Despite advancements in pharmacological therapy and refinement of the tools and technique of primary percutaneous coronary intervention (PCI) and coronary artery bypass surgery, patients with acute myocardial infarction (AMI) complicated by profound cardiogenic shock (CS) still have unacceptably high in-hospital mortality and unfavorable long-term outcome. Thus, there is an imminent need of a new and safe treatment modality in the management of AMI complicated by profound CS. Growing evidence suggests that extracorporeal membrane oxygenator (ECMO)-supported primary PCI is an effective therapeutic option for saving lives under such conditions. In this review, we describe and interpret the potential role of circulatory mechanical support by ECMO in the setting of AMI complicated by profound CS for improving clinical outcomes. (Circ J 2016; 80: 572–578)

Key Words: Acute myocardial infarction; Extracorporeal membrane oxygenator; Profound cardiogenic shock

Over the past decade, with the advancement of pharmacological therapy,1–6 continuous improvement of the instruments7–16 and skills for percutaneous coronary intervention (PCI) and coronary artery bypass surgery, patients with acute myocardial infarction (AMI) complicated by profound cardiogenic shock (CS) still have unacceptably high in-hospital mortality and unfavorable long-term outcome. Thus, there is an imminent need of a new and safe treatment modality in the management of AMI complicated by profound CS. Growing evidence suggests that extracorporeal membrane oxygenator (ECMO)-supported primary PCI is an effective therapeutic option for saving lives under such conditions. In this review, we describe and interpret the potential role of circulatory mechanical support by ECMO in the setting of AMI complicated by profound CS for improving clinical outcomes. (Circ J 2016; 80: 572–578)

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What Is the Clinical Value of IABP in AMI Complicated by CS or Profound CS?

Intriguingly, although some clinical trials29,36–38 have demonstrated that IABP support does not reduce in-hospital mortality, in their daily clinical practice many interventional cardiologists currently still frequently utilize IABP for those patients with AMI complicated by CS15 or for those with acute coronary syndrome and hemodynamic instability.46,47 In fact, current guidelines still recommend that IABP support should
ECMO-Assisted Primary PCI

be considered for those patients with AMI complicated by CS.39,48

IABP is the most widely accepted circulatory assist device for patients with unstable hemodynamic status. The underlying mechanism of IABP is believed to be increasing coronary perfusion in the diastolic phase by inflation of the balloon in the descending aorta (ie, flow augmentation in the diastolic phase) and to reduce afterload in the systolic phase by deflation of the balloon (ie, systolic unloading). In fact, in the setting of STEMI complicated by CS, the hemodynamic status is extremely unstable during the primary PCI procedure.15–17,28,30–35,42–44 In this situation, application of primary PCI for re-canalization of the infarct-related artery (IRA) to achieve a final Thrombolysis in Myocardial Infarction (TIMI)-3 flow is frequently “mission impossible”. On the other hand, IABP support with or without inotropic drugs could offer at least temporarily stable hemodynamics, which is crucial for interventional cardiologists to have enough time to complete the primary PCI procedure and achieve TIMI-3 flow in the IRA. Abundant previous data have shown that a final TIMI-3 flow is a strong and independent predictor of favorable clinical outcome in AMI patients undergoing reperfusion therapy.9,10,16,22,27,32,48

Based on these findings, one may wonder why IABP support failed to offer any benefit to clinical outcome in this condition in recent clinical trials.29,36–38 In fact, this remains an issue of continuous debate in interventional cardiology.29,36–42

The Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial is by far the most important randomized clinical trial29 to study the role of IABP in post-AMI CS. The results of the study concluded that IABP did not significantly reduce the 30-day mortality rate in AMI patients complicated by CS for whom an early revascularization strategy was planned. In a recent review article, Acharji et al challenged the conclusion from the IABP-SHOCK II trial.47 They identified major shortcomings that may have explain the discrepant findings between this trial and many other registries.8,10,16,22,27,32,48 These include: (1) time intervals from chest pain onset or AMI recognition to revascularization, patient enrollment, and IABP initiation were not divulged; (2) 86.6% of the treatment arm had IABP initiated only after the index PCI procedure while 4.3% did not receive IABP at all; (3)
fields; low SBP unrelated to cardiac arrhythmia, showing no response to adequate fluid supply and requiring vasopressor agent infusion. Profound CS was defined as SBP <75 mmHg despite intravenous inotropic agent administration and IABP support, and associated with altered mental status and respiratory failure. The results of our study showed that the in-hospital mortality rate was substantially higher in patients with profound CS than in those with non-profound CS (71.4% vs. 22.1%) (Table). Furthermore, profound CS was strongly and independently predictive of 30-day mortality. Our study had important clinical implications. As the in-hospital mortality rate of profound CS patients was comparable to that in the pre-reperfusion era, our study results suggested an ineffectiveness of IABP-supported primary PCI in this patient subgroup. Therefore, it raised the need to use more powerful mechanical circulatory support for patients with profound CS undergoing primary PCI.

