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ORIGINAL STUDIES

Improved Outcomes Associated with the use of Shock Protocols: Updates from the National Cardiogenic Shock Initiative

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Abstract

Background: The National Cardiogenic Shock Initiative is a single-arm, prospective, multicenter study to assess outcomes associated with early mechanical circulatory support (MCS) in patients presenting with acute myocardial infarction and cardiogenic shock (AMICS) treated with percutaneous coronary intervention (PCI).

Methods: Between July 2016 and February 2019, 35 sites participated and enrolled into the study. All centers agreed to treat patients with AMICS using a standard protocol emphasizing invasive hemodynamic monitoring and rapid initiation of MCS. Inclusion and exclusion criteria mimicked those of the "SHOCK" trial with an additional exclusion criteria of intra-aortic balloon pump counter-pulsation prior to MCS.

Results: A total of 171 consecutive patients were enrolled. Patients had an average age of 63 years, 77% were male, and 68% were admitted with AMICS. About 83% of patients were on vasopressors or inotropes, 20% had a witnessed out of hospital cardiac arrest, 29% had in-hospital cardiac arrest, and 10% were under active cardiopulmonary resuscitation during MCS implantation. In accordance with the protocol, 74% of patients had MCS implanted prior to PCI. Right heart catheterization was performed in 92%. About 78% of patients presented with ST-elevation myocardial infarction with average door to support times of 85 ± 63 min and door to balloon times of 87 ± 58 min.

Survival to discharge was 72%. Creatinine ≥2, lactate >4, cardiac power output (CPO) <0.6 W, and age ≥ 70 years were predictors of mortality. Lactate and CPO measurements at 12–24 hr reliably predicted overall mortality postindex procedure.

Conclusion: In contemporary practice, use of a shock protocol emphasizing best practices is associated with improved outcomes.

KEYWORDS
ACS/NSTEMI, acute myocardial infarction/STEMI, ECMO/IABP/Tandem/Impella, heart failure, hemodynamics, mechanical circulatory support, shock, cardiogenic

1 | INTRODUCTION

Cardiogenic shock remains the most feared and deadly complication of an acute myocardial infarction. With decades of advancements in ST-elevation myocardial infarction (STEMI) systems of care there is now a <2% risk of death from STEMI in patients who present without cardiogenic shock.[1] In patients who develop cardiogenic shock, however, there remains a >40% mortality.[1] Frustratingly, there has been no significant advancement in survival in the past two decades. The "Should we emergently revascularize Occluded Coronaries for cardiogenic shocK (SHOCK)" trial published in 1999 was the last significant advancement in the field and cemented early revascularization as the cornerstone of therapy in acute myocardial infarction and cardiogenic shock (AMICS).[2] To safely intervene and provide revascularization clinicians often require mechanical circulatory support (MCS). Multiple trials have shown that intra-aortic balloon pump (IABP) counterpulsation provides insufficient support in AMICS to improve survival and therefore many clinicians have opted to use more robust MCS devices such as Impella (Abiomed, Danvers, MA), Tandem Heart (Cardiac Assist Inc, Pittsburgh, PA), and veno-arterial extracorporeal membrane oxygenation (VA-ECMO).[3–6]

In 2016, the Food and Drug Administration (FDA) approved Impella, a percutaneous microaxial MCS device, for use in patients with cardiogenic shock. The basis of Impella's FDA approval and increasing use in the United States has been significant improvements in hemodynamics when compared with IABP.[7] In 2016, after the FDA's approval of Impella for AMICS, investigators in Detroit began the "Detroit Cardiogenic Shock Initiative," a single-arm study evaluating hemodynamic changes and in-hospital survival with the implementation of the following best practices[1]: early identification and catheterization laboratory activation in AMICS[2]; early delivery of MCS (prior to percutaneous coronary intervention [PCI], prior to escalating inotropes, and as quickly from shock onset as possible, ideally within 90 min)[3]; and routine use of invasive hemodynamics and[4] limiting device-related complications. The results of the pilot study have been previously published.[8] The initiative has continued to grow and at present over 65 sites around the country are using the algorithm and best practices now referred to as the "National Cardiogenic Shock Initiative" (NCSI; ClinicalTrials.gov Identifier: NCT03677180). We sought to evaluate early predicators of outcomes in patients treated in the NCSI to improve upon the implemented best practices.

2 | METHODS

Eligible patients were those who developed an AMICS and underwent PCI. All patients received MCS with an Impella device. The diagnosis of AMI was confirmed 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 was defined as the presence of at least two of the following: (a) prolonged hypotension (systolic blood pressure [SBP] <90 mmHg, or inotropes/vasopressors to maintain SBP >90 mmHg), (b) signs of end organ hypoperfusion (cool extremities, oliguria or anuria, or elevated lactate levels), and (c) hemodynamic criteria represented by cardiac index <2.2 L/min/m^2 or cardiac power output (CPO) <0.6 W. Operators were highly encouraged to follow the treatment algorithm and place MCS prior to PCI.

