primary percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) that can be performed within 90 minutes of first contact now has a class I, level A indication according to current American College of Cardiology/American Heart Association (ACC/AHA) Guidelines.1 In experienced centers and in the vast majority of cases, this can be performed without any hemodynamic (pharmacologic or mechanical) support. Patients presenting with AMI and cardiogenic shock, however, represent a very high-risk subset that requires hemodynamic support. This article discusses hemodynamic support, focusing on the therapeutic device alternatives that are currently available for patients with AMI in cardiogenic shock, as well as the theoretical advantages that these devices may offer in limiting infarct size in patients with AMI without cardiogenic shock.

**BACKGROUND**

Table 1 lists the potential etiologies of cardiogenic shock. Acute left ventricular failure is the most common etiology of cardiogenic shock among patients with AMI.2 The landmark SHOCK trial first reported in 1999 that emergency revascularization versus medical stabilization resulted in a survival advantage at 6 months (not at 30 days).3 It should also be noted that emergency revascularization in this trial meant that it took place within 12 hours, which is not very emergent by current standards. This advantage was confirmed at long-term follow-up at 1 year and 6 years.4 The SHOCK trial registry (composed of those patients eligible but not randomized to emergency revascularization versus medical stabilization) recorded the various etiologies of shock and found that predominant left ventricular failure accounted for 75% of cases with acute severe mitral regurgitation, ventricular septal rupture, isolated right ventricular shock, cardiac tamponade, and various other causes accounting for the remaining 25% of cases.2 Although acute left ventricular failure accounts for the vast majority of cases, it is imperative that a thorough clinical evaluation (including physical examination and laboratory and hemodynamic scrutiny) confirm the correct diagnosis so that the appropriate therapy can be instituted. Once the diagnosis is confirmed, appropriate measures are undertaken, such as

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<th>AMI</th>
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<td>• Acute left ventricular failure</td>
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<td>• Refractory arrhythmia</td>
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<td>• Mechanical complications of AMI</td>
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<td>• Ventricular septal rupture</td>
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<td>Acute right ventricular failure</td>
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<td>Acute and chronic progressive cardiomyopathy</td>
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<td>Acute and chronic valvular disease</td>
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<td>Failure to separate from cardiopulmonary bypass</td>
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<td>Sepsis with myocardial depression</td>
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correction of acid/base abnormalities, restoration of perfusion pressure with pressors and inotropic agents as indicated, and the use of mechanical devices, if the preceding maneuvers fail. It should be noted that restoration of blood pressure alone is not necessarily an indication that the shock state has been corrected. An adequate systemic pressure with continued evidence of shock with a low cardiac index and poor perfusion is not sufficient to sustain the patient over the long term.

The currently available mechanical assist devices in the United States that may be instituted in the setting of AMI and cardiogenic shock include the intra-aortic balloon pump (IABP), the TandemHeart (CardiacAssist, Inc., Pittsburgh, PA), and the Impella 2.5.

IABP

The IABP may help restore systemic and coronary perfusion pressure but has little effect on cardiac output, and its use in the setting of acute ST-elevation myocardial infarction remains controversial to this day despite decades of experience with this device. The major advantages of the IABP are its ready availability in all cardiac catheterization laboratories that perform emergency PCI, ease of insertion, relative low cost, and potential for longer-term use. The disadvantage of this device is its lack of significant effect on cardiac output and microvascular flow. As with the other percutaneous devices listed, the IABP has never been shown to improve survival in randomized clinical trials. In a recent meta-analysis of IABP therapy in ST-elevation myocardial infarction, the pooled randomized data did not support the use of this device. It is of note that in the SHOCK trial, more than 80% of patients in both arms (emergency revascularization vs medical stabilization) were on an IABP before randomization, indicating the failure of this device alone to reverse cardiogenic shock in most patients, with the crucial therapy ultimately being prompt revascularization.

