Intra-Aortic Balloon Pump Counterpulsation: Old Friend or Foe?

The hemodynamics and utility of IABP counterpulsation in current practice.

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Mechanical support in patients who present in the catheterization laboratory can serve several purposes but is generally related to three indications: high-risk percutaneous coronary intervention (PCI), acute myocardial infarction (AMI), and cardiogenic shock. During PCI in patients with depressed ejection fraction or large areas of ischemic myocardium, the hemodynamic consequences of periprocedural ischemia during balloon inflation may be disastrous by inducing a vicious circle of ischemia-induced deterioration in ejection fraction, hemodynamic compromise, and cardiogenic shock, ultimately resulting in death. Therefore, mechanical assist devices are regularly considered to support the circulation during these high-risk procedures.[1] In AMI, hemodynamic support is thought to reduce infarct size due to unloading of the left ventricle in the acute setting, which reduces workload of the heart and possibly limits infarct size. Finally, profound depression of myocardial contractility caused by the lack of adequate blood supply to the heart during AMI can result in cardiogenic shock. In this setting, mechanical support is primarily intended to restore normal blood flow and blood pressure for adequate organ perfusion.

Mechanical support options have expanded in recent years, ranging from the minimally invasive intra-aortic balloon pump (IABP) and transvalvular microaxial flow pump (Impella, Abiomed, Inc.) to ventricular assist devices requiring open surgery for implantation. The currently available range of mechanical support options should not be seen as competitive devices, but rather as a range of escalating treatment options, in which a choice can be made based on pathophysiologic considerations, the goal of hemodynamic support (myocardial protection or restoring organ perfusion), and ease of use. Although IABP is a good choice for myocardial protection purposes, in case of nonischemic cardiogenic shock, the choice for a more potent assist device (ie, Impella) might be more useful. Extracorporeal life support is much more complicated than these percutaneous mechanical support devices and increases afterload and myocardial workload.

IABP is the most widely used circulatory support device worldwide due to its ease of use, low complication rate, and quick insertion.[2] Appropriate use of IABP counterpulsation has been extensively discussed over the past 5 years. Other than conflicting trial results in the three main indications for mechanical support, many interventional cardiologists have had firsthand experiences and varying results with IABP therapy. These range from immediate reversal of hemodynamic deterioration in some patients to no noticeable change in hemodynamic conditions in others. These confusing results may be due to insufficient understanding of the prerequisites needed for effective IABP therapy, as well as the inclusion of very broad, nonspecific patient populations in the large trials where the benefit of IABPs could not be expected in the majority of patients on pathophysiologic grounds.

This article aims to clarify the conflicting results seen in the literature and to elaborate on the prerequisites needed for effective IABP therapy, enabling physicians to distinguish between patients who will and will not benefit from IABP support. Selective application of IABP support based on pathophysiologic considerations is a much more promising strategy than a one-size-fits-all approach.

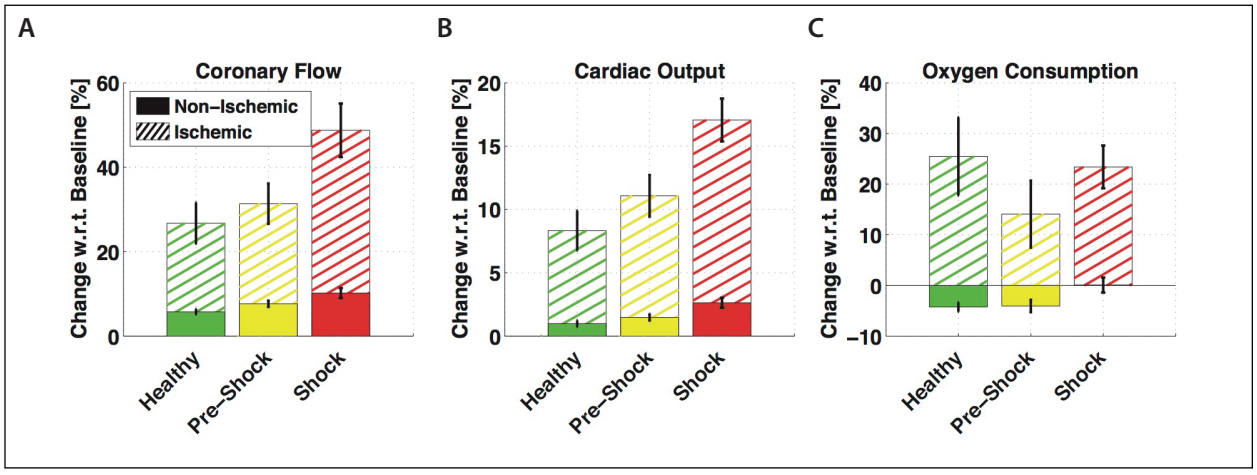

Figure 1. Effect of IABP on coronary blood flow, cardiac output, and myocardial oxygen consumption in 12 beating pig hearts. Mean change (standard error) by IABP support compared with the status without IABP of coronary blood flow (A), cardiac output (B), and myocardial oxygen consumption (C) for different clinical scenarios, ranging from healthy to cardiogenic shock, whether (hatched lines) or not (solid bar) in the presence of global myocardial ischemia. Reprinted with permission from Schampaert S, van Nunen LX, Pijls NH, et al. Intra-aortic balloon pump support in the isolated beating porcine heart in nonischemic and ischemic pump failure. Artif Organs. 2015;39:931–938.