Between July 2016 and February 2019, 35 sites participated and enrolled in the study. Institutional review board (IRB) approval was obtained at each of the participating sites. Consent was obtained from patients, patient surrogates, or capturing of deidentified data for patients who did not survive and would not require follow-up according to local IRB requirements. The centers agreed to treat all patients with AMICS using a similar, mutually agreed-upon, best practice algorithm. Inclusion and exclusion criteria mimicked those from the "SHOCK" trial with an additional exclusion of patients treated with an IABP. AMICS comprises a heterogeneous cohort of patients; therefore, these inclusion and exclusion criteria were included to limit those who present in preshock as well as those with refractory shock associated with prolonged cardiac arrest. About 171 patients met all inclusion and no exclusion criteria and were included in the analysis (Figure 1).

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Continuous variables were described using the mean and standard deviation. Categorical variables were described with the frequency

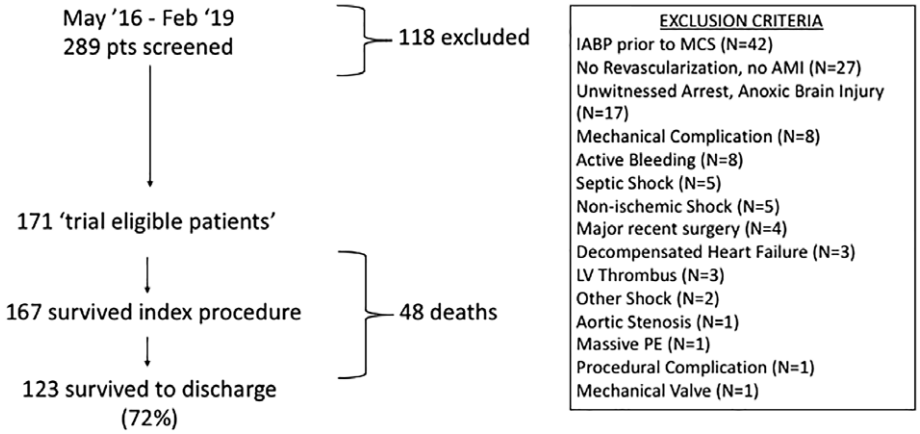

FIGURE 1 Enrollment and exclusion into the National Cardiogenic Shock Initiative. Abbreviations: AMI, acute myocardial infarction; IABP, intra-aortic balloon pump; LV, left ventricular; MCS, mechanical circulatory support; PE, Pulmonary Embolism

TABLE 1 Patient demographics and admission characteristics

	All (*N* = 171 patients)	Nonsurvivors (*N* = 48)	Survivors (*N* = 123)	*p* value
Demographics				
Age (years)	63.4 ± 12.4	68.5 ± 10.2	61.4 ± 12.6	<.01
Gender—Male (%)	77.2% (132)	68.8% (33)	80.5% (99)	.10
Diabetes mellitus	39.5% (66)	50.0% (23)	35.5% (43)	.18
Cerebrovascular disease	10.4% (17)	26.7% (12)	4.2% (5)	<.01
Renal insufficiency	15.7% (26)	22.2% (10)	13.2% (16)	.16
Dialysis	4.2% (7)	4.3% (2)	4.1% (5)	.95
Congestive heart failure	31.4% (50)	39.5% (17)	28.4% (33)	.18
Prior myocardial infarction	21.5% (35)	26.7% (12)	19.5% (23)	.32
Prior percutaneous coronary intervention	26.5% (43)	13.1% (14)	24.8% (29)	.41
Prior coronary artery bypass graft	6.6% (11)	11.1% (5)	5.0% (6)	.16
Admission characteristics				
Patient transferred from another hospital	27.1% (46)	12.8% (6)	32.5% (40)	<.01
Support prior to transfer	28.9% (13)	0.0% (0)	32.5% (13)	.13
Shock present on admission	67.5% (114)	69.6% (32)	66.7% (82)	.72
Out of hospital arrest	20.5% (35)	12.5% (6)	23.6% (29)	.60
In-hospital arrest	29.2% (50)	29.2% (14)	29.2% (36)	.60
CPR at the time of Impella insertion	9.9% (17)	8.3% (4)	10.6% (13)	.71
STEMI	77.6% (132)	78.7% (37)	77.2% (95)	.84

Abbreviations: CPR, Cardiopulmonary Resuscitation; STEMI, ST-elevation myocardial infarction.

and percentage. Student's *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 two-sided *p* value = .05. Univariate and multivariate logistical regression models were used to assess the effect of variables on hospital mortality. In the subset of patients with CPO or lactate data, logistical regression was performed to determine correlates with hospital mortality. In addition, ROC curves were performed on CPO and lactate for hospital mortality.

3 | RESULTS

A total of 289 patients were screened for inclusion of which 171 were included in this single arm, prospective, multicenter study (Figure 1). Patients had an average age of 63 ± 12 years, 77% were male, and 68% of patients were admitted to the hospital in cardiogenic shock; baseline demographics are listed in Table 1. About 83% of patients were on vasopressors or inotropes prior to or during the index procedure, 20% had witnessed out of hospital cardiac arrest with return of spontaneous circulation within 30 min, 29% had an in-hospital cardiac arrest, and 10% were under active cardiopulmonary resuscitation while MCS was being implanted; admission characteristics are listed in Table 1.

Patients were presented with elevated heart rates (88.3 ± 29.6 bpm), poor hemodynamics (SBP 78.6 ± 19.7 mmHg) despite continuous infusion of vasopressors and inotropes, signs of tissue hypoperfusion, and end-organ dysfunction (creatinine 1.8 ± 2.2 mg/dL and lactate 5.4 ± 4.4 mg/dL); complete hemodynamics are available for the following four intervals: preprocedure, immediately postprocedure, 12 hr postprocedure, and 24 hr postprocedure and are listed in Table 2.