IMPELLA 2.5

The Impella 2.5 (Figure 1), which is approved for short-term use by the US Food and Drug Administration, may be inserted percutaneously in the cardiac catheterization laboratory through a 13-F sheath. The device is inserted over a guidewire and placed retrograde across the aortic valve. The caged turbine in the left ventricle spins at 55,000 rpm and expels blood from the left ventricle into the ascending aorta. The Impella 2.5 is currently being investigated in the setting of AMI in the RECOVER II trial sponsored by Abiomed. This a multicenter, randomized, open-label, parallel assignment trial that compares the Impella 2.5 to the IABP in patients who have AMI and hemodynamic instability with the primary outcome being major adverse cardiac events at 30 days. The RECOVER II trial is still recruiting patients. In the ISAR-SHOCK trial, a small study comparing the Impella 2.5 to the IABP in patients with AMI and cardiogenic shock, the cardiac index was initially significantly improved in the Impella 2.5 group compared to the IABP group, but there was no difference at 4 or 30 hours between the two groups. Similarly, there was no difference in the need or duration of pressors between the two groups. There was one case of limb ischemia in the Impella 2.5
group after implantation, and there was significantly increased hemolysis in this group as well (at 24 hours), although these adverse events were not significantly different compared to the control group. During intensive care treatment, there was a greater need for transfusion (packed red blood cells and fresh frozen plasma) in the Impella 2.5 group, although again, this was not statistically significant. There was no difference in mortality; however, this study was obviously not powered to detect a difference. The major limitation of this study was the small number of patients studied and the lack of longer-term follow-up.

**TANDEMHEART**

The TandemHeart device (Figure 2) has four major components: (1) a 21-F transseptal cannula, (2) a 12- to 17-F arterial cannula, (3) an extracorporeal continuous flow pump that allows for up to 5 L/min of flow depending on the size of the arterial cannula and the speed of the pump, and (4) a microprocessor-based controller. The use of this pump was first reported in the setting of cardiogenic shock and AMI by Thiele et al, who demonstrated that cardiogenic shock could be reversed in all patients, with a significant increase in cardiac index and mean arterial pressure and a concomitant significant decrease in the pulmonary capillary wedge pressure. Survival in this group of 18 patients was 56%, similar to the SHOCK trial; however, it should be noted that five of the 18 patients had ventricular septal rupture in the setting of AMI, a condition associated with a mortality rate in excess of 80%. Excluding the patients with ventricular septal rupture from consideration, 10 of 13 patients survived to 30 days. The small number of patients and lack of long-term follow-up also limit this study, but it suggests that the TandemHeart percutaneous left ventricular assist device (LVAD) may provide a survival benefit in the setting of AMI and cardiogenic shock. In a small randomized trial of the TandemHeart versus the IABP in AMI complicated by cardiogenic shock, Thiele et al again reported an improvement in hemodynamic and metabolic parameters but an increase in bleeding and vascular complications. The latter complications are not unexpected in view of the fact that in the TandemHeart group, all patients required large cannula (21-F venous and 12- to 17-F arterial compared to an 8-F IABP), and 48% and 33% received thrombolytic and glycoprotein IIb/IIIa receptor antagonist therapy, respectively. In addition, although severe peripheral vascular disease was an exclusion criterion, a preinsertion abdominal aortogram and runoff study were not routinely performed in these patients to rule out significant peripheral vascular disease and to pick the most favorable side for the large arterial cannula. The preoperative use of thrombolytic therapy and severe peripheral vascular disease are relative contraindications for the use of the TandemHeart, and excessive bleeding and peripheral vascular compromise are to be expected unless appropriate precautions are undertaken and inappropriate patients are excluded from treatment.

