Percutaneous left ventricular assist devices in acute myocardial infarction complicated by cardiogenic shock

Holger Thiele1*, Richard W. Smalling2, and Gerhard C. Schuler1

1Department of Internal Medicine/Cardiology, University of Leipzig—Heart Center, Strümpellstr. 39, 04289 Leipzig, Germany and 2Division of Cardiovascular Medicine, Department of Internal Medicine, The Memorial Hermann Heart and Vascular Institute, University of Texas, Houston, TX, USA

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Cardiogenic shock (CS) remains the most common cause of death in patients with acute myocardial infarction (AMI). In addition to percutaneous coronary intervention, inotropes, and fluids, intraaortic balloon pumping (IABP) is most widely used for initial haemodynamic stabilization. However, the main limitation of IABP is the lack of active circulatory support and the requirement of a certain level of left ventricular (LV) function. In many patients with severe depression of LV function, haemodynamic support and LV unloading derived from IABP is insufficient to reverse CS. The use of percutaneous LV assist devices (LVAD) with active circulatory support might be beneficial in CS patients not responding to standard treatment including IABP support. This review reports the current experience of percutaneous LVAD in CS complicating AMI.

KEYWORDS
Shock; Heart-assist device; Heart failure; Haemodynamics; Myocardial infarction

Introduction
The incidence of cardiogenic shock (CS) in patients with AMI ranges from 7 to 10% after acute myocardial infarction (AMI).1,2 Despite aggressive treatment modalities such as percutaneous coronary interventions (PCI) and use of intraaortic balloon support, mortality of CS remains unacceptably high (50–70%).1,3,4 Recovery of myocardial performance following successful revascularization of the infarct related artery may require several days. During this period many patients succumb to low cardiac output. Therefore, intraaortic balloon pumping (IABP) is the method of choice for mechanical assistance,5 since IABP can result in initial haemodynamic stabilization.6–8 Systematic reviews on the mode of action, physiological response and clinical studies have been published elsewhere.9,10 The main limitations of IABP include the lack of active cardiac support, need for accurate synchronization with the cardiac cycle, and requirement of a certain level of left ventricular (LV) function. In many patients with severe depression of cardiac function or persistent tachyarrhythmias, haemodynamic support and LV unloading derived from IABP are insufficient to reverse CS.11

Therefore, the use of percutaneous LV assist devices (LVAD) with active circulatory support might be beneficial in patients with CS not responding to standard treatment, although this is currently not supported by randomized controlled clinical data (Figure 1). Usually these devices are used as a bridge-to-recovery, which may last several days. In patients with mechanical complications after AMI, LVAD are used as a bridge-to-surgery, or in patients without recovery, the surgical implantation of a long-term LVAD,12,13 or emergent heart transplantation might be necessary (Figure 1). Therefore, percutaneous LVAD are usually designed for a maximum use of 14 days.

Currently, there are several different devices and modes of operation.

Percutaneous cardiopulmonary bypass

After introduction of the first cardiopulmonary bypass (CPB) system with oxygenation in 1953, further developments led to percutaneously implantable devices.14 Such systems consist mainly of a blood pump and an oxygenator; 16–18 French arterial cannulae in the descending aorta and 18 French venous cannula advanced into the right atrium are used (Figure 2). These cannulae are connected to an external pump and a membrane oxygenator. After pump priming with normal saline, blood is withdrawn from the right atrium and pumped through a heat exchanger, membrane oxygenator, and ultimately returned into the femoral artery. The pump provides a continuous flow with maintenance of pulsatile arterial pressure unless the circulation is completely supported by the CPB device. There are several drawbacks of CPB such as large cannulae sizes with subsequent lower limb ischaemic complications, requirement of perfusionists, lack of direct LV unloading, increased afterload, and a limited support time (usually <6 h).15 Therefore, percutaneous CPB has mainly been used for patients with cardiopulmonary collapse in the cath lab.
Those patients with abrupt closure of a vessel may be supported until the situation is resolved by either PCI or until transfer in a stable condition to the operating room for emergency cardiac surgery. Since the introduction of a percutaneous approach, >200 patients have been treated during resuscitation efforts or in acute severe CS.\textsuperscript{14,16-23} The survival rates of these reports range from 4–64% with a mean survival rate of approximately 25%. There are only limited experiences in CS after AMI,\textsuperscript{24} and for patients with mechanical complications.\textsuperscript{25}