The majority of patients presented with STEMI (78%). Patients were revascularized promptly with a mean door to balloon time of 87 ± 58 min in STEMI. Angiographic success was achieved in the vast majority with 90% of patients achieving thrombolysis in myocardial infarction III flow after PCI. In accordance to the algorithm, 74% of patients had implementation of MCS prior to PCI. Right heart catheterization and hemodynamic monitoring was performed in 92% of patients. An Impella CP device was used in the majority of cases (92%). Rapid door to support times was achieved and averaged 85 ± 63 min in STEMI; procedural characteristics are listed in Table 3.

Survivors had higher cardiac output (4.6 ± 1.8 vs. 3.8 ± 1.3 L/min; $p < .01$), cardiac index (2.3 ± 0.8 vs. 1.9 ± 0.6 L/min/m^2; $p = .03$), and pulmonary artery oxygen saturations (62.0 ± 11.5 vs. 53.8 ± 14.2%; $p = .02$) immediately postprocedure. Immediately post-MCS and revascularization, invasive hemodynamics were measured in 113 patients. Using a combination of CPO and the number of inotropes used, a simple predictive model was developed, see Figure 2.

About 12–24 hr after MCS, 51% of patients reduced the number of inotropes used, 25% remained on a similar number of inotropes, and 24% increased the number of inotropes used. Twelve hours postprocedure, survivors had higher cardiac output (4.8 ± 1.9 vs. 3.9 ± 1.6 L/min; $p = .03$), pulmonary artery oxygen saturations (60.5 ± 14.1 vs. 45.0 ± 21.5%; $p = .02$), mean arterial blood pressure (85.2 ± 16.0

TABLE 2 Hemodynamic trends within the first 24 hr

Hemodynamic variable	All (*N* = 171 patients)	Nonsurvivors (*N* = 48)	Survivors (*N* = 123)	*p* value
Preprocedure				
HR	88.3 ± 29.6 (155)	86.5 ± 31.6 (43)	89.0 ± 28.9 (112)	.64
SBP	78.6 ± 19.7 (156)	78.2 ± 20.6 (43)	78.7 ± 19.5 (113)	.88
DBP	50.3 ± 15.4 (156)	50.8 ± 15.5 (43)	50.1 ± 15.4 (113)	.81
MAP	59.5 ± 16.8 (156)	59.2 ± 17.6 (43)	59.6 ± 16.5 (113)	.90
AST	134.1 ± 193.7 (80)	194.9 ± 285.2 (20)	113.9 ± 149.5 (60)	.11
Cardiac output	4.0 ± 1.4 (60)	3.5 ± 1.0 (16)	4.1 ± 1.6 (44)	.15
CPO	0.7 ± 0.3 (58)	0.6 ± 0.2 (14)	0.7 ± 0.3 (44)	.08
PAPI	1.3 ± 0.8 (47)	1.1 ± 0.4 (11)	1.4 ± 0.9 (36)	.29
LVEDP	29.3 ± 9.8 (76)	31.1 ± 10.9 (21)	28.6 ± 9.4 (55)	.31
PA sat	55.9 ± 14.2 (28)	48.8 ± 15.4 (7)	58.3 ± 13.3 (21)	.13
Cardiac index	2.1 ± 0.7 (60)	1.9 ± 0.6 (15)	2.1 ± 0.7 (45)	.34
PCWP	26.7 ± 9.8 (53)	23.9 ± 8.1 (12)	27.5 ± 10.2 (41)	.26
Troponin	15.8 ± 71.4 (129)	43.4 ± 137.0 (33)	6.3 ± 14.1 (96)	<.01
Creatinine	1.8 ± 2.2 (151)	1.9 ± 1.7 (43)	1.8 ± 2.4 (108)	.72
Lactate	5.4 ± 4.4 (97)	6.5 ± 5.0 (32)	4.9 ± 4.1 (65)	.08
Hgb	13.1 ± 2.5 (155)	12.7 ± 2.7 (44)	13.3 ± 2.4 (111)	.22
Postprocedure				
HR	93.4 ± 22.9 (159)	98.3 ± 28.7 (43)	91.6 ± 20.1 (116)	.10
SBP	113.8 ± 25.5 (155)	113.8 ± 28.4 (41)	113.8 ± 24.6 (114)	.99
DBP	78.9 ± 20.0 (155)	80.3 ± 22.5 (41)	78.4 ± 19.1 (114)	.61
MAP	90.6 ± 21.0 (156)	91.4 ± 23.7 (42)	90.4 ± 20.0 (114)	.79
PCWP	22.4 ± 9.6 (109)	23.1 ± 9.2 (32)	22.1 ± 9.8 (77)	.65
Cardiac output	4.4 ± 1.7 (131)	3.8 ± 1.3 (38)	4.6 ± 1.8 (93)	<.01
Cardiac index	2.2 ± 0.8 (123)	1.9 ± 0.6 (33)	2.3 ± 0.8 (90)	.03
CPO	0.9 ± 0.4 (129)	0.7 ± 0.3 (37)	1.0 ± 0.5 (92)	<.01
PAPI	1.5 ± 1.0 (113)	1.3 ± 1.0 (32)	1.5 ± 1.0 (81)	.25
PA sat	59.1 ± 13.0 (*N* = 60)	53.8 ± 14.2 (*N* = 21)	62.0 ± 11.5 (*N* = 39)	.02
12 hr postprocedure				
HR	88.4 ± 18.0 (147)	93.8 ± 21.7 (36)	86.6 ± 16.4 (111)	.04
SBP	106.3 ± 20.8 (148)	98.5 ± 21.0 (36)	108.8 ± 20.2 (112)	<.01
DBP	73.3 ± 15.1 (148)	69.5 ± 13.3 (36)	74.6 ± 15.5 (112)	.08
MAP	83.5 ± 15.7 (149)	78.4 ± 13.8 (37)	85.2 ± 16.0 (112)	.02
Troponin	40 (13.4–75) (111)	40 (13.5–75) (25)	40 (13.4–75) (86)	.71
Creatinine	1.9 ± 2.0 (141)	2.2 ± 1.8 (35)	1.8 ± 2.1 (106)	.30
AST	350 (172–732) (107)	762 (243–1,394) (27)	293 (171–528) (80)	<.01
Hgb	11.4 ± 2.4 (142)	11.1 ± 2.4 (36)	11.5 ± 2.4 (106)	.38
Lactate	3.9 ± 4.1 (125)	7.0 ± 5.3 (34)	2.8 ± 2.7 (91)	<.01
PCWP	16.5 ± 7.8 (32)	18.3 ± 5.5 (7)	16.0 ± 8.4 (25)	.51
Cardiac output	4.6 ± 1.9 (123)	3.9 ± 1.6 (29)	4.8 ± 1.9 (94)	.03
Cardiac index	2.3 ± 0.8 (119)	2.0 ± 0.7 (29)	2.3 ± 0.8 (90)	.11
CPO	0.9 ± 0.4 (117)	0.7 ± 0.3 (29)	0.9 ± 0.4 (88)	<.01
PAPI	1.7 ± 1.1 (101)	1.4 ± 0.9 (25)	1.8 ± 1.1 (76)	.14
PA sat	56.8 ± 17.1 (38)	45.0 ± 21.5 (9)	60.5 ± 14.1 (29)	.02
24 hr postprocedure				
HR	89.9 ± 19.9 (113)	96.7 ± 25.4 (30)	87.4 ± 16.9 (83)	.03

