mortality in each cohort. Each higher age group was associated with progressively higher adjusted 30-day mortality compared to patients aged <50 years in the Mayo Clinic cohort (Supplementary material online, *Figure S4*); a similar trend was observed in the University Clinic Hamburg cohort, but the effect sizes were smaller and between-groups differences were significant only for patients aged ≥70 years ($P < 0.01$).

Exploratory analyses

When patients in the Mayo Clinic cohort had their SCAI stage reclassified using the algorithm from the University Clinic Hamburg cohort (Supplementary material online, *Table S1B*), the distribution of SCAI shock stages and the associated 30-day survival for each SCAI shock stage changed (Supplementary material online, *Figure S2A*). Our main findings did not change materially regarding the effects of age (adjusted HR 1.33 per 10 years, $P < 0.001$) or SCAI shock stage (adjusted HR 1.42 per stage, $P < 0.001$) on adjusted 30-day mortality, and older age was associated with higher mortality in each SCAI shock stage (all $P < 0.05$ except SCAI shock stage E, $P = 0.05$).

Patients with missing lactate levels in the Mayo Clinic cohort had their SCAI shock stage reclassified using imputed lactate levels to determine hypoperfusion (Supplementary material online, *Table S2*). A total of 29 patients in SCAI shock stage B (7.5% of Mayo Clinic SCAI shock stage B patients) were predicted to have an elevated lactate level and had their SCAI shock stage reclassified (17 to SCAI shock stage C and 12 to SCAI shock stage D). Using these imputed SCAI shock stages, our main findings did not change materially regarding the effects of age (adjusted HR 1.39 per 10 years, $P < 0.001$) or SCAI shock stage (adjusted HR 1.49 per stage, $P < 0.001$) on adjusted 30-day mortality, and older age was associated with higher mortality in each SCAI shock stage (all $P < 0.05$).

Discussion

In this multicentre study of almost 1750 unselected patients with CS, we observed a strong and graded relationship between older age and lower 30-day survival that was additive to the effect of shock severity. Older patients were more likely to die at each level of shock severity, and higher shock severity was associated with increased mortality risk in each age group. The use of MCS was not associated with 30-day survival, and older age was associated with lower survival among patients who did and did not receive MCS. Age and SCAI shock stage were among the strongest predictors of survival in both cohorts. Our findings were remarkably consistent despite significant differences between these two distinct cohorts from separate continents during different time periods, with substantially higher illness severity and greater use of advanced percutaneous MCS devices in the University Clinic Hamburg cohort and a stronger association between age and outcomes in the Mayo Clinic cohort. Furthermore,

