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Review

ST Elevation Myocardial Infarction Complicated by Cardiogenic Shock: Systematic Review of Survival Predictors

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A B S T R A C T

Background: Cardiogenic shock complicating acute myocardial infarction is associated with reduced survival despite advancements in the treatment of acute coronary syndromes. Characterizing predictors of morbidity and mortality in this setting is crucial to improving risk stratification and management. Notwithstanding, the interplay of factors determining survival in this condition remains poorly studied.

Methods: Embase, MEDLINE, and CINAHL databases were searched for original studies evaluating predictors of short-term (30-day or in-hospital) survival in ST elevation myocardial infarction with cardiogenic shock (STEMI-CS). Included studies were analyzed by way of vote counting, identifying variables that predicted mortality or survival.

Results: Twenty-four studies, consisting of 14,735 patients (5649 nonsurvivors and 9086 survivors) were included. All studies were observational by design (17 retrospective and 7 prospective) with clinical and statistical heterogeneity. Unsuccessful revascularization, reduced left ventricular ejection fraction, renal impairment, and other variables were identified as key independent predictors of mortality.

Conclusion: Several key variables have been shown to independently increase mortality in STEMI-CS populations. Future prospective studies examining the prognostic role of multivariate scoring systems incorporating these domains are required.

Introduction

Cardiogenic shock (CS) is a hemodynamically complex syndrome whereby low cardiac output results in global tissue hypoperfusion, culminating in multiorgan failure and eventual death if left untreated.[1] Despite advances in treatment, acute myocardial infarction (AMI) is the most common cause of CS, and CS is the leading cause of in-hospital death in patients presenting with AMI.[2] Persistently high mortality rates suggest many questions regarding the evolution from AMI to CS remain unanswered.[3]

To date, acute myocardial infarction with cardiogenic shock (AMI-CS) cohorts have been demonstrated to be widely heterogenous. This includes a range of preexisting comorbidities, time to presentation, coronary findings, mechanical sequelae, electrical complications, end-organ injury, and treatments accessed.[4] Assessment of predictors of survival is therefore exceedingly complex; however, there remains an urgent and unmet need to better understand the determinants of mortality in this group.[4,5]

The main objective of this systematic review was to identify independent predictors of in-hospital and 30-day mortality in ST elevation myocardial infarction with cardiogenic shock (STEMI-CS). This is key to improving future prognostication, shock team decision making, and patient selection for mechanical circulatory support in STEMI-CS.[5]

Methods

This systematic review was registered on PROSPERO (CRD42021272438) and reported according to the Meta-analysis of Observational Studies (MOOSE) guidelines.[6] An experienced researcher was consulted on all aspects of study design and helped in

Abbreviations: AMI, Acute myocardial infarction; AMI-CS, Acute myocardial infarction with cardiogenic shock; CS, Cardiogenic shock; LVEF, Left ventricular ejection fraction; PCI, Percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; STEMI-CS, ST elevation myocardial infarction with cardiogenic shock; TIMI, thrombolysis in myocardial infarction..

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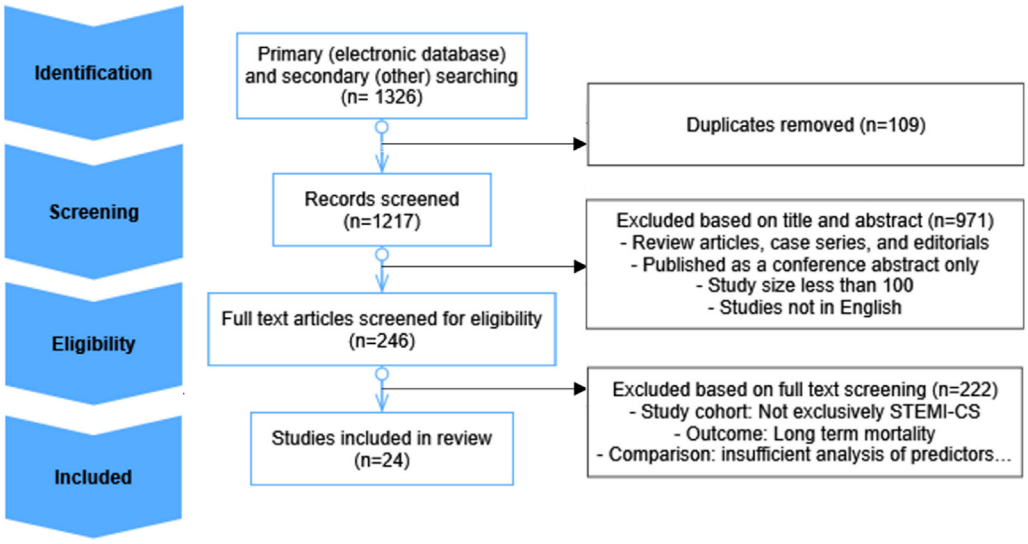

