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Editorial

Clinical Significance of Low-flow Time in Patients Treated with Extracorporeal Cardiopulmonary Resuscitation

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▸ See the article "Relationship between Clinical Outcomes and Cardiopulmonary Resuscitation Time in Patients with Acute Myocardial Infarction Treated by Extracorporeal Membrane Oxygenation-Assisted Primary Percutaneous Coronary Intervention" in volume 48 on page 705.

Despite advances in treatment techniques and mechanical circulatory support for acute myocardial infarction (AMI), AMI complicated by cardiogenic shock is still a leading cause of death. Under these circumstances, accompanied by cardiopulmonary collapse, extracorporeal membrane oxygenation (ECMO)-assisted cardiopulmonary resuscitation (ECPR) has been increasingly utilized.[1] Several observational studies have shown an improved survival rate with this method compared to conventional CPR in patients with in-hospital cardiac arrest.[2] In addition, a recently published meta-analysis including 856 in-hospital cardiac arrest patients treated with ECPR showed acceptable clinical outcomes, with 324 (37.9%) patients surviving to discharge, and good neurological outcomes (Cerebral Performance Category 1 or 2) occurred in 222 of 263 (84.4%) survivors.[3] In previous studies, a shorter low-flow time, age, initial shockable rhythm, pulse pressure, lower lactate level, and lower Sequential Organ Failure Assessment score were predictors of poor overall survival after ECPR.[1][3]

In this issue of the *Korean Circulation Journal*, Cho et al.[4] investigated the association between CPR time and clinical outcome in 42 AMI patients complicated by cardiac arrest and who were treated by ECMO-assisted primary percutaneous coronary intervention from July 2008 to March 2016. The authors showed that AMI patients with complications from cardiac arrest remain in poor condition despite ECMO support, and that CPR time >12 min is a unique prognostic factor for in-hospital mortality in this population treated with ECMO-assisted primary percutaneous coronary intervention. Based on these findings, the authors suggest that both an experienced ECMO team for priming ECMO circuits and application of ECMO as soon as possible should be required to improve survival after cardiac arrest. Actually, the prognosis of AMI patients treated with ECPR may be affected by pre-ECMO factors (e.g., age, comorbidities, obesity, low Glasgow Coma Score, elevated lactate, and an initial arrest rhythm), intra-ECMO factors (e.g., successful revascularization, CPR to ECMO time, and vascular complications), and post-ECMO factors (e.g., bleeding, limb ischemia, left ventricular distension, and Harlequin syndrome), as well as by further treatment options, like implanted left ventricular assist devices or cardiac transplantation. Among these factors, CPR to ECMO time representative of low-flow time is a clinically unique modifiable factor. The authors used CPR time instead of CPR to ECMO pump-on time to evaluate the impact of low-flow time on clinical

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outcomes of ECPR. However, most previous papers have used CPR to ECMO time because it reflects low-flow time better in clinical situations with low incidence of return of spontaneous circulation or recurrent cardiac arrest prior to pump-on, such as in the study population of this paper. Previous several studies reported that CPR to ECMO time ranged from 30 to 60 minutes.[1)3)5)] Based on our experiences, the paper regarding the prognosis of ECPR indicated that the probability of survival to discharge decreased to 0.45, 0.37, 0.30, 0.24, and 0.18 as the ECMO pump-on time was delayed to 20, 30, 40, 50, and 60 min, respectively.[1)] Considering findings from previous and the current study, it seems clear that we can achieve improved survival when a patient receives ECMO pump-on as soon as possible. Thus, it may be necessary to establish a hospital-specific strategy for ECMO pump-on within acceptable low-flow time from initiation of CPR, with availability to do so 24 hours per day, seven days per week.

Theoretically, low-flow time might be more closely associated with worse neurological outcomes rather than with higher mortality in patients who undergo ECPR. The clinical significance of low-flow time should be interpreted after considering an interaction with age. The relationship between low-flow time and poor neurological outcome appeared to be attenuated in younger patients.[6)] Not uncommonly, in real-world practice, younger patients have been found to have better neurological outcomes even with a prolonged duration of CPR. Although the reason for these findings is unclear, young brains might have increased reserve and tolerance to hypoxic-ischemic injury and secondary injury, which is characterized by an imbalance in post-resuscitation reperfusion.[6)] In addition, neurologic examinations, body temperature pattern, gray-to-white matter ratio, optic nerve sheath diameter, and cortical sulcal effacement on initial brain CT scans could provide better information to physicians regarding brain injury caused by low-flow time in patients who underwent ECPR[5)]. Recently, Lamhaut et al.[7)] showed that ECPR, including prehospital ECPR, in the management of refractory cardiac arrest is feasible and can lead to a significant increase in neurologically intact survivors. Based on these findings, in addition to in-hospital treatments such as high-quality CPR, rapid implementation of ECMO, and the strategy of primary percutaneous coronary intervention to reduce low-flow time, it would be beneficial to establish pre-hospital optimal management in order to improve the neurologic prognosis in AMI patients complicated by cardiac arrest.[8)] Although it is not possible to determine the relationship between low-flow time and neurologic outcomes from this study because it is difficult to identify brain death or not due to nature of retrospective study and to perform a powerful multivariable analysis for prognostic factors after ECPR due to the limited number of participants, Cho et al.[4)] added valuable evidence that low-flow time might be associated with higher in-hospital mortality, even in selected AMI patients treated with ECPR.

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