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Biventricular unloading in patients with refractory cardiogenic shock

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ABSTRACT

Background: Cardiogenic shock remains a clinical challenge with high mortality rate. Mechanical circulatory support (MCS) devices have become an integral component of the therapeutic armamentarium expanding the treatment options for refractory cardiogenic shock (RCS).
Methods: We included all consecutive patients with biventricular unloading with Impella-2.5 and VA-ECMO admitted for RCS between October 2013 and March 2015. Outcome data included survival to discharge, bridging to VAD and 28-day mortality.
Results: A total of 17 patients were included. Mean age was 63.3 ± 10.5 and 15 (88%) patients were male. RCS resulted from acute myocardial infarction in 14 (82%), acute myocarditis in 1 (6%) dilated cardiomyopathy in 2 (12%) patients. Mean SAPS II and SOFA score on admission was 74.7 ± 16.86 and 11.16 ± 1.79, respectively. Vasopressor doses and lactate levels were significantly decreased within 72 h on biventricular support ($p = 0.025$ for norepinephrine and $p = 0.005$ for lactate). Nine (53%) patients died while on support. Of the remaining 8 patients, 5 (29%) patients were weaned successfully and discharged in cardiac rehabilitation and 3 (18%) patients were successfully bridged to VAD. All 5 patients who were discharged to rehabilitation survived at day 28 after discharge, while 1 of 3 VAD patients died after VAD implantation, corresponding to an overall 28-day survival rate of 41%.
Conclusions: Biventricular support with Impella-2.5 and VA-ECMO in patients with RCS is feasible and led to significant hemodynamic improvement and reduction of lactate levels. Despite high severity scores, ICU- and 28-day mortality rates were better than predicted.

1. Introduction

Cardiogenic shock refractory to standard therapy with inotropes, vasopressors and revascularization remains a clinical challenge with high mortality rate [1]. Percutaneous mechanical circulatory support (MCS) devices have become an integral component of the cardiovascular therapeutic armamentarium expanding the treatment options for refractory cardiogenic shock (RCS). Accordingly, there has been a rise in the use of percutaneous MCS for RCS [2], such as the Impella microaxial flow pump and peripheral veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

Although the treatment of RCS with MCS plays a crucial role in clinical practice, the best strategy is still uncertain. The ESC and AHA/ACC guidelines on ST-elevation myocardial infarction state that LV assist devices may be considered for circulatory support in RCS with a IIb/C recommendation [3,4]. Despite the variety of devices for MCS in cardiogenic shock (CS) [1,5], there are only few prospective randomized trials. Recently, the large randomized IABP Shock II Trial did not show a significant reduction in 30-day [6] or 12-month [7] mortality with IABP insertion in patients with CS complicating myocardial infarction. For RCS due to LV failure minimally invasively placed short-term LV assist devices, like Impella, are the most optimal mechanisms of treatment. The Impella-2.5 is a 9F catheter-mounted microaxial rotary flow pump, which can be rapidly inserted percutaneously and provides continuous blood flow up to 2.5 L/min. Short-term circulatory support with Impella-2.5 has been demonstrated to be safe and feasible in patients with high-risk coronary interventions [8] but also in patients with acute cardiogenic shock [9].

One other option for support includes the VA-ECMO system. The VA-ECMO can also be implanted percutaneously and provides cardiopulmonary support. VA-ECMO can be used in various cardiac emergencies, including refractory cardiogenic shock [10] due to uni- or biventricular failure and cardiopulmonary resuscitation [11]. However, despite good systemic blood flow and biventricular support, ECMO pressurizes the arterial circuit increasing LV afterload resulting in insufficient LV-unloading, LV-distention and worsening pulmonary edema, especially in patients with severely depressed LV function [12].

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Patients with CS may present with LV-failure, biventricular failure or even combined cardiopulmonary failure. Therefore, selection of the appropriate MCS should be tailored according to the underlying pathophysiology and properties of the respective MCS device. In patients who present with biventricular failure or combined cardiopulmonary failure the implantation of a VA-ECMO seems most appropriate, whereas patients with univentricular LV failure are particularly suitable for Impella device implantation. However, in some cases, despite optimal medical treatment, revascularization and even MCS with Impella or VA-ECMO, CS evolves and progresses rapidly. Patients with Impella who initially presented with univentricular LV failure may develop additionally RV dysfunction or pulmonary failure whereas patients with VA-ECMO may show signs of LV overloading, causing pulmonary edema, LV distension and thus compromising LV myocardial recovery. In the setting of RCS, these life-threatening situations have to be identified quickly and managed aggressively. Therefore, at our institution we adopted a standard operating procedure regarding the management of these complications. Accordingly, VA-ECMO induced LV overload can be managed successfully with the additional implantation of an Impella device. On the other hand, additional VA-ECMO implantation in patients with Impella and secondary RV failure (e.g. biventricular failure) or pulmonary failure will provide the appropriate support due to RV unloading and oxygenation support.

Patients with CS often develop a systemic inflammatory response syndrome (SIRS) progressing to multi-organ dysfunction syndrome (MODS) and subsequent death, despite intensive therapy. The available evidence suggests that the development of SIRS plays a central role in the pathogenesis of shock and the adverse outcome of patients with CS [13]. It is therefore critical to identify these patients and cumulative data suggest that intensive care and MODS severity scoring systems scores (e.g. SAPS II) can play an important role in predicting mortality in patients with CS [14–16].

