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Vasopressors independently associated with mortality in acute myocardial infarction and cardiogenic shock

Mir B. Basir
Henry Ford Health, mbasir1@hfhs.org

Alejandro Lemor
Henry Ford Health, ALemor1@hfhs.org

Sarah Gorgis
Henry Ford Health, SGORGIS1@hfhs.org

Angela M. Taylor

Behnam Tehrani

See next page for additional authors

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Authors

Mir B. Basir, Alejandro Lemor, Sarah Gorgis, Angela M. Taylor, Behnam Tehrani, Alexander G. Truesdell, Aditya Bharadwaj, Brian Kolski, Kirit Patel, Joseph Gelormini, Josh Todd, David Lasorda, Craig Smith, Robert Riley, Steve Marso, Robert Federici, Navin K. Kapur, and William W. O'Neill

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Vasopressors independently associated with mortality in acute myocardial infarction and cardiogenic shock

Mir B. Basir DO[1] | Alejandro Lemor MD[1] | Sarah Gorgis MD[1] | Angela M. Taylor MD[2] | Behnam Tehrani MD[3] | Alexander G. Truesdell[3] | Aditya Bharadwaj MD[4] | Brian Kolski MD[5] | Kirit Patel MD[6] | Joseph Gelormini MD[7] | Josh Todd MD[8] | David Lasorda MD[9] | Craig Smith MD[10] | Robert Riley MD[11] | Steve Marso MD[12] | Robert Federici MD[13] | Navin K. Kapur MD[14] | William W. O'Neill[1] | The National Cardiogenic Shock Initiative Investigators

[1]Cardiology, Henry Ford Health System, Detroit, MI, USA

[2]Cardiology, University of Virginia, Charlottesville, VA, USA

[3]Cardiology, Inova Heart and Vascular Institute, Fairfax, VA, USA

[4]Cardiology, Loma Linda University Medical Center, Loma LInda, VA, USA

[5]Cardiology, St. Joseph Hospital of Orange, Orange, CA, USA

[6]Cardiology, St. Joseph Mercy Oakland, Pontiac, MI, USA

[7]Cardiology, Mercy Hospital of Buffalo, Buffalo, NY, USA

[8]Cardiology, Fort Sanders Medical Center, Knoxville, TN, USA

[9]Cardiology, Allegheny General Hospital, Pittsburgh, PA, USA

[10]Cardiology, UMass Memorial Medical Center, Worcester, MA, USA

[11]Cardiology, Christ Hospital, Cincinnati, OH, USA

[12]Cardiology, Overland Park Regional Medical Center & Research Medical Center, Overland Park, KS, USA

[13]Cardiology, Presbyterian Hospital, Alburqurque, NM, USA

[14]Cardiology, Tufts Medical Center, Boston, MA, USA

Correspondence
Mir B. Basir, Director of Acute Mechanical Circulatory Support, Director of STEMI, K-2 Cardiac Catheterization Laboratory, Henry Ford Hospital, 2799 W. Grand Blvd. Detroit, MI 48202, USA.
Email: mbasir1@hfhs.org

Abstract

Background: Increasing vasopressor dose is associated with increasing mortality in patients presenting with acute myocardial infarction and cardiogenic shock (AMICS). It is unknown whether the use of vasopressors is independently harmful or if their use is secondary to decreasing intrinsic cardiac power output (CPO). Mechanical circulatory support (MCS) devices enhance CPO. We sought to evaluate the independent impact of increasing vasopressor dose on survival in the National Cardiogenic Shock Initiative (NCSI).

Methods: The NCSI is a single arm prospective trial evaluating outcomes associated with the use of MCS using Impella in patients with AMICS. Early initiation of MCS placement before percutaneous coronary intervention (PCI) and rapid de-escalation of vasopressors guided by systematic use of invasive hemodynamic measures led to 70% in-hospital survival for the first 300 patients enrolled from July 2016 to December 2019 in 57 U.S. sites.

Results: Hemodynamic measures were obtained immediately after MCS and PCI. Survival curves were constructed based on CPO and use of vasopressors. For patients with CPO ≤0.6 W, survival was 77.3%, 45.0%, and 35.3% when 0, 1, or ≥ 2 vasopressors were used ($p = 0.02$). Similarly, for patients with CPO >0.6 W survival was 81.7%, 72.6%, and 56.8%, respectively ($p = 0.01$). Logistic regression analysis demonstrated that increasing vasopressor requirements were independently associated with increasing mortality ($p = 0.02$).

Conclusion: Increasing vasopressor requirement is associated with increased mortality in AMICS independent of underlying CPO. Methods to decrease the need for vasopressors may enhance survival in AMICS.

