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Timing of Impella In Acute Myocardial Infarction Complicated With Cardiogenic Shock Impacts Survival: A Meta-Analysis

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Abstract

Background: Acute myocardial infarction (AMI) complicated by cardiogenic shock (AMICS) is often fatal, despite early revascularization. We sought to analyze whether mortality could be favorably impacted by the early implementation of mechanical circulatory support (MCS) before revascularization during AMICS.

Methods and Results:

In this large study of 811 patients, the largest study to date, we performed a meta-analysis of eight studies comparing the impact of 'Early' versus 'Late' Impella implantation on early (In-hospital-to30 days) and late (6-12 month) mortality during AMICS. Pooled analysis showed significantly lower short-term mortality (RR: 0.61, 95 % CI: 0.49-0.75, p < 0.001, I2 = 0 %) and long-term mortality (RR: 0.64, 95 % CI: 0.48-0.84, p=0.002, I2 = 0 %) with early Impella implantation compared to late Impella implantation.

Conclusion: Our findings suggest increased survival is associated with early implantation of Impella, before revascularization, in patients presenting with AMICS. Although further exploration of this finding is warranted, these data support a new protective strategy with Impella use in AMICS.

Non-standard Abbreviations and Acronyms

Percutaneous coronary intervention (PCI) Mechanical circulatory support (MCS) Acute myocardial infarction complicated by cardiogenic shock (AMICS)

Keywords: Acute myocardial infarction, cardiogenic shock, AMICS, Impella, pre PCI, Post PCI

Introduction

Mortality remains high (~50 %) in patients presenting with acute myocardial infarction (AMI) complicated by cardiogenic shock (AMICS) despite early revascularization. Decreased AMICS-related survival persists despite the addition of supportive therapies; in particular, the historical widespread use of intra-aortic balloon pumps (IABP) and the undirected, random use of partial percutaneous mechanical circulatory support (MCS). **[1]** However, when contemporary standardized AMICS protocols are deployed utilizing early MCS of the left and/or right ventricle(s) before revascularization, survival outcomes as high as ~77 % have been observed. **[2]** Yet, current guidelines do not provide specific guidance for the appropriate timing of MCS use in AMICS. **[3]** Therefore, we performed a meta-analysis of the current literature related to the use of Impella MCS in the treatment of AMICS to determine the overall survival impact of an early Impella implantation strategy.

Methods

This meta-analysis was performed following the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis. PubMed, Embase, and Cochrane Central databases were searched from inception till April 2022. Two reviewers (A.M., M.S.K) independently assessed the eligibility of the studies and extracted data. Studies reporting outcomes on 'Early' and 'Late' Impella implantation were included. Studies with overlapping patient populations were excluded. 'Early' and 'Late' Impella implantation were defined as Impella placement before or following coronary revascularization, respectively. The outcome assessed was mortality in short term (In-hospital or 30-day) and in long term (6-12 months). Risk ratios (RR) were calculated and the generic inverse variance method was used to pool data into a fixed effect model meta-analysis. Heterogeneity among studies was assessed using I2 statistics

Results

After applying the eligibility criteria, 8 studies were included in our analysis.1,4-10 Two studies were prospective **[1,9]** and the rest were observational in design. Of the 811 participants, 64 % were men, mean age was 65 years. Utilization of inotropes and the need for mechanical ventilation were prevalent, 85 % and 82 %, respectively. Cardiac arrest occurred in 54 % of all included patients. All 8 studies reported short-term mortality and 3 studies reported long-term mortality. **[4,5,10]** Cardiogenic shock was defined as systolic blood pressure (SBP) < 90 mm Hg or the need for inotropic support for more than 30 minutes to maintain SBP > 90 min despite adequate fluid loading. Exclusion criteria encompassed patients with severe aortoiliac disease and known severe aortic valve disease and patients who received Impella support after the first 24 hours following PCI.1,4-10 Patient demographics and studies' characteristics are summarized in **Tables 1 and 2,** respectively. Pooled analysis showed significantly lower short-term mortality (RR: 0.61, 95 % CI: 0.49-0.75, p < 0.001, I2 = 0 %) and long-term mortality (RR: 0.64, 95 % CI: 0.48-0.84, p=0.002, I2 = 0 %) with early Impella implantation compared to late Impella implantation **(Figure 1: A and B, respectively)**.