Therapeutic Role of ECMO in Patients With Profound CS Undergoing Primary PCI

Our previous study demonstrated that the 30-day mortality in STEMI patients with profound CS undergoing primary PCI was remarkably lower with combined IABP and ECMO support than in those who only received IABP support (72.0% vs. 39.1%, P=0.008) (Figures 1, 2), resulting in a relative risk reduction of 45.8%. The finding suggested that 1 life can be saved for every 3 uses of ECMO in these patients. Accordingly, it underscores the potential role of ECMO-supported primary PCI to reduce the mortality in STEMI patients with profound CS. Because the study assessed mostly the efficacy and safety of IABP initiated after PCI, Acharji et al remarked that the study conclusion should not be extrapolated to situations in which IABP is being utilized before or during PCI in patients with CS.

Of particular issue in the IABP-SHOCK II trial was that it did not clarify the mortality rate between patients with profound CS and those patients with non-profound CS. These 2 groups of patients have been identified by our previous studies as having entirely different rates of in-hospital mortality (Table). Our studies further demonstrated that in patients with STEMI complicated by profound CS, even undergoing IABP-assisted primary PCI, the 30-day mortality remained as high as 80%. Accordingly, we concluded that IABP-assisted primary PCI did not offer additional benefit for STEMI patients complicated by profound CS. Therefore, early upgrade to a more effective mechanical circulatory support should be considered in such patients undergoing primary PCI.

Importance of Stratifying CS as Profound or Non-Profound in STEMI

To the best of our knowledge, we have been the first to stratify STEMI patients with CS at presentation into 2 groups: (1) profound shock and (2) non-profound shock (Figure 1, Table). In our studies, non-profound CS was defined as patients who met the following 2 prospective criteria upon presentation or in the cardiac catheterization laboratory: chest X-ray showing pulmonary edema with systolic blood pressure (SBP) <90 mmHg or persistent hypotension with SBP <90 mmHg associated with low cardiac output and clear lung fields; low SBP unrelated to cardiac arrhythmia, showing no response to adequate fluid supply and requiring vasopressor agent infusion. Profound CS was defined as SBP <75 mmHg despite intravenous inotropic agent administration and IABP support, and associated with altered mental status and respiratory failure. The results of our study showed that the in-hospital mortality rate was substantially higher in patients with profound CS than in those with non-profound CS (71.4% vs. 22.1%) (Table). Furthermore, profound CS was strongly and independently predictive of 30-day mortality. Our study had important clinical implications. As the in-hospital mortality rate of profound CS patients was comparable to that in the pre-reperfusion era, our study results suggested an ineffectiveness of IABP-supported primary PCI in this patient subgroup. Therefore, it raised the need to use more powerful mechanical circulatory support for patients with profound CS undergoing primary PCI.

Figure 2. Kaplan Meyer analysis comparing the survival rate of profound cardiogenic shock patients with and without ECMO support, demonstrating the 30-day mortality was notably reduced in patients with ECMO support compared with those without ECMO support. ECMO, extracorporeal membrane oxygenator. (Adapted with permission from Sheu JJ, et al.)

