# Novel prediction tool for veno-arterial extracorporeal membranous oxygenation in acute myocardial infarction patients

### Yosuke Matsumura, Taka-Aki Nakada, Ryuzo Abe

Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine, Chuo, Chiba 260-8677, Japan *Correspondence to*: Taka-Aki Nakada, MD, PhD. Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine, 1-8-1 Inohana, Chuo, Chiba 260-8677, Japan. Email: taka.nakada@nifty.com.

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Cardiogenic shock is a state of critical hypoperfusion due to impaired cardiac function (1). Ischemia can induce impaired myocardial contraction, which involves a vicious cycle of low cardiac function and hypotension, resulting in systemic tissue hypoperfusion (1,2). Acute myocardial infarction (AMI) is the most frequent cause of cardiogenic shock, accounting for 80% (3). Despite recent advances in early revascularization, cardiogenic shock is still the leading cause of mortality in AMI, and remains high at 40-50% (4-6). Venoarterial extracorporeal oxygenation (VA-ECMO) provides temporary circulatory and respiratory support in refractory shock, including cardiogenic shock patients (7-9). It ensures systemic organ perfusion during the wait for cardiac function recovery, transplantation, or a left ventricular assist device (8). Early revascularization with VA-ECMO support was reported to improve outcomes in AMI presenting with cardiogenic shock (10,11); however, in-hospital mortality of refractory cardiogenic shock patients with VA-ECMO is still high at 40-94% (12). Complications related to ECMO, such as bleeding or infection, were seen frequently (13). Thus, nonselective implementation of ECMO should be questioned and early identification of mortality risk among cardiogenic shock patients treated with ECMO has been needed. The survival after veno-arterial-ECMO (SAVE)score was published to identify pre-ECMO factors that predict survival in refractory cardiogenic shock (not only AMI) patients with VA-ECMO (14). The SAVE score was based on analysis of 3,846 cardiogenic shock patients who received VA-ECMO from 2003 to 2013, extracted from the Extracorporeal Life Support Organization (ELSO) registry. It evaluates 11 items: diagnosis group, age, weight, acute pre-ECMO organ failure, chronic renal failure, duration of intubation, peak inspiratory pressure, pre-ECMO cardiac arrest, diastolic pressure before ECMO, pulse pressure before ECMO, and HCO<sub>3</sub> before ECMO. Total SAVE score ranges from -35 to 17, and hospital survival was grouped into 5 risk classes: >5 (75%), 1 to 5 (58%), -4 to 0 (42%), -9 to -5 (30%), and  $\leq$ -10 (18%). However, few studies have focused on cardiogenic shock due to AMI with use of ECMO (15).

In this context, Muller et al. identified pre-ECMO factors associated with ICU mortality, and created a mortality risk score (prEdictioN of Cardiogenic shock OUtcome foR AMI patients salvaGed by VA-ECMO: the ENCOURAGE score) that would help physicians decide the indication for VA-ECMO in AMI patients (16). They also evaluated health-related quality of life (HRQOL) and mental status among long-term survivors using the Medical Outcome Study Short-Form 36 (SF-36), Hospital Anxiety and Depression (HAD) Scale, and the Impact of Event Scale (IES). They analyzed 138 AMI patients who received VA-ECMO at two French intensive care units (ICUs) from 2008 to 2013. This population resulted in 65 patients (47%) surviving to ICU discharge. Multivariable logistic regression analyses identified seven pre-ECMO mortality risk factors: age, female, body mass index (BMI), Glasgow coma scale (GCS) score, creatinine, lactate level, and prothrombin activity. These variables enabled the ENCOURAGE score to predict ICU mortality. With these results, the probabilities of survival 6 months after ECMO were grouped into five classes. In receiver operating characteristic (ROC) analyses, area under the curve (AUC) (95% confidence interval) was 0.84 (0.77-0.91), which was significantly higher than the SAVE, Simplified Acute Physiology (SAPS) II, and Sequential Organ Failure Assessment (SOFA) scores. Fifty-seven patients survived

beyond 6 months post-ICU admission, and 41 long-term survivors undertook HRQOL and psychological evaluation. These survivors had significantly poorer SF-36 self-assessed HRQOL scores compared to age-and-sex matched controls, and persistent mental problems were revealed.

ENCOURAGE is the first mortality risk score for AMI-cardiogenic shock patients treated by VA-ECMO. This score has higher AUC than other prediction scores and uses seven variables, making it simpler than the SAVE score (11 parameters). The number in the analyzed population is much smaller than that for the SAVE score, but large enough for a 2-center study. This study included evaluation of long-term survival outcomes, HRQOL, and psychological status, which is the strength of this study, since it is difficult to achieve in the current ELSO registry. ECMO is a potentially effective life-saving device in refractory shock patients. To reduce futile ECMO implementation in unsalvageable patients, evaluation of pre-ECMO factors and prediction of mortality are desirable.

Schmidt *et al.* reported the PRedicting dEath for SEvere ARDS on VV-ECMO (PRESERVE) score to predict the 6-month post-ICU mortality in acute respiratory distress syndrome (ARDS) patients treated by ECMO (17). It includes eight parameters: age, BMI, immune compromise, SOFA score, mechanical ventilation duration, no prone positioning, positive end-expiratory pressure (PEEP), and plateau pressure. Despite using the same ECMO devices, ARDS and cardiogenic shock are different in pathophysiology and treatment. Specific scoring for each disease is reasonable, and it may help physicians decide on appropriate ECMO implementation.

There are limitations in this study. First, the two centers studied are experienced high-volume centers, and patient characteristics and critical care policy might differ from those of other centers or countries. Thus, survival analysis of ECMO patients is often difficult to apply to other hospitals. Second, validation of the ENCOURAGE score in other cohorts was not performed. Determination of VA-ECMO indications in AMI-cardiogenic shock patients using the ENCOURAGE score from ECMO-treated patients alone is of equivocal value. As noted above, a multiinstitutional prospective study will establish the usefulness.

Poorer HRQOL and some mental disorders were reported in long-term survivors. It is difficult to determine whether this was the result of cardiogenic shock, VA-ECMO management, prolonged ICU stay, or other factors. However, medical practitioners understand the significance of long-term outcomes including physical function and mental or cognitive status in the field of critical care. The mechanisms of cognitive impairment or psychological disorders should be clarified in further investigations.

Predictive variables for neurological outcome in inhospital cardiac arrest (IHCA) patients have been reported: younger age; initial cardiac arrest rhythm of ventricular fibrillation or pulseless ventricular tachycardia, with a defibrillation time of <2 minutes; baseline neurological status without disability; arrest location in a monitored unit, shorted duration of resuscitation, and absence of mechanical ventilation; renal insufficiency; hepatic insufficiency; sepsis; malignancy; and hypotension prior to arrest (18). Accurate prediction of outcome after cardiac arrest or refractory shock is always challenging, but an estimation would provide critical information for physicians, patients, and families. Importantly, the ENCOURAGE score does not prevent current clinical decision-making, but we can add the findings to clinical practice and existing knowledge. Sharing the predicted mortality with family and caregivers will contribute to the appropriate decision for treatment withdrawal after ECMO implementation.

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# Footnote

*Provenance:* This is an invited Commentary commissioned by the Section Editor Zhongheng Zhang (Department of Critical Care Medicine, Jinhua Municipal Central Hospital, Jinhua Hospital of Zhejiang University, Jinhua, China). *Conflicts of Interest:* The authors have no conflicts of interest to declare.

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