

Mechanical circulatory support in cardiogenic shock – what every interventional cardiologist should know

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Postep Kardiol Inter 2014; 10, 3 (37): 195–200
DOI: 10.5114/pwki.2014.45147

Abstract

Cardiogenic shock (CS) remains the main cause of death in patients with myocardial infarction. Conservative treatment alone does not sufficiently improve prognosis. Mortality in CS can only be significantly reduced with revascularization, both surgical and percutaneous. However some patients present with haemodynamic instability despite optimal medical treatment and complete revascularization, resulting in very high mortality rates. These patients require the implementation of mechanical circulatory support in order to increase systemic blood flow, protect against organ hypoperfusion and protect the myocardium through a decrease in oxygen consumption. In contemporary interventional cardiology it seems that every operator should be aware of all available mechanical circulatory support methods for their patients. This article aims to present the current state of knowledge and technical possibilities in this area.

Key words: mechanical circulatory support, shock, extracorporeal membrane oxygenation, percutaneous ventricular assist devices.

Cardiogenic shock

Cardiogenic shock (CS) is the main cause of death in patients with myocardial infarction. The prevalence of this complication is estimated at 2–8% of cases and is significantly higher in ST segment elevation myocardial infarction (STEMI) patients when compared do non-ST segment elevation myocardial infarction (NSTEMI) [1–3]. It has been shown that the prognosis of CS patients is worse than in non-CS subjects. The in-hospital mortality of STEMI patients is 38% vs. 1.9% in CS vs. non-CS groups, respectively [4]. This is also observed in long-term analysis. In the TRACE study 30-day (62% vs. 9%) and 6-year mortality (88% vs. 45%) were significantly higher in myocardial infarction complicated by CS. In a multivariate analysis CS was a predictor of higher mortality [5]. Similarly, a higher 30-day mortality in STEMI CS patients was shown by Singh *et al.* (49.6% vs. 11.1%). After exclusion of patients dead within 30 days from myocardial infarction (MI) in 11-year observation the mortality in the CS group was still significantly higher (44.8% vs. 30.6%). Moreover, CS was an independent risk factor of 11-year mortality [6].

Mortality in CS patients is high and is dependant on the administered therapy. Medical treatment is associated with an 80% mortality rate [7]. Thrombolysis also does not significantly alter the prognosis of these patients. In a randomised GISSI-1 trial (Grupppo Italiano per lo Suddiodella Streptochinasi nell'Infarto Miocardico), which assessed the efficacy of streptokinase treatment in myocardial infarction, the CS patients had similar in-hospital mortality with no regard to the administered treatment (71.1% in the thrombolysis group vs. 69.9% in the no-thrombolysis group) [8]. Nevertheless, it was proven that thrombolysis led to a reduction of CS occurrence. The CAPTIM trial (Comparison of Angioplasty and Pre-hospital Thrombolysis In Acute Myocardial infarction), which compared pre-hospital fibrinolysis to primary percutaneous coronary intervention (PCI), a significantly lower percentage of CS prior to hospital admission was shown in subjects who were pre-treated with fibrinolysis (0% vs. 3.6%). This relationship was proven mainly in patients with chest pain onset < 2 h [9].

The mortality of CS patients may only be decreased by revascularisation. In the Shock Trial Registry the in-hos-

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Received: 11.05.2014, **accepted:** 18.07.2014.

pital mortality rate was 27.9% in patients treated with coronary artery bypass grafting (CABG), 45.5% in the PCI group, and 59.6% in patients without revascularisation. In a multivariate analysis, revascularisation was associated with decreased mortality [10]. A similar correlation was observed by Carnendran *et al.* In-hospital mortality in patients that had undergone revascularisation was 41%, while in the non-revascularization group it was 79% [11]. The correlation between revascularisation and long-term survival was analysed in the Shock Trial [12]. Thirty-day mortality was similar regardless of the implemented treatment. In subjects < 75 years old, who had undergone revascularisation procedures, mortality was significantly lower. In 6-month assessment mortality was 50.3% vs. 63.1% in favour of revascularisation. In a multivariate analysis this form of treatment was identified as an independent factor of better 6 – and 12-month survival. Correspondingly, in an analysis by Hochman *et al.*, patients who had undergone revascularisation had lower 3-year (58.6% vs. 71.7%) and 6-year (67.2 vs. 80.4%) mortality. In a multivariate analysis, revascularisation was an independent factor of lower mortality [13].

