# Effect of Early Initiation of Mechanical Circulatory Support on Survival in Cardiogenic Shock

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**The role and timing of percutaneous mechanical circulatory support (MCS) devices in the treatment of acute myocardial infarction complicated by cardiogenic shock (AMICS) are not well understood. We sought to evaluate patient characteristics and predictors of outcomes in patients presenting with AMICS supported with an axial flow percutaneous MCS device; 287 consecutive unselected patients enrolled in the catheter-based ventricular assist device registry presenting with AMICS who underwent percutaneous coronary intervention (PCI) were included in this analysis. All patients were supported with either the Impella 2.5 or Impella CP. Mean patient age was 66 ± 12.5 years, 76% were men, and mean left ventricular ejection fraction was 25 ± 12%. Before receiving MCS, 80% of patients required inotropes or vasopressors and 40% were supported with intra-aortic balloon pump; 9% of patients were under active cardiopulmonary resuscitation at the time of MCS implantation. Survival to discharge was 44%. In a multivariate analysis, early implantation of a MCS device before PCI ($p = 0.04$) and before requiring inotropes and vasopressors ($p = 0.05$) was associated with increased survival. Survival was 66% when MCS was initiated <1.25 hours from shock onset, 37% when initiated within 1.25 to 4.25 hours, and 26% when initiated after 4.25 hours ($p = 0.017$). Survival was 68%, 46%, 35%, 35%, and 26% for patients requiring 0, 1, 2, 3, and ≥4 inotropes before MCS support, respectively ($p < 0.001$). In conclusion, MCS implantation early after shock onset, before initiation of inotropes or vasopressors and before PCI, is independently associated with improved survival in patients presenting with AMICS.** **© 2016 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2016;■:■−■)**

Novel percutaneous axial flow mechanical circulatory support (MCS) devices have been shown to safely and efficiently provide rapid and superior hemodynamic support compared with intra-aortic balloon pump (IABP) in patients who present with AMICS.[1] These devices reduce pulmonary capillary wedge pressure, increase coronary perfusion, and provide increase end-organ perfusion.[1−6] When used early, before percutaneous coronary intervention (PCI), MCS devices have been shown to allow for more complete revascularization and improve survival.[7] Currently, American and European societies give a class IIb recommendation for the use of MCS in patients presenting with AMICS.[8,9] The present study provides data on the use and clinical outcomes associated with using Impella devices (Abiomed, Danvers, Massachusetts) in AMICS. The analysis was conducted on real-world data from the global catheter-based ventricular assist device (cVAD) Registry and constitutes the largest cohort to date of such patients.

## Methods

The cVAD Registry is an on-going multicenter voluntary registry open to centers in the United States and Canada. The registry protocol was reviewed and approved by the Institutional Review Board at each participating site. Sites are invited to report all consecutive patients treated with Impella devices. To avoid patient selection bias, patients who were identified as having received an Impella device in the commercial database were expected to be reported in the cVAD Registry database; otherwise, sites were notified of the obligation to enter and report the cases to ensure consecutiveness. Data were abstracted retrospectively from the medical record to a standard electronic case report form by the sites' study coordinators. All patients reported in the registry who met the listed inclusion criteria of AMICS were included in the current analysis without pre-selection of patients or sites. An independent clinical event committee, consisting of 1 cardiovascular surgeon and 2 interventional cardiologists, adjudicated the in hospital study end points and their relatedness to the device (all-cause of death, re-infarction, stroke, repeat revascularization, renal insufficiency, and vascular complications requiring surgical repair) against prespecified standard definitions.

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See page 6 for disclosure information.