Figure 1. Study search and selection flowchart.

the primary literature search during January 2021. The bibliographic databases EMBASE, MEDLINE, and CINAHL were searched for published journal articles limited to English as well as human studies, with no time restrictions set. A secondary search of Google Scholar was performed. Detailed search strategies are outlined in Supplementary Table S3 (available online). In addition, a manual search of secondary sources including the bibliographies of relevant reviews and editorials was conducted.

All studies retrieved were transferred to EndNote (Windows Version X9.3.1, 2020), and duplicates were removed. Using Covidence (Covidence systematic review software, 2021), the remaining studies were independently screened according to title and abstract by 2 experienced reviewers (JKK and SH). Full texts were assessed against the following predefined inclusion criteria: (1) randomized control trials or observational studies; (2) study populations with STEMI and CS; (3) study populations of 100 or more patients; (4) short-term (30-day or in-hospital) mortality outcomes; and (5) analysis of predictors of short-term mortality. Studies were therefore excluded based on: (i) design, including case series; (ii) population, including non-STEMI patients; (iii) outcomes, including long-term mortality only; and (iv) methodology, including failure to compare survivors and nonsurvivors for predictors of mortality. A third reviewer (AA) verified the selection and extraction process. Disagreements were resolved by consensus among the 3 reviewers.

Study characteristics and outcomes were extracted manually from each study, including data from the main text, figures, and supplementary material. This data was tabulated in a Microsoft Excel (Microsoft 365, 2021) file. Reviewers JKK and SH extracted and tabulated data, and any disagreements were adjudicated by consensus with reviewer AA. Statistical synthesis of predictors was performed using the vote counting method according to the *Cochrane Handbook for Systematic Reviews of Interventions*.[7] This was chosen given the lack of consistent effect measures across studies.[7] It involved two steps. First a binary metric was used to classify independent determinants of the outcome by their direction of effect, either associated with survival or associated with mortality.[7] Second a tally of the number associated with survival and mortality was calculated and compared.[7]

The risk of bias of observational studies was assessed using the Newcastle-Ottawa Scale.[8] Quantitative global judgments about risk of bias were not derived. Risk of bias was determined based on the adequacy of case-control selection, case-control comparison, and ascertainment of exposures.[8] Due to clinical and methodological diversity, the studies have broad statistical heterogeneity precluding significant quantitative heterogeneity analyses. The studies also lack homogeneity preventing meaningful graphical assessment of publication bias with a funnel plot. The overall quality of evidence and recommendation was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results

The initial search revealed a total of 1217 studies. Following title and abstract screening 246 studies remained. After full text assessment 24 observational studies (17 retrospective and 7 prospective) of 14,735 STEMI-CS patients (5649 nonsurvivors and 9086 survivors) were included. Of note, 2 of the studies divided populations into separate cohorts for analysis. Yang et al.[9] analyzed diabetic and nondiabetic patients separately. Kochar et al.[10] analyzed patients directly presenting to a percutaneous coronary intervention (PCI) facility and patients transferred from a non-PCI facility separately. The 2 studies thus yielded 4 cohorts. Therefore, a total of 26 cohorts made up this review. The study selection flowchart is shown in Figure 1.

Publication year ranged from 2006 to 2021, while study period ranged from 1990 to 2018. All studies were observational by design and demonstrated significant clinical diversity, with differences in prespecified inclusion criteria, STEMI subgroups, exclusion criteria, and definitions for CS. Study and baseline population characteristics are outlined in Table 1 and Supplementary Table S1 (available online), respectively. Newcastle-Ottawa Scale scores for risk of bias ranged from 4 to 6 and are shown in Table 2.

Short-term mortality ranged from 13.5% to 65.2%. Collectively, outcomes of 14,735 patients with a total of 9086 survivors and 5649 nonsurvivors (38.3% mortality) were studied. Mortality in each cohort was found to have at least 1 independent predictor. Predictors that were analyzed varied widely, and in some studies variables were not specified. Vote counting results for independent predictors of mortality are presented in Figure 2. Tabulated data of all variable analysis can be found in Supplementary Table S2 (available online).