In this retrospective, single-center study, we report our experience with biventricular support with Impella-2.5 and peripheral VA-ECMO on intensive care unit (ICU)-mortality and bridging to long-term ventricular assist device (VAD) in patients with RCS.

2. Materials and methods

2.1. Patients

We retrospectively reviewed our cardiac intensive care database from October 2013 to March 2015 to identify all patients admitted for RCS with biventricular support with Impella-2.5 and VA-ECMO. Among 221 MCS cases (135 with Impella and 86 with VA-ECMO), 17 (8%) patients with RCS were on biventricular support with these both devices. In 12 (71%) patients the Impella-2.5 device was implanted first, whereas 5 (29%) patients were placed first on VA-ECMO. The decision algorithm for the choice of mechanical circulatory support in severe cardiogenic shock is outlined in Fig. 1. In brief, the Impella device is our first choice of MCS in patients with cardiogenic shock due to isolated left ventricular (LV) failure. In cases of biventricular failure or cases with LV failure and pulmonary failure or persistent cardiac arrest, we implant a VA-ECMO first. If peripheral VA-ECMO support results in insufficient LV unloading with left ventricular distension and worsening pulmonary edema, an Impella-2.5 is additionally inserted. The development of right ventricular (RV) failure, hypoxemic respiratory failure, further hemodynamic deterioration or progressive multi-organ failure during Impella support is, according to our algorithm, an indication for supplementary implantation of a VA-ECMO (Fig. 1).

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee. The local ethics committee waived the need for informed consent due to the retrospective nature of the study.

2.2. Definitions

Refractory cardiogenic shock was defined by persistent hypotension (systolic blood pressure < 90 mmHg or mean arterial pressure < 65 mmHg) and sustained evidence of impaired end-organ perfusion despite adequate fluid administration and high dose of inotropes and vasopressors. Isolated LV failure was defined by reduced systolic LV ejection fraction below 40% without RV dysfunction. Insufficient LV unloading during VA-ECMO support was defined as worsening pulmonary edema on chest radiography and increasing LV dilatation or the presence of spontaneous echocontrast in the LV cavity or insufficient opening of the aortic valve due to ECMO-induced afterload. In the absence of a standardized definition, right ventricular dysfunction was defined by the presence of RV dilatation (basal diameter > 42 mm) and systolic dysfunction (TAPSE < 16 mm). Hypoxemic lung failure was defined as PaO_2/FIO_2 < 200 mmHg with PEEP > 5 cmH_2O.

2.3. Implantation of MCS and patients management during circulatory support

All MCS devices were implanted under fluoroscopic control in catheterization laboratory. The Impella-2.5 (Abiomed Europe GmbH, Aachen, Germany) was inserted percutaneously in the femoral artery and positioned retrogradely across the aortic valve under fluoroscopy to allow for LV support. The Impella-2.5 provides up to 2.5 L/min of forward flow expelling blood from the LV into the ascending aorta. The degree of support can be managed by graduation of the pump speed (maximal rotation pump speed of 51.000 rpm) on the impella console.

The VA-ECMO circuit (Maquet Getinge Group) consisted of a centrifugal pump and an membrane oxygenator for complete cardiopulmonary support. The arterial (17F) and venous femoral (21 for female or 23F for male) canulae (Maquet Getinge Group) with an additional antegrade 7 F femoral limb perfusion cannula were percutaneously inserted in the catheterization laboratory. VA-ECMO is the only device to provide complete respiratory support in addition to circulatory support.

Echocardiographic studies were systematically performed during mechanical circulatory support for monitoring Impella position, LV-, RV- and cardiac valve function, as well as signs of insufficient LV-unloading. Unfractionated heparin was administered to

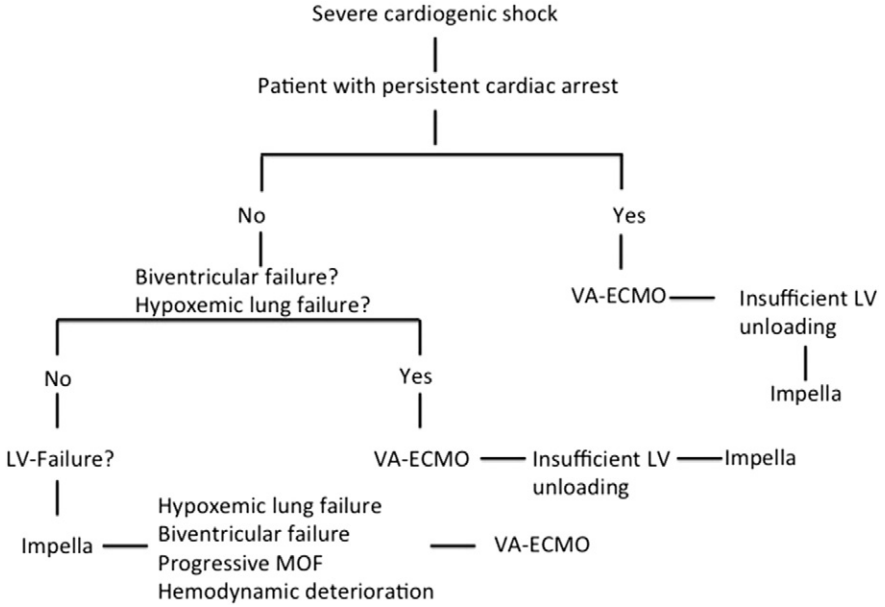

Fig. 1. Decision algorithm on mechanical circulatory support in severe cardiogenic shock.