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Table 1
Patient demographics and baseline characteristics

| | All (N=287 patients) | Survivors (N=127 Patients) | Non-Survivors (N=160 Patients) | P-Value |
|---|---|---|---|---|
| Age* | 66 | 61 | 68 | <0.01 |
| Gender – Male (%) | 219/287 (76.3%) | 100/127 (78.8%) | 119/160 (74.4%) | 0.4 |
| Body Surface Area ($m^2$) | 274/287 (2.0±0.3) | 123/127 (2.0±0.3) | 151/160 (2.0±0.3) | 0.4 |
| Smoker | 129/263 (49.1%) | 64/122 (52.5%) | 65/141 (46.1%) | 0.3 |
| Hyperlipidemia† | 155/268 (57.8%) | 71/122 (58.2%) | 84/146 (57.5%) | 0.9 |
| Hypertension† | 194/273 (71.1%) | 85/125 (68.0%) | 109/148 (73.7%) | 0.3 |
| Diabetes Mellitus | 117/271 (43.2%) | 50/124 (40.3%) | 67/147 (45.6%) | 0.4 |
| Cerebrovascular Disease | 32/266 (12.0%) | 11/122 (9.0%) | 21/144 (14.6%) | 0.2 |
| Renal Insufficiency | 64/266 (24.0%) | 27/122 (22.1%) | 37/144 (25.7%) | 0.6 |
| Dialysis | 15/63 (23.8%) | 7/27 (25.9%) | 8/362 (2.2%) | 0.8 |
| Liver Insufficiency | 7/259 (2.7%) | 3/120 (2.5%) | 4/139 (2.9%) | 0.9 |
| Chronic Obstructive Pulmonary Disease | 45/265 (17.0%) | 23/123 (18.7%) | 22/142 (15.5%) | 0.5 |
| Peripheral Vascular Disease | 39/260 (15.0%) | 21/121 (17.4%) | 18/139 (13.0%) | 0.4 |
| Congestive Heart Failure | 44/245 (18.0%) | 20/113 (17.7%) | 24/132 (18.2%) | 0.9 |
| Prior Myocardial Infarction | 80/268 (29.9%) | 35/123 (28.5%) | 45/145 (31.0%) | 0.7 |
| Prior Percutaneous Coronary Intervention | 88/271 (32.5%) | 43/126 (34.1%) | 45/145 (31.0%) | 0.6 |
| Prior Coronary Artery Bypass Graft | 31/277 (11.2%) | 14/126 (11.1%) | 17/151 (11.3%) | 0.9 |

* Median.
† Defined as treated Hyperlipidemia, treated Hypertension.

Table 2
Hemodynamic and laboratory values

| Hemodynamics Prior to MCS | All (N=287 Patients) | Survivors (N=127 Patients) | Non-Survivors (N=160 Patients) | p Value |
|---|---|---|---|---|
| Heart Rate (beats per minute) | 92.6±33.0 (278) | 94.1±32.1 (126) | 91.3±33.8 (152) | 0.5 |
| Systolic Blood Pressure (mmHg) | 95.8±27.8 (276) | 97.9±23.7 (127) | 94.0±30.8 (149) | 0.2 |
| Diastolic Blood Pressure (mmHg) | 58.4±20.7 (275) | 61.2±17.8 (126) | 56.0±22.6 (149) | 0.04 |
| Mean Arterial Pressure (mmHg) | 71.6±21.8 (277) | 74.3±18.6 (127) | 69.4±24.0 (150) | 0.06 |
| Cardiac Index (L/min/$m^2$) | 2.1±0.8 (55) | 2.2±0.8 (28) | 2.1±0.8 (27) | 0.5 |
| Pulmonary Capillary Wedge Pressure (mmHg) | 29.5±10.0 (70) | 30.6±10.8 (33) | 28.5±9.2 (37) | 0.4 |
| Creatinine Kinase-MB (ng/mL) | 66.9±133.7 (123) | 44.4±107.4 (55) | 85.1±150.1 (68) | 0.08 |
| Troponin T (ng/mL) | 7.2±17.4 (59) | 4.8±6.9 (26) | 9.0±22.5 (33) | 0.3 |
| Troponin I (ng/mL) | 43.3±275.1 (147) | 69.2±417.5 (63) | 23.9±44.2 (84) | 0.4 |
| Total Bilirubin (mg/dL) | 1.2±3.4 (112) | 0.8±0.5 (49) | 1.5±4.5 (63) | 0.3 |
| Creatinine (mg/dL) | 1.7±1.3 (247) | 1.6±1.4 (112) | 1.8±1.3 (135) | 0.3 |
| Lactate (mg/dL) | 43.1±112.1 (38) | 51.2±120.5 (13) | 38.9±109.9 (25) | 0.8 |
| Aspartate Aminotransferase (U/L) | 193.3±340.8 (118) | 127.6±194.1 (54) | 248.7±421.0 (64) | 0.04 |
| Alanine Aminotransferase (U/L) | 121.5±252.4 (120) | 92.5±148.5 (55) | 146.0±313.9 (65) | 0.2 |