Baseline Characteristics

Age was the most widely reported demographic variable, analyzed in 20 of the 26 cohorts. In 10 of these cohorts, advanced age was found to be an independent predictor of mortality. Age was reported as a continuous variable in 8 of these cohorts,[10-16] while an age cutoff of 75 years

Table 1
Study Characteristics

Author	Publication year	Study period	Location	Observational study design	Population	Exclusion criteria	CS definition	Time	Patients *n*	Mortality *n* (%)	Survival *n* (%)
Feng et al.	2021	2011-2018	China	Retrospective	AMI-CS with emergency PCI to IRA only under IABP support	Other heart disease, aortic dissection, MI in last month, or comorbidities that could affect prognosis	SBP <90 mmHg for ≥30 min, or SBP decreased by >30% for ≥30 min; and clinical end-organ hypoperfusion or pulmonary congestion	30-day	141	92 (65.2)	49 (34.8)
Kumar et al.	2020	2011-2016	USA	Prospective	STEMI-CS with PCI	Nil	SBP <90 mmHg (or CI <2.2 L/min/m^2 for >30 min); or vasopressors or inotropes or mechanical support to maintain SBP and CI	In-hospital	137	35 (25.5)	102 (74.5)
Joshi et al.	2020	2011-2014	Denmark	Retrospective	STEMI-CS with primary PCI	Nil	SBP <90 mmHg for ≥30 mins, or vasopressors to maintain SBP ≥90 mmHg; pulmonary congestion or elevated filling pressures; and clinical end-organ hypoperfusion, or lactate ≥2.5 mmol/L	30-day	128	69 (53.9)	59 (46.1)
Hayıroğlu et al.	2019	2013-2016	Turkey	Retrospective	STEMI-CS with primary PCI	Nil	SBP ≤90 mmHg for ≥30 min, or vasopressors to maintain SBP >90 mmHg; clinical end organ hypoperfusion; and elevated filling pressures	In-hospital	329	202 (61.3)	127 (38.7)
Sharma et al.	2019	2015-2018	India	Prospective	STEMI-CS presenting ≥12 h post symptom onset	Nil	SBP <90 mmHg for ≥30 min, or supportive measures to maintain SBP ≥90 mmHg; and clinical end organ hypoperfusion	In-hospital	147	63 (42.9)	84 (57.1)
Raja et al.	2018	2001-2017	India	Retrospective	STEMI-CS with primary or rescue PCI	Mechanical complications, isolated RV infarction, or iatrogenic shock	SBP ≤90 mmHg for ≥30 min, or inotropes or vasopressors or mechanical support to maintain SBP ≥90 mmHg; and a congruent clinical presentation	In-hospital	114	61 (53.5)	53 (46.5)
Kochar et al.	2018	2012-2014	USA	Retrospective	STEMI-CS	Nil	SBP <90 mmHg or CI <2.2 L/min/m^2 for >30 min; or inotropes or vasopressors or mechanical support to maintain SBP (or CI)	In-hospital	1993	686 (34.4)	1307 (65.6)
Backhaus et al.	2018	2006-2016	Germany	Retrospective	STEMI-CS	Nil	SBP <90 mmHg for ≥30 min, or catecholamines to maintain SBP >90 mmHg; and end organ hypoperfusion	In-hospital	981	363 (37.0)	618 (63.0)
Costa et al.	2017	2013-2015	Argentina	Retrospective	STEMI-CS	Nil	SBP ≤90 mmHg for ≥30 min, or vasopressors or inotropes to maintain SBP ≥90 mmHg; and clinical hypoperfusion or pulmonary congestion	In-hospital	124	67 (54.0)	57 (46.0)
Cheng et al.	2016	2000-2012	Netherlands	Retrospective	STEMI-CS with primary PCI	Nil	SBP <90 mmHg not responsive to fluid resuscitation, or inotropes or mechanical support to maintain SBP; and clinical hypoperfusion	30-day	544	209 (38.4)	335 (61.6)
Park et al.	2015	2006-2013	Korea	Prospective	STEMI-CS with MVD receiving primary PCI	Missing vital signs data	SBP <90 mmHg for >30 min, or supportive measures to maintain SBP ≥90 mmHg; and clinical end organ hypoperfusion	In-hospital	510	69 (13.5)	441 (86.5)
Jensen et al.	2014	2002-2010	Denmark	Retrospective	STEMI-CS with primary PCI	Patients undergoing a later primary PCI for acute MI after the first index procedure	SBP <90 mmHg with need for catecholamines to maintain SBP; and clinical congestion; and end-organ hypoperfusion; or use of IABP in first 24 h of admission	30-day	286	164 (57.3)	122 (42.7)
Ho et al.	2014	2009-2010	Singapore	Retrospective	STEMI-CS with primary PCI	Nil	SBP <90 mmHg for >30 min, or supportive measures to maintain SBP >90 mmHg; and end organ hypoperfusion	In-hospital	145	40 (27.6)	105 (72.4)
Tomassini et al.	2013	2001-2010	Italy	Retrospective	STEMI-CS with primary PCI	Mechanical complications (tamponade, septum or wall rupture, or acute MR due to papillary muscle rupture)	SBP <90 mmHg (without inotropes or IABP); and end-organ hypoperfusion	In-hospital	155	63 (40.6)	92 (59.4)