Table 1: Patient Clinical Characteristics and Demographics

	O'Neill et al (n=154)	Basir et al. (n=287)	Schroeter et al (n=68)	Ouweneel et al (n=24)	Meraj et al (n=36)	Loehn et al (n=73)	Hemradj et al (n=88)	Chatzis et al (n=81)
Mean age	64	66	63	58	69	69	60	68
Male	110	219	49	18	28	53	72	68
Hypertension	119	193	NA	4	23	53	31	62
Diabetes Mellitus	68	117	16	2	13	28	14	27
Prior stroke	14	32	5	0	1	9	2	6
Prior MI	59	80	11	1	9	19	16	34
Mechanical ventilation	NA	218	55	24	26	55	78	81
Cardiac arrest	35	153	33	24	16	61	53	64
Inotropes/vasopressors	NA	230	NA	24	36	60	78	71
EF	26.4+/-13.4	25.3 +/- 12	27 +/-15	NA	24.6+/-12	29 +/-12	NA	32.9+/-7

Table 2: Studies characteristics

Study/Year	**Design**	**Patients (number)**	**Impella**	**Indication**
O'Neill et al. 2014	Retrospective, observational, USpella registry	154	2.5	Cardiogenic shock due to Acute MI
Basir et al. 2016	Retrospective, observational, cVAD registry	287	2.5/CP	Cardiogenic shock due to Acute MI
Schroeter et al. 2016	Retrospective observational, single-center	68	2.5	Cardiogenic shock due to Acute MI
Ouweneel et al. 2016	Randomized Controlled Trail, Multi-center	48	CP	Cardiogenic shock due to Acute MI
Meraj et al. 2017	Retrospective, observational, cVAD registry	36	2.5	Cardiogenic shock due to Acute MI
Loehn et al. 2020	Retrospective Observational , single center	73	CP	Cardiogenic shock due to Acute MI
Hemredj et al. 2020	Prospective observational, single-center	88	2.5/CP/5	Cardiogenic shock due to Acute MI
Chatzis et al. 2021	Retrospective Observational , single center	81	2.5	Cardiogenic shock due to Acute MI