HEMODYNAMICS OF IABP THERAPY

In 1953, the counterpulsation principle was developed, which postulated that by perfusing the coronary bed with higher pressure during diastole, coronary blood flow would increase; this led to the introduction of the IABP in 1968.[3,4] The helium-filled balloon is positioned in the descending thoracic aorta through the femoral artery and inflates and deflates in synchrony with the cardiac cycle.[5] The hypothetical hemodynamic effects of IABP counterpulsation consist of a combined increase of coronary blood flow by diastolic inflation and afterload and workload reduction by systolic deflation, resulting in decreased myocardial workload and oxygen demand.[6]

However, these mechanical effects on coronary perfusion pressure and coronary blood flow are highly dependent on the state of the so-called coronary autoregulation. This autoregulatory mechanism ensures constant myocardial blood flow over a wide range of aortic pressures by controlling sphincters at the entrance of coronary arterioles, which can constrict or dilate in response to the coronary perfusion pressure.[7] As such, the supposed direct mechanical effect of counterpulsation on coronary blood flow can be easily undone. The importance of the status of the coronary autoregulation during IABP counterpulsation was proven using intravenous adenosine infusion to turn off coronary autoregulation.[8] With autoregulation still intact, balloon pump augmentation led to an increase in coronary pressure as well as a reactive increase in microvascular resistance that resulted in unchanged coronary blood flow. In contrast, with autoregulation "switched off," the balloon pump augmentation led to an increase in distal coronary pressure and coronary blood flow, whereas microvascular resistance remained unchanged. These results were corroborated by recent studies performed in isolated beating pig hearts, which showed a linear relationship between diastolic aortic pressure and coronary blood flow is present with exhausted autoregulation and an increase in coronary blood flow by up to 50% in the presence of acute ischemic pump failure (Figure 1).[9,10]

In physiologic conditions with intact coronary autoregulation, myocardial blood flow is not dependent on perfusion pressure. In these conditions, no effect on coronary blood flow caused by higher perfusion pressure can be expected by IABP counterpulsation. Coronary autoregulation is exhausted in the presence of a subtotal coronary artery stenosis, in the setting of AMI complicated by persistent ischemia, in cardiogenic shock with mean arterial pressures outside the autoregulatory range, and in myocardial stunning after open heart surgery.

TRIALS AND TRIBULATIONS IN IABP THERAPY

Numerous studies have investigated the benefit of IABP in the three general indications for mechanical support. Overall, retrospective studies seem to indicate a benefit of PCI, although these results cannot be

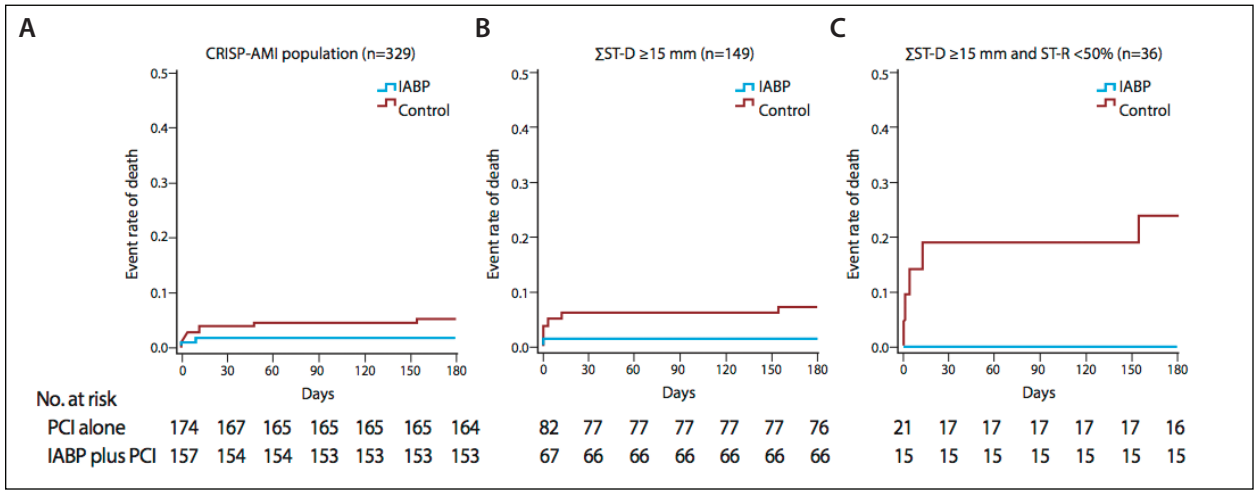

Figure 2. All-cause mortality at 6 months in different (sub)populations of the CRISP AMI trial. All-cause mortality rates at 6 months in all patients receiving IABP as adjunct to PCI (blue line) or PCI alone (red line) in the CRISP AMI population (A; three vs nine deaths; log-rank *P* = .12); in patients with large myocardial infarction (B; one vs six deaths; log-rank *P* = .10); in patients with large myocardial infarction complicated by persistent ischemia (C; zero vs five deaths; log-rank *P* = .046). Abbreviations: ST-D, ST-segment deviation; ST-R, ST-segment resolution. Reprinted from EuroIntervention 11(3); van Nunen LX, van 't Veer M, Schampaert S, et al. Intra-aortic balloon counterpulsation reduces mortality in large anterior myocardial infarction complicated by persistent ischaemia: a CRISP-AMI substudy; p. 286–292, 2015, with permission from Europa Digital & Publishing.

reproduced in randomized trials. In high-risk PCI, retrospective studies with standard IABP support