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# Mechanical circulatory support following out-of-hospital cardiac arrest: Insights from the National Cardiogenic Shock Initiative

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ABSTRACT

*Background:* Evidence is limited regarding the role of mechanical circulatory support (MCS) in patients with acute coronary syndromes (ACS) complicated by cardiogenic shock (CGS). In particular, the role of MCS in patients with out-of-hospital cardiac arrest (OHCA) is unknown.
*Methods:* The National Cardiogenic Shock Initiative (NCSI) is a multicenter United States registry of patients with ACS complicated by CGS treated with MCS. We compared the rate of survival to hospital discharge among patients with OHCA, in-hospital cardiac arrest (IHCA), or no cardiac arrest. We subsequently used multivariable analyses to determine independent predictors of OHCA survival.
*Results:* Survival to hospital discharge occurred in 85.7% (42/49) of OHCA, 72.4% (50/69) of IHCA, and 74.5% (111/149) of non-cardiac arrest patients. By multivariable analysis, pre-procedural predictors of survival included younger age, female sex, fewer diseased vessels, left anterior descending coronary artery culprit, lower troponin, higher lactate, and delayed initiation of MCS. Procedural and post-procedural predictors of survival included fewer vessels treated, complete revascularization, higher post-MCS cardiac power output, and fewer inotropic medications required.
*Conclusions:* This study demonstrates that excellent outcomes may be achieved following OHCA when MCS is employed for patients appropriately selected by prognostic demographic, anatomic, and health status characteristics. A larger study population, currently being enrolled, is needed to validate the observation further.


## 1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a devastating event associated with poor outcomes. Non-traumatic OHCA is estimated to affect 347,322 adults per year in the United States with a dismal rate of only 11.4% survival to hospital discharge [1]. Coronary artery disease (CAD) is strongly associated with OHCA, with CAD present in >70% of patients resuscitated from OHCA [2]. Data from the Parisian Region Out of hospital Cardiac ArresT (PROCAT) Registry suggest that early angiography and percutaneous coronary intervention (PCI) improve survival in OHCA, irrespective of the presence of ST elevation on electrocardiogram (ECG) [3,4]. The 2015 American Heart Association guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care include a Class I (level of evidence [LOE] B non-randomized [NR]) recommendation to perform emergent coronary angiography for patients with OHCA of suspected cardiac etiology and ST elevation on ECG; for patients without ST elevation on ECG, emergent coronary angiography is reasonable in select electrically or hemodynamically unstable patients, even if they are comatose (class IIa, LOE B-NR) [5].

The National Cardiogenic Shock Initiative (NCSI) is a multicenter study of patients presenting with acute coronary syndrome (ACS) complicated by cardiogenic shock (CGS). Per the single-arm NCSI protocol, patients are treated with early initiation of mechanical circulatory

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support (MCS) with the Impella device (Abiomed, Danvers, MA) as well as PCI. Interim results from 171 patients demonstrated 72% survival to discharge [6], a significant improvement over the historical survival rate of 40% reported by the PROCAT Registry [3].

However, no study to date has examined the effect of MCS on OHCA survival. Therefore, we undertook to study OHCA survival in the subset of patients enrolled in NCSI who presented with OHCA. An understanding of the efficacy of MCS following OHCA and predictors of survival will allow for optimal use of MCS in strategies to maximize OHCA survival.

## 2. Methods

The NCSI protocol has been previously published [7]. Briefly, NCSI enrolls patients with ACS, defined as non-ST-elevation myocardial infarction (NSTEMI) or STEMI, and CGS, defined as the presence of at least two of the following: hypotension (systolic blood pressure ≤ 90 mmHg, or inotropes/vasopressors to maintain systolic blood pressure ≥ 90 mmHg), signs of end organ hypoperfusion (cool extremities, oliguria or anuria, or elevated lactate levels), or hemodynamic criteria (cardiac index of <2.2 L/min/m$^2$ or a cardiac power output ≤0.6 W). Data collected include demographics, admission characteristics, timings from presentation and shock to support and intracoronary balloon inflation, coronary artery disease anatomy, hemodynamics, medications, and survival.