Mechanical circulatory support

Various levels of left ventricular dysfunction during MI are the reason for a certain heterogeneity of CS patients, resulting in different reactions to treatment. This is reflected in the analysis by Samuels *et al.* of 3462 patients who underwent cardiovascular surgery. The authors assessed in-hospital mortality with regard to the quantity and dosage of inotropic drugs. The mortality was respectively 2% (no inotropes), 3% (low dose), 7.5% (medium dose), 21% (high dose of a single agent), 42% (high doses of two agents), and 80% (high doses of three agents) [14].

It is also clear that patients with CS benefit from revascularisation. Angiographically optimal reperfusion, with persistent haemodynamic instability (low blood pressure) is associated with worse clinical outcomes. Such a condition, referred to as “profound shock”, is defined as systolic blood pressure (SBP) < 75 mm Hg despite introduced treatment. Yip *et al.*, in a group of 89 patients with MI, diagnosed profound shock in 24% of subjects. In-hospital mortality in this particular group was 71.4%, as opposed to 22.1% in patients haemodynamically stable after reperfusion. In a multivariate analysis profound shock was an independent factor of higher mortality [15]. Haemodynamic instability in patients with CS despite optimal medical treatment and complete revascularisation justifies the implementation of mechanical circulatory support. These devices are meant to increase systemic blood flow, protect against organ hypoperfusion, and protect the myocardium through a decrease in oxygen consumption. These methods are as follows: intra-aortic balloon pumping (IABP) and percutaneous ventricular assist devices (pVAD) such as extracorporeal membrane oxygenation (ECMO), TandemHeart, and Impella (Table I).

Intra-aortic balloon pump

The relationship between IABP and patient prognosis was assessed in the Shock Trial Registry (SHould we emergently revascularise Occluded Coronaries for cardiogenic shock?). Significantly lower in-hospital mortality was proven in patients with CS treated with thrombolysis, in whom IABP was used (50% vs. 72%). The authors explain this by the fact that in patients with IABP there was a higher possibility of subsequent revascularisation [16]. The NRMI-2 registry assessed 23180 patients. It confirmed that patients treated with thrombolysis benefit-

Table I. Mechanical circulatory support options – summary

Parameter	IABP	ECMO	Impella 2.5/CP/5.0	TandemHeart	Pulsatile VAD	Constant flow VAD
Pump mechanism	Pneumatic	Pneumatic/centrifugal	Axial	Centrifugal	Pneumatic	Centrifugal/axial
Implantation	7–8 Fr via femoral artery	15–19 Fr via femoral artery and 23–28 Fr via femoral vein	13 Fr/14 Fr/surgical cutdown; femoral artery	15–17 Fr via femoral artery and 21 Fr via femoral vein	Via sternotomy	Via sternotomy
Maximal flow	0.5 l/min	~4 l/min	2.5/3.7/5.0 l/min	4 l/min	~ 8 l/min	Up to 10 l/min
Implantation time	+	+++	++	++++	++++	++++
Anticoagulation	+	++	++	+++	++++	++++
Requires stable heart rhythm	Yes	No	Yes (RV function)	No	Yes	Yes
Support period	Prolonged use possible relatively to clinical state	< 14 days	< 10 days (reported cases up to 14 days)	< 14 days	Long-term use possible	Long-term use possible
Treatment method	Bridge-to-recovery, bridge-to-bridge, bridge-to-transplant	Bridge-to-recovery, bridge-to-bridge, bridge-to-transplant	Bridge-to-recovery, bridge-to-bridge, bridge-to-transplant	Bridge-to-recovery, bridge-to-bridge, bridge-to-transplant	Bridge-to-recovery, bridge-to-transplant	Bridge-to-recovery, bridge-to-transplant, destination therapy