(Continues)

TABLE 2 (Continued)

Hemodynamic variable	All (*N* = 171 patients)	Nonsurvivors (*N* = 48)	Survivors (*N* = 123)	*p* value
SBP	106.9 ± 20.1 (111)	99.2 ± 20.9 (30)	109.8 ± 19.1 (81)	.01
DBP	67.6 ± 12.0 (111)	65.8 ± 12.6 (30)	68.3 ± 11.7 (81)	.33
MAP	79.3 ± 13.6 (114)	76.5 ± 14.2 (31)	80.4 ± 13.3 (83)	.17
Troponin	43 (10.6–80) (71)	45 (14.9–75) (20)	43 (7.9–100) (51)	.81
Creatinine	2.0 ± 2.3 (101)	2.4 ± 1.5 (26)	1.9 ± 2.6 (75)	.35
AST	226 (121–571) (67)	755 (151–1,649) (18)	181 (113–301) (49)	<.01
Hgb	10.2 ± 1.9 (100)	9.4 ± 1.6 (28)	10.5 ± 1.9 (72)	<.01
Lactate	2.9 ± 3.0 (93)	4.6 ± 4.1 (29)	2.2 ± 2.1 (64)	<.01
PCWP	15.5 ± 6.4 (28)	19.3 ± 8.3 (10)	13.3 ± 4.0 (18)	.02
Cardiac output	5.2 ± 1.8 (88)	4.4 ± 1.3 (22)	5.5 ± 1.9 (66)	.02
Cardiac index	2.6 ± 0.8 (88)	2.3 ± 0.6 (22)	2.7 ± 0.9 (66)	.04
CPO	0.9 ± 0.3 (83)	0.7 ± 0.2 (20)	0.9 ± 0.3 (63)	<.01
PAPI	1.7 ± 2.2 (77)	2.2 ± 4.1 (19)	1.5 ± 0.9 (58)	.20
PA sat	59.7 ± 16.9 (33)	50.5 ± 25.6 (7)	62.2 ± 13.3 (26)	.11

Abbreviations: AST, aspartate aminotransferase; CPO, cardiac power output; DBP, diastolic blood pressure; Hgb, hemoglobin; HR, hear rate; LVEDP, left ventricular end diastolic pressure; MAP, mean arterial pressure; PA; pulmonary artery pressure; PAPI, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure.

vs. 78.4 ± 13.8 mmHg; p = .02), SBP (108.8 ± 20.2 vs. 98.5 ± 21 mmHg; p < .01), as well as lower heart rates (86.6 ± 16.4 vs. 93.8 ± 21.7 bpm; p = .04) and hepatic enzymes (aspartate aminotransferase [AST] 293 [171–528] vs. 762 [243–1,394] U/L; p < .01). Similarly, 24 hr postprocedure survivors had higher cardiac output (5.5 ± 1.9 vs. 4.4 ± 1.3 L/min; p = .02), cardiac index (2.7 ± 0.9 vs. 2.3 ± 0.6 L/min/m^2; p = .04), hemoglobin (10.5 ± 1.9 vs. 9.4 ± 1.6; p < .01), SBP (109.8 ± 19.1 vs. 99.2 ± 20.9 mmHg; p = .01), as well as lower heart rates (87.4 ± 16.9 vs. 96.7 ± 25.4 mmHg; p = .03) and hepatic enzymes (AST 181 [113–301] vs. 755 [151–1,649] U/L; p < .01).