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 new or presumed new ischemia (new ST-T changes or new left bundle branch block), detection of elevated cardiac biomarkers, or angiographic findings of an infarct-related artery on coronary angiogram in a clinical setting of myocardial ischemia (symptoms of ischemia). Cardiogenic shock was defined based on clinical criteria including (1) hypotension (systolic blood pressure <90 mm Hg for 30 minutes before inotropes/vasopressors or inotropes/vasopressors or IABP required to maintain systolic blood pressure >90 mm Hg), (2) signs of end organ hypoperfusion (cool extremities, oliguria with urine output of <30 ml/h or anuria, and altered mental status), (3) tachycardia and/or hemodynamic criteria represented by cardiac index of <2.2 L/min/$m^2$ and pulmonary capillary wedge pressure of >15 mm Hg. Patients who received Impella support after the first 24 hours post-PCI were excluded from this analysis. Timing of Impella insertion (pre, during, or post PCI) was at the operating physician's discretion. From January 2009 to June 2014, 59 US sites participated in the cVAD Registry and a total of 287 consecutive unselected patients were reported in the cVAD Registry to have met the above inclusion criteria. The Impella 2.5 patients were those supported from its market introduction in 2008 through June 1, 2013, before the introduction of the Impella CP. The Impella CP supported patients were those who received the device from June 1, 2013, to June 30, 2014.

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Table 3
Admission, procedural, post-procedural characteristics