We identified the cohort of NCSI patients who presented with OHCA, defined as the absence of a palpable pulse. For enrollment of OHCA patients, NCSI study criteria included witnessed arrest, <30 min of total cardiopulmonary resuscitation (CPR), and no clinical evidence of anoxic brain injury (seizure, posturing) upon initial presentation prior to MCS or PCI.

As a primary outcome, we determined the rate of survival to discharge of OHCA patients treated per the NCSI protocol. We then compared this survival rate with in-hospital CA (IHCA, principally patients who presented with ACS with CGS and arrested in the emergency department, in transport, or in the catheterization laboratory prior to PCI) as well as with non-OHCA NCSI patients. As a secondary outcome, we determined and quantified the variables that independently predicted increased OHCA survival in patients treated with MCS using multivariable analyses.

## 3. Results

Among patients enrolled in NCSI, 49 had OHCA, and 85.7% of these (42/49) survived to discharge. By contrast, among the 69 patients that had IHCA (whether or not they also had OHCA), the rate of survival to discharge was 72.5% (50/69) (Fig. 1). Of the 149 patients with no cardiac arrest, the rate of survival to discharge was 74.5% (111/149). Society for Cardiovascular Angiography and Interventions (SCAI) Shock Stage [8] at the time of PCI was highest for the IHCA group, intermediate for the OHCA group, and lowest for the group without cardiac arrest (Table 1), although some SCAI Shock Stage data were missing, particularly in the group without cardiac arrest.

Due to the emergent nature of OHCA, patient presentation data were limited. Data on bystander cardiopulmonary resuscitation (CPR) were available for 32/49 patients: 23/32 received bystander CPR (survival to discharge 20/23), and 9 did not receive bystander CPR (survival to discharge 8/9). Data on presenting EKG were available for 39/49 patients: 21/39 had documented ST-segment elevations, and 31/39 had documented ventricular tachycardia or fibrillation. Interhospital transfers accounted for 9/49 OHCA patients, with 8/9 surviving to discharge. Therapeutic hypothermia was administered in 19/49 patients: survival to discharge was 14/19 with hypothermia and 18/20 without hypothermia.

By multivariable analysis, pre-MCS/PCI predictors of OHCA survival included younger age, female sex, fewer diseased vessels, left anterior descending (LAD) culprit, lower troponin, and higher lactate (Fig. 2).

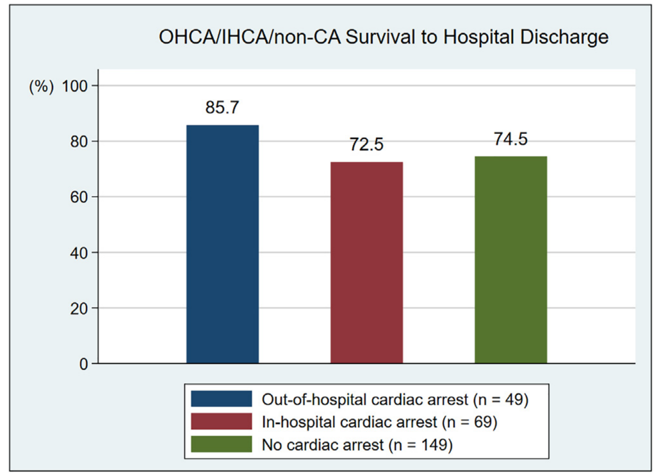


**Fig. 1.** Rates of survival to hospital discharge for NCSI patients with OHCA, IHCA, and no cardiac arrest.

Average patient age was 65.4 years and 55.9 years among non-survivors and survivors, respectively, and survival rate was higher among women (90.0%) than men (84.6%) (panels (A)–(C)). For diseased vessels, 85.7% of non-survivors and 61.9% of survivors had more than one diseased vessel (panel (D)). The culprit lesion was in the LAD in 19.0% percent of the survivors but none of the non-survivors. Pre-Impella troponin (1.17 vs. 2.21 ng/dL) and pre-Impella lactate (5.14 vs. 7.28 mmol/L) level were higher among survivors compared to non-survivors (panels (E)–(G)).