In summary, the percutaneous CPB system has been lifesaving for a small group of patients with abrupt haemodynamic collapse in the cath lab. Its use is limited by high associated complications, need of extracorporeal circulation and a membrane oxygenator with subsequent activation of cellular elements, and limited support time. The clinical impact of new, smaller, and portable devices such as the Lifebridge B\textsubscript{2}T\textsuperscript{TM} needs to be determined in future trials.\textsuperscript{26}

### Axial flow pumps

These pumps are usually positioned across the aortic valve to provide active support by transvalvular LV assistance (Figure 3). In 1988, Wampler et al.\textsuperscript{27} were the first to describe an axial, catheter-mounted LVAD inserted by surgical arteriotomy via the femoral artery. The outer diameter was 21 French and the length 26 cm. The axial flow pump consisted of a disposable suction cannula with a turbine driven by an external motor (Figure 4). The pumping system consisted of an axial flow blood pump, which was positioned in the aortic arch or the descending aorta, an inlet cannula, and a drive cable in a polymeric sheath and a motor. Depending on the aortic pressure, the pump capacity was up to 3.5 L/min at a speed of 25 000 r.p.m. In a canine infarct model, the effects of LV unloading were assessed. Treatment with the Hemopump\textsuperscript{TM} (Medtronic Inc., Minneapolis, MN, USA) resulted in significant myocardial salvage as compared with reperfusion alone.\textsuperscript{28} In addition, it provided superior LV unloading in comparison to IABP.\textsuperscript{28} Similar positive results on LV unloading, myocardial perfusion pressure, and serum lactate levels were obtained in a sheep model.\textsuperscript{29,30}

In a subsequent small pilot study, the 21 French Hemopump\textsuperscript{TM} was used in 11 patients with CS after AMI.\textsuperscript{31} Haemodynamic parameters and catecholamine requirements improved significantly during the initial 24 h of haemodynamic support. Overall mortality in this trial was 64%.\textsuperscript{31} However, a transfemoral placement of the pump via the aortic valve was possible in only two thirds of the patients despite surgical cutdown of the femoral artery. In another multiinstitutional study including patients with CS, the insertion rate of this LVAD was 77%; 30-day-mortality was 68%.\textsuperscript{32}

A smaller 14 French Hemopump\textsuperscript{TM} (Medtronic Inc.) was devised that could be inserted percutaneously.\textsuperscript{33} At a speed of 40 000 r.p.m. the system delivered flow of up to 2.2 L/min. In a multicentre registry of the percutaneous Hemopump\textsuperscript{TM} during high-risk PCI, the overall mortality was 12.5% for 32 patients not in CS.\textsuperscript{34} In addition, despite the short-term use, there were significant procedure and device-related vascular access problems (16% limb ischaemia, 25% bleeding complications).\textsuperscript{34} As a cause of the high complication rate, the Hemopump\textsuperscript{TM} never received FDA approval and further development was not pursued.

Recently, new axial flow devices have been developed. The Impella Recover\textsuperscript{L} LP 5.0 (Impella CardioSystems GmbH, Aachen, Germany) axial flow pump is a microaxial
flow pump capable of delivering a continuous flow of up to 5 L/min (Table 1), which is also available as a surgical insertion LVAD. By use of this device in a sheep infarction model, oxygen consumption was reduced during ischaemia and led to infarct size reduction. A drawback was the requirement of femoral artery surgical cutdown. However, in comparison to the Hemopump, positioning across the aortic valve appears to be successful in a higher proportion of patients as a guidewire can be positioned across the device tip. Currently, the Impella Recover LP® has been used in approximately 200 cases, is under investigational use in a FDA approval study, and has received CE mark for use in Europe.