ed from IABP implementation. In-hospital mortality was 49% vs. 67%, respectively, in patients with and without IABP. In a multivariate analysis this form of treatment was an independent predictor of lower mortality. However, in patients treated with primary PCI, there were no significant in-hospital mortality differences (47% vs. 45%, with and without IABP) [17]. Similar results were presented in a meta-analysis of nine studies assessing IABP in CS STEMI patients by Sjauw *et al.* The authors showed that using IABP in the thrombolysis group resulted in lower 30-day mortality, while patients treated with primary PCI and IABP had a risk of 30-day mortality increased by 6% [18]. Significantly though, none of the studies included in the meta-analysis were randomised. Primary angioplasty was the reperfusion method in only two of the studies; in one study, medical treatment only was administered; and in the others there was only thrombolysis and rescue PCI. Moreover, in eight of the studies, patient inclusion was performed before the year 2000. The results of a subsequent meta-analysis in this subject were presented in 2012 by Bahekar *et al.* They showed that in MI complicated by CS the implementation of IABP correlated with a significantly lower in-hospital mortality (RR = 0.72; 95% CI: 0.60–0.86). This was based on the results of six studies (one randomized, two prospective, and three retrospective) [19]. Based on this meta-analysis, ESC 2012 STEMI guidelines have changed the evidence level for IABP use (from IC to IIbB) [20]. IABP-SHOCK II, published in 2012, was a randomised trial analysing the treatment of CS patients with the use of IABP. Six hundred patients were included with STEMI and NSTEMI complicated by CS, treated with revascularisation (IABP was used in 301 subjects). Thirty-day observation showed no significant differences between the groups. Mortality was 39.7% vs. 41.3% in the IABP vs. non-IABP groups. The risk of second MI, stroke, or bleeding were also comparable. Of note, the use of IABP in patients < 50 years old, without MI history, was related to lower mortality. However, it seems that the results of this study should be treated with a certain degree of caution. A quarter of patients were excluded from final analysis. The exclusion criteria were CS symptom onset > 12 h, mechanical MI complications, massive pulmonary embolism, reanimation > 30 min, CNS damage, age > 90, and significant peripheral atherosclerosis. The patients characteristics (mean age 70 years, mean SBP prior to randomization ~ 90 mm Hg, mean creatinine clearance 60 ml/min) and the mortality rate (around 40%) lead us to believe that the study group was relatively “healthy and young” compared to typical CS patients usually treated in clinical settings. Moreover, 10% of the patients primarily randomised to the control group were finally treated with IABP, and in the IABP group 4.3% of patients died before balloon introduction. Mean time of IABP use was 3 days. There are no data as to the percentage of subjects with profound shock in the analysed groups. Also significant, in the non-IABP group

there was a higher frequency of ventricular assist device implantation [21]. In a post-IABP-SHOCK world, present-day clinical practice shows a tendency away from IABP use. Still, there are reports emerging that suggest the device should still be considered in certain situations, such as CS without complete revascularisation or with the presence of MI mechanical complications [22].

Intra-aortic balloon pump – technical aspect

Intra-aortic balloon pump remains the most commonly used method of short – and mid-term circulatory support in cardiology wards. The balloon is introduced in a cathlab via femoral artery (8–9 Fr sheath), and then placed in the descending aorta, below the left subclavian artery. The balloon is filled after aortic valve closure (synchronisation is performed via ECG or BP curve analysis), causing both distal and proximal blood flow. As a result, there is a decrease of late diastolic pressure in the aorta, a decrease of after load and improved coronary perfusion. The increase of cardiac output is estimated to be around 0.5 l/min or around 20%. The main advantages of IABP are ease of use and short time needed to introduce the device, as well as the possibility of prolonged application. However, IABP requires haemodynamically effective cardiac function as well as a stable heart rhythm.

Extracorporeal membrane oxygenation

The studies concerning the use of ECMO in CS are based on relatively small patient groups. Also, the aetiology of CS varies among studies. Analysis by Chung *et al.* assessed 134 patients after sudden cardiac arrest and effective reanimation, with persistent CS symptoms (SBP < 75 mm Hg) despite inotropes and IABP, in whom ECMO was implemented. In the study group there were only 53 patients with MI. Mean blood pressure in the group was 50/30 mm Hg. The ECMO was used for 5.1 days. After haemodynamic stabilisation 50.7% of patients were successfully weaned from ECMO. In this subgroup, in-hospital survival was 83.8%. Significantly, all the subjects who were permanently dependent on ECMO support, without possibility to wean, have since died. In-hospital mortality in the whole group was 57.5% (40.5% in STEMI, 68.7% in NSTEMI). In a multivariate analysis the implementation of ECMO and successful weaning were factors of lower in-hospital mortality [23]. The results of a study assessing the use of ECMO in a group of MI CS patients treated by revascularisation were presented by Kim *et al.* Twenty-seven patients were included. ECMO was weaned in a larger percentage of patients than in the previous study (81.5%), resulting in lower in-hospital mortality (40.8%) [24]. Another observational study assessing the role of ECMO, on a larger group of patients (334) with MI complicated by CS treated by primary PCI, was performed by Sheu *et al.* Only subjects qualified for immediate cardiovascular surgery were excluded. The authors di-

