REVIEW ARTICLE

Future Perspectives of Intra-Aortic Balloon Pumping for Cardiogenic Shock

Takeo Fujino, MD, Teruhiko Imamura, MD and Koichiro Kinugawa, MD

Summary
An intra-aortic balloon pump (IABP) is a device of internal counterpulsation. Inflation of the balloon in diastole results in a potential increase in coronary blood flow and an improvement in systemic perfusion, and deflation at the end of diastole reduces left ventricular afterload, although the hemodynamic effects are relatively small. With its favorable safety profile due to fewer adverse events, IABP has been used for more than 5 decades as the most common mechanical circulatory support device for cardiogenic shock. Recently, however, other short-term devices have become available, and the position of IABP for cardiogenic shock is rapidly changing. Meanwhile, novel improvements in knowledge and technology are pushing the boundaries of this device. In this review, we summarize the basic physiology and current evidence of this device and then discuss the outlook and implications of IABP in the future.

Key words: Mechanical circulatory support, Heart failure, Acute myocardial infarction

Hemodynamic Effects of IABP
The concept of counterpulsation was first conceived by Kantrovitz, et al. After several years of animal experiments and device development, the first clinical application of a successful treatment with IABP was reported in 1968 for a patient with acute myocardial infarction complicated by severe CS. Subsequently, IABP has been widely used for CS with several etiologies, and has become the most common MCS device for the failing heart.

With a balloon placed in the descending aorta, inflation of the balloon in diastole and active deflation in systole induce “volume displacement” of blood within the aorta at both proximal and distal locations. The inflation of the balloon in diastole results in a potential increase in coronary blood flow and an improvement in systemic perfusion, and the deflation at the end of diastole reduces left ventricle (LV) afterload. Hemodynamic effects expected with IABP are listed below (Table I).

- a decrease in systolic aortic pressure
- a decrease in end-diastolic aortic pressure
- an increase in diastolic aortic pressure with a potential increase in coronary blood flow
- an increase in stroke volume and cardiac output (by 0.5-1.0 L/minute)
- a decrease in LV preload
- a decrease in LV afterload
- a decrease in myocardial oxygen demand

The magnitude of the effect of IABP is affected by (1) balloon volume, (2) balloon position, (3) heart rate, (4) timing of inflation, (5) stroke volume, and (6) aortic compliance.

Indications, Contraindications, and Complications
There are several indications for IABP, including CS, unstable angina refractory to medical therapy, and hemodynamic support for high-risk percutaneous coronary intervention or coronary artery bypass grafting. The common etiologies of CS are listed in Table II. IABP can be indicated for various types of CS; however, because of its ability to predominantly support LV, generally it is not indicated for CS due to right ventricular (RV) failure in-
including pulmonary embolism and RV infarction. Like other MCS devices, the goal of therapy should be clarified before initiating the therapy; that is, 1) bridge to recovery; provide circulatory support while the heart recovers, 2) bridge to decision; determine reversibility of end-organ damage with circulatory support, 3) bridge to bridge, or 4) bridge to transplantation; achieve a period of temporary stability until durable device therapy or heart transplantation. Lack of a solution or a potential to recovery should discourage IABP initiation; however, as we discussed below, there is a possibility of 5) destination therapy with an ambulatory implantable counterpulsation device.

IABP is contraindicated in patients with significant aortic regurgitation because it worsens regurgitation. IABP device insertion should not be attempted in a patient with suspected or known aortic dissection. Aortic rupture is a potential consequence of IABP device insertion in patients with aortic dissection or aortic aneurysms. IABP may be associated with vascular complications, including bleeding, systemic embolization, limb ischemia, and amputation; therefore it should be avoided in patients with severe peripheral vascular disease. In addition, as with any indwelling catheter, IABP may cause blood stream infection. The presence of a fever in a patient with IABP, in the absence of another clear source, requires balloon removal. In a large multi-center registry, 7.0% of IABP recipients experienced IABP-related complications. Among them, 2.6% had major vascular complications, including severe access site bleeding in 0.8%, limb ischemia in 0.9%, limb amputation in 0.1%, and IABP-related mortality in 0.05%.13 Thrombocytopenia during IABP support is reported to be found in 43-58% of patients, but generally mild. Thrombocytopenia was unrelated to concomitant heparin use and not associated with an increased risk of major bleeding or in-hospital death.11,14