| Characteristics | All (N=287 Patients) | Survivors (N=127 Patients) | Non-Survivors (N=160 Patients) | P-Value |
|---|---|---|---|---|
| Patient transferred from another hospital | 123/286 (43.0%) | 54/126 (42.9%) | 69/160 (43.1%) | 0.9 |
| Shock present on admission | 170/280 (60.7%) | 66/124 (53.2%) | 104/156 (66.7%) | 0.03 |
| Intra-Aortic Balloon Pump prior to Impella support | 114/285 (40.0%) | 49/127 (38.6%) | 65/158 (41.1%) | 0.7 |
| Duration of shock (hours) | | | | |
| <6 | 142/258 (55.0%) | 59/110 (53.6%) | 83/148 (56.1%) | 0.7 |
| 6-12 | 33/258 (12.8%) | 14/110 (12.7%) | 19/148 (12.8%) | 0.9 |
| 12-24 | 28/258 (10.9%) | 12/110 (10.9%) | 16/148 (10.8%) | 0.9 |
| >24 | 55/258 (21.3%) | 25/110 (22.7%) | 30/148 (20.3%) | 0.6 |
| Patient experienced any of the following | | | | |
| Anoxic brain damage | 51/271 (18.8%) | 6/122 (4.9%) | 45/149 (30.2%) | <0.001 |
| End-organ hypoperfusion | 83/271 (30.6%) | 22/122 (18.0%) | 61/149 (40.9%) | <0.001 |
| Cardiac arrest | 153/284 (53.9%) | 42/126 (33.3%) | 111/158 (70.3%) | <0.001 |
| Cardiac arrest before admission for index procedure | 58/145 (40.0%) | 16/41 (39.0%) | 42/104 (40.4%) | 0.9 |
| Patient required any of the following | | | | |
| Mechanical Ventilation | 218/285 (76.5%) | 77/126 (61.1%) | 141/159 (88.7%) | <0.001 |
| Cardiopulmonary Resuscitation | 147/281 (52.3%) | 40/124 (32.3%) | 107/157 (68.2%) | <0.001 |
| Cardiopulmonary Resuscitation during Impella placement | 25/129 (19.4%) | 6/35 (17.1%) | 19/94 (20.2%) | 0.8 |
| Patient required inotrope or vasopressor prior to Impella support | 230/287 (80.1%) | 88/127 (69.3%) | 142/160 (88.8%) | <0.001 |
| If yes, maximum number of different agents used | 2.03±1.1 (230) | 1.88±1.0 (88) | 2.1±1.1 (142) | 0.1 |
| Ejection Fraction (%) | 25.3±12.7 (213) | 24.7±12.0 (100) | 25.8±13.3 (113) | 0.5 |
| STS Mortality Score | 21.6±17.1 (263) | 18.1±16.4 (117) | 24.4±17.2 (146) | 0.003 |
| STS Morbidity Score | 61.1±21.4 (263) | 56.3±22.4 (117) | 65.0±19.8 (146) | 0.001 |
| Intensive Care Unit length of stay (days) | 8.9±14.5 (237) | 13.6±19.1 (111) | 4.9±6.4 (126) | <0.001 |
| Duration of Index Hospitalization (days) | 11.8±20.0 (283) | 18.1±20.9 (127) | 6.6±17.7 (156) | <0.001 |
| Patients required Inotropes or vasopressors during support | 253/286 (88.5%) | 102/127 (80.3%) | 151/159 (95.0%) | <0.001 |
| Impella Pump Flow (L/min) | 2.4±0.5 (219) | 2.4±0.6 (105) | 2.4±0.5 (114) | 0.808 |
| Acute Myocardial Infarction | | | | |
| STEMI | 204/287 (71%) | 88/127 (69%) | 116/60 (73%) | 0.6 |
| NSTEMI | 83/287 (29%) | 39/127 (31%) | 44/160 (28%) | 0.6 |
| Number of diseased vessels (>50% stenosis) | 1.68±0.78 (276) | 1.67±0.79 (121) | 1.70±0.77 (142) | 0.8 |
| Number of Vessels Treated | 1.38±0.66 (276) | 1.37±0.66 (121) | 1.39±0.67 (142) | 0.9 |
| Patients with 1 vessel treated | 56% | 58% | 54% | 0.6 |
| Patients with 2 vessels treated | 34% | 32% | 35% | 0.6 |
| Patients with 3 vessels treated | 5% | 5% | 5% | 1.0 |
| Patients with 100% stenosis in at least one lesion prior to PCI | 179/276 (65%) | 80/121 (66%) | 99/155 (64%) | 0.7 |
| Number of stents placed | 1.79±0.95 (262) | 1.72±0.85 (119) | 1.84±1.03 (143) | 0.3 |
| Door to Baloon Time (hours) in STEMI* | 1.35 | 1.40 | 1.32 | 0.8 |
| Onset of cardiogenic shock to Impella implantation (hours)* | 2.24 | 1.29 | 2.75 | 0.03 |
| Onset of acute myocardial infarction to Impella implantation (hours)* | 2.32 | 1.32 | 2.75 | 0.03 |
| TIMI Flow "0" Pre PCI | 52.6 % | 51.6 % | 53.3 % | 0.8 |
| TIMI Flow "0 or 1" Post PCI | 4.1 % | 4.9 % | 3.4 % | 0.4 |
| TIMI Flow "3" Post PCI | 82.7 % | 90.2 % | 77.1 % | <0.001 |

* Median value.

Data are expressed as mean ± SD or median as appropriate. Qualitative data are presented as proportion with its 95% confidence interval. Parametric tests were used when possible. Alternatively, nonparametric tests were used for very small sample size comparisons or in the case of skewed distributions. Categorical variables were tested using Pearson's chi-square test for contingency tables or Fisher's exact test, as appropriate. Continuous variables were analyzed by a 1-way ANOVA or paired *t* test. Kaplan-Meier survival estimates were calculated, and a log-rank test was used to compare the clinical outcomes between groups when appropriate. A multivariate stepwise logistic regression analysis was performed to identify independent predictors for inhospital mortality. All statistical tests and/or confidence intervals, as appropriate, were performed with a 2-sided p value = 0.05. Statistical analysis was performed using SAS software, v10.