**ASSIST DEVICES IN NONSHOCK AMI TO REDUCE INFARCT SIZE?**

Although studies in humans have not consistently demonstrated an improvement in left ventricular function with an assist device in the setting of nonshock AMI, there
are considerable experimental data to suggest that this is possible. The current mantra of reperfusion in AMI, however accomplished, is that “time is muscle.” Multiple studies have demonstrated that the earlier reperfusion is accomplished, the greater the myocardial salvage and the lower the mortality.\textsuperscript{12,13} This is reflected in the ACC/AHA class I, level A recommendation for PCI if the door-to-balloon time can be accomplished within 90 minutes. There is accumulating evidence, however, that the milieu of reperfusion is of profound importance. It has been known for some time now that reperfusion preconditioning limits infarct size in the canine model of myocardial infarction,\textsuperscript{14} and subsequently, preconditioning and postconditioning have also been demonstrated to limit infarct size in humans as well.\textsuperscript{15,16} In an effort to change the setting of reperfusion, drug therapy has also been utilized in an effort to reduce infarct size. The use of high-dose intravenous adenosine in the AMISTAD II trial was found to have a favorable effect on infarct size in AMI.\textsuperscript{17} More recently, it has been demonstrated that the administration of cyclosporine, as well as acadesine, can reduce infarct size.\textsuperscript{18,19} This suggests that, although time is of crucial importance, the milieu of reperfusion is critically important as well. In the canine infarct model, a substantial percentage of the final infarct size is due to reperfusion injury.\textsuperscript{20} Therefore, preventing reperfusion injury may substantially reduce final infarct size, improve left ventricular function, and ultimately improve survival.

In 1983, Catinella et al demonstrated that left ventricular unloading with left atrial to left femoral artery bypass in the canine experimental model could substantially reduce the area of infarction as a percentage of the left ventricle as well as the area of infarction compared to the area at risk.\textsuperscript{21} In 2003, Meyns et al demonstrated that infarct size could be reduced as well with left ventricular unloading in the ovine experimental model, with the greatest reduction occurring with the highest level of support instituted as early as possible.\textsuperscript{22} Although it is not always possible to translate experimental animal data to humans, a percutaneous left ventricular support device certainly has the potential to reduce infarct size in patients. Trials in patients with AMI will be required to determine whether this theoretical construct, which works so well in the animal model, can be translated into meaningful human use.

A recent meta-analysis of controlled trials by Cheng et al compared percutaneous LVADs (TandemHeart and Impella 2.5) to the IABP for treating cardiogenic shock.\textsuperscript{23} There were only three trials with 100 patients total for analysis.\textsuperscript{5,8,11} The main conclusion of this study was that the use of the percutaneous LVAD resulted in a better hemodynamic profile; however, this did not translate into an improved 30-day outcome. In addition, the patients treated with the LVAD had a higher incidence of lower extremity ischemia and device-related bleeding. As noted in the preceding discussion, with more experience and better patient selection, some of these complications may be avoidable. The study confirmed that the LVADs were more powerful devices than the IABP, and this was reflected in better hemodynamic profiles in the LVAD patients.

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Clearly, there is no ideal percutaneous LVAD in terms of safety and efficacy. For any device to be widely accepted, it must first be safe as well as efficacious. The IABP, Impella 2.5, and TandemHeart all have significant safety issues, with the LVADs clearly having the edge on efficacy with a tradeoff in safety due to the larger caliber of the cannulas. Therefore, LVADs should only be used in patients who are at significantly increased risk and are failing medical therapy and an IABP. Continued improvement with each of these devices, as well as increased experience with each of them, will hopefully allow patients to avoid complications and to improve outcomes. The efficacy of the devices may be judged by the level of support that they provide, and ultimately, by the improvement in outcomes that accrue because of their use. Hemodynamics may provide evidence of efficacy in terms of cardiac index, cardiac power index, left ventricular filling pressure, and mean arterial pressure, as well as left ventricular pressure volume loops. Efficacy may be judged in terms of survival benefit, but this is hard to prove in view of the difficulty in enrolling cardiogenic shock patients in a trial large enough to prove this endpoint. Finally, there is the important issue of cost, particularly in the politically and economically charged health care reform environment. A device may be both safe and effective, but if it is too costly in terms of cost/benefit analysis, its widespread adoption cannot be expected. The ultimate value of these devices may be as a bridge to recovery or as a bridge to more definitive therapy, such as coronary artery bypass/valve surgery, cardiac transplantation, or LVADs as destination therapy.

**CONCLUSION**

With technical refinements and increased experience, the still rather grim prognosis of cardiogenic shock can hopefully be improved with the use of percutaneous LVADs. Larger trials and/or improved devices will be required to prove this point. The use of these devices to
reduce infarct size in the setting of nonshock AMI has been demonstrated in various animal models but has yet to be demonstrated in humans.

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