KEYWORDS

acute myocardial infarction, cardiogenic shock, ECMO/IABP/Tandem/Impella, mechanical circulatory support, STEMI

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1 | INTRODUCTION

Vasopressors are frequently used to provide hemodynamic stabilization in patients presenting with acute myocardial infarction and cardiogenic shock (AMICS). These medications are routinely used to temporize circulatory collapse until definitive therapies can be provided. European and US guidelines provide a class IIb recommendation, evidence level C, for their use in AMICS.[1–3]

Vasopressors unfortunately have adverse effects and can increase left ventricular afterload thereby increasing myocardial oxygen demand, arrhythmia and infarct size.[4–6] The time-dependent effects of vasopressors have not been well studied. Observational studies have demonstrated that increasing doses of vasopressors are associated with increasing mortality in patients with AMICS.[7–9] A causal link to independent harm however is confounded by the fact that higher levels of vasopressors may be needed for decreasing intrinsic cardiac power output (CPO). Since mechanical circulatory support (MCS) devices enhance CPO, we sought to assess the impact of vasopressors on survival in the National Cardiogenic Shock Initiative (NCSI).

2 | METHODS

The National Cardiogenic Shock Initiative (ClinicalTrials.gov Identifier: NCT03677180) is a single-arm, prospective, multi-center study assessing outcomes associated with early MCS in patients presenting with AMICS treated with percutaneous coronary intervention (PCI). Eligible patients are those who develop AMICS and are treated with early revascularization with PCI. AMI is defined by electrocardiographic changes indicative of presumed new ischemia (ST-T changes), detection of elevated cardiac biomarkers or angiographic findings of an infarct related artery on coronary angiogram in the presence of ischemic symptoms. Cardiogenic shock must be present prior to PCI and is defined as the presence of at least two of the following[1]: prolonged hypotension (systolic blood pressure < 90 mm Hg, or use of vasopressors to maintain systolic blood pressure > 90 mmHg)[2] signs of end organ hypo-perfusion (cool extremities, oliguria or anuria, or an elevated lactate) or[3] hemodynamic criteria for shock (cardiac index <2.2 L/min/m^2 or cardiac power output <0.6 watts [W]). Operators are highly encouraged to follow the treatment algorithm and place MCS prior to PCI and use a pulmonary artery (PA) catheter to

TABLE 1 Demographics and admission characteristics

	All (N = 267)	0 (N = 98)	1 (N = 115)	≥2 (N = 54)	*p* value
Demographics					
Age (years) (SD)	63.7 (12.08)	61.4 (11.83)	64.7 (12.53)	65.9 (11.04)	0.05
Female	23% (62/267)	27% (26/98)	21% (24/115)	22% (12/54)	0.61
DM	40% (105/261)	43% (42/98)	35% (39/110)	45% (24/53)	0.39
CVA/TIA	10% (25/259)	8% (8/98)	9% (10/108)	13% (7/53)	0.60
CKD	11% (30/261)	13% (13/97)	11% (12/110)	9% (5/54)	0.72
ESRD	4% (10/264)	5% (5/98)	4% (4/112)	2% (1/54)	0.60
CHF	25% (63/248)	29% (28/95)	22% (23/103)	24% (12/50)	0.50
Prior MI	19% (49/259)	20% (19/96)	18% (20/110)	19% (10/53)	0.96
Prior PCI	24% (62/260)	24% (23/95)	23% (26/112)	25% (13/53)	0.98
Prior CABG	6% (15/264)	3% (3/97)	8% (9/113)	6% (3/54)	0.31
Admission characteristics					
Transferred	24% (63/267)	28% (27/98)	21% (24/115)	22% (12/54)	0.50
Support prior to transfer	20% (12/60)	23% (6/26)	21% (5/24)	10% (1/10)	0.67
Shock on admission	67% (177/265)	63% (62/98)	67% (77/115)	73% (38/52)	0.48
In-hospital arrest	30% (79/267)	26% (25/98)	30% (35/115)	35% (19/54)	0.91
Out of hospital arrest	19% (50/267)	16% (16/98)	20% (23/115)	20% (11/54)	0.91
Active CPR	9% (24/267)	6% (6/98)	10% (11/115)	13% (7/54)	0.35
Hypothermia	13% (31/240)	11% (10/92)	12% (12/99)	18% (9/49)	0.30

Abbreviations: CABG, coronary artery bypass grafting; CHF, congestive heart failure; CKD, chronic kidney disease; CPR, cardio-pulmonary resuscitation; CVA/TIA, cerebral vascular event/transient ischemic attack; DM, diabetes mellitus; ESRD, end stage renal disease; MI, myocardial infarction; PCI, percutaneous coronary intervention.