vided the patients into two groups: 263 patients in whom the use of inotropic drugs and IABP led to haemodynamic stability, and 71 patients (21%) with SBP < 75 mm Hg despite such treatment. Subsequently, in the second group ECMO was used. The efficacy of ECMO weaning, defined as 72-hour post-wean survival, was 78.3%. Furthermore, despite the fact that the primary characteristics of both groups were similar, in the ECMO group TIMI 3 flow was obtained more frequently after PCI. In this group there was also a significantly lower 30-day mortality in comparison to the non-ECMO group (39.1% vs. 72%). The mortality in the ECMO group was only slightly higher than in the group of patients not presenting with profound CS (30%). The multivariate analysis has shown that ECMO is an independent predictor of lower 30-day mortality (OR = 0.223; 95% CI: 0.062–0.801) [25]. An analogical group of patients was assessed by Tsao *et al.* They divided the subjects into two study groups: 25 patients with IABP and 33 patients with IABP with/without ECMO. The ECMO was finally used in 18 patients (54.6%). In-hospital mortality in the study groups was respectively 68% and 33.3%. Patient mortality was mainly observed in the in-hospital period (1-month mortality 68% vs. 33.3%, 6-month mortality 68% vs. 36.4%, 12-month mortality 76% vs. 36.4%) [26].

An interesting evolution of the ECMO concept was presented by the Maquet company in the form of a Cardiohelp device – a minimised, portable, percutaneous VA ECMO support. The aim of the device is to enable rapid haemodynamic support in the settings of a cathlab, allowing at the same time for patient transfer to a tertiary cardiovascular centre. Initial reports of Cardiohelp use are promising, showing up to 62% patient recovery rates [27, 28].

Extracorporeal membrane oxygenation – technical aspect

The archetype of ECMO was the cardio-pulmonary bypass system. The principle of the ECMO function is unburdening the circulatory and respiratory system, oxygenation of blood, and elimination of carbon dioxide. In respiratory failure veno-venous ECMO (VV) is used, in which the main function is extracorporeal oxygenation of blood. When circulatory support is the major necessity, veno-arterial ECMO (VA) is required, in which the extracorporeal pump generates additional blood flow, and blood oxygenation is not obligatory (however often used due to insufficient blood oxygenation, as ECMO pumps via the venous sheath from the right atrium). Implantation of VA ECMO in a cathlab requires the introduction of large sheaths in the arterial (femoral artery, 15–17 Fr sheath in females, 17–19 Fr in males) and venous line (femoral vein, sheath 23–28 Fr). The femoral access occasionally requires also an antegrade cannulation of the vessel to obtain proper limb perfusion.

The ECMO is a method of short-term support, mainly during the acute phase. It provides an extra 4 l/min

of blood flow, allows for both circulatory and respiratory support. The use of this method is mainly limited by significant blood trauma and the risk of left-ventricular distension due to blood stasis. The aortic blood flow is mostly retrograde; therefore, oxygenation in the regions supplied by the aortic arch arteries should always be assessed (saturation measurement mandatory). Also, mechanical respiratory support should always be considered, especially when an ECMO oxygenator is not used. Finally, the use of ECMO requires constant control of a perfusionist.

As previously mentioned, the main obstacles against prolonged ECMO use are: blood cell trauma and left ventricle distension. The first can be partially avoided with the use of modern, centrifugal pumps, such as Levitronix CentriMag. The latter, by unburdening the left ventricle, either with percutaneous devices such as pVAD Impella 2.5 or by surgical venting. In such cases, after obtaining surgical access, the ECMO pump may be used as a temporary VAD, in a typical bridge-to-decision setting (VAD or transplantation). Minimisation of blood cell trauma and unburdening of the LV may prolong ECMO use by up to 14 days (and in some reports even longer).

Impella and TandemHeart

Long-term results of percutaneous VAD (pVAD) implantation were presented by Engström *et al.* In a group of 34 patients with STEMI and profound CS, treated by primary PCI, the use of Impella 2.5 and Impella 5.0 pumps was assessed. The clinical characteristics showed that the culprit lesion was in the left main in 38% of cases and the left anterior descending (LAD) in 53%. Angiography in all of the cases revealed TIMI 0 flow in the culprit lesion. The PCI efficacy (defined as final TIMI 3 flow) was 59%. The Authors reported that 30-day mortality was high, around 73.5% (76% Impella 2.5; 67% Impella 5.0) [29]. A similarly high 30-day mortality was observed in a 2013 Impella-EUROSHOCK registry, which included a large group of patients with MI complicated by CS (120 subjects) treated with Impella 2.5. Thirty-day mortality was 64.2%. Age > 65 and lactate level on admission > 3.8 mmol/l were both predictors of higher mortality [30]. There is also a meta-analysis of three randomised trials by Cheng *et al.*, which compares pVAD vs. IABP plus optimal medical treatment. Inclusion criterion for those analyses were as follows: MI complicated by CS (two studies) and MI complicated by CS or decompensated chronic heart failure (one study). Exclusion criteria were as follows: reanimation > 30 min, mechanical MI complications, CS symptoms onset > 12 h, age > 75 years, significant peripheral atherosclerosis, significant aortic regurgitation, right ventricle failure, brain damage, stroke < 6 months, sepsis, severe bleeding, and coagulopathy. These criteria were the reason for excluding 52% of the subjects from a trial by Thiele *et al.*, and 21% from a trial by Burkhoff *et al.* In the final meta-analysis 100 patients were included. Implantation of pVAD was