(*continued on next page*)

Table 1 (*continued*)

Author	Publication year	Study period	Location	Observational study design	Population	Exclusion criteria	CS definition	Time	Patients *n*	Mortality *n* (%)	Survival *n* (%)
Yang et al.	2013	2005-2010	Korea	Prospective	STEMI-CS	Mechanical complications (VSD or acute MR) or unavailable blood glucose level at admission	SBP persistently <90 mmHg or vasopressors to maintain SBP >90 mmHg; signs of hypoperfusion; and elevated filling pressures (pulmonary congestion)	30-day	816	261 (32.0)	555 (68.0)
Greenberg et al.	2012	2001-2011	Israel	Prospective	STEMI-CS with primary PCI	Dominant valvular pathology, mechanical complication, or accompanying sepsis	SBP <90 mmHg and organ hypoperfusion despite fluid challenge, associated with LV dysfunction with or without RV dysfunction by echocardiography	30-day	170	85 (50.0)	85 (50.0)
Hoebers et al.	2013	1997-2008	Netherlands	Retrospective	STEMI-CS with primary PCI	Nil	SBP persistently <90 mmHg, or vasopressors to maintain SBP >90 mmHg; and elevated filling pressures; and end-organ hypoperfusion	30-day	609	228 (37.4)	381 (62.6)
Bataille et al.	2012	2006-2011	Canada	Retrospective	STEMI-CS <12 h post symptom onset, receiving primary PCI	Previous CABG, no significant coronary lesion found, or CS that developed during or after PCI	SBP <90 mmHg for ≥30 min, or supportive measures to maintain SBP ≥90 mmHg; and end-organ hypoperfusion	30-day	141	69 (48.9)	72 (51.1)
Tsai et al.	2010	2001-2009	Taiwan	Prospective	STEMI-CS treated with primary PCI	Left main occlusion	SBP <90 mmHg and pulmonary edema; or persistent SBP <90 mmHg due to low cardiac output, not related to dysrhythmia, unresponsive to fluid supply and requiring vasopressors.	30-day	212	63 (29.7)	149 (70.3)
Sheu et al.	2010	1993-2009	Taiwan	Prospective	STEMI-CS <12 h post symptom onset, receiving primary PCI	Urgent cardiovascular surgery (VSD or left main with triple vessel disease)	Persistent SBP <90 mmHg (not responsive to fluid), or hypotension needing vasopressors; and low CO or pulmonary edema. (Profound CS refers to SBP <75 mmHg despite inotropes and IABP).	30-day	334	114 (34.1)	220 (65.9)
Pres et al.	2010	1998-2006	Poland	Retrospective	STEMI-CS with PCI	Nil	SBP <90 mmHg for ≥30 min, or SBP decreased by >30% for ≥30 min, or SBP <110 mmHg with the use of inotropes or IABP; and clinical end-organ hypoperfusion	In-hospital	258	97 (37.6)	161 (62.4)
Mehta et al.	2009	2004-2007	USA	Retrospective	STEMI-CS with primary PCI	Transferred from another facility for PCI or missing data on post-PCI TIMI flow grade	SBP ≤80 mmHg (or CI <1.8 L/min/m^2) despite maximal treatment, or inotropes or IABP to maintain SBP >80 mmHg (or CI ≥1.8 L/min/m^2)	In-hospital	4731	1528 (32.3)	3203 (67.7)
Mehta et al.	2007	1990-1993, 1995-1997	International	Retrospective	STEMI-CS <6 h post symptom onset, receiving fibrinolysis	Missing data on age or gender	SBP <90 mmHg for ≥1 h unresponsive to fluid; and signs of hypoperfusion or CI ≤2.2 L/min/m^2	30-day	761	457 (60.1)	304 (39.9)
Jeger et al.	2006	1993-1998	International	Retrospective	STEMI-CS (CS <36 h post STEMI onset)	Severe valvular disease, mechanical complications, isolated RV infarction, known dilated CM, excess beta-blockade or calcium channel blockade, or complication from PCI	SBP <90 mmHg (or CI ≤2.2 L/min/m^2) for ≥30 min, or vasopressors or IABP to maintain SBP ≥90 mmHg; and evidence of end-organ hypoperfusion; and pulmonary congestion or PCWP ≥15 mmHg	In-hospital	969	564 (58.2)	405 (41.8)
All Studies Combined	2006-2021	1990-2018	–	–	–	–	–	Short-term	14,735	5649 (38.3%)	9086 (61.7%)