TABLE 2 Serial hemodynamic and laboratory variables

	All (N = 267)	0 (N = 98)	1 (N = 115)	≥2 (N = 54)	*p*-value
Worst shock					
HR	87.0 ± 30.0 (249)	90.8 ± 29.6 (90)	87.2 ± 31.8 (107)	79.9 ± 25.8 (52)	0.11
SBP	77.6 ± 17.9 (250)	80.8 ± 18.7 (90)	76.0 ± 18.1 (108)	75.2 ± 15.3 (52)	0.09
DBP	50.7 ± 14.5 (248)	52.9 ± 15.1 (90)	49.5 ± 14.8 (106)	49.6 ± 12.5 (52)	0.21
MAP	59.7 ± 14.7 (248)	62.3 ± 15.6 (90)	58.2 ± 14.8 (106)	58.6 ± 12.4 (52)	0.12
Pre-MCS					
HR	95.4 ± 32.0 (253)	98.8 ± 30.5 (89)	95.6 ± 34.6 (112)	89.3 ± 28.4 (52)	0.79
SBP	94.7 ± 26.1 (254)	99.0 ± 26.3 (90)	93.7 ± 26.5 (112)	89.4 ± 24.0 (52)	0.89
DBP	61.1 ± 19.8 (253)	64.7 ± 20.1 (90)	60.7 ± 19.3 (112)	55.5 ± 19.4 (51)	0.26
MAP	72.5 ± 21.3 (250)	76.3 ± 21.4 (89)	72.1 ± 21.1 (111)	66.7 ± 20.6 (50)	0.21
Creatinine	1.7 ± 1.6 (240)	1.8 ± 2.2 (88)	1.7 ± 1.4 (102)	1.3 ± 0.7 (50)	0.57
AST	176.9 ± 444.8 (139)	101.1 ± 95.3 (54)	178.6 ± 287.0 (54)	306.2 ± 849.1 (31)	0.57
Hgb	13.3 ± 2.5 (240)	13.5 ± 2.3 (87)	13.4 ± 2.6 (102)	12.8 ± 2.4 (51)	0.46
Lactate	5.4 ± 4.9 (161)	4.5 ± 3.9 (56)	5.2 ± 4.1 (67)	6.9 ± 7.0 (38)	0.46
PCWP	26.0 ± 9.9 (66)	28.7 ± 8.1 (30)	21.4 ± 11.1 (23)	27.7 ± 9.0 (13)	0.28
CO	3.9 ± 1.4 (72)	3.9 ± 1.6 (37)	3.8 ± 1.3 (22)	3.9 ± 1.1 (13)	0.50
CI	2.0 ± 0.7 (70)	2.0 ± 0.7 (36)	2.0 ± 0.6 (21)	2.1 ± 0.6 (13)	0.45
CPO	0.7 ± 0.3 (66)	0.7 ± 0.3 (34)	0.7 ± 0.3 (20)	0.6 ± 0.2 (12)	0.72
PAPI	2.2 ± 5.5 (64)	1.4 ± 0.7 (29)	2.5 ± 6.1 (21)	3.6 ± 9.0 (14)	0.72
LVEDP	32.3 ± 29.2 (132)	32.5 ± 10.4 (56)	27.1 ± 8.9 (51)	42.7 ± 63.7 (25)	0.15
PA Sat	56.3 ± 15.5 (55)	56.3 ± 11.6 (30)	56.1 ± 19.5 (14)	56.5 ± 20.4 (11)	0.18
RA	16.0 ± 6.9 (71)	15.2 ± 5.2 (31)	14.3 ± 4.8 (26)	21.0 ± 10.7 (14)	0.08
Post-MCS					
HR	94.1 ± 23.0 (260)	93.4 ± 24.0 (94)	94.7 ± 22.0 (114)	94.2 ± 23.6 (52)	0.64
SBP	114.8 ± 24.3 (256)	119.4 ± 23.6 (94)	114.4 ± 24.6 (112)	107.0 ± 23.5 (50)	0.39
DBP	79.2 ± 18.5 (256)	84.8 ± 17.0 (94)	77.8 ± 18.5 (112)	71.8 ± 18.5 (50)	0.27
MAP	91.2 ± 19.5 (260)	96.7 ± 18.5 (95)	90.1 ± 19.0 (114)	83.4 ± 19.6 (51)	0.41
PCWP	22.3 ± 9.1 (183)	21.2 ± 8.6 (60)	22.8 ± 9.4 (88)	22.6 ± 9.1 (35)	0.30
CO	4.3 ± 1.6 (204)	4.1 ± 1.5 (73)	4.5 ± 1.7 (91)	4.0 ± 1.6 (40)	0.33
CI	2.1 ± 0.8 (194)	2.1 ± 0.7 (69)	2.2 ± 0.8 (83)	2.1 ± 0.8 (42)	0.40
CPO	0.9 ± 0.4 (199)	0.9 ± 0.4 (70)	0.9 ± 0.4 (90)	0.7 ± 0.3 (39)	0.56
PAPI	1.7 ± 1.9 (194)	1.7 ± 1.1 (64)	1.8 ± 2.5 (89)	1.3 ± 1.0 (41)	0.71
PA Sat	60.1 ± 13.3 (128)	61.8 ± 10.9 (51)	60.5 ± 14.5 (48)	56.6 ± 14.9 (29)	0.28
RA	14.5 ± 6.2 (201)	12.9 ± 6.1 (66)	14.9 ± 5.9 (92)	15.8 ± 6.6 (43)	0.51
12 h					
HR	87.5 ± 18.5 (236)	89.0 ± 18.5 (91)	85.0 ± 18.9 (103)	90.4 ± 16.9 (42)	0.59
SBP	105.5 ± 19.6 (239)	107.2 ± 19.3 (92)	105.0 ± 20.1 (106)	102.9 ± 19.4 (41)	0.61
DBP	72.5 ± 13.5 (238)	75.5 ± 14.2 (91)	71.0 ± 12.9 (106)	69.8 ± 12.6 (41)	0.24
MAP	83.1 ± 14.3 (240)	85.7 ± 15.0 (91)	82.0 ± 14.1 (106)	80.4 ± 12.6 (43)	0.65
Creatinine	1.8 ± 1.5 (221)	1.7 ± 1.7 (87)	1.8 ± 1.4 (97)	1.7 ± 0.8 (37)	0.46
AST	742.5 ± 1313.0 (166)	559.7 ± 1241.2 (65)	792.4 ± 1159.0 (73)	1036.8 ± 1767.6 (28)	0.46
Hgb	11.4 ± 2.5 (222)	11.7 ± 2.4 (85)	11.4 ± 2.4 (97)	10.8 ± 2.8 (40)	0.34
Lactate	4.0 ± 4.0 (201)	2.9 ± 2.9 (79)	4.0 ± 4.0 (84)	6.3 ± 5.0 (38)	0.09
PCWP	17.8 ± 7.6 (52)	19.8 ± 9.4 (19)	17.6 ± 6.5 (24)	13.9 ± 3.8 (9)	0.40
CO	4.5 ± 1.7 (197)	4.5 ± 1.5 (76)	4.6 ± 1.8 (86)	4.4 ± 2.0 (35)	0.36