CPO was higher in survivors postprocedure (1.0 ± 0.5 vs. 0.7 ± 0.3 W; p < .01), at 12 hr (0.9 ± 0.4 vs. 0.7 ± 0.3 W; p < .01) and at 24 hr (0.9 ± 0.3 vs. 0.7 ± 0.2 W; p < .01). Lactate was lower in survivors at 12 hr (2.8 ± 2.7 vs. 7.0 ± 5.3 mg/dL; p < .01) and at 24 hr (2.2 ± 2.1 vs. 4.6 ± 4.1 mg/dL; p < .01). Nonsurvivors had a numerically higher admission lactate when compared with survivors (6.5 ± 5.0 vs. 4.9 ± 4.1 mg/dL; p = .08). More importantly nonsurvivors had a plateau or increase in lactate levels within the first 12–24 hr, whereas survivors had a 55% reduction of their baseline lactate at 24 hr. Both lactate and CPO were independent predicators of survival (Figure 3; Table 4). Lactate ≥4 mg/dL demonstrated a 44% sensitivity and 89% specificity for predicting mortality. A CPO ≤0.6 (irrespective of the use of inotropes) demonstrated a 38% sensitivity and 88% specificity for predicting mortality. The combination of lactate <4 mg/dL and CPO >0.6 W at 12–24 hr was associated with a high likelihood of survival (Survival 95% vs. 50%; p < .01); see Figure 4.

Complications included seven reported cases of ischemic limb requiring intervention (such as removal of MCS, percutaneous or operative intervention). Four cases reported the need for percutaneous intervention. Five cases reported the need for surgical intervention including one case of compartment syndrome. Twelve cases of major bleeding requiring transfusion including one case of fatal access site bleeding, four cases of access site bleeding requiring removal of MCS, and one case of retroperitoneal hematoma. Two cases of thrombus on the Impella inlet cannula requiring removal or replacement of MCS were also reported. Major complications are well documented in the NCSI, however, it is important to note that other complications are less often captured and likely under-reported given limitations of the study design.

Fifteen patients required escalation of MCS and were subsequently transferred or evaluated for durable left ventricular assist device (LVAD) or transplant. Three patient had an Impella RP placed in conjunction with an Impella CP (Bipella) with two of three patients surviving to discharge. Five patients had escalation with VA-ECMO in conjunction with Impella (ECPella) with three of five patients surviving to discharge.[10] Two patients had escalation to VA-ECMO with no patients surviving to discharge. One patient was escalated to an Impella 5.0 and survived to discharge. One patient had escalation to temporary surgical LVAD and survived to discharge. Lastly, one patient underwent treatment with durable LVAD and survived to discharge.

In the above cohort, 72% of patients survived to discharge. Survival was high across a variety of subgroups including those with active CPR at the time of MCS, in and out of hospital cardiac arrest, multivessel coronary artery disease, and those with left main coronary artery disease. Overall adherence to the protocol was high and mortality rates were lower than previous trials, see Figure 5 and Table 5.

4 | DISCUSSION

There has been a rapid growth in the use of percutaneous MCS over the past decade. Stretch et al. reported a 1,511% increase in the use of such devices between 2007 and 2011.[9] Despite the increasing use of MCS, there has been an unfortunate void in common practice