A smaller device, the Impella Recover LP® approved for 5 day use in Europe, can be inserted percutaneously and provides continuous flow up to 2.5 L/min (Table 1). The device is equipped with a pigtail-catheter at the tip to ensure stable positioning in the LV and to prevent it from adhering to the myocardium (Figure 3). So far, there is only limited clinical experience, in particular in stable patients with high-risk PCI, and it remains unclear if 2.5 L/min is adequate to reverse CS.

Limitations of axial support devices are related to the position in the aortic valve. The presence of a mechanical aortic valve or an aortic stenosis is a contraindication for the

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**Table 1** Technical features of currently available percutaneous left ventricular assist devices for haemodynamic support in the cath lab

<table>
<thead>
<tr>
<th></th>
<th>Tandem Heart®</th>
<th>Impella Recover® LP 5.0</th>
<th>Impella Recover® LP 2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter size (French)</td>
<td>--</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Cannula size (French)</td>
<td>21 venous</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>Flow (L/min)</td>
<td>12–19 arterial</td>
<td>Max. 4.0</td>
<td>Max. 5.0</td>
</tr>
<tr>
<td>Pump speed (r.p.m.)</td>
<td>Max. 7500</td>
<td>Max. 33 000</td>
<td>Max. 33 000</td>
</tr>
<tr>
<td>Insertion/placement</td>
<td>Peripheral (femoral artery + left atrium after transseptal puncture)</td>
<td>Peripheral surgical cutdown (femoral artery)</td>
<td>Percutaneous (femoral artery)</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recommended duration of use</td>
<td>-- -- 14 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
<tr>
<td>CE-certification FDA</td>
<td>PMN</td>
<td>IDE trial</td>
<td>IDE trial</td>
</tr>
<tr>
<td>Relative costs in comparison to intraaortic balloon pumping</td>
<td>+++</td>
<td>+++</td>
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</table>

PMN, pre-market notification; IDE, investigational device exception.
+ + + + +, high relative costs in comparison to IABP; + + + + + + very high relative costs in comparison to IABP.
implantation. Furthermore, these devices might be inefficient in severe aortic regurgitation, and some need surgical cutdown of the femoral artery. Due to the high rotation speed of the impeller, these devices might provoke significant haemolysis.\textsuperscript{38}

**Left atrial-to-femoral arterial left ventricular assist devices**

In 1962, this system was first described by the jugular approach.\textsuperscript{40} Initially, left atrial-to-femoral arterial LVAD were used in patients not weanable from CPB after cardiothoracic surgery.\textsuperscript{41} Subsequently, percutaneous approaches for patients undergoing high-risk interventions for short-term use have been reported.\textsuperscript{42} Due to the lack of a transseptal cannula that can accommodate flow rates necessary to provide adequate circulatory support, due to risk of thrombus formation at the impeller, and due to inherent haemolysis of high-speed centrifugal pumps, this technique has not achieved widespread popularity. Therefore, new developments have been made to avoid the inherent risk of thrombus formation and haemolysis by centrifugal pumps.