(Continues)

TABLE 2 (Continued)

	All (N = 267)	0 (N = 98)	1 (N = 115)	≥2 (N = 54)	*p*-value
CI	2.2 ± 0.8 (191)	2.3 ± 0.8 (73)	2.2 ± 0.7 (85)	2.3 ± 1.0 (33)	0.50
CPO	0.8 ± 0.3 (188)	0.9 ± 0.3 (71)	0.8 ± 0.4 (82)	0.8 ± 0.4 (35)	0.68
PAPI	1.8 ± 2.2 (172)	1.8 ± 0.8 (61)	2.1 ± 3.1 (77)	1.4 ± 1.0 (34)	0.48
PA Sat	60.9 ± 15.5 (81)	61.6 ± 12.2 (33)	60.0 ± 18.0 (30)	61.3 ± 17.2 (18)	0.48
RA	11.8 ± 5.1 (168)	11.4 ± 5.5 (66)	11.9 ± 5.0 (70)	12.2 ± 4.5 (32)	0.66
24 h					
HR	89.3 ± 19.5 (188)	93.0 ± 19.0 (73)	86.3 ± 20.0 (82)	88.5 ± 18.5 (33)	0.44
SBP	104.6 ± 18.5 (190)	106.5 ± 15.9 (73)	104.8 ± 20.4 (85)	99.7 ± 18.6 (32)	0.43
DBP	66.6 ± 12.3 (190)	69.8 ± 10.6 (73)	64.9 ± 12.1 (85)	63.7 ± 14.8 (32)	0.36
MAP	78.8 ± 12.7 (193)	81.8 ± 11.1 (74)	77.5 ± 13.1 (85)	75.3 ± 14.0 (34)	0.05
Creatinine	1.9 ± 2.0 (167)	1.6 ± 1.4 (57)	2.1 ± 2.4 (78)	2.0 ± 1.5 (32)	0.41
AST	821.8 ± 2078.5 (114)	811.9 ± 3252.1 (37)	817.1 ± 1243.1 (54)	848.6 ± 1077.3 (23)	0.41
Hgb	10.4 ± 1.9 (168)	10.6 ± 2.0 (59)	10.4 ± 1.8 (78)	9.8 ± 1.7 (31)	0.54
Lactate	2.8 ± 2.9 (151)	1.7 ± 1.7 (56)	3.2 ± 3.1 (64)	3.8 ± 3.6 (31)	0.22
PCWP	16.3 ± 7.0 (48)	16.2 ± 6.2 (17)	16.8 ± 7.4 (22)	15.1 ± 8.3 (9)	0.39
CO	5.1 ± 1.6 (157)	5.2 ± 1.4 (62)	5.2 ± 1.7 (69)	4.8 ± 2.0 (26)	0.48
CI	2.6 ± 0.8 (156)	2.7 ± 0.7 (61)	2.6 ± 0.8 (68)	2.4 ± 0.9 (27)	0.48
CPO	0.9 ± 0.3 (148)	0.9 ± 0.2 (56)	0.9 ± 0.3 (66)	0.8 ± 0.5 (26)	0.41
PAPI	1.9 ± 1.9 (139)	2.1 ± 1.6 (48)	1.9 ± 2.4 (65)	1.5 ± 1.1 (26)	0.49
PA Sat	62.6 ± 13.9 (58)	64.3 ± 9.3 (24)	62.6 ± 16.8 (21)	59.6 ± 16.3 (13)	0.34
RA	10.9 ± 4.4 (146)	10.2 ± 4.6 (56)	11.5 ± 4.7 (62)	10.9 ± 2.9 (28)	0.35

