LETTER TO EDITOR

Comparison of Inotropes for Use With the Impella Device in Cardiogenic Shock

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Management of cardiogenic shock includes pharmacologic and non-pharmacologic interventions to restore end organ perfusion.[1,2] Temporary mechanical circulatory support devices (MCS) such as the Impella device (Abiomed, Inc. Danvers, Massachusetts) can restore cardiac output and have shown promise in improving outcomes.[3-5] The Impella device is a catheter-based, impeller-driven temporary percutaneous MCS device approved by the Food and Drug Administration (FDA) for the treatment of ongoing cardiogenic shock and has shown potential mortality benefit.[4,5] Despite frequent combination therapy between the Impella device and inotropes for the management of patients with cardiogenic shock, limited evidence exists regarding optimal agent selection.[6,7] Milrinone and dobutamine increase cardiac output via different mechanisms of action but despite mechanistic differences, the prospective DOREMI trial demonstrated no difference in clinical outcomes including a composite cardiac outcome and in-hospital mortality.[8] To date, no prospective trials have directly compared milrinone and dobutamine in patients requiring Impella support. Due to the lack of high-quality comparative evidence, the choice of inotropic agent is primarily driven by patient specific factors and clinician preference.[6]

The purpose of this study was to explore the effects of milrinone and dobutamine on the duration of Impella support and clinical outcomes in patients with cardiogenic shock. This was a retrospective, single-center cohort study. Adult patients admitted to the cardiac intensive care unit (ICU) with Impella support and concomitant milrinone or dobutamine from January 1, 2011 to March 31, 2022 were included. Patients were excluded if more than 1 inotrope was used during Impella support to prevent confounding. The primary outcome was the difference in duration of Impella support between patients treated with milrinone and dobutamine. Secondary outcomes included hospital and ICU length of stay, duration of mechanical ventilation, in-hospital mortality, mortality during Impella support, and transitions to comfort care compared between inotrope groups. The difference in duration of Impella support was analyzed using the Mann-Whitney *U* test and median and IQR were reported. Mortality proportions were compared using Chi-squared test and all other secondary outcomes were assessed using Mann Whitney *U*-tests. Statistical significance was assessed using an alpha ⩽.05. All statistical analyses were performed using IBM® SPSS® Statistics for Windows, version 28 (IBM Corp., Armonk, NY, USA).

A total of 43 patients were included, of which 33 were treated with milrinone and 10 were treated with dobutamine. Baseline demographics were similar between milrinone and dobutamine groups with the exception of preexisting heart failure with reduced ejection fraction (20% vs 57%, $P = .037$) and a higher proportion of patients in the milrinone group being intubated prior to MCS (Table 1). Patients also had significant differences in etiology of cardiogenic shock with patients in the dobutamine group having more acute myocardial infarction (39% vs 80%, $P = .024$) and those in the milrinone group having more decompensated heart failure (52% vs 10%, $P = .019$). We observed no difference in the primary outcome of duration of Impella support between those receiving concomitant milrinone or dobutamine therapy (66.2 hours vs 31.7 hours, $P = .164$). Patients treated with milrinone were found to have a significantly longer hospital length of stay compared to those treated with dobutamine (9.34 days vs 4.32 days, $P = .042$). No differences were observed between ICU length of stay, duration of mechanical ventilation, in-hospital mortality, mortality on Impella, or transition to comfort care.

To our knowledge, this is the first report to describe the effects of milrinone and dobutamine in patients with cardiogenic shock requiring Impella support. We observed no statistically significant differences in duration of Impella support between the milrinone and dobutamine groups, similar to previous literature.[8] Though there was no significant difference in the duration of Impella use between inotrope groups, the median time on support was roughly double in the milrinone group when compared to dobutamine, potentially revealing a clinically relevant difference especially if corroborated by future reports. In addition to a longer duration of MCS, patients in the milrinone group had a significantly longer hospital length of stay. This may be attributed to the longer time required to reach steady-state concentrations of milrinone given the longer half-life of 2.3 to 2.4 hours compared with the shorter, 2-minute, half-life of dobutamine. While a longer duration of MCS and length of stay is not preferred, this outcome may be offset by the lower proportion of mortality in the milrinone group; however, this was non-significant, and we are not powered to measure this difference. There are no reports

Table 1. Patient characteristics and outcomes.

	MILRINONE (N = 33)	DOBUTAMINE (N = 10)	*P*-VALUE
Baseline characteristics			
Age, years, median (IQR)	64.2 (53-72.3)	59.5 (57.3-69.5)	.509
Male, n (%)	25 (75.8)	7 (70)	.714
BMI, kg/m^2, median (IQR)	28.6 (22.5-32.5)	31.0 (29-35.8)	.250
Impella indication			
Acute MI, n (%)	13 (39)	8 (80)	.024
Cardiomyopathy, n (%)	14 (42)	1 (10)	.059
Heart failure decompensation, n (%)	17 (52)	1 (10)	.019
Mechanical ventilation at insertion, n (%)	18 (55)	2 (20)	.055
IABP prior to Impella insertion, n (%)	6 (18)	3 (30)	.420
Clinical outcomes			
Impella duration, hours, median (IQR)	66.2 (42.4-97)	31.6 (17.6-76.9)	.164
Hospital length of stay, days, median (IQR)	9.34 (3.5-26.1)	4.32 (1.7-8.0)	.042
ICU length of stay, days, median (IQR)	6.18 (2.5-12)	4.18 (1.7-6.9)	.114
Mechanical ventilation duration, days, median (IQR)	3.21 (1.4-6.3)	2.68 (1.6-3.7)	.362
Mortality on Impella, n (%)	14 (42.4)	8 (80.0)	.085
In-hospital mortality, n (%)	19 (57.6)	8 (80.0)	.198
Transition to comfort care, n (%)	9 (27.3)	4 (40.0)	.707

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HFpEF, heart failure with preserved ejection fraction; HFrEF, Heart failure with reduced ejection fraction; IABP, intra-aortic balloon pump; ICM, ischemic cardiomyopathy; MI, myocardial infarction; NICM, non-ischemic cardiomyopathy.

directly comparing milrinone to dobutamine in patients requiring Impella support for the management of cardiogenic shock, highlighting the large gap in knowledge for optimizing inotropic and vasoactive medications in these patients. Due to the very heterogeneous nature of cardiogenic shock precluding large-scale evaluation, prospective evidence is unlikely to be available soon. Our study attempts to contribute to this critical gap in knowledge by reporting the characteristics of patients treated with concomitant inotrope and Impella support and describing their associated outcomes.

Our study has several limitations. First, the retrospective single-center nature precludes drawing causative conclusions, and the small sample size (n = 43) limits our ability to robustly compare patient outcomes such as mortality and adverse effects. Second, we observed significant baseline imbalances between prior diagnoses and etiology of cardiogenic shock representing significant heterogeneity in our study population. Lastly, outcomes following hospital stay were not evaluated, precluding our ability to identify differences in long-term clinical outcomes between groups following discharge. Nevertheless, our study provides insight into concomitant inotrope use with Impella support and highlights the need for more robust comparative evidence in patients requiring MCS and inotropic support.

In critically ill patients with cardiogenic shock requiring Impella support and concomitant inotrope therapy, no significant difference between milrinone and dobutamine was found with respect to the duration of Impella support. Further appropriately powered prospective studies with more homogenous populations are warranted to better elucidate the relationship between inotrope use, Impella device duration, and clinical outcomes.

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