AMI-CS = acute myocardial infarction with cardiogenic shock; CABG = coronary artery bypass graft; CI = cardiac index; CM = cardiomyopathy; CO = cardiac output; CS = cardiogenic shock; h = hours; IABP = intraaortic balloon pump; IRA = infarct-related artery; LV = left ventricular; min = minutes; MR = mitral regurgitation; MVD = multivessel disease; PCI = percutaneous coronary intervention; PCWP = pulmonary capillary wedge pressure; RV = right ventricular; SBP = systolic blood pressure; STEMI = ST elevation myocardial infarction; STEMI-CS = ST elevation myocardial infarction with cardiogenic shock; TIMI = thrombolysis in myocardial infarction; USA = United States of America; VSD = ventricular septal defect.

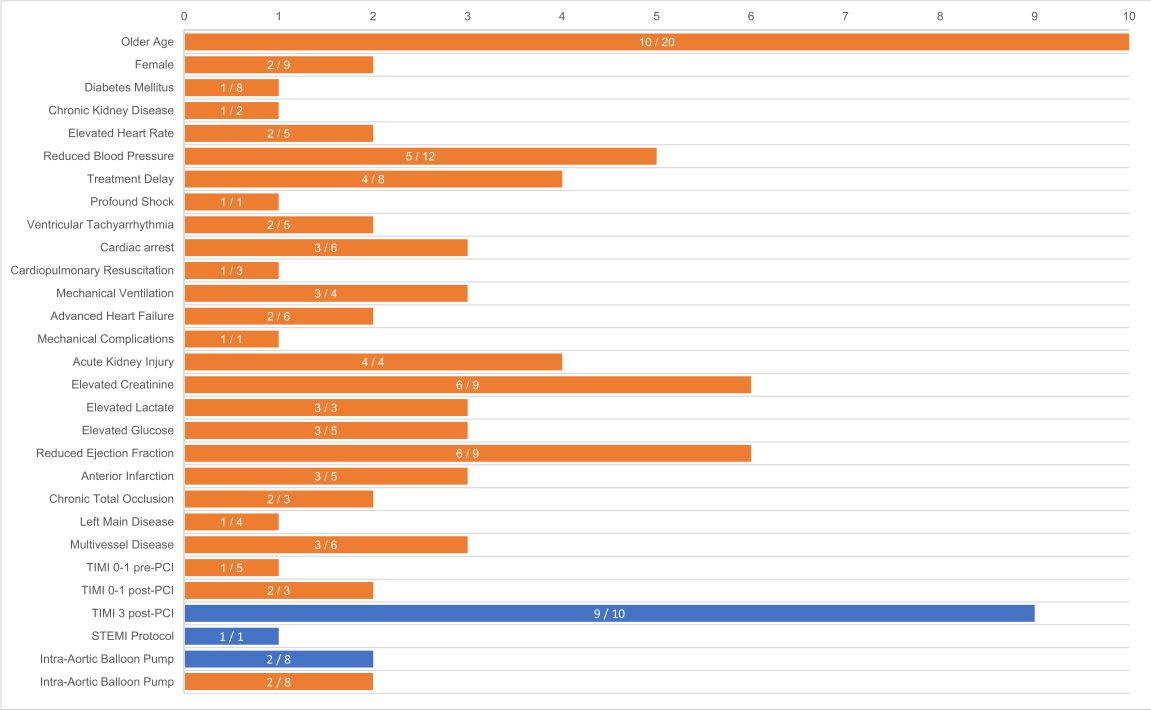

Figure 2. Bar graph of the number of cohorts that found each variable to be an independent predictor. The ratio to the total number of cohorts is written in each bar. Orange bars indicate mortality. Blue bars indicate survival.