By multivariable analysis, survivors had delayed MCS and PCI compared to non-survivors (Fig. 3). Average times for door to support (92.2 ± 77.4 vs. 166.9 ± 369.8 min), onset of shock to support (107.6 ± 73.0 vs. 230.6 ± 467.8 min), and door to balloon (92.8 ± 70.0 vs. 182.0 ± 369.8 min) were higher among the survivors compared to the non-survivors. In addition, the variations in these times (measured in standard deviations) were greater among the survivors than among the non-survivors for all three measurements.

MCS/PCI predictors of survival included fewer vessels treated, complete revascularization, higher post-Impella cardiac power output (CPO), and few inotropes (Fig. 4). Compared to non-survivors, survivors were less likely to have more than one treated vessel (42.8% vs. 38.1%), while they were more likely to have complete revascularization (66.7% vs. 75.0%) (panels (A)–(B)). The post-Impella CPO was 0.67 W among non-survivors while 0.97 W among survivors (panel (C)). The average number of post-Impella vasopressors/inotropes (i.e., total number of norepinephrine, epinephrine, vasopressin, dobutamine, milrinone, phenylephrine, and other vasopressors/inotropes) was lower among the survivors (1.14 vs. 0.55).

Notably, at the present stage of on-going NCSI data collection, the sample size remains small, so many of these preliminary results were not statistically significant by a $p < 0.05$ threshold.

**Table 1**
SCAI Shock Stages at the time of PCI for OHCA, IHCA, and no cardiac arrest cohorts. Due to rounding, percentages may not add up to 100%.

| | | SCAI Shock Stage at PCI | | | n (%) of total cohort with SCAI Shock Data available |
|---|---|---|---|---|---|
| | | C | D | E | |
| OHCA | n (%) | 27 (59%) | 0 (0%) | 19 (41%) | 46/49 (94%) |
| IHCA | n (%) | 23 (37%) | 4 (6%) | 35 (56%) | 62/69 (90%) |
| No cardiac arrest | n (%) | 18 (78%) | 2 (9%) | 3 (13%) | 23/149 (15%) |