TABLE 3 Procedural characteristics

Characteristics	All (*N* = 171 patients)	Nonsurvivors (*N* = 48)	Survivors (*N* = 123)	*p* value
Impella insertion				
Pre-PCI	74.0% (125)	78.7% (37)	72.1% (88)	.67
Intraprocedural	7.1 (12)	6.4% (3)	7.4% (9)	
Post-PCI	18.9% (32)	14.9% (7)	20.5% (25)	
RHC insertion				
Pre-Impella	29.8% (50)	29.8% (14)	29.8% (36)	.99
Post-Impella	61.9% (104)	61.7% (29)	62.0 (75)	
RHC not performed	8.3% (14)	8.5% (4)	8.3% (10)	
Initial device used				
Impella 2.5	6.4% (11)	8.3% (4)	5.6% (7)	.32
Impella CP	91.8% (157)	91.7 (44)	91.8% (113)	
Impella RP	1.8% (3)	0.0% (0)	2.4% (3)	
Impella access				
Femoral	97.6% (165)	100% (46)	96.7% (119)	.58
Axillary	2.4% (4)	0.0% (0)	3.3% (4)	
PCI access				
Radial	19.9% (34)	18.8% (9)	20.3% (25)	.82
Femoral	80.1% (137)	81.3% (39)	79.7% (98)	
Thrombectomy used	30.8% (52)	30.4% (14)	30.9% (38)	.95
Atherectomy used	7.2% (12)	10.9% (5)	5.8% (7)	.31
Culprit vessel (*n* = 104 culprit vessels)				
Left Main	12.5% (13)	(4)	(9)	.76
Left anterior descending	45.2% (47)	(14)	(33)	.76
Left circumflex	13.4% (14)	(2)	(12)	.35
Right coronary artery	26.9% (28)	(8)	(20)	.95
Ramus	1.9% (2)	(0)	(2)	.99
Number of diseased vessels (>70% stenosis)				.96
1 vessel	38.3% (64)	38.3% (18)	38.3% (46)	
2 vessels	30.5% (51)	31.9% (15)	30.0% (36)	
3 vessels	31.1% (52)	29.8% (14)	31.7% (38)	
Number of vessels treated				
1 vessel treated	62.1% (105)	61.7% (29)	62.3% (76)	.96
2 vessels treated	30.8% (52)	31.9% (15)	30.3% (37)	
3 vessels treated	7.1% (12)	6.4% (3)	7.4% (9)	
Number of stents placed[a]	1.7 ± 1.2	1.8 ± 1.1	1.6 ± 1.2	.20
Door to balloon time in STEMI (min)[a]	87.1 ± 57.8	94.2 ± 71.6	84.15 ± 51.3	.80
Door to support time in STEMI (min)[a]	85.4 ± 63.21	92.3 ± 70.6	83.0 ± 60.7	.40
TIMI flow pre PCI				.07
0	71.7% (114)	75.0% (33)	70.4% (81)	
1	10.7% (17)	9.1% (4)	11.3% (13)	
2	7.5% (12)	13.6% (6)	5.2% (6)	
3	10.1% (16)	2.3% (1)	13.0% (15)	
TIMI flow post PCI				.05
0	1.2% (2)	4.3% (2)	0.0% (0)	
1	1.8% (3)	4.3% (2)	0.8% (1)	
2	6.7% (11)	4.3% (2)	7.6% (9)	
3	90.2% (148)	87.0% (40)	91.5% (108)	

Abbreviations: PCI, percutaneous coronary intervention; RHC, right heart catheterization; STEMI, ST-elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

[a]*SD* included.

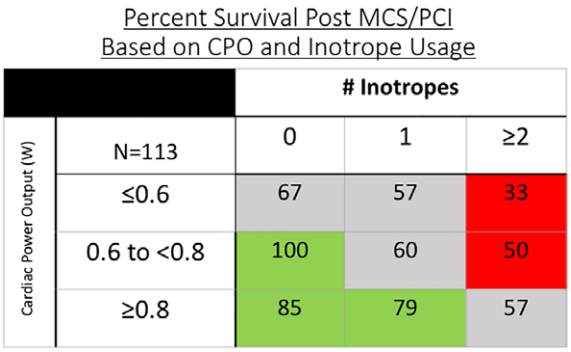

FIGURE 2 In hospital survival as it relates to CPO and the use of inotropes immediately post mechanical circulatory support and revascularization. Abbreviations: CPO, cardiac power output; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention [Color figure can be viewed at wileyonlinelibrary.com]

patterns, which has resulted in tremendous variability in the use of MCS in AMICS.[10] We have previously identified that delivery of MCS prior to PCI, prior to escalating doses of inotropes and within 1.25 hr from the onset of shock are associated with improved survival.[11] Similarly, data from over 15,000 patients treated with Impella have shown that the use of invasive hemodynamics (i.e., right heart catheterization) and institutional volume is similarly associated with improved survival.[10] Using these best practices, investigators organized the construct of a shock protocol and team who mutually agreed to treat patients according to the aforementioned best practices.

The investigators of the NCSI represent the largest working group studying the effects of MCS in AMICS in the Unites States. The current analysis includes the first 171 patients enrolled in the NCSI including 41 patients from the Detroit pilot study. In this analysis, we have demonstrated that a protocol-based approach emphasizing "best practices" is reproducible in institutions outside of Detroit and across academic and community programs. Furthermore, we have demonstrated that overall adherence to the protocol is associated with improved outcomes.

TABLE 4 Predictors of clinical outcomes

Univariate analysis		
Variable	**Univariate OR (95% CI)**	***p* value**
Age ≥70 vs. <70	2.41 (1.21–4.80)	.013
SBP ≥75 vs. <75	0.73 (0.18–3.00)	.67
Lactate >4 vs. <4	6.90 (2.97–16.03)	<.001
CPO <0.6 vs. >0.6	3.79 (1.55–9.24)	.004
TIMI 3 flow post-PCI	0.62 (0.21–1.81)	.38
TIMI 0 flow pre-PCI	1.26 (0.57–2.78)	.57
Creatinine >2 vs. <2	3.75 (1.67–8.42)	.001
PAPI >0.9 vs. <0.9	0.60 (0.22–1.61)	.31
Sites w/ >10 enrolled patients	1.22 (0.63–2.38)	.56
Multivariate analysis		
Variable	**aOR (95% CI)**	***p* value**
Age <70 vs. ≥70	0.5 (0.151–1.658)	.26
Lactate ≥4 vs. <4	7.246 (2.241–23.436)	<.001
CPO <0.6 vs. ≥ 0.6	8.275 (2.184–31.350)	.002
Creatinine ≥2 vs. <2	6.726 (1.685–26.840)	.007

Abbreviations: aOR, Adjusted odds ratio; CPO, cardiac power output; OR, odds ratio; SBP, systolic blood pressure; TIMI, thrombolysis in myocardial infarction.

