

BRIEF REPORT

Optimal Mechanical Circulatory Support Timing in Patients With Acute Myocardial Infarction With Cardiogenic Shock



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In patients with acute myocardial infarction (AMI)-cardiogenic shock (CS), early revascularization has been shown to improve survival,¹ but the high mortality is attributed to hypoperfusion of end organs that cannot be recovered through early primary percutaneous coronary intervention (PCI) alone, and various studies to improve it have persisted.² One of several studies to address end-organ hypoperfusion used temporary mechanical circulatory support (MCS), followed by efforts to determine the optimal use that could improve survival in patients with CS. However, recent randomized controlled trials (RCT) related to the early initiation of venoarterial extracorporeal membrane oxygenation (VA-ECMO) in patients with infarct-related CS have failed to show a survival benefit.^{3,4} Nevertheless, the application of VA-ECMO cannot be excluded in patients with AMI-CS because the factors associated with VA-ECMO use (left ventricular unloading, weaning, complications), primary strategies, and the timing of VA-ECMO initiation were not fully considered in current RCTs.⁵

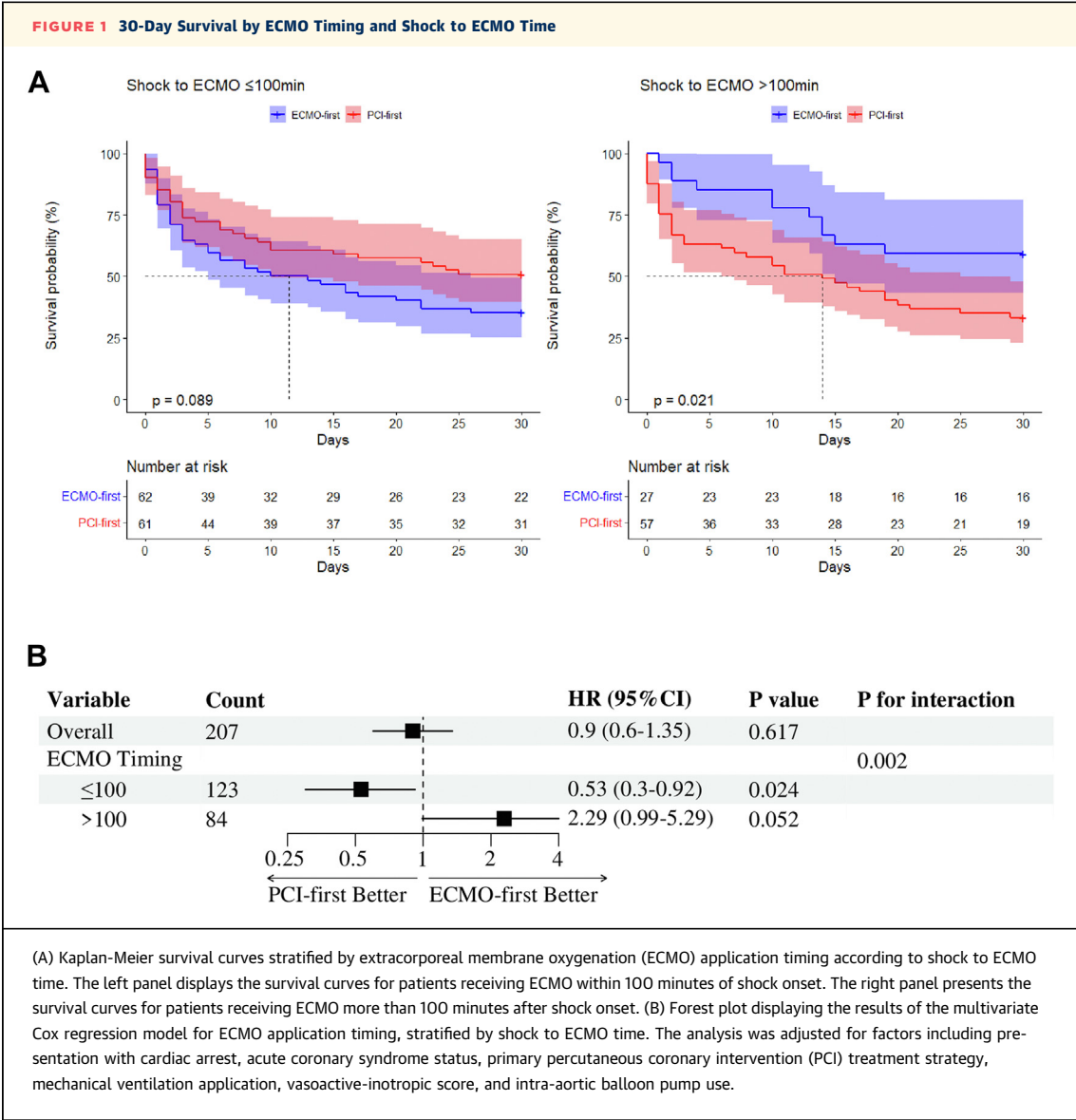
Our study compared 30-day survival in AMI patients with refractory CS who received VA-ECMO before vs after PCI, aiming to determine the optimal timing for VA-ECMO.

