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DEBATE

Percutaneous transvalvular microaxial flow pump is underused in infarct-related cardiogenic shock: pros and cons

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Cardiogenic shock (CS) is among the most feared complications of myocardial infarction and leads to high rates of mortality. Percutaneous transvalvular microaxial flow pumps have emerged as an alternative treatment option in the setting of infarct-related CS, offering an alternative to venoarterial extracorporeal membrane oxygenation (VA-ECMO). The principle behind the use of a percutaneous transvalvular microaxial flow pump is to sustain blood flow in the systemic circulation by pumping blood from the left ventricle to the ascending aorta. However, the use of this device is not exempt from complications, mainly including severe bleeding and peripheral vascular complications. In addition, randomised data on the use of percutaneous transvalvular microaxial flow pumps are limited due to the complexity of the clinical scenario, and the profile of optimal candidates is yet to be defined. Based on current evidence, whether a percutaneous transvalvular microaxial flow pump should be used more in patients presenting with myocardial infarction complicated by CS remains an area of uncertainty

Pros

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ST-segment elevation myocardial infarction (STEMI) is complicated by its most severe manifestation, CS, in up to 10% of cases[1]. For decades, the mortality rate in patients with STEMI and CS has plateaued at approximately 50%, despite several attempts to improve survival[1]. In 1999, the SHOCK Trial demonstrated a 6-month survival benefit of acute percutaneous coronary intervention (PCI) in patients with STEMI complicated by CS[2]. Since then, there has been a lack of breakthrough treatments, and the results of subsequent randomised clinical trials have been disappointing[2].

CS is characterised by the hypoperfusion of vital organs due to the severe reduction in cardiac output that is caused by myocardial injury. Therefore, recent attempts to improve the survival of patients with STEMI complicated by CS have focused on percutaneous mechanical circulatory support (MCS)[2]. These include both complete haemodynamic support with VA-ECMO[3] and partial haemodynamic support by unloading the left ventricle using implantation of an intra-aortic balloon pump (IABP) or microaxial left ventricle assist device (LVAD)[2]. Yet, randomised clinical trials investigating the use of MCS in patients with CS have failed to show a reduction in mortality[2]. Of note, the acute manifestation of CS challenges the conduction of randomised trials, and very few exist[2]. Thus, the existing trials encompass heterogeneous patient populations which may have obfuscated the results.

The recently published Danish Cardiogenic Shock Trial (DanGer Shock; ClinicalTrials.gov: NCT01633502) found an absolute 13% reduction in all-cause mortality at 180 days in patients with STEMI and CS treated with a microaxial flow pump (Impella CP [ABIOMED]) plus standard of care compared with standard of care alone[4]. DanGer Shock included 360 patients and is the first trial to show a survival benefit for the use of MCS in patients with STEMI and CS, marking a pivotal cornerstone in treatment of these patients. DanGer Shock followed very strict inclusion and exclusion criteria, and as opposed to previous trials, the trial excluded patients who had an out-of-hospital cardiac arrest (OHCA)[2,4]. Consequently, the DanGer Shock cohort was more homogeneous, emphasising that patient selection is a key component in terms of who may benefit from

a microaxial flow pump in the acute setting of STEMI and CS. The caveats are, of course, adverse events – including major bleeding, limb ischaemia, and renal replacement therapy – which were higher in patients treated with a microaxial flow pump compared with placebo[4]. These severe complications are normally associated with a high mortality rate, and prevention hereof is therefore of crucial importance[5]. However, it is noteworthy that despite a higher complication rate in patients treated with a microaxial flow pump, the mortality in these patients remained significantly lower as compared with standard of care; the number needed to treat (NNT) to avoid 1 death was, remarkably, only 8. Overall, the microaxial flow pump saves lives of patients with STEMI and CS.

Conflict of interest statement

T. Engstrøm is on advisory boards for Abbott and Novo Nordisk; and has received speaker fees from Boston Scientific, Abbott, and Novo Nordisk. J.M. Madsen has no conflicts of interest to declare.