Table 2
Newcastle-Ottawa Scale Quality Assessment A star system is used to allow a semiquantitative assessment of study quality. A study can be awarded a maximum of 4 stars for the selection domain, 2 stars for comparability, and 3 stars for exposure. The Newcastle-Ottawa Scale ranges from 0 to 9 stars.[8]

Author	Year	Selection	Comparability	Exposure	Total score
Feng	2021	★★	★★	★	5
Kumar	2020	★	★★	★★	5
Joshi	2020	★	★★	★	4
Hayıroğlu	2019	★★	★★	★★	6
Sharma	2019	★★	★★	★★	6
Raja	2018	★★	★★	★★	6
Kochar	2018	★★	★★	★	5
Backhaus	2018	★★	★★	★	5
Costa	2017	★★	★★	★	5
Cheng	2016	★★	★★	★	5
Park	2015	★★	★★	★★	6
Jensen	2014	★★	★	★	4
Ho	2014	★	★★	★	4
Tomassini	2013	★★	★★	★	5
Yang	2013	★★	★★	★★	6
Greenberg	2012	★★	★	★	4
Hoebers	2013	★★	★★	★★	6
Bataille	2012	★★	★★	★	5
Tsai	2010	★★	★★	★★	6
Sheu	2010	★★	★★	★★	6
Pres	2010	★★	★★	★	5
Mehta	2009	★★	★★	★	5
Mehta	2007	★	★★	★	4
Jeger	2006	★★	★★	★	5

A star system is used to allow a semiquantitative assessment of study quality. A study can be awarded a maximum of 4 stars for the selection domain, 2 stars for comparability, and 3 stars for exposure. The Newcastle-Ottawa Scale ranges from 0 to 9 stars.

was reported in the other 2 cohorts.[9,17] Additional demographic or comorbidity variables found to independently predict mortality included female sex,[9] diabetes mellitus,[18] and chronic kidney disease.[19]

Time to Treatment

Revascularization timing and delay to treatment predicted mortality in 4 cohorts, although there was considerable heterogeneity in study terms. Raja et al.[20] defined revascularization timing as the total ischemic time ("time from symptom onset to PCI"), whereas Jeger et al.[12] reported a revascularization (PCI or bypass grafting) time cutoff of 6 h from randomization (with randomization being performed within 12 h from CS onset). Costa et al.[21] defined delayed treatment as >240 min from symptom onset to admission, while Kochar et al.[10] used first medical contact to device time >90 min in direct presenters to a PCI facility.

Regardless, comprehensive STEMI protocols which expedited revascularization timing were found to be favorable prognostically and associated with improved survival.[22] Kumar et al. identified the following 4 key aspects of a successful revascularization protocol: (1) emergency department activation of the catheterization laboratory; (2) standardized patient triage and handover; (3) transfer to an available catheterization laboratory; and (4) a "radial-first" approach.[22]

Angiography and Revascularization

Procedural success defined based on Thrombolysis in Myocardial Infarction (TIMI) flow post-PCI was analyzed in 13 cohorts and independently predicted survival in 11. Of these, TIMI 3 flow was defined as the cutoff in 9 cohorts,[15,16,19,20,23-27] while TIMI 0-1 flow was reported in the other 2 cohorts.[14,17] Additional angiographic factors independently predictive of mortality included the presence of one or more chronic total occlusions,[28,29] multivessel disease,[17,24,29] left main disease,[11] and anterior infarction.[9,24]

Left Ventricular Ejection Fraction

The association between left ventricular ejection fraction (LVEF) and mortality was analyzed in 9 of the 26 study cohorts. Unfortunately, between all 9 cohorts specific in-hospital timing and method of LVEF assessment varied or was not stated. Nevertheless, reduced LVEF was

found to be an independent predictor of mortality in 6 cohorts. Of these, LVEF was analyzed as a continuous variable in 4 cohorts,[14,19,20,24] while LVEF cutoffs of <40%[18] and <30%[28] were used in the other 2 cohorts.