## Results

A total of 287 consecutive, unselected patients were included in the analysis. Patients had a median age of 66 years (Table 1). Survivors were younger than nonsurvivors (61 to 68 years, p <0.01) and the majority were men (76%). Patients presented with elevated heart rates, poor hemodynamics despite continuous infusion of vasopressors and inotropes, signs of tissue hypoperfusion, and end-organ dysfunction (Table 2); 61% of patients were admitted to the hospital in cardiogenic shock. Patients had an average left ventricular ejection fraction of 25 ± 12%.

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Table 4
Multivariate analysis of predictors of inhospital mortality

| Variable | Odds Ratio Estimate | Lower 95% Confidence Limit for Odds Ratio | Upper 95% Confidence Limit for Odds Ratio | p-value |
|---|---|---|---|---|
| Age | 1.073 | 1.041 | 1.107 | <.0001 |
| Male | 1.002 | 0.459 | 2.188 | 0.9961 |
| Anoxic Brain Injury | 7.707 | 2.887 | 20.570 | <.0001 |
| Mechanical Ventilation | 2.810 | 1.272 | 6.207 | 0.0106 |
| ST-Elevation Myocardial Infarction | 1.246 | 0.576 | 2.698 | 0.5762 |
| Creatinine | 1.188 | 0.934 | 1.510 | 0.1600 |
| Mean Arterial Pressure | 0.995 | 0.980 | 1.010 | 0.4948 |
| Inotropes or Vasopressors Required Prior to Impella Support | 2.302 | 0.997 | 5.317 | 0.0509 |
| Impella Implanted pre-Percutaneous Coronary Intervention | 0.485 | 0.240 | 0.981 | 0.0442 |
| Cardiac Arrest Prior to Admission | 1.377 | 0.533 | 3.555 | 0.5087 |
| Shock Prior to Admission | 2.410 | 1.205 | 4.820 | 0.0128 |

Before receiving MCS, 80% of patients were on vasopressors or inotropes with the majority requiring ≥2 agents and 40% were supported with IABP. Moreover, 9% were under active cardiopulmonary resuscitation as the Impella was being implanted. Patients were revascularized promptly with a median door-to-balloon time for patients with STEMI of 1.35 hours (Table 3). Angiographic success was achieved in most of the patients with only 4% continuing to have a Thrombolysis In Myocardial Infarction score of 0 or 1 post-PCI.

Overall survival to discharge for the entire cohort was 44%. Survivors and nonsurvivors had similar hemodynamics before initiation of MCS. Occurrence of anoxic brain injury, end organ hypoperfusion, or need for mechanical ventilation before Impella insertion were all significantly less yet prevalent in the survivors group ($p < 0.001$, Table 3). Survivors had significantly shorter times from the onset of cardiogenic shock to MCS initiation (1.3 vs 2.8 hours, $p = 0.03$). In a multivariate analysis, Impella implantation before PCI and before initiation of inotropes or vasopressors was independently associated with survival. Variables included in the multivariate analysis are listed in Table 4. Patients who received MCS before PCI (i.e., before the first angioplasty/stent balloon inflation) had a higher survival rate to discharge compared with those who received MCS post-PCI (survival 46% vs 35%, odds ratio 0.485, 95% confidence interval 0.24 to 0.98, $p = 0.04$, Figure 1). This difference in survival was observed despite equivalent angiographic success rate (Thrombolysis In Myocardial Infarction score 2 to 3, flow >95%) between the pre-PCI and post-PCI groups. The rate of survival to discharge was inversely proportional to the amount of inotropic support used before initiation of MCS. Patients who received 0, 1, 2, 3, or 4 or more inotropes had a 68%, 45%, 35%, 35%, and 26% rate of survival to discharge, respectively (odds ratio 2.3, 95% confidence interval 0.99 to 5.32, $p = 0.05$, Figure 2). Similarly, patients who received MCS early with a duration of shock before MCS initiation of <1.25 hours (first tercile of the duration of cardiogenic shock distribution) had higher survival to discharge (66%) compared with those who received MCS within 1.25 to 4.25 hours (second tercile) or >4.25 hours (third tercile) of cardiogenic shock with survival to discharge of 37% and 26%, respectively (Figure 3). Older age, presence of anoxic brain injury, and mechanical ventilation before initiation of MCS were independent predictors of mortality. Survivors were less likely to have experienced cardiopulmonary resuscitation, ventricular arrhythmia, and acidosis and were more likely to experience vascular complications requiring surgery and hematomas. There was no difference in the rates of myocardial re-infarction, stroke, bleeding, or hemolysis between survivors and nonsurvivors.