The Tandem Heart\textsuperscript{TM} pVAD (Cardiac Assist Technologies, Inc., Pittsburgh, PA, USA), which is approved for short-term haemodynamic support (6 h) by the FDA and which is currently marketed in the USA and Europe, is a new generation low speed centrifugal continuous flow pump with a low blood surface contact area resulting in reduced potential for haemolysis and thromboemboli. The implantation procedure has been described in detail elsewhere.\textsuperscript{43} In brief, after standard transeptal puncture and pre-dilatation of the fossa ovalis, a venous inflow cannula is inserted into the left atrium (Figure 5). Afterwards an arterial cannula (usually 17 French) needs to be inserted into the femoral artery. Once all air has been removed from the system, the cannulae are connected to the extracorporeal centrifugal pump by standard tygon tubing. Oxygenated blood is drawn from the left atrium and returned via the centrifugal pump and via the arterial cannula in the femoral artery to the lower abdominal aorta (Figure 5). After a short learning curve this device can be inserted and LV assist instituted in 30 min in the cath lab setting. The system is capable of delivering flow up to 4.0 L/min at 7500 r.p.m. In a feasibility trial, 18 patients with CS were enrolled.\textsuperscript{43} With the device, CS could be reversed efficiently as monitored by haemodynamic and metabolic parameters, and the overall mortality rate was as low as 44%.\textsuperscript{43} In a subsequent randomized trial comparing the Tandem Heart\textsuperscript{TM} and IABP in 41 patients with revascularized AMI complicated by CS, the device was able to improve the haemodynamic and metabolic variables more effectively than with IABP support.\textsuperscript{44} However, complications like severe bleeding, limb ischaemia, or fever were encountered more frequently after LVAD support, whereas the 30-day-mortality was similar (IABP 45% vs. LVAD 42%, log-rank, $P = 0.86$).\textsuperscript{44}

Figure 5  Diagram of the percutaneously inserted transseptal and arterial cannulae connected to the Tandem Heart\textsuperscript{TM} centrifugal pump. Right upper corner: close-up of the transseptal catheter with large end hole and 14 side holes in the left atrium.
Similar results with increased complications without a significant mortality benefit were obtained in a second multi-centre trial of the Tandem Heart™ in comparison to IABP for CS. The most important drawback of the left atrial-to-femoral arterial bypass support is the need for large arterial cannulae to achieve the required flow. Furthermore, currently little is known about the fate of the transseptal puncture site. However, in recent series, no relevant left-to-right shunt has been observed by careful echocardiographic monitoring.

An overview of the technical features of currently available LVAD for percutaneous support or those that can be inserted by peripheral surgical cutdown is shown in Table 1.

Effects of left ventricular unloading

Besides the haemodynamic effects of an active LVAD in comparison to IABP support, the recovery of the myocardium after revascularization occurs by a reduction of the LV filling pressure, cardiac workload, and oxygen demand. Previous animal studies have demonstrated a substantial decrease in infarct size by use of CPB with venting of the LV and by axial and left atrial-to-femoral LVAD with or without revascularization of the infarct related artery. In animal models, LV unloading prior to revascularization of the infarcted artery led to significant myocardial salvage in comparison to the implementation of unloading after reperfusion. A clinical trial supporting this hypothesis is still pending.

In patients with end-stage heart failure, long-term implantable LVAD were useful in improving symptoms and in preventing or reversing heart failure by inducing neuro-endocrine modulation and reverse remodelling. In terms of neurohormonal modulation, LVAD support decreased plasma levels of epinephrine, norepinephrine, angiotensin II, and arginine vasopressin. Furthermore, serum levels of interleukins 6 and 8 and TNF-α content in the failing myocardium could be reduced. In terms of remodelling, long-term LVAD support has been shown to significantly reduce collagen content and decrease myocyte size. In addition, improvement in myocyte contractility and myocardial response to β-adrenergic stimulation has been observed. However, whether these neuroendocrine and reverse remodelling effects can be translated into the acutely failing heart in patients with CS after AMI with short-term assisted circulatory support is not known.

Limitations

As all percutaneous implantable LVAD provide continuous flow, this also affects the flow in the coronary arteries, which leads to non-physiological flow. The debate regarding the effect of non-pulsatile flow on organ function and the hormonal situation is extensive and remains controversial and has not been finally determined.

Active circulatory support LVAD have been used so far only in small trials with limited number of patients enrolled. Except the two randomized Tandem Heart™ vs. IABP trials, there are no randomized trials that have proven a substantial benefit of these devices over standard treatment. Although the haemodynamic effects of active support LVAD have been proven in several trials, there is no trial that had the power to detect differences in mortality. A large clinical trial, supporting the theoretical advantages of an active LVAD (in particular in patients with a significant amount of stunned myocardium not responding to standard treatment) is warranted; however, currently there is no larger trial on the horizon. In addition, there are no trials assessing the merits of risks of each LVAD against the other. Therefore, no conclusion can be drawn regarding the different risk of embolic complication, haemolysis, inducement of aortic regurgitation, or the dislodgment risk from the optimal site in the left atrium or LV.