Cardiovascular Complications

Major cardiorespiratory sequelae predicted mortality, including cardiac arrest in 3 cohorts,[10,31] cardiopulmonary resuscitation in 1 cohort,[20] ventricular fibrillation/tachycardia in 2 cohorts,[11,30] advanced congestive heart failure in 2 cohorts,[15,25] mechanical complications in 1 cohort,[30] and mechanical ventilation in 3 cohorts.[9,11,16]

End-Organ Complications and Biochemistry

Acute kidney injury, elevated serum creatinine, increased serum lactate, and elevated serum glucose were all found to be independent predictors of mortality. Serum creatinine predicted mortality in 6 cohorts. This was analyzed as a continuous variable in 2 cohorts,[10,14] while the other 4 cohorts used varying creatinine cutoff values (ie, creatinine >115 μmol/L in males or >90 μmol/L in females,[11] creatinine >1.5 mg/dL,[9] creatinine clearance <60 mL/min,[28] and eGFR <60[18]). Serum lactate was analyzed as a continuous variable in 3 cohorts[11,16,19] and independently predicted mortality in each. Serum glucose predicted mortality in 3 cohorts. Of these, glucose was reported as a continuous variable in 2 cohorts,[19,24] while in the other nondiabetic cohort a cutoff of ≥11 mmol/L was associated with increased risk of mortality.[9]

Discussion

To our knowledge this is the first systematic review of predictors of short-term mortality in STEMI-CS. Several key independent predictors of mortality were identified, including unsuccessful revascularization, reduced LVEF, and renal impairment. Despite comprehensively reviewing the available literature, however, these findings are derived entirely from observational studies and therefore carry a risk of bias. Few randomized control trials on the subject exist, and those published did not meet inclusion criteria owing to a lack of reporting on predictors of short-term survival.[32]

Importantly, failure to restore TIMI 3 flow was a strong indicator of mortality. This supports prior studies in which successful revascularization was demonstrated to be critical for STEMI patient survival.[4,5] The present review also identified other angiographic variables to be associated with mortality, including chronic total occlusions,[28,29] multivessel disease,[17,24,29] left main disease,[11] and anterior infarction.[9,24] Our review extends prior literature[4] and gives scope to predict short-term prognosis by factoring in high-risk angiographic variables. Of note, surgical revascularization was not well studied. Current practice is that bypass is reserved for mechanical complications, suitable coronary anatomies, rescuing failed PCI, or hybrid approaches.[3] However, as this review demonstrates, bypass graft surgery was analyzed in only 1 cohort and was not found to be significant.[17] There remains a paucity of data on bypass surgery in STEMI-CS and presently no randomized study has compared it to PCI.[4]

Lower LVEF was identified as an important predictor of mortality in this review. Greenberg et al.[18] and Bataille et al.[28] found an LVEF <40% and <30% to be significant, respectively. Acharya et al.[4] also identified an AMI-CS cohort in which LVEF <30% was associated with mortality. Collectively, these studies support the inclusion of LVEF <40% in the CardShock risk score, a multivariate risk calculator that predicts short-term mortality in CS of any cause.[5] Reduced baseline and postprocedural LVEF should be factored into prognosis for AMI-CS patients going forward.[3]

Of the hemodynamic variables studied, reduced blood pressure and elevated heart rate predicted increased mortality in 5 cohorts.[9,10,12,13] Sheu et al. further identified profound CS, defined as systolic blood pressure <75 mmHg, to be a predictor of mortality, and among these patients PCI supported by early extracorporeal membrane oxygenation improved 30-day outcomes.[15] Previous studies in AMI with refractory CS have similarly demonstrated association between mortality and blood pressure. The TRIUMPH trial found on posthoc analysis that decreases in systolic blood pressure predicted 30-day mortality in refractory CS.[4] The findings of this review support the SAVE (Survival after Veno-Arterial ECMO) Score. The SAVE Score was developed based on registry data and incorporates baseline diastolic blood pressure and pulse pressure as predictors of in-hospital mortality in refractory CS.[5]

Delays to treatment predicted mortality in 4 cohorts.[10,12,20,21] However, different time measures were used and we were not able to establish any standard interval per se. Regardless, our findings reinforce the importance of reducing time from symptom onset to admission, as well as time from symptom onset to PCI, so as to reduce mortality.[4] The present review also affirms systems of care which focus on the importance of early intervention.[3]