## Discussion

This analysis encompasses the largest number of patients treated with MCS in the setting of AMICS. The cohort consisted of a critically ill population in which MCS was primarily used for salvage purposes; 40% of all patients experienced cardiac arrest before MCS implantation, including 9% of those who underwent active cardiopulmonary resuscitation at the time of Impella implantation, of whom a quarter survived their hospitalization. These patients are understandably under-represented in prospective randomized trials.[10,11] Patients who presented with anoxic brain injury before MCS, pre-hospital cardiac arrest, or patient transfers, all major exclusion criteria in previous randomized controlled trials, represented >60% of the total cohort. Therefore, the survival reported in our study appears favorable even compared with previous AMICS registries, such as the Euroshock and Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) registries.[12,13] In fact, our cohort presented with more profound hemodynamic compromise on admission and lower ejection fraction and were more likely to have sustained cardiac arrests than either of the aforementioned registries.

The most important finding in our analysis is the temporal relation of early use of percutaneous MCS and improved clinical outcomes. Survival was found to be significantly improved if MCS implantation was initiated before PCI. Survival was inversely proportional to the amount of inotropic support required before MCS implantation. Although intuitive, this is the first time that an association between early initiation of MCS and improved survival was reported in patients presenting with AMICS.

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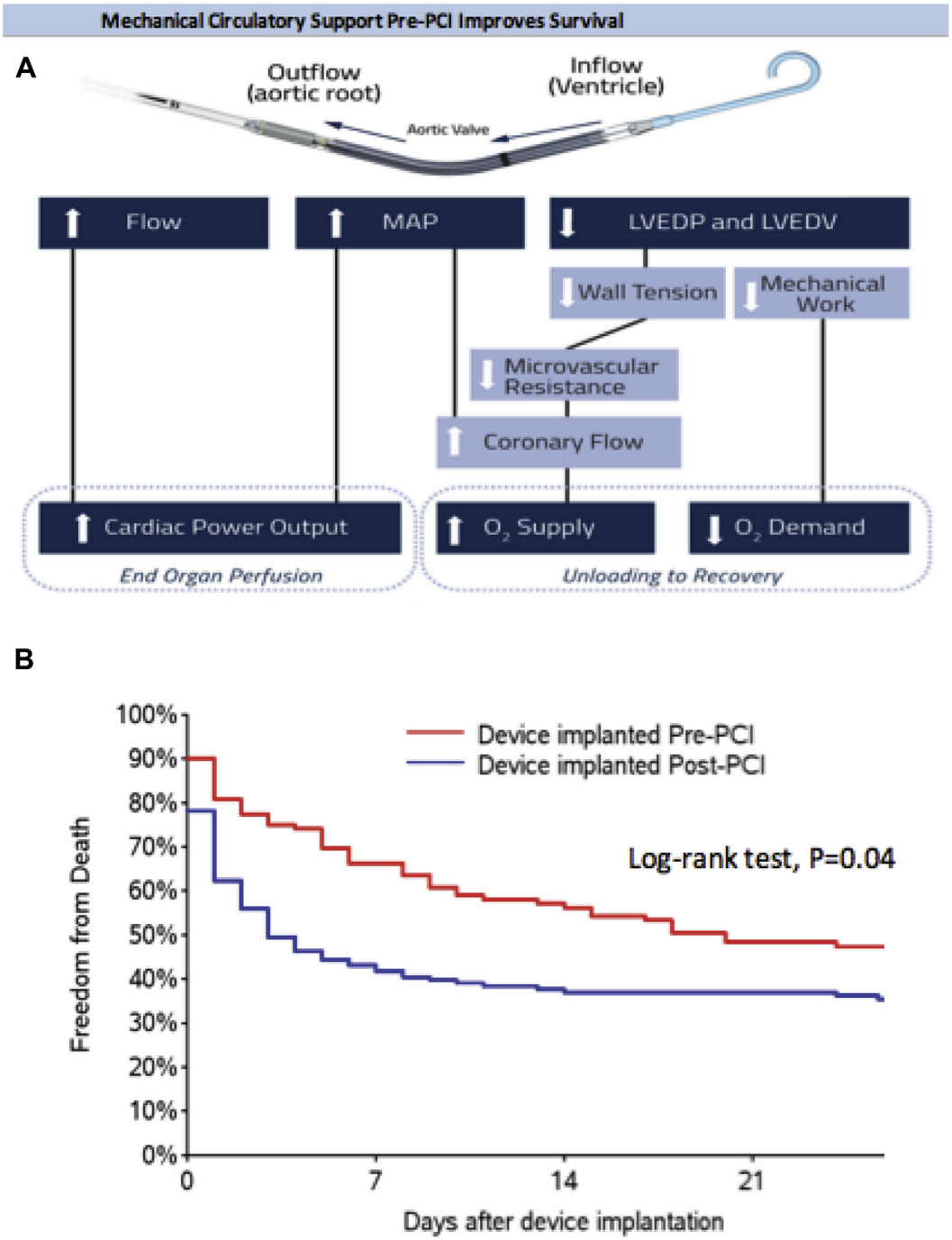