Overall survival using a protocol-based approach to treat AMICS with MCS resulted in numerically higher survival when compared with previously reported studies[1–5,7,9–15]; see Table 5. This was in lieu of comparable blood pressures, rates of cardiac arrest, and lactate levels. MCS has not been shown to improve survival in previous studies; however, these devices are used inconsistently among clinicians and used in a heterogeneous cohort of patients.[3,5,7,13–15] In the absence of data from randomized control trials (RCT), the present analysis represents the highest survival reported in AMICS albeit with the limitations of an observational single arm study. Therefore, in lieu of evidence from RCT, the authors believe it is reasonable for centers that have adopted MCS as a treatment in AMICS to implement the

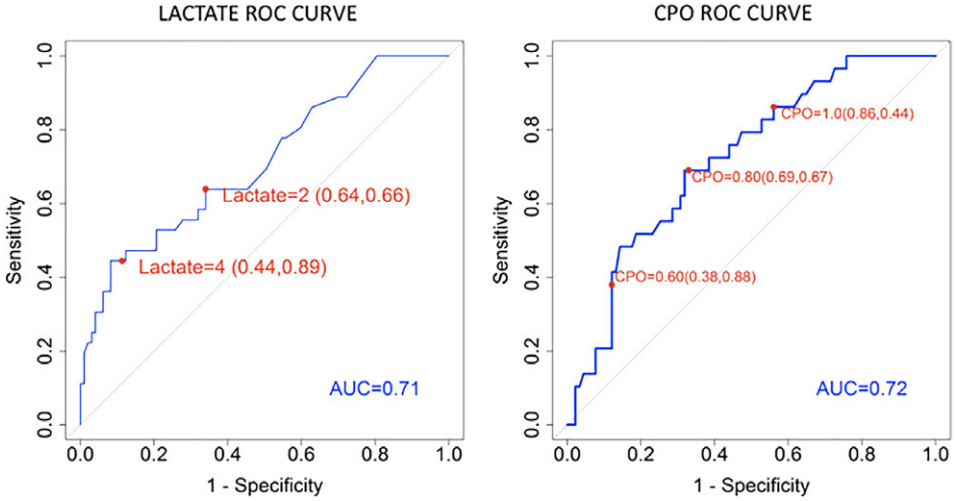

FIGURE 3 About 12–24 hr lactate and cardiac power output ROC curves. Variable (sensitivity, specificity): lactate 4 (0.44, 0.89), lactate 2 (0.64, 0.66), CPO 0.60 (0.38, 0.88), CPO 0.80 (0.69, 0.67), CPO 1.0 (0.86, 0.44). Abbreviations: AUC, area under the curve; CPO, cardiac power output; ROC, receiver operating characteristics [Color figure can be viewed at wileyonlinelibrary.com]

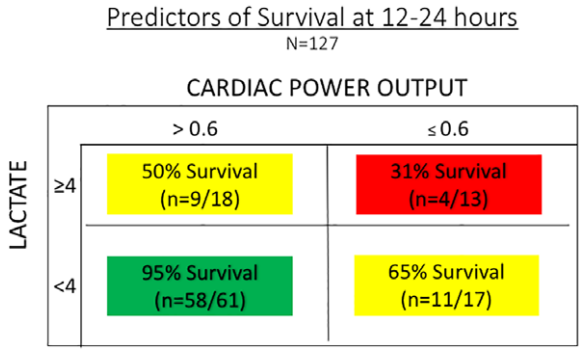

FIGURE 4 In hospital survival as it relates to lactate and CPO at 12 to 24 hr postprocedure. Abbreviation: CPO, cardiac power output [Color figure can be viewed at wileyonlinelibrary.com]

best practices emphasized in the NCSI and develop local protocols and teams in an effort to improve care of these critical ill patients.

The main objective of the present analysis was to identify important clinical and hemodynamic variables to assist clinicians who have adopted the above best practices. CPO, cardiac output, cardiac index, pulmonary artery oxygen saturation, PAPI, hepatic enzymes, and lactate have been found to be useful predicators for survival. Stratifying patients according to CPO (> or <0.6 W) and lactate (> or <4 mg/dL) provides a reliable and useful tool in predicting outcomes; see Figure 4. Patients who had a CPO > 0.6 W along with a lactate <4 md/dL within 12–24 hr of their procedure had a 95% overall survival. In such an example, the aforementioned variables direct clinicians to remain aggressive in their care, focus on limiting device related complications and provide optimism to patients and their families. Contrary to the above example a patient who had a CPO <0.6 W and a lactate >4 mg/dL has a 30% predicted survival and warrants evaluation for escalation of MCS, consideration of transfer to a LVAD and transplant center or if not a candidate for either of the aforementioned therapies cautious care with consideration for palliative measures in the event of continued hemodynamic decline.

CPO is a simple calculation using the mean arterial pressure and multiplying it by the cardiac output and dividing by a constant of 451. CPO has been shown to be the strongest hemodynamic predictor of mortality in the shock trial.[16–18] It was demonstrated that a CPO of 0.53 W was the most accurate value in predicting hospital mortality. In the above analysis, we corroborate those findings in patients who are treated with early MCS. CPO is superior to SBP measurements in AMICS. SBP can be raised with use of high-dose inotropes but at the expense of marked increase in peripheral resistance. In addition, in the presence of inotropes, augmented diastolic pressure with IABP makes it appear that blood pressure is maintained when in fact no increase in forward cardiac output occurs.[19,20] It is important to note that inotropes though needed to support patients early in their course of shock result in increasing myocardial oxygen demand at a time when the myocardium oxygen consumption is at its highest. In the above analysis, an improvement in CPO with MCS and PCI is achieved while reducing doses of inotropes therefore possibly leading to less myocardial injury; see Table 6. We have found that the combination of increase cardiac power with lowered lactate levels is the best predictor of survival. This pattern demonstrates that cardiac work is sufficient to provide end organ and peripheral perfusion.