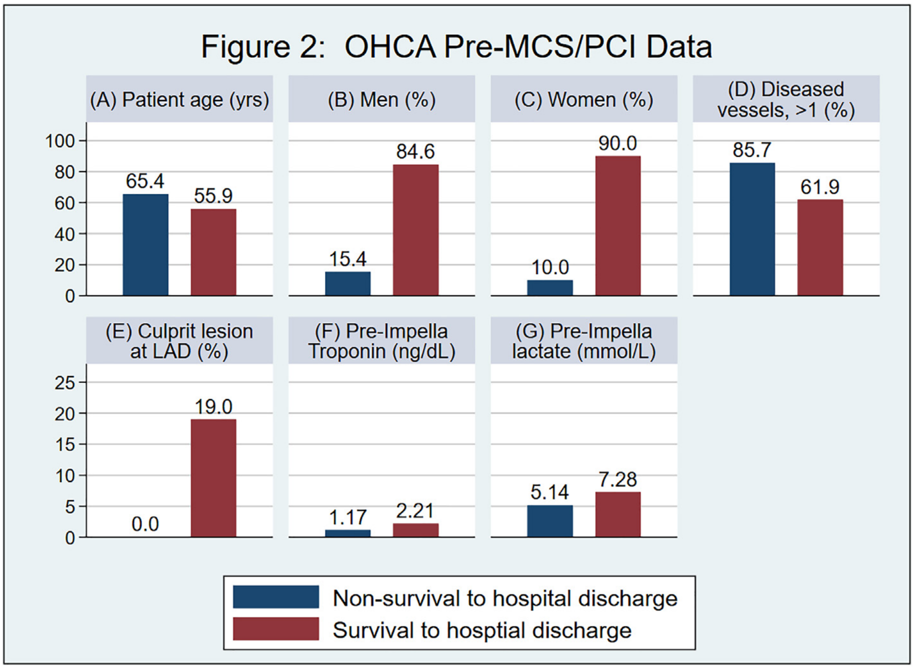


**Fig. 2.** Pre-MCS/PCI predictors of OHCA survival included younger age, female sex, fewer diseased vessels, left anterior descending (LAD) culprit, lower troponin, and higher lactate.

## 4. Discussion

In our study of 49 NCSI patients presenting with OHCA, we report a high rate of 85.7% survival to discharge. While this high survival rate may not be generalizable to all OHCA patients, the key implication of the study is that, within a population of patients with CGS treated with MCS, excellent outcomes can be achieved in an appropriately selected subset of OHCA patients. Among these patients, utilization of MCS within a streamlined, protocolized approach to CGS may contribute to survival.

First, OHCA patients were more likely to survive to discharge than IHCA patients. The fact that enrolled OHCA patients had survived long enough to reach a hospital and undergo MCS and PCI selects for a survival-prone population within the population of all OHCA victims. Conversely, enrolled IHCA patients may be sicker and more prone not to survive, but they reach the catheterization laboratory and are enrolled simply because they were in the hospital when their arrests occurred. Consistent with this explanation, the SCAI Shock Stage at the time of PCI was indeed highest for the IHCA group, intermediate for the OHCA group, and lowest for the group without cardiac arrest, although statistical significance was not achieved.

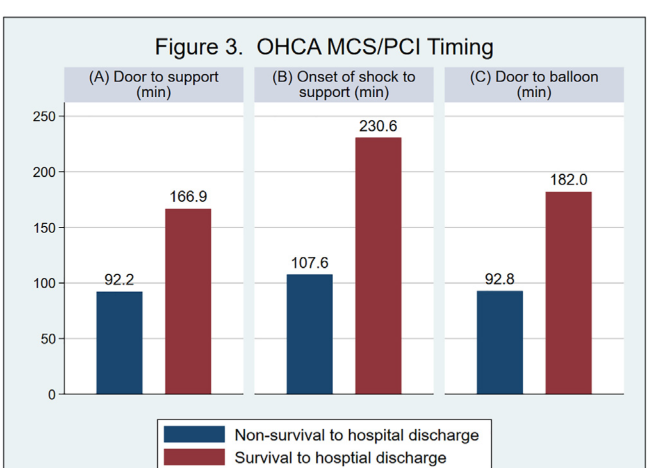


**Fig. 3.** Survivors actually had delayed MCS and PCI compared to non-survivors.

Not surprisingly, we found that OHCA patients with better baseline health were more likely to survive. Younger age, fewer diseased vessels, and lower troponin were associated with survival. An LAD culprit for ACS with CGS may also be prognostically favorable: because the LAD typically supplies around 50% of the myocardium, an LAD lesion alone can cause CGS, whereas a patient with CGS and a non-LAD culprit is likely to have other significant coronary disease, allowing a non-LAD culprit to cause CGS. The interpretation of a slightly higher initial lactate in survivors could relate to more acute shock in these patients from sudden occlusion of a single major coronary artery as opposed to better compensated shock in patients with diffuse, multi-vessel disease. Acute dysfunction of an otherwise healthy heart may be easier to reverse than more insidious pathology, and the relative contributions of reperfusion and MCS to survival cannot be separated in this study.

Counterintuitively, we observed that door to support, shock to support, and door to balloon times were higher among survivors than non-survivors. The finding of greater survival despite delayed care suggests an underlying propensity of these patients to survive, perhaps related to their younger age, fewer disease vessels, and lower troponin levels. This highlights the critical importance of research to define precisely the population of CGS and OHCA patients likely to benefit from MCS. That survivors received slower care than non-survivors emphasizes that patient selection may be the important predictor of survival. Of note, this observation runs contrary to a pre-MCS era study of patients with witnessed arrest that reported 74% survival if first defibrillation was administered within 3 min and 49% survival if defibrillation was first administered after more than 3 min [9].