Figure 1. *(A)* Hemodynamic and clinical effects of Impella demonstrated in previous studies. Use of MCS results in numerous beneficial effects including increasing cardiac power output, unloading of the left ventricle, and increasing coronary flow. *(B)* The Kaplan-Meier curve for Freedom from Death (to 30 days) by device implanted pre/post-PCI. The separation of the Kaplan-Meier curves occurs very early post-PCI reinforcing that early hemodynamic support is a key determinant in clinical outcomes.

This observation is strengthened by the fact that initial hemodynamics were similar between survivors and non-survivors. Patients who received MCS devices early were more likely to survive than those who received MCS later. Poor outcomes were associated with longer durations to MCS initiation. Patients who had MCS initiated at the first signs of shock, before inotropic support, had a significantly higher survival rate compared with those who received MCS after inotropic support. In fact, delayed MCS initiation in lieu of continuous increases of inotropes yielded stepwise poorer outcomes. This suggests that inotropes may not be beneficial in AMICS and may even be detrimental because of their associated ischemic effect that may aggravate the neurohormonal and molecular cascade associated with cardiogenic shock and further negatively affect cardiac and end-organ function.[14–16] These results suggest that the

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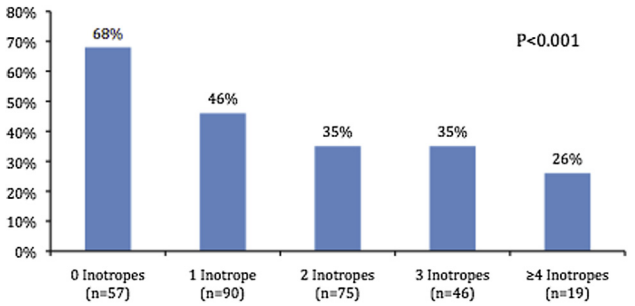


Figure 2. Inhospital survival rates as a function of inotropic support to MCS implantation.

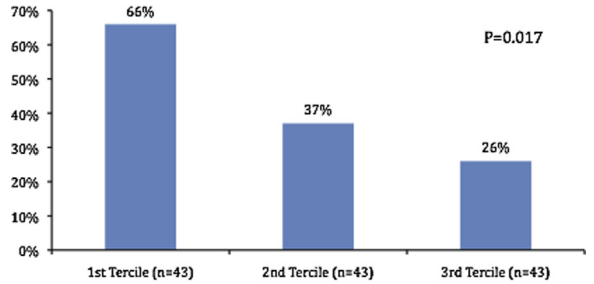


Figure 3. Inhospital survival rates as a function of shock onset to MCS implantation.

focus in AMICS should revolve around system improvements that will shorten onset of "shock to support" times in a similar fashion to "door-to-balloon" times in STEMI.