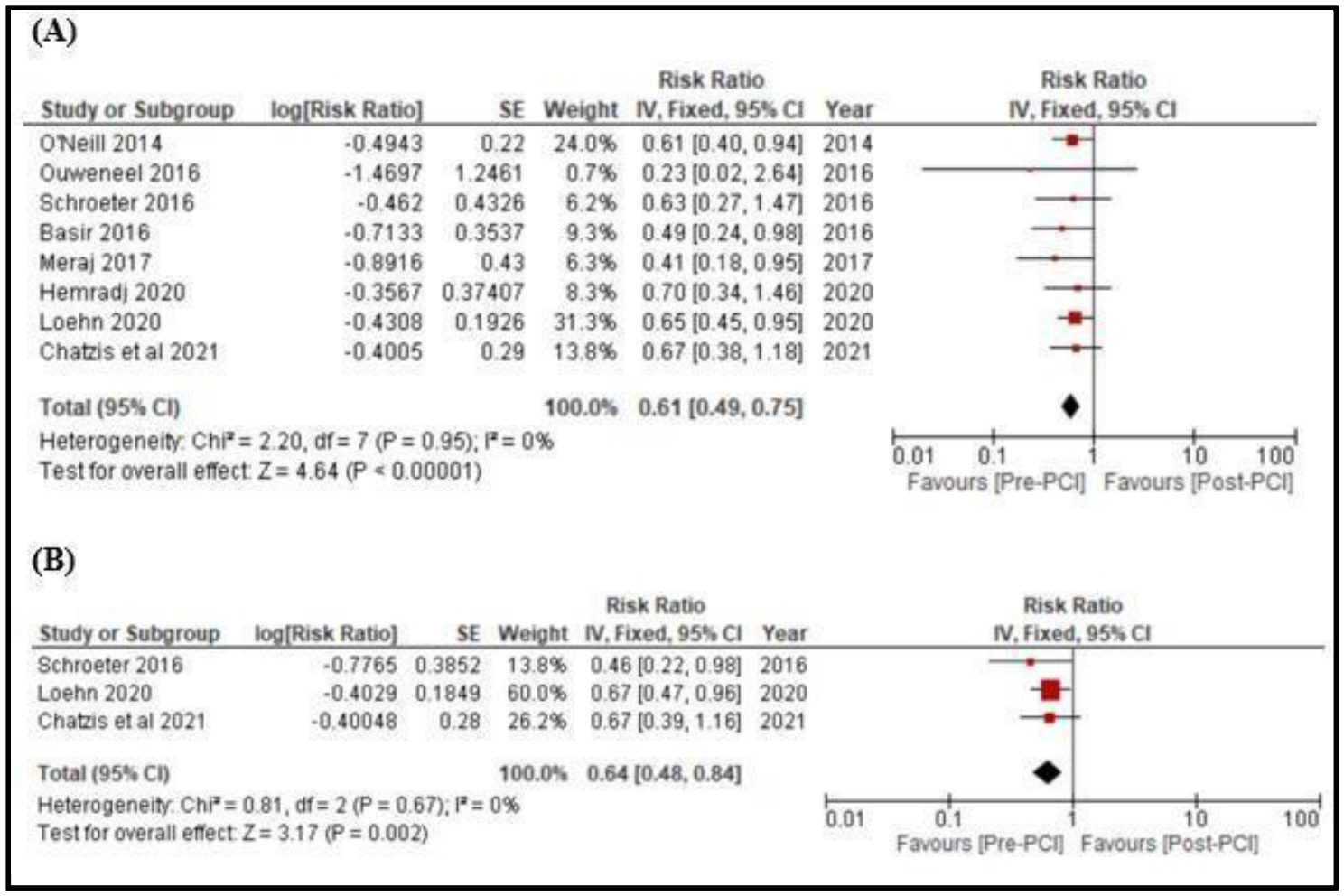

Figure 1: Forest Plot Comparing In-Hospital-30-Day (A) and 6-12 month (B) Mortality in "Early" vs. "Late" Impella use for AMICS.

Discussion

This analysis of 811 patients is currently the largest study investigating the role of percutaneous MCS timing in the treatment of AMICS. Our data suggest a significant survival benefit with early compared to late Impella implantation in patients presenting with AMICS. Early Impella initiation was associated with a 59 % reduction in short-term mortality (In-hospital/30 days) and a 36 % reduction in long-term mortality in AMICS patients. Early left ventricular unloading in AMICS demonstrated a reduction in infarction size as shown in animal models. **[11]** As previously reported, this early initiation of MCS may play a key role in halting the downward spiral of escalating vasopressor dosage, peripheral vasoconstriction, hypoperfusion, arrhythmias, systemic inflammatory response syndrome, and multi-organ failure. **[5,6]**

In line with our data, the Detroit Cardiogenic Shock Initiative Pilot Study demonstrated a significant improvement in survival to explant compared with historical data with early initiation of mechanical cardiac support. **[12]** Others demonstrate a well-documented proportional increase in survival rate with shorter doors to Impella times were observed in a retrospective study. **[13]** Whereas, contemporary data are scarce and mixed about the survival benefit from early use of other MCS devices compared to Impella. **[1,14,15]** Finally, O'Neill et al, in ostensibly the sickest non-AMICS cohorts studied to data, reported higher survival to explant with pre-PCI impeller support when compared to pre-PCI intra-aortic balloon pump use in a large cohort of AMICS.**[16]**

Study

Limitations: There are several limitations in our analysis. Despite the lack of heterogeneity in our analysis, variability in the study population exists allowing for both known and unknown confounders. Outcomes-based on Impella initiation is subject to treatment bias wherein those treated late with Impella were treated as such due to a complication or unexpected hemodynamic compromise, therefore, self-selecting a higher risk cohort. These limitations can only be assessed by way of an individual patient-data meta-analysis or adequately powered randomized controlled trial. Additionally, we do not establish causation, due to the observational design and lack of a comparator group in the included studies, which makes our results purely hypothesis generating.

Conclusions

Collectively, when taken together with our data, the contemporary literature is replete with data underscoring the 'timing' of Impella support initiation as a crucial variable impacting outcome in AMICS. Our data are in line with previous analyses and other registry data reporting improved overall survival with an early MCS strategy as well as shorter door-to-MCS times.**[12,17]** However, larger adequately powered prospective studies (undoubtedly those aforementioned here) are needed to confirm our findings and alter future practice patterns.

Conflicts of Interest

Drs. Flaherty, Kapur, Kaki, Schreiber, and O'Neill receive modest speaker honoraria from Abiomed; Dr. Basir is a consultant and receives research funding from Abiomed; Drs. Moustafa, Khan MS, and Khan AR have no conflicts of interest to disclose.

Author's contribution

Conception and design: Abdelmoniem Moustafa, Michael Flaherty, Abdur R. Khan. Data collection and analysis: Abdelmoniem Moustafa, Mohammad Saud Khan. Writing: Michael Flaherty, Abdelmoniem Moustafa, Mohammad Saud Khan. Reviewing and Editing: Mir Basir, Navin Kapur, Amir Kaki, Theodore Schreiber, and William O'Neill

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