Abbreviations: CI, cardiac index (L/min/m^2); CO, cardiac output (L/min); CPO, cardiac power output (Watts); Creatinine (mg/dl) AST, aspartate aminotransferase (u/L); DBP, diastolic blood pressure (mmHg); Hgb, hemoglobin (g/dl); HR, heart rate (beats per minute); Lactate (mmol/L); MAP, mean arterial blood pressure (mmHg); PA Sat, pulmonary artery oxygen saturation; PAPI, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure (mmHg); RA, right atrial pressure (mmHg); SBP, systolic blood pressure (mmHg).

guide therapy. However, patients treated outside of these best practices are included if they meet all other inclusion and exclusion criteria listed below.

Between July 2016 and February 2019, 57 sites participated and enrolled patients into the study. Institutional review board approval was obtained at each of the participating sites. Consent was obtained from patients or health surrogates. Capturing of de-identified data was performed for patients who did not survive and would not require follow up, or if electronic follow up was expected, according to local IRB requirements. Participating centers agreed to treat the majority of patients with AMICS using a mutually agreed-upon shock algorithm. Inclusion criteria included patients who were greater than 18 years of age, presented with an AMI within 12 h of symptom onset, presented in cardiogenic shock prior to PCI and were treated with Impella. Exclusion criteria included patients treated with intra-aortic balloon pump as a first line MCS, patients treated with surgical revascularization, any unwitnessed cardiac arrest, any cardiac arrest in which return of spontaneous circulation did not occur within 30 minutes, concern for anoxic brain injury prior to PCI, mechanical complications of AMI, active bleeding, shock from an etiology other than AMICS, presence of a left ventricular thrombus, severe aortic stenosis or a mechanical aortic valve. AMICS comprises a heterogeneous cohort of patients, therefore these inclusion and exclusion criteria were included to limit patients who present in pre-shock as well as those with refractory shock associated with prolonged cardiac arrest. These patients were all considered to be in SCAI shock stages C-E. 300 patients met all inclusion and no exclusion criteria and were included in the analysis. Patients were classified according to the use of vasopressors after MCS and PCI.

Continuous variables were described using mean and standard deviation. Categorical variables were described with frequency and percentage. Student t test was used for continuous variables. Chi square test or Fisher's exact tests were used for categorical variables, as appropriate. All statistical tests and/or confidence intervals, as appropriate, were performed with a 2-sided p value = 0.05. Univariate and multivariate logistical regression models were used to assess the effect of vasopressors on hospital mortality. In the subset of patients with CPO and number of vasopressors used, logistical regression was performed to determine correlates with hospital mortality.