Procedural recommendations outlined by Kumar et al. highlight the importance of adopting early comprehensive care in STEMI-CS.[22] Kumar et al. reported that a 4-component model was associated with increased guideline-based care, decreased time to intervention, reduced infarct size, and lower in-hospital mortality.[22] The benefit of protocolized care in AMI-CS is echoed by recommendations from the American Heart Association.[3] In addition to CS protocols, models of current care are moving toward CS centers, networks, and multidisciplinary teams in order to coordinate the best timely management.[5] Clearly ongoing challenges in AMI-CS care include minimizing time losses and identifying a standard time measure.

End organ dysfunction and serum biomarkers, namely acute kidney injury, elevated creatinine, increased lactate, and elevated glucose, were identified as predictors of mortality. Acute kidney injury was significant in 4 out of 4 cohorts, highlighting the impact of this complication in CS with end-organ ischemia.[2] Our findings support previous studies into CS of various etiologies, which found that acute renal impairment predicted mortality.[5] Our review also affirms the use of initial serum creatinine in the AMI-CS mortality risk scores, IABP-SHOCK II, and ENCOURAGE.[5] As such these straightforward and readily obtained biomarkers should be maintained in scoring systems going forward.

With respect to cardiovascular sequelae mechanical complications predicted mortality[30] and not requiring mechanical ventilation predicted survival.[9,11,16] Cardiac arrest was also associated with mortality; however, analysis was limited by studies using different variables, including ventricular fibrillation, cardiopulmonary resuscitation, in-hospital arrest, and out-of-hospital arrest.[10,11,20,30,31] Included among these are successfully resuscitated out-of-hospital arrests, and their outcomes are naturally complicated by hypoxic ischemic brain injury.[3] However, separate data and analysis of these patients was not provided. These findings, while not surprising, highlight the need for identification of early demographic, biochemical, and clinical predictors prior to the development of overt cardiovascular sequelae.

Analysis of circulatory supports was limited mainly to intraaortic balloon pump, which showed mixed survival and mortality signals.[9,11,14,16,19,20,33] The mixed results align with past studies and explain the current class two recommendations for balloon pumps in international guidelines.[2] Other circulatory supports were not well represented. Extracorporeal membrane oxygenation[15] and Impella[16] were each only analyzed in one study. In these studies, circulatory support was reserved for sicker patients[15] and involved a small number of patients,[16] limiting the ability to draw meaningful conclusions. Randomized control trials evaluating the prognostic utility of newer mechanical circulatory support systems are urgently required.

Regarding demographic variables, the most widely analyzed factor was age, which was studied in twenty cohorts. In half of these studies,

advanced age independently predicted mortality. Although age is common to many risk scores, based on the findings of this review, age should continue to be coupled with other variables in AMI-CS cohorts, to improve baseline risk assessment as well as aid clinical decision making and prognostication.[4]

Study Limitations

There are several limitations. This study was not a metaanalysis, owing in part to the fact that randomized trials in CS have been historically difficult to perform. This review is limited to observational and mostly retrospective studies, which cannot fully account for confounding and selection bias. The studies therefore have a high risk of bias. Further, studies lack comprehensive inclusion and exclusion criteria, engendering diverse study populations. Additionally, the studies have clinical and methodological diversity, owing to differences in criteria, treatment strategies, definitions for CS, and definitions for variables. A solution exists in part by adopting a standard classification such as that provided by the Society for Cardiovascular Angiography and Interventions.[1]

The heterogeneity of studies in this review precluded meaningful quantitative analysis and propagated uncertainty when comparing studies. Analysis was done using vote counting, which does not account for the relative sizes of studies.[7] Therefore, underpowered studies that do not rule out clinically important effects are considered nonsignificant.[7] Also, multiple significant predictors of mortality were supported only by 1 study. These findings are less robust as removing one of the studies changes the results.

Conclusion

In this systematic review, we present several factors that have been shown to portend a higher risk of mortality in STEMI-CS. Unsuccessful revascularization, reduced LVEF, and renal impairment stand out as 3 of the most significant predictors. This review is a step toward better patient prognostication and potentially better patient selection for advanced therapies. It is our intention that this body of work invites future studies to embrace a consistent set of definitions, variables, and outcomes, which will allow more meaningful quantitative analysis and future research.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajmo.2023.100057.

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