Cons

Uwe Zeymer, MD; Holger Thiele, MD

Until recently, the only proven therapy to reduce mortality in patients with acute myocardial infarction complicated by CS has been early revascularisation of the infarct-related coronary artery, preferably with PCI[6]. Based on the belief that it improves prognosis, MCS devices are increasingly used, despite the fact that all randomised controlled trials with MCS devices in CS were neutral. Until recently, only 2 randomised clinical trials with MCS that were powered for mortality were available, IABP-SHOCK II[7] and ECLS-SHOCK[3], neither of which showed any mortality benefit with the routine use of an IABP or extracorporeal life support, also called VA-ECMO. In contrast, the recently published DanGer Shock Trial[4] reports a significant reduction in 6-month mortality with the use of the microaxial flow pump (Impella CP) in patients with STEMI-related CS. The absolute risk reduction of nearly 13% and the NNT of 8 is clinically important; however, the number needed to harm (NNH) was 6 (severe bleeding, peripheral vascular complications, significant haemolysis, device failure, and damage to the aortic valve).

Importantly, DanGer Shock included a selected patient population with minimal risk of possible hypoxic brain injury and excluded patients with non-STEMI (NSTEMI). Therefore, patients who had suffered an OHCA and remained comatose after the return of spontaneous circulation (ROSC) were not eligible, while patients experiencing cardiac arrest during transfer to the hospital or in-hospital with ROSC were eligible. This is in strong contrast to the ECLS-SHOCK trial, which excluded only patients with a duration of cardiopulmonary resuscitation (CPR) >45 minutes and ultimately randomised 77% of patients after cardiac arrest[3]. Consequently, the main reason for death was neurological in only 6/355 (1.7%) in DanGer Shock in contrast to 20% in ECLS-SHOCK. As a consequence, the results of DanGer Shock do not apply to about 50% of patients with CS, i.e., those with OHCA. These patients were included in the IMPRESS in Severe Shock trial, which did not show any benefit of the microaxial flow pump[8]. In addition, those with non-STEMI were excluded, which is equivalent to another 30% of patients with CS. So, only roughly 20% of patients with infarct-related CS would be eligible for the microaxial flow pump based on the DanGer Shock inclusion criteria.

Although it is always difficult to draw firm conclusions from subgroup analyses, there were 2 relevant populations in DanGer Shock who did not display a benefit from the device. The first were females, in whom mortality was high (65%), with no difference between the pump and standard of care (hazard ratio [HR] 1.01, 95% confidence interval [CI]: 0.58-1.79). The reasons for this finding remain unclear but might be due to the usually older age of female patients (not reported previously), which seems to be in line with the result of a lower benefit in patients with an age >67 years (HR 0.85, 95% CI: 0.59-1.24).

Another important subgroup is patients with a mean arterial pressure >63 mmHg (n=173, 50%). While there was an impressive benefit in those with a mean arterial pressure <63 mmHg (HR 0.61, 95% CI: 0.41-0.92), the reduction in mortality was not significant in the subgroup with higher mean arterial blood pressure (HR 0.88, 95% CI: 0.57-1.34). This difference makes sense from a pathophysiological point of view, since the main effect of the microaxial flow pump is to increase blood flow and blood pressure in the aorta.

Table 1 summarises the patient populations in whom the benefit of the microaxial flow pump has been proven and those in whom this benefit does not seem to have been shown thus far.

As indicated above and also confirmed in a retrospective single-centre analysis of 1,305 patients with CS, only about 20% would have been eligible for DanGer Shock[9], so a widespread application of the DanGer Shock results to a broader CS population does not seem justified.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Table 1. Pros and cons of microaxial flow pump use.

Pro use of microaxial flow pump	Contra use of microaxial flow pump
STEMI	Non-STEMI
Male	Female
Younger age	Older age
Mean arterial pressure <63 mmHg	Mean arterial pressure >63 mmHg
	Right ventricular failure
	Need for oxygenation
	Out-of-hospital cardiac arrest

STEMI: ST-segment elevation myocardial infarction

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