Post-procedurally, we again found that OHCA patients with better health status were more likely to survive. Complete revascularization in conjunction with fewer vessels treated, higher CPO, and fewer vasopressors/inotropes were associated with increased survival.

Despite the evidence and guidelines, rates of coronary angiography and subsequent PCI in OHCA patients are low. Among the 407,974

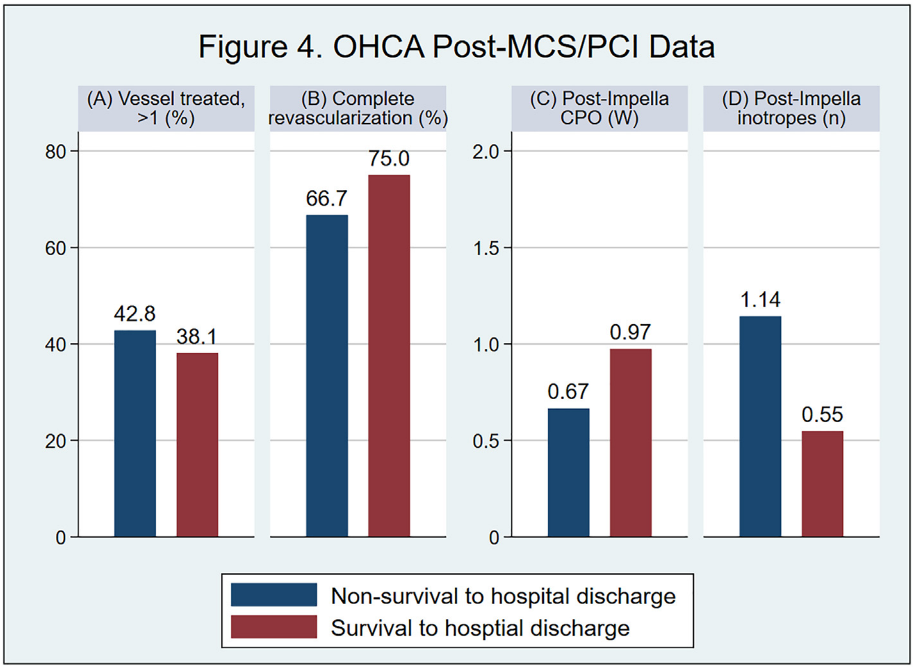


**Fig. 4.** MCS/PCI predictors of survival included fewer vessels treated, complete revascularization, higher post-Impella cardiac power output, and few inotropes.

patients in the Nationwide Inpatient Sample (NIS) hospitalized with out-of-hospital ventricular tachycardia or fibrillation from 2000 to 2012, only 35% underwent coronary angiography [10]. This rate is extremely low given that a culprit vessel may be identified in 80.2% of patients with STEMI but also in 33.2% of patients without ST-segment elevation [11]. The current study suggests that coronary angiography, MCS, and PCI may be associated with increased OHCA survival when applied to appropriately selected patients. Again, patient selection is critical: The Coronary Angiography after Cardiac Arrest (COACT) study of 552 patients without ST-segment elevation found no difference in survival between patients undergoing early or delayed angiography [12]. The Cardiac Arrest Hospital Prognosis (CAHP) score identifies the likelihood of survival to discharge based upon presentation characteristics: age, shockable rhythm, time from collapse to CPR, time from CPR to return of spontaneous circulation, location of cardiac arrest, epinephrine dose, and arterial pH [13]. Now, our work has identified additional prognostically-valuable demographic, anatomic, and health status characteristics associated with such patients who may benefit from MCS and are more likely to survive to discharge.