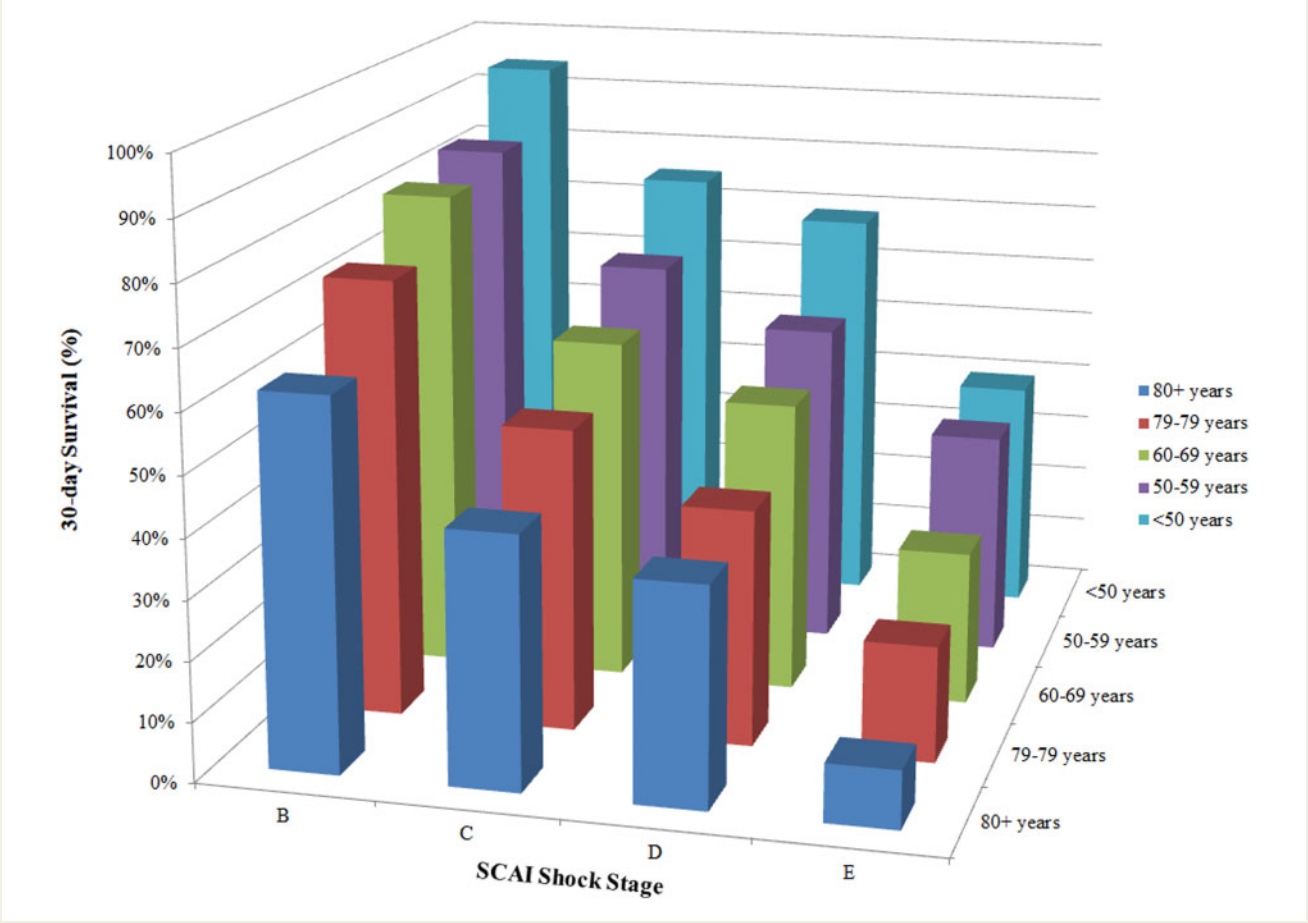

Figure 2 Crude 30-day survival (*Y* axis) as a function of Society for Cardiovascular Angiography and Intervention shock stage (*X* axis) and age group (colour-coded) in the combined cohort.

our results were robust to changes in the SCAI shock stages classification within the Mayo Clinic cohort. The observed 30-day survival rates among older patients with severe shock were very low, emphasizing the substantial hazard faced by CS patients of advanced age that cannot be completely explained by higher shock severity or commonly-measured clinical variables.

Our study is congruent with prior studies identifying older age as a risk factor for mortality among patients with CS, which have led to inclusion of age in CS-specific mortality risk scores.[6–9,15,18–28] Our findings echo those of Baran *et al.*[15] who reported that age was the most important risk factor for mortality in patients with CS after SCAI shock stage. We observed a graded relationship between age and mortality, although the strength of this relationship differed between cohorts—only patients aged ≥70 years were at significantly higher risk of dying in both cohorts. This age cut-off of ≥70 years for identification of high-risk CS patients is consistent with prior studies that have identified age cut-offs ranging from ≥65 to >75 years for prediction of higher mortality among patients with CS.[2,5–7,26–28,33,34]

Older patients had more co-morbidities, worse kidney function, and decreased use of MCS devices, but had a significantly higher risk of mortality despite adjusting for these factors in addition to shock severity (which did not differ significantly as a function of age). Therefore, it is challenging to determine which specific factors may have led to worse outcomes among our older patients. Although we observed different patterns of MCS device use as a function of age and cohort, there was no significant association between MCS use and outcomes in either cohort, consistent with published randomized trials of percutaneous MCS devices in CS.[4,35] Older age was associated with lower survival in patients who did and did not receive MCS, although the relationship between age and survival appeared stronger for patients who did not receive MCS; this could potentially reflect differential responses to MCS as a function or age or selection bias in the use of MCS in older vs. younger patients.

Older patients have consistently fared worse in randomized trials of CS populations.[2–5] In the randomized SHOCK trial, patients aged ≥75 years with acute myocardial infarction-related CS (AMICS) appeared less likely to benefit from early revascularization despite an important benefit in the overall study population.[2,33] Subsequent nonrandomized studies have suggested a survival benefit from revascularization among older patients with AMICS, but their outcomes remain worse than younger patients.[34] Zeymer *et al.*[24] reported that older AMICS patients had more severe coronary disease, a lower likelihood of successful percutaneous coronary intervention, and higher mortality (especially if they did not have successful

Table 2 Predictors of 30-day mortality on Cox proportional-hazards analysis in each cohort analysed separately; all of these variables were include in the Cox models