As the use of MCS in AMICS increases, there are significant challenges in predicting outcomes in these complex patients. In the above analysis, we have identified a useful and predictive model to guide clinical decision making. Most importantly, the NCSI is a starting point for sites around the country to help identify key components in the

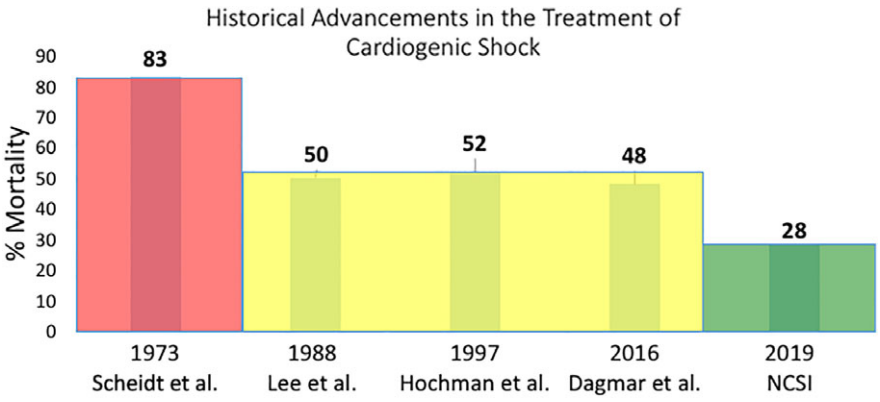

FIGURE 5 Timeline depicting the mortality associated with acute myocardial infarction and cardiogenic shock over the past five decades. Abbreviation: NCSI, National Cardiogenic Shock Initiative [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 5 Trials in AMICS to date

	Sample size	Age	Inotropes	HR	BP	Lactate	Lactate >2 mmol/L	Survival
SHOCK	302	66	99	102	89/54	N/A	N/A	53
IABP SHOCK	600	70	90	92	90/55	4.1	74%	60
Culprit SHOCK	686	70	90	91	100/60	5.1	66%	49
NCSI	171	63	83	89	79/51	5.3	77%	72

Abbreviations: AMICS, acute myocardial infarction and cardiogenic shock; BP, blood pressure; HR, heart rate; IABP, intra-aortic balloon pump; NCSI, National Cardiogenic Shock Initiative.

TABLE 6 Hemodynamic trends within the first 24 hr

	Pre-MCS	Post-MCS	12 hr	24 hr
HR (bpm)	88	93	88	89
SBP (mmHg)	79	114	106	107
DBP (mmHg)	50	79	73	67
LVEDP (mmHg)	29 (n = 76)	—	—	—
dPA (mmHg)	25 (n = 53)	23 (n = 133)	20 (n = 91)	19 (n = 76)
% on inotropes	70 (n = 95)	65 (n = 93)	64 (n = 84)	60 (n = 61)
Lactate (mg/dL)	5.4 (n = 97)	—	3.9 (n = 125)	2.6 (n = 88)
CPO (W)	0.7 (n = 58)	0.9 (n = 129)	0.9 (n = 117)	0.93 (n = 83)

Abbreviations: CPO, cardiac power output; HR, heart rate; MCS, mechanical circulatory support; SBP, systolic blood pressure.

TABLE 7 NCSI report card

Best practice	Metric achieved to date
MCS pre-PCI	74%
Door to support <90 min	85 ± 63 min
Achieve TIMI 3 flow	90%
RHC usage	92%
Maintain CPO >0.6 W	62%
Survival to discharge	72%

Abbreviations: CPO, cardiac power output; MCS, mechanical circulatory support; NCSI, National Cardiogenic Shock Initiative; PCI, percutaneous coronary intervention; RHC, right heart catheterization; TIMI, thrombolysis in myocardial infarction.

establishment of local and regional shock care models, see Table 7. With a 50% mortality for the past two decades, it behooves use as a medical community to focus our efforts in improving the quality of care we provide patients with AMICS. Establishing shock teams and protocols are a logical step to achieving this goal.

5 | LIMITATIONS

The major limitation of this study is that it is a single-arm study in which all patients received MCS, therefore the improved observed survival may be due to selection bias, MCS, improvement in the overall delivery of care, a combination of the above, or by chance.

6 | CONCLUSIONS

The NCSI is a single-arm multicenter study evaluating the use of early MCS in patients who present with AMICS who are treated with PCI. In the above analysis, we have demonstrated that a protocol-based approach emphasizing "best practices" is reproducible in institutions across the country in both academic and community programs. We have also demonstrated that lactate and CPO measured at 12–24 hr postprocedure are predictive of overall outcomes and can help guide clinical decisions early in the course of these critically ill patients. Further studies are needed to demonstrate which patients gain the most benefit from MCS and escalation of support.

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