More broadly, the in-hospital mortality rate associated with acute MI complicated by cardiogenic shock has remained unchanged for 3 decades despite significant advances in cardiovascular care. In 1988, early in the era of emergent coronary angioplasty, Lee et al. reported 50% mortality at 30 days following acute MI complicated by cardiogenic shock treated with coronary angioplasty [14]. In 1999, in a similar patient population, the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial showed a similar 30-day mortality of 46.7% for patients treated with revascularization (angioplasty or bypass surgery) and 56.0% for patients treated medically ($p = 0.11$). As recently as 2016, Ouweneel found a similar 30-day mortality rate of 46% in patients treated with MCS following PCI [15]. Therefore, the NCSI paradigm of immediate MCS, with its initial report of only 28% in-hospital mortality [6], has the potential to save thousands of lives if applied to the appropriate patients. Within the population of CGS patients, OHCA patients may derive particular benefit from immediate MCS given their propensity to delays in care. This paradigm must be explored further in cardiac arrest patients as suggested by the present study.

## 5. Strengths and limitations

Studies of OHCA are notoriously difficult to conduct due to the challenges of obtaining informed consent and collecting data in an emergent setting. NCSI represents a paradigm shift in the management of such patients: the standard of care at participating institutions is benchmarked to the NCSI protocol, and consent from patients or family members must only be obtained after the fact to allow inclusion of protected health information in the NCSI registry. Thus, the present study represents one of the most extensive prospective analyses of OHCA patients treated with MCS to date.

However, the NCSI study population is still quite small. Therefore, many of these preliminary observations did not achieve statistical significance. NCSI data collection continues, and with expanded NCSI enrollment, these observations can be evaluated further.

Furthermore, due to the pace of emergent care for OHCA patients, data about patient history, bystander CPR, and pre-procedure laboratory and EKG findings could not always be collected reliably. These factors are major determinants of outcomes after OHCA. The present findings are therefore only hypothesis-generating regarding predictors of survival following OHCA treated with MCS and PCI and appropriate patient selection for these procedures. The International Liaison Committee on Resuscitation has recommended a detailed reporting template for OHCA, emphasizing documentation of bystander witnesses, dispatcher-assisted CPR, automated external defibrillators, and shockable rhythms [16]. For future studies, we have begun to develop an interdisciplinary partnership with our emergency services colleagues to implement this template for data collection, systematically recording data immediately in the hospital emergency department instead of performing retrospective reviews later in the hospital course.

Indeed, we fully acknowledge the major limitation of selection bias. However, in the context of OHCA, selection bias can be viewed conversely as guidance for appropriate selection of OHCA patients most likely to benefit from treatment with an NCSI-style protocol. Accordingly, the study results may not be generalizable to all OHCA patients. Furthermore, given the baseline characteristics of the OHCA survivors studied and the fact that all NCSI subjects were treated with MCS, the precise contribution of MCS to OHCA survival cannot be quantified.

## 6. Conclusion

This study is consistent with the hypothesis that, within a population of patients with CGS treated with MCS, excellent outcomes may be achieved even in those presenting with OHCA when appropriately selected by prognostic demographic, anatomic, and health status characteristics. A larger study population is needed to validate these observations.

## CRediT authorship contribution statement

**Andrew M. Goldsweig:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Supervision, Project administration. **Hyo Jung Tak:** Conceptualization, Methodology, Software, Formal analysis, Writing – original draft, Writing – review & editing. **M. Chadi Alraies:** Methodology, Investigation, Writing – review & editing. **James Park:** Methodology, Investigation, Writing – review & editing. **Craig Smith:** Methodology, Investigation, Writing – review & editing. **John Baker:** Methodology, Investigation, Writing – review & editing. **Lang Lin:** Methodology, Investigation, Writing – review & editing. **Nainesh Patel:** Methodology, Investigation, Writing – review & editing. **William W. O'Neill:** Conceptualization, Methodology, Investigation, Resources, Data curation, Writing – review & editing, Supervision, Project administration. **Mir B. Basir:** Conceptualization, Methodology, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Supervision, Project administration.

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