**Current Evidence for Cardiogenic Shock (CS)**

**Definition of CS:** CS is a state in which ineffective cardiac output caused by a primary cardiac disorder results in both clinical and biochemical manifestations of inadequate tissue perfusion. The clinical presentation is typically characterized by persistent hypotension unresponsive to volume replacement and is accompanied by clinical features of end-organ hypoperfusion requiring intervention with pharmacological and/or mechanical support.1,12 There are a number of causes of CS, including acute myocardial infarction, chronic heart failure (HF) with decompensation, acute myocarditis, and post-cardiomyotomy shock (Table II). Commonly accepted hemodynamic parameters of CS were defined in the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) Trial, including systolic blood pressure < 90 mmHg, cardiac index < 2.2 L/minute/m², and pulmonary capillary wedge pressure > 15 mmHg.13,14 However, we should be aware that absolute cutoffs of these parameters are often impractical because some cases have end-organ hypoperfusion even with higher cardiac output.15 Recovery is rare with pharmacological therapy alone and MCS devices are often required.

**Current evidence for CS:** Although IABP has been widely used for CS for decades, the clinical efficacy was unclear because the evidence was derived only from small clinical trials and registry data.16 In the early era of IABP, the first registry cooperative trial published in 1973 showed that IABP for CS decreased systolic blood pressure from 76 ± 22 to 57 ± 17 mmHg, increased diastolic blood pressure from 53 ± 12 to 83 ± 19 mmHg, and increased cardiac output from 2.4 to 2.9 L/minute; however, mortality was high with only 15 survivors among 87 patients.17 In 2013, the IABP-SHOCK II Trial, which was the largest randomized controlled trial in patients with CS after acute myocardial infarction (AMI) undergoing early revascularization, demonstrated that IABP did not improve 30-day mortality (39.7% in the IABP group versus 41.3% in the control group, \( P = 0.69 \)).18 IABP did not show any clinical benefits in 1-year and 6-year follow-up.19,20 Recent meta-analysis including this study also revealed no benefit of IABP in this population.21

There are possible explanations for the absence of benefit in that study. Although experimental and clinical studies have shown hemodynamic improvements with IABP, its effect on cardiac output was only modest, and furthermore, most clinical studies had no control group.17,18 In a small randomized pilot trial, cardiac output in patients with AMI and revascularization increased in both the IABP arm and the control arm, and no significant differences were shown between the arms, suggesting that initial hemodynamic improvement might be more af-

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**Table I. Hemodynamic Effects of IABP**

| Parameter                        | Change  |
|----------------------------------|---------|
| Diastolic aortic pressure        | Increase|
| End-diastolic aortic pressure    | Decrease|
| Systolic aortic pressure         | Decrease|
| Left ventricular preload         | Decrease|
| Left ventricular afterload       | Decrease|
| Stroke volume                    | Increase|
| Coronary perfusion               | Increase|
| Peripheral tissue perfusion      | Increase|
| Myocardial oxygen demand         | Decrease|

Note that these changes can be modulated by mechanical or patients’ factors.

**Table II. Major Etiologies of Cardiogenic Shock**

| Etiology                          |
|-----------------------------------|
| Acute myocardial infarction (acute pump failure / mechanical complications) |
| Acute (fulminant) myocarditis     |
| Pulmonary embolism                |
| Post-cardiomyotomy shock          |
| Cardiomyopathy (ischemic / non-ischemic) |
| Right ventricular failure during LVAD support |
| After heart transplantation (primary graft failure / acute rejection) |
| Arrhythmia (atrial arrhythmia / ventricular tachycardia / bradycardia) |
| Endocrine disorders (hypothyroidism / hyperthyroidism / pheochromocytoma) |
| Overdose of cardiotoxic drugs     |

LVAD indicates left ventricular assist device.
fected by revascularization as well as inotropic optimization than IABP.23)

The findings of the IABP-SHOCK II Trial have led to a paradigm shift away from routine IABP use in these cohorts. A Guideline from the European Society of Cardiology downgraded that routine use of IABP for CS as a Class III recommendation.46) In parallel with the downgrade of guideline recommendations, the use of IABP in clinical practice decreased rapidly.24,25)

However, CS is recognized as a condition with a spectrum with varying etiologies, phenotypes, and degrees of severity.26) We should focus on the possibility of alternative use and efficacy of IABP for other types of CS.