There are new hypotheses that in the development and maintenance of CS peripheral factors play an important role besides extensive myocardial necrosis. Theoretically, extracorporeal support and contact with artificial surfaces of LVAD might further promote the systemic inflammatory response syndrome with subsequent deterioration to a multiorgan dysfunction syndrome. A second, potentially deleterious effect of extracorporeal circulation, besides the propagation of systemic inflammatory response, is the activation of complement and the development of coagulation with subsequent fibrinolysis, which may progress to disseminated intravascular coagulation leading to severe bleeding complications.

Furthermore, these devices are expensive in comparison to standard IABP treatment resulting in up to 30-fold higher costs (Table 1). In view of these limitations, there are some general contraindications for LVAD in addition to specific contraindications of the different systems, such as contraindication to anticoagulation, severe aortic regurgitation, terminal disease with limited life expectancy, advanced multiorgan dysfunction syndrome, central nervous system injury, right ventricular failure, severe bleeding, sepsis, uncontrolled by antibiotics, and severe peripheral arterial obstructive disease.

Conclusions

LVAD with active circulatory support reverse haemodynamic and metabolic parameters in CS more effectively than with standard IABP treatment alone. The use of these newer percutaneous devices is still in its infancy. The easier and safer deployment of the newly developed devices may increase their use for patients not responding to PCI, fluids, inotropes, and IABP. Although, from a theoretical point of view, these active LVAD might be beneficial, it remains to be proven that these actually alter the high mortality of CS patients. Furthermore, these devices are associated with more complications as a result of the highly invasive procedure and the extracorporeal support in some of these devices. Therefore, the decision making process on how to treat CS complicating AMI in addition to standard treatment requires an integrated stepwise approach, although the evidence supporting this is very limited. An LVAD might be considered on the basis of individual risk, success rates of standard treatment, and potential peri-procedural event rates.

Conflict of interest: none declared.

References


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**Clinical vignette**

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**The heart of coronary arteries**

Marco Valgimigli1,2* and Patrizia Malagutti1,2

1Institute of Cardiology, University of Ferrara, C.rosso Giovecca 203, 44100 Ferrara, Italy and 2Cardiovascular Research Centre, Salvatore Maugeri Foundation, IRCCS Gussago (BS), Italy

*Corresponding author. Tel: +39 0532 202143; fax: +39 0532 241885. E-mail address: vlgmrc@unife.it

A 67-year-old man with a medical history notable for treated type II diabetes, dyslipidaemia and hypertension, was admitted to the hospital for repeated episodes of angina with mild effort or at rest. A coronary angiogram showed lumen stenosis in the mid-tract of the right coronary artery and in the first obtuse marginal branch (Panel A). In the proximal tract of left anterior descending artery, a severe stenosis (Panel A, arrow) was also observed, followed by giant heart-shaped coronary artery aneurysm (CAA) (Panel B, magnified in the insert). The patient underwent coronary artery bypass grafting of the three main coronary vessels. The 1-year follow-up was uneventful.

CAA, defined as a localized dilatation of the coronary artery with a diameter ≥ 1.5 times that of an adjacent coronary segment, has been observed in 0.2–5.3% of patients undergoing coronary angiography. CAA most often involves the right coronary artery followed in frequency by the left anterior descending. Most CAA are atherosclerotic in origin, although other aetiologies include congenital aneurysms, Kawasaki syndrome, infectious arteries, and coronary trauma, including those related to percutaneous coronary intervention.

The catheter-based treatment of coronary aneurysm through polytetrafluoroethylene-covered stent implantation or core embolization is feasible in selected cases. The safety and efficacy of the percutaneous approach in comparison with conventional surgical treatment remain to be established.