The RESCUE (Retrospective and Prospective Observational Study to Investigate Clinical Outcomes and Efficacy of Left Ventricular Assist Device for Korean Patients With CS) study, a retrospective and prospective registry study conducted at multiple centers, aimed to investigate the clinical outcomes and efficacy of left ventricular devices in Korean patients with cardiogenic shock. Between January 2014 and December 2018, 1,247 patients with CS were enrolled from 12 major centers in Korea. Among them, 238 of the 693 patients who underwent PCI for acute coronary syndrome received VA-ECMO. To evaluate the prognostic effect of the timing of VA-ECMO initiation in patients with acute coronary syndrome and CS undergoing PCI, 207 eligible patients were included in the final analysis. For this analysis, the enrolled patients were divided into 2 groups: ECMO initiation before PCI (n = 89) and ECMO initiation during or after PCI for refractory CS (n = 118).

To analyze the effect of the timing of ECMO initiation and primary PCI on 30-day mortality, Kaplan-Meier survival curves were used. This study used retrospective data and employed a multivariate Cox proportional hazards model to adjust for covariates affecting the outcome. Additionally, in a post hoc

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analysis, we calculate interaction *P* values to compare 2 HRs. Statistical significance was set at *P* < 0.05. Statistical analyses were performed using the R Statistical Software version 4.1.2 (R Foundation for Statistical Computing).

The comparison between the ECMO- and PCI-first groups did not reveal a statistically significant difference in 30-day survival among patients with cardiogenic shock caused by myocardial infarction, as determined using the Kaplan-Meier survival curve. However, upon stratification based on the duration between CS onset and MCS administration, the 30-day survival outcomes varied according to the timing of ECMO initiation. In the univariate analysis, the Kaplan-Meier survival curves showed relatively

high 30-day survival in the PCI-first group, where ECMO was applied within 100 minutes, and in the ECMO-first group, where ECMO was applied after more than 100 minutes (Figure 1A). In addition, the multivariate Cox regression results adjusting for related factors showed similar results (PCI-first better; HR: 0.53 [95% CI: 0.3-0.92]; *P* = 0.024 in shock to ECMO time ≤ 100 minutes, ECMO-first better; HR: 2.29 [95% CI: 0.99-5.29]; *P* = 0.052 in shock to ECMO time >100 min). There was a significant interaction between shock and ECMO duration (*P* = 0.002). (Figure 1B).

In this study, as in recent RCTs,^{3,4} it was consistently observed that performing ECMO before primary PCI did not improve survival rates. However,

when the comparison was stratified based on the time from shock onset to ECMO initiation, a significant difference in 30-day survival was observed depending on the timing of ECMO initiation. This study is based on observational data, and it is important to consider that the use of ECMO was entirely at the discretion of the attending physician. The fact that ECMO was initiated first suggests that the patient's condition was that much more unstable. Therefore, if ECMO is started first within 100 minutes of shock onset, this group is more likely to include critically ill patients compared with those who receive PCI first. This suggests that the potential benefits of VA-ECMO might have been offset by the greater severity of the patients' conditions.

Conversely, this study also demonstrates that when the time from shock onset to ECMO initiation—in other words, the duration of hypoperfusion—increases, starting ECMO first may improve 30-day survival. Additionally, in analyzing the timing of ECMO initiation while considering stratification variables, we observed a clear difference in survival rates depending on whether ECMO was initiated before or after 90 to 100 minutes following the onset of shock. However, it is important to note that the 100-minute threshold is not based on definitive evidence but rather on observations made during the serial comparison of these variables.

Although this was not a study where ECMO application was uniformly controlled, which limits the interpretation, the findings suggest that when shock persists despite strict adherence to guidelines for treating initial shock patients with medication, continuous renal replacement therapy, and mechanical ventilation, prioritizing ECMO to first address hypoperfusion may provide a survival benefit.

As mentioned at the beginning of this report, VA-ECMO is a device that is inherently challenging to use optimally. Without employing it according to prespecified, strict criteria, it becomes difficult to accurately assess its effectiveness. Therefore, the biggest limitation of this study is the lack of explicit criteria for ECMO use. Moreover, there were no defined criteria for revascularization during primary PCI, which necessitates caution in interpreting the results. Although this variable was included as a covariate in the multivariate Cox regression analysis, it remains a source of variability. Both primary PCI and ECMO were performed according to the most recent clinical guidelines by well-trained cardiologists and thoracic surgeons, but these limitations should be taken into account when evaluating the finding of this study.

In conclusion, carefully planning the timing of VA-ECMO and PCI based on the time since shock onset suggests that this approach may offer additional survival benefits. It is plausible that the maximum benefit of temporary MCS in infarct-related cardiogenic shock can be achieved by prioritizing the initiation of VA-ECMO, particularly in cases where PCI is not feasible during hypoperfusion.

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REFERENCES

1. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. *N Engl J Med*. 1999;341:625-634.
2. Samsky MD, Morrow DA, Proudfoot AG, Hochman JS, Thiele H, Rao SV. Cardiogenic shock after acute myocardial infarction: a review. *JAMA*. 2021;326:1840-1850.
3. Thiele H, Zeymer U, Akin I, et al. Extracorporeal life support in infarct-related cardiogenic shock. *N Engl J Med*. 2023;389:1286-1297.
4. Banning AS, Sabaté M, Orban M, et al. Venoarterial extracorporeal membrane oxygenation or standard care in patients with cardiogenic shock complicating acute myocardial infarction: the multicentre, randomised EURO SHOCK trial. *EuroIntervention*. 2023;19:482-492.
5. Rao SV. Mechanical circulatory support in cardiogenic shock — persistence and progress. *N Engl J Med*. 2024;390:1436-1438.

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