performed in 53 patients (TandemHeart in two studies and Impella 2.5 in one study); in other subjects IABP alone was used. In the pVAD group a significant improvement of haemodynamics was observed (increased cardiac output, higher SBP, lower wedge pressure) in comparison to the IABP group. Thirty-day mortality, however, showed no significant difference – 45% (pVAD) vs. 43% (IABP). The main complication was the increased incidence of bleeding [31–34]. These trials have limited the pVAD use to a preselected group of patients. The Authors have not proposed a treatment algorithm in this complicated group of patients. There is a clear need for a sufficiently powered randomised clinical trial concerning pVADs. The RECOVER II trial was prematurely stopped due to insufficient recruitment and funding problems. The DanShock trial (currently recruiting) is a randomised, multicentre trial, aimed to assess the efficacy of the Impella device vs. conventional treatment of cardiogenic shock, and may bring many greatly-anticipated answers in the field of pVADs.

pVADImpella – technical aspect

Impella 2.5 is an axial micropump, enabling short-term left ventricular support (7 days). It is a device completely implantable in the settings of a cathlab. It requires an arterial-only access route via a 12–13 Fr sheath. It is then stabilised on the level of the aortic valve. It pumps blood from the left ventricle directly into the aorta, resulting in an additional output of 2.5 l/min. The use of an Impella may also be considered as a way of unburdening left ventricle during VA ECMO use. The main objection to the device is related to the flow limitation, so now there are two modified versions of the Impella device. Impella CP provides 4 l/min flow, but requires a 14 Fr sheath. The relatively large tear-away sheaths are used solely for device introduction; the Impella device is permanently managed via a 9 Fr arterial sheath. Impella 5.0 provides 5 l/min flow, but a surgical cut down is required to access the femoral artery. In order to provide right ventricular support, another modification of the device, the Impella RD, was introduced (at this moment commercially not yet available), showing promise in first-in-man cases [35, 36].

pVADTandemHeart – technical aspect

TandemHeart is a centrifugal pump system for short – and mid-term left ventricular support (14 days) implantable in the settings of a cathlab. The implantation of TandemHeart requires introduction of a 21 Fr sheath into the femoral vein, and then a trans-septal puncture in order to catheterise the left atrium. In the second stage a 15–17 Fr sheath is inserted into the femoral artery. A 30-cm catheter is introduced and the TandemHeart pump is connected. The effective blood flow generated by the device is estimated at 4–5 l/min. The main disadvantage of TandemHeart is the gauge of required vascular sheaths, corresponding to possible peripheral vascular complications.

Future perspectives and summary

Cardiogenic shock is the main cause of death in patients with myocardial infarction. Despite proper revascularisation, the prognosis in this group is still unsatisfying. The IABP use promotes haemodynamic stability and increases the possibility of implementing all available treatment methods. However, even with such therapy, haemodynamic stability sometimes cannot be achieved. In these circumstances the less commonly used methods of mechanical support (ECMO and pVAD) may significantly improve patient outcome.

Rapid development of mechanical circulatory support devices will most likely lead to more common implementation of mechanical circulatory support in CS. Improved pumps, allowing increased flow as well as right ventricular support systems (under development), are likely to lead to improved patient prognosis. Facilitated use of mechanical support as well as introduction of mobile ECMO devices may improve the availability of such treatment for CS patients even in primary cardiac care centres. Perhaps in the near future, in MI complicated by cardiogenic shock, “door-to-support time” might replace the long standing “door-to-balloon time” concept.

Still, it is vital to create an evidence-based algorithm for proper use of these methods in cardiogenic shock. Current data does not provide adequate information concerning questions such as proper time of implantation (pre – or post-PCI) or the selection of patient groups in which the benefit of MCS will be maximal and will outweigh the still significant proportion of complications. This requires randomised trials assessing MCS efficacy and safety in this complicated patient population.

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