Chronic HF patients with acute decompensation and CS may represent a different physiologic phenotype compared with the above-discussed AMI population. Recent studies have reported acute hemodynamic improvement as well as the clinical utility of IABP in chronic HF patients.27-29) The efficacy of IABP as “bridge to bridge” in chronic HF patients was also shown.30-32) Furthermore, considering its physiological effect, IABP is believed to be more effective in CS patients with mechanical complications of AMI such as acute mitral regurgitation or a ventricular septal defect, and small trials support this hypothesis.12,23,34) The concomitant use of IABP with VA-ECMO in severe CS patients might be associated with better clinical outcomes than VA-ECMO alone, although Impella could be the first-line strategy in this situation.35,36) Even though the routine use of IABP for AMI with CS patients is not recommended, further studies are still warranted to determine the utility of IABP in carefully selected specific situations and patients. In addition, further studies to investigate the predictive factors for IABP responders are also warranted.37)

**Figure.** Scheme of intravascular ventricular assist system (reused with permission of NuPulseCV Inc). ECG indicates electrocardiogram.

**How to select optimal devices for CS:** Recently, novel percutaneous short-term devices including the Impella family (2.5, CP, and 5.0) and Tandem Heart have become available. Although these devices have shown more favorable hemodynamic effects compared to IABP, no significant differences have been observed in the mortality of CS patients.2,38-40) Furthermore, a recent observational study showed that Impella use for patients undergoing percutaneous coronary intervention was associated with what higher rates of adverse events than IABP. After propensity score matching, Impella use was associated with death (odds ratio (OR) 1.24, 95% confidence interval (CI) 1.13-1.36), bleeding (OR 1.10, 95% CI 1.00-1.21), and stroke (OR 1.24, 95% CI 1.18-1.53).41) Further studies are warranted to prove the advantage of Impella in CS patients.42) The use of percutaneous VA-ECMO for CS is also rapidly increasing, but there has been no randomized clinical trial to investigate the efficacy of VA-ECMO in this population so far.43)

Currently, which device is the optimal option for CS? Compared to the other devices, the advantages of IABP are an easy and quick procedure for insertion and placement and a good safety profile with fewer adverse events. The major disadvantage is its limited hemodynamic support and short-term support. As noted above, there is a wide spectrum of CS severity from pre-CS to refractory CS, or from stage A to D, and the optimal therapeutic strategies might vary depending on the severity of CS.24,45) In patients with severe CS, VA-ECMO is indicated based on its ability to provide full biventricular and respiratory support. In contrast, considering the advantages of IABP, the initiation of IABP in the early stage of CS might be a good therapeutic option, although there is also a possibility that medical therapy alone might be better than any concomitantly used devices in this situation. The optimal therapeutic strategy in each stage of CS should be investigated in future studies.

**Implantable counterpulsation device:** Generally, IABP is inserted from a femoral artery; however, patients with femoral IABP have restricted mobilization, limiting the duration of support into days to weeks. Recently, the safety and efficacy of subclavian IABP was reported, which enabled patient mobilization and then longer-term IABP support as “bridge to bridge” or “bridge to transplantation”.44,45)

An ambulatory implantable intra-aortic counterpulsation through the subclavian artery was also proposed recently (implantable ventricular assist system; Figure ). The first-in-human clinical trial of this device was performed for patients who had been listed for heart transplantation (“bridge to transplantation”), and showed that there were no deaths or thromboembolic events at 30 days and all patients were successfully transplanted. There were no intraoperative complications or blood transfusions.46) In Japan it is difficult to use this device as “bridge to transplantation” because of the extremely longer waiting time, but it can be used as a bridge to durable mechanical support (“bridge to bridge”). Improved mobilization enables patients to discharge and probably increases patient qual-

**Future Perspectives**
it of life, suggesting its indication as “destination therapy”. Furthermore, because IABP reduces myocardial oxygen demand, it is expected that longer-term IABP support using this system can promote myocardial recovery. This system can achieve biventricular unloading and improves not only LV but also RV function. A prospective multi-center feasibility study is now ongoing to demonstrate the implications of the implantable ventricular assist system on cardiac recovery. Longer-term ambulatory IABP systems might be a novel strategy for advanced HF and CS patients, particularly relatively less sick cohorts, in the near future.

Disclosure

Conflicts of interest: None.

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