3 | RESULTS

A total of 300 patients were included in this analysis, of whom 267 had complete information regarding use of vasopressors and

TABLE 3 Procedural characteristics

	All (N = 267)	0 (N = 98)	1 (N = 115)	≥2 (N = 54)	*p*-value
Impella insertion					
Pre-PCI	70% (186/266)	73% (72/98)	68% (77/114)	69% (37/54)	0.86
Intra-procedural	21% (55/266)	19% (19/98)	22% (25/114)	20% (11/54)	
Post-PCI	9% (25/266)	7% (7/98)	11% (12/114)	11% (6/54)	
RHC insertion					
Pre-Impella	24% (64/263)	34% (33/97)	16% (18/112)	24% (13/54)	0.03
Post-Impella	67% (177/263)	56% (54/97)	77% (86/112)	69% (37/54)	
Not performed	8% (22/263)	10% (10/97)	7% (8/112)	7% (4/54)	
Initial MCS					
Impella 2.5	4% (12/267)	6% (6/98)	4% (5/115)	2% (1/54)	0.47
Impella CP	93% (249/267)	92% (90/98)	95% (109/115)	93% (50/54)	0.68
Impella RP	4% (10/267)	0% (0/98)	3% (4/115)	11% (6/54)	<0.01
Impella access					
Femoral	99% (263/265)	98% (95/97)	100% (115/115)	100% (53/53)	0.17
Axillary	1% (2/265)	2% (2/97)	0% (0/115)	0% (0/53)	
PCI					
STEMI	79% (212/267)	74% (73/98)	83% (95/115)	81% (44/54)	0.31
Thrombectomy	27% (71/265)	26% (25/97)	26% (30/115)	30%(16/53)	0.82
# stents	1.8 ± 1.16 (253)	1.8 ± 1.29 (94)	1.7 ± 1.06 (109)	1.9 ± 1.09 (50)	0.45
PCI access					
Radial	21% (55/267)	28% (27/98)	20% (23/115)	9% (5/54)	0.03
Femoral	78% (209/267)	71% (70/98)	78% (90/115)	91% (49/54)	0.02
Diseased vessels					
1 vessel	36% (94/262)	38% (36/95)	39% (44/114)	26% (14/53)	0.44
2 vessels	33% (87/262)	31% (29/95)	31% (35/114)	43% (23/53)	
3 vessels	31% (81/262)	32% (30/95)	31% (35/114)	30% (16/53)	
Vessels treated					
1 vessel	59% (158/266)	57% (56/98)	67% (76/114)	48% (26/54)	0.06
2 vessels	33% (89/266)	34% (33/98)	26% (30/114)	48% (26/54)	
3 vessels	7% (19/266)	9% (9/98)	7% (8/114)	4% (2/54)	
TIMI flow (pre)					
0	70% (178/253)	63% (58/92)	71% (80/112)	82% (40/49)	0.42
1	11% (28/253)	14% (13/92)	9% (10/112)	10% (5/49)	
2	11% (27/253)	13% (12/92)	12% (13/112)	4% (2/49)	
3	8% (19/253)	10% (9/92)	7% (8/112)	4% (2/49)	
TIMI flow (post)					
0	1% (3/260)	0% (0/94)	1% (1/114)	4% (2/52)	0.45
1	1% (3/260)	1% (1/94)	1% (1/114)	2% (1/52)	
2	5% (12/260)	3% (3/94)	4% (5/114)	8% (4/52)	
3	93% (241/260)	96% (90/94)	93% (106/114)	87% (45/52)	

cardiac power output. 98 patients (37%) were on 0 vasopressors after MCS and PCI; 115 patients (43%) were on 1 vasopressor; and 54 patients (20%) were on ≥2 vasopressors. Of those on vasopressors norephinephrine (48%), dopamine (19%), epinephrine (13%) were the most commonly used medications. Baseline demographics for the cohorts are given in Table 1; patients requiring vasopressors were older but other baseline characteristics were similar.