The importance of shorter "shock to support" times is most clearly demonstrated in the difference between patients who underwent MCS implantation pre-PCI as opposed to post-PCI. As previously shown by O'Neill and colleagues[7] in a smaller patient cohort, patients in the pre-PCI MCS implantation arm of the study had significantly higher survival. On average, PCI was delayed by 17 minutes to accommodate MCS implantation. Despite the 17-minute delay in reperfusion observed in the group that received MCS pre-PCI compared with the group that received it post-PCI, survival was significantly higher in the pre-PCI group. It is important to note that the separation of the Kaplan-Meier curves between these 2 groups occur very early post-PCI reinforcing that early hemodynamic support is a key determinant in clinical outcomes (Figure 1).

The improved clinical outcomes associated with early MCS use have been attributed to unloading of the left ventricle before reperfusion. This was first demonstrated in numerous animal models.[17–19] These initial studies demonstrated that the early use of MCS can limit infarct size and augment the neurohormonal cascade associated with reperfusion injury. Unloading of the left ventricle, therefore, results in increases in cardioprotective signaling, reducing apoptosis, and limiting myocardial damage in AMI. This effect can be seen even with a relatively small amount of left ventricular unloading as demonstrated in the CRISP AMI trial, in which a 58% reduction in mortality, shock, or heart failure occurred at 6 months post-AMI when IABP was initiated before PCI in patients with large anterior STEMI compared with PCI alone.[20]

Importantly, the observations seen in our study serve as a call to action for clinicians caring for patients presenting with AMICS in identifying the appropriate timing for MCS initiation.[21] Although inotropes and vasopressors are needed for rapid early stabilization, initiation of these vasoconstrictive agents can result in arrhythmias, increase myocardial oxygen consumption leading to further ischemia, and decrease peripheral perfusion and microcirculation, all of which can further worsen end-organ dysfunction. As opposed to chronic systolic heart failure leading to cardiogenic shock, patients presenting with AMICS are less likely to have developed compensatory responses and are, thus, more susceptible to rapid cardiovascular collapse. In AMICS, medical therapy should serves as a temporizing measure until a more robust form of MCS is achieved. As shown in our study, early initiation of temporary mechanical support, before inotropic and vasopressor therapy escalation, could potentially lead to improved outcomes in these critically ill patients.

Careful consideration and attention should be placed on vascular access and closure techniques when using percutaneous MCS to treat AMICS. Although our study suggests that the risk of major vascular complications was relatively limited (9%), nevertheless, operators and institutions should have a high degree of competency to achieve large bore access and delivery.[22] Other adverse events potentially associated with using MCS were relatively low in this series compared with previous reports using more invasive MCS devices, such as surgical ventricular assist devices or extracorporeal membrane oxygenation. This suggests that early support with an Impella device is a reasonable strategy to treat patients presenting with AMICS to improve outcomes.

There are several limitations to consider for our study. (1) Because of the retrospective nature of the registry design, there is a risk that some adverse events may not be properly documented. Adverse events that are defined based on temporal trends (such as biomarkers and rapid hemodynamic changes) may not be properly documented if accounted for retrospectively based on patient chart review. We, therefore, focused on mortality outcomes that were well documented in the cVAD Registry. (2) The observational nature of this study limits definitive causal relationships. Timing of MCS, decision of the extent of revascularization, and all other adjunctive therapies were left to the operating physician and are, therefore, subject to treatment biases. (3) Lastly long-term follow-up was not available for most of the patients. Prospective studies will be needed in the future to further evaluate these observations and validate the temporal relationships from cardiogenic shock onset to MCS implantation to short- and long-term clinical outcomes.

## Disclosures

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