	Mayo Clinic cohort		University Clinic Hamburg cohort	
Variable	**Adjusted HR (95% CI)**	***P* value**	**Adjusted HR (95% CI)**	***P* value**
Demographics				
Age (per 10 years)	1.387 (1.257–1.534)	<0.001	1.305 (1.173–1.451)	<0.001
Female sex	0.936 (0.739–1.187)	NS	1.516 (1.170–1.965)	0.002
BMI (per 1 mg/m^2)	1.008 (0.991–1.026)	NS	0.988 (0.962–1.015)	NS
Co-morbidities and diagnoses				
Hypertension	0.728 (0.577–0.920)	0.005	0.916 (0.708–1.185)	NS
Diabetes mellitus	1.016 (0.756–1.323)	NS	0.993 (0.752–1.310)	NS
CKD	0.992 (0.734–1.340)	NS	0.770 (0.542–1.094)	NS
Prior MI	0.931 (0.696–1.246)	NS	0.980 (0.735–1.308)	NS
Prior stroke	1.242 (0.891–1.732)	NS	1.172 (0.782–1.756)	NS
Acute coronary syndrome	0.795 (0.624–1.012)	0.06	1.014 (0.793–1.230)	NS
Cardiac arrest	2.606 (2.035–3.337)	<0.001	1.022 (0.721–1.448)	NS
Admission vital signs and labs				
Systolic BP (per 1 mmHg)	0.992 (0.987–0.997)	<0.001	1.001 (0.995–1.005)	NS
Diastolic BP (per 1 mmHg)	1.000 (0.993–1.007)	NS	0.998 (0.990–1.005)	NS
Heart rate (per 1 b.p.m.)	1.002 (0.997–1.007)	NS	0.999 (0.996–1.003)	NS
Estimated GFR (per 1 mL/min)	0.992 (0.987–0.998)	0.004	0.994 (0.988–1.001)	0.07
Supportive therapies				
Invasive mechanical ventilation	1.139 (0.888–1.462)	NS	1.735 (1.173–2.566)	0.006
Vasoactive drugs	1.049 (0.826–1.332)	NS	1.157 (0.732–1.830)	NS
Impella®	0.670 (0.209–2.145)	NS	1.135 (0.831–1.550)	NS
ECMO	1.054 (0.624–1.779)	NS	1.043 (0.752–1.448)	NS
SCAI shock stage (per stage)	1.511 (1.341–1.707)	<0.001	1.488 (1.261–1.757)	<0.0001

Hazard ratio (HR) and 95% confidence interval (CI) values are reported. *P* values >0.1 are reported as non-significant (NS).

revascularization). Numerous other age-related factors can potentially contribute to worse outcomes in older patients, including frailty, delayed or atypical clinical presentation, multimorbidity, impaired organ function, altered drug metabolism, reduced functional reserve, and abnormal cardiovascular physiology.[29]

This study provides real-world survival estimates for CS patients as a function of both age and shock severity, to enable more accurate risk stratification in clinical practice that can inform patients and families about expected outcomes. More accurate risk estimates can facilitate CS patient triage and mortality benchmarking, but the low survival rates we observed in older patients with severe shock should not be interpreted as futility of care. The selection of older patients for specific therapies must be individualized by incorporating other prognostic factors including organ function and baseline health status. Despite the poor survival observed among older patients with AMICS, withholding potentially life-sustaining therapies, such as revascularization on the basis of age alone is not appropriate.[2,24,33,34] Older patients may have different goals of care from younger patients and may request limitations on the aggressiveness of care in the setting of critical illness and a poor anticipated prognosis.[29] Our data can help to inform these crucial discussions using real-world outcomes in CS patients, helping providers to determine the best approach for an individual patient.

Limitations

This retrospective observational study design has inherent limitations which prevent drawing causal inferences, including the potential that unmeasured confounding variables (such as frailty) or missing data could have influenced the results. We did not have available data to calculate CS mortality risk scores in both cohorts to allow full adjustment for predicted mortality, and patients with missing data were not included in the Cox analysis.[6–8] The two cohorts included in this study differed substantially, including patients from different countries and time periods with divergent care patterns using distinct definitions of SCAI shock stages which were assigned retrospectively and led to

substantially different distributions of SCAI shock stages between cohorts. Our consistent findings in these disparate patient populations strengthen our message that age and shock severity are strongly and independently associated with mortality in patients with CS. The use of ICD-9 diagnosis codes to identify patients with CS remains an important limitation, particularly because the primary admission diagnosis could not be confirmed for the Mayo Clinic cohort.[14,31] This led to inclusion of a substantial number of lower risk (SCAI shock stage B) patients with ICD diagnoses of CS, who were haemodynamically unstable but did not have hypoperfusion at the time of CICU admission; these patients may have either had previously stabilized shock or subsequent development of shock. Notably, lactate levels were missing for a substantial number of patients in the Mayo Clinic cohort, and missing lactate levels were considered normal for the purpose of determining SCAI shock stage; this could potentially have led to misclassification of patients with hypoperfusion as having SCAI shock stage B. When we reclassified the SCAI shock stages in the Mayo Clinic cohort using imputation of missing lactate levels, the results did not change materially. Data were not available regarding frailty or patient goals of care including limitations on therapies, such as 'Do-Not-Resuscitate' orders, which are particularly relevant when considering the effects of age on outcomes in critically ill patients.[29]

Conclusions

Increasing age is associated with lower survival in patients with CS at each level of shock severity, and increasing SCAI shock stage is associated with lower survival in each age group. Our results highlight the graded worsening in survival rates among older patients with more severe CS, providing much-needed data regarding the interaction between age and shock severity. Older patients had lower adjusted 30-day survival even though they did not have higher shock severity than younger patients, implying that other clinical factors are responsible for their worse outcomes. Further research is needed to understand the biologic underpinnings of the poor outcomes observed in the oldest patients and to identify which patients may benefit from more aggressive treatment strategies. Future studies examining the relationship between age and outcomes in CS patients need to better quantify frailty, which may help to better recognize which older patients with CS are more likely to survive their illness.

Supplementary material

Supplementary material is available at *European Heart Journal: Acute Cardiovascular Care*.

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Data availability

The authors declare that all supporting data are available within the article and its online supplementary files.

Conflict of interest: none declared.

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