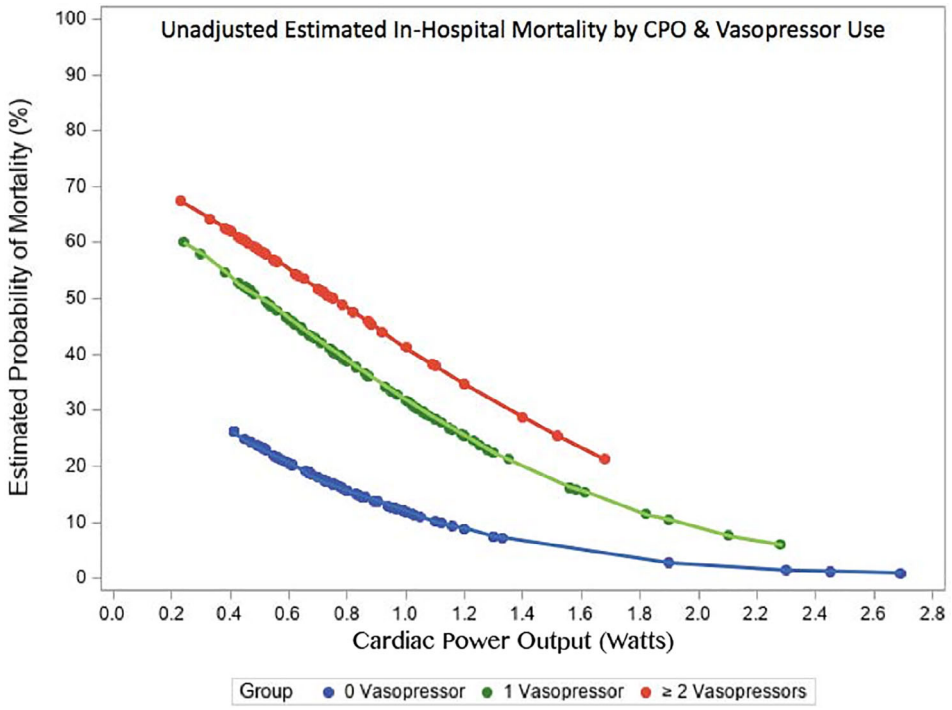

FIGURE 1 Unadjusted estimated in-hospital morality based upon cardiac power output (CPO) and vasopressor use [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 4 Outcomes of vasopressors and survival in AMICS

Survival	Odds ratio	95% CI	*p* value
Unadjusted			
No vasopressors	Reference	Reference	Reference
1 vasopressor	0.50	0.28–0.89	0.019
≥2 vasopressors	0.24	0.12–0.47	<0.001
Adjusted for post-PCI CPO, pre-PCI lactate, age, gender, past medical history			
No vasopressors	Reference	Reference	Reference
1 vasopressor	0.22	0.06–0.79	0.02
≥2 vasopressors	0.18	0.4–0.84	0.029

TABLE 5 Outcomes of vasopressors in various subgroups

	Number of vasopressors after PCI			0 versus 1		0 versus 2	
Survival	0	1	≥2	Odds ratio	*p* value	Odds ratio	*p* value
CPO after PCI ≤0.6	77.3%	45.0%	35.3%	0.24	0.04	0.16	0.01
CPO after PCI > 0.6	87.5%	68.6%	59.1%	0.31	0.01	0.21	0.01
Lactate <4	92.9%	65.7%	72.2%	0.39	0.09	0.54	0.35
Lactate ≥4	74.2%	56.3%	35.0%	0.45	0.14	0.19	0.01
Age < 65 years old	82.9%	83.3%	65.4%	1.03	0.95	0.39	0.07
Age ≥ 65 years old	78.2%	53.3%	35.7%	0.32	0.01	0.16	0.01

Overall, 67% of patients had shock on admission, 19% of patients presented with a witnessed out-of-hospital cardiac arrest with ROSC within 30 minutes, 30% had an in-hospital cardiac arrest with ROSC within 30 minutes, 9% were under active cardiopulmonary resuscitation while MCS was being implanted and 13% received therapeutic hypothermia; admission characteristics are given in Table 1.

Patients presented with a heart rate of 87.0 ± 30 bpm, poor hemodynamics (SBP 77.6 ± 17 mmHg) despite 83% of patients

receiving continuous infusion of vasopressors prior to MCS and PCI, and signs of tissue hypoperfusion and end-organ dysfunction (creatinine 1.7 ± 1.6 mg/dl, AST 176.9 ± 444.8 and lactate 5.4 ± 4.9 mg/dl). Serial hemodynamic measures were available for the following four intervals in the NCSI: pre-procedure, post-procedure, post-procedure at 12 and 24 h, and are given in Table 2.

The majority of patients presented with STEMI (79%). Patients were supported and revascularized promptly with a median door to support time of 79 (IQR 52–117) minutes and a median door to balloon time of 79 (IQR 54–117) minutes in STEMI. Angiographic success was achieved in the vast majority, with 93% of patients achieving thrombolysis in myocardial infarction (TIMI) III flow in the culprit vessel after PCI. In accordance with the algorithm, 70% of patients had implantation of MCS prior to PCI and right heart catheterization with hemodynamic monitoring was performed in 92% of patients. An Impella CP device was used in the majority of cases (93%). Procedural characteristics are given in Table 3.