Table 1. Comparison of survival rate between the ECMO and the non-ECMO group

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<tr>
<th>Follow-up (Days)</th>
<th>With ECMO</th>
<th>Without ECMO</th>
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<tr>
<td>0</td>
<td>46</td>
<td>25</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>7</td>
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<tr>
<td>2</td>
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<td>3</td>
<td>28</td>
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of profound CS suggests a synergistic effect of ECMO providing cardiopulmonary circulatory support, which relieves the workload of the heart and the lung, while IABP augments diastolic perfusion and reduces afterload. In fact, in STEMI patients with profound CS, complete revascularization is usually difficult and the chance of achieving a normal blood flow (ie, TIMI-3) in the IRA is often very low. This further contributes to the very unstable blood pressure in these patients. On the other hand, with the use of ECMO support, the patient’s hemodynamic condition can be stabilized while the interventionist gains enough time to completely revascularize the IRA. Of paramount importance is that combined IABP-ECMO-supported PCI offers dual benefits; namely, stabilized hemodynamics and increased coronary artery perfusion. Therefore, the chance of having normal blood flow in the IRA will be maximized. Consistent with this, Tsao et al demonstrated that in patients with profound CS undergoing primary PCI, the 1-year mortality rate was significantly lower with combined IABP and ECMO support than in those with only ECMO support. These findings reinforce the concept that combined IABP and ECMO support is better than only ECMO or only IABP support for improving the prognosis of profound CS patients undergoing primary PCI.

In the study that confirmed the positive role of ECMO in profound CS patients undergoing primary PCI, it was dependent on several critical factors. First, a prompt decision to initiate ECMO as a hemodynamic salvaging procedure in the cardiac catheterization laboratory or even the Emergency Room should be made. This means that whenever the patient fulfills criteria of profound CS, ECMO should be implanted without delay. Second, early and rapid primary PCI should be performed by experienced interventional cardiologists. Third, a trained and dedicated ECMO team should be established, comprising interventional cardiologists, cardiovascular surgeons, technicians and senior nurses who work closely with other colleagues who manage STEMI patients.

Another important observation in our experience is that the duration of hospitalization in patients with profound shock who received ECMO was significantly longer (35.3±38.2 vs. 2.9±3.4 days, P=0.0005). This is because ECMO support may serve as a bridging procedure to subsequent definitive therapeutic intervention such as heart transplantation for pump failure or other treatment strategies for this high-risk patient population.

**ECMO Support for Hemodynamic Collapse Patients in Other Clinical Settings**

The role of ECMO in patients with cardiac arrest has also been examined. The study by Chen et al studied patients undergoing...
Sung PH et al.

That study implied the potentially beneficial role of ECMO-assisted CPR for patients with cardiac arrest, which warrants further studies.

In our hospital, a program of portable ECMO for patients with profound CS was set up in May 2003; the ECMO team consists of 3 senior cardiovascular surgeons, 2 senior interventional cardiologists, several senior coronary artery bypass cardiopulmonary resuscitation (CPR) who were assisted by ECMO vs. conventional CPR in adults with in-hospital cardiac arrest. In this observational study, they prospectively enrolled patients within 3 years who had experienced an in-hospital cardiac arrest and underwent CPR for longer than 10 min. A total of 113 patients were enrolled in the conventional CPR group and 59 were enrolled in the ECMO-assisted CPR group. The results of the study demonstrated that ECMO-assisted CPR patients had significantly higher survival rates at discharge (28.8% vs. 12.3%, P<0.0001), 30 days (P=0.003) and 1 year (P=0.006) as compared with the conventional CPR group. That study implied the potentially beneficial role of ECMO-assisted CPR for patients with cardiac arrest, which warrants further studies.
surgery technicians and a senior nurse. Being a rapid-response team allows the procedure of ECMO implantation to be performed in the cardiac catheterization laboratory, at the bedside, in an operation theatre, in the Emergency Room, or in a coronary care unit (Figure 3). Between 2003 and 2010, 134 patients with profound CS unrelated to STEMI (Figure 4) who underwent 10–15 min of CPR with ECMO support were prospectively identified to elucidate the effect of ECMO on clinical outcome. The results demonstrated that the in-hospital mortality was 57.5%. Kaplan-Meier analysis identified a 30-day free survival rate of 54.5% in the study patients (Figure 5); 68 patients (50.7%) were successfully weaned from ECMO and 57 (42.5%) were discharged alive. These findings, corroborated with those from Chen et al, suggest that ECMO-assisted CPR may offer additional benefit on improving short-term and intermediate-term survival over conventional CPR in patients with in-hospital cardiac arrest of cardiac origin.47,49

Conclusions

Growing evidence supports ECMO as a new interventional tool to improve the prognosis of patients with STEMI complicated by profound CS undergoing primary PCI. Apart from STEMI, ECMO has proved to be a good mechanical circulatory supportive device for saving the lives and improving the short-term and intermediate-term prognosis in patients with profound CS of cardiac origin. In order to effectively incorporate ECMO into the routine management of profound CS, it is prudent to set up a dedicated team that has the ability to quickly set up the system and work with a multidisciplinary approach.

References