Using invasive hemodynamics to calculate a cardiac power output and the number of vasopressors utilized immediately after MCS and PCI, a simple predictive model was developed (Figure 1). For patients with a CPO ≤0.6 W, survival was 77.3%, 45.0%, and 35.3% when 0, 1, or ≥ 2 vasopressors were used ($p = 0.02$). Similarly, for patients with CPO ≥0.6 W survival was 81.7%, 72.6%, and 56.8%, respectively ($p = 0.01$). Logistic regression analysis demonstrated that a higher number of vasopressors used was independently associated with an increase in mortality ($p = 0.02$), (Tables 4 and 5).

4 | DISCUSSION

Acute myocardial infarction complicated by cardiogenic shock (AMICS) is a common and deadly condition. European and US guidelines support the early use of vasopressors, however, little evidence exists regarding a survival benefit with the use of these agents. Vasopressors provide early hemodynamic stabilization by increasing blood pressure and cardiac output, however they also increase myocardial oxygen consumption.

Vasopressors have complex effects on multiple receptors to different degrees.[10] Alpha-adrenergic agents cause peripheral vasoconstriction and increased afterload, including increasing pulmonary venous resistance which can be particularly harmful in patient with right ventricular shock. Beta-adrenergic agents increase inotropy, chronotropy, cellular metabolism, and myocardial consumption. Dopaminergic agents lead to increase splanchnic and renal perfusion and with increasing dosing cause vasoconstriction and increased afterload. Each vasopressor has an individualized effect on the above receptors, therefore, dosing and utilization of specific agents is highly variable among clinicians.

In the largest randomized controlled trial evaluating outcomes of vasopressors in shock, dopamine was found to be associated with increased mortality when compared to norepinephrine in the prespecified cardiogenic shock subgroup.[4] Dopamine was associated with increased heart rate and more arrhythmic events. Levy et al compared norepinephrine and dobutamine to epinephrine in a small randomized pilot study in non-AMI cardiogenic shock.[5] They found that hemodynamic effects were similar but there were significantly higher lactate levels, increased tachycardia and arrhythmia, as well as decreased gastric perfusion with the use of epinephrine. In a separate study, Levy et al evaluated the use of epinephrine and norepinephrine in an AMI-CS population.[6] In this 57-patient randomized study use of epinephrine was associated with an increase in cardiac double product and increased lactate levels. Observational studies have also associated increasing use of vasopressors to increased mortality.[7–9] A causal link to independent harm however is confounded by the fact that higher levels of vasopressors may be needed for decreasing intrinsic CPO.

CPO is a value that is calculated by multiplying the mean arterial pressure and cardiac output then dividing by 451, a constant. CPO has been shown to be the strongest hemodynamic predictor of mortality in cardiogenic shock.[11,12] Finke et al demonstrated in the SHould we emergently revascularize Occluded Coronaries for cardiogenic shocK, ("SHOCK") trial, a CPO of 0.53 W was the most sensitive and specific value in predicting hospital mortality.[11] The NCSI provides a unique opportunity to evaluate outcomes of patients treated with MCS - which increases CPO independently. The main findings of our study are that increasing doses of vasopressors are associated with increased mortality in AMICS independent of CPO. More importantly, unlike prior observational work, this study takes into account the intrinsic CPO of patients and demonstrates independent harm.

5 | LIMITATIONS

The major limitation of this study is its observational design and therefore conclusions are hypothesis generating. In addition, despite the number of vasopressors required being a part of our dataset, the specific dose is unknown, hence is not known if one agent is used at moderate or maximum dose versus multiple agents at low doses. Also for the purposes of this manuscript inotropes such as dobutamine or milrinone, vasopressors such as vasopressin and neosynephrine and ino-pressors such as norepinephrine, dopamine and epinephrine were not differentiated. Lastly despite adjusting for post-PCI CPO, pre-PCI lactate, age, gender and past medical history it remains that's patients who required more vasopressors may have had larger myocardial infarcts resulting in more significant left ventricular damage and hemodynamic compromise that is unable to be fully adjusted for.

6 | CONCLUSIONS

Increasing requirements for vasopressors are associated with increasing mortality in AMICS irrespective of underlying CPO. Methods to decrease need for vasopressors may enhance survival in AMICS.

CONFLICT OF INTEREST

The NCSI is funded by unrestricted research grants from Abiomed and Chiesi Pharmaceuticals Inc. Neither company had direct involvement in the study design or the present analysis.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Mir B. Basir https://orcid.org/0000-0003-3486-6753
Behnam Tehrani https://orcid.org/0000-0002-8037-7021
Alexander G. Truesdell https://orcid.org/0000-0001-5656-4401
Robert Riley https://orcid.org/0000-0003-3467-1737
Navin K. Kapur https://orcid.org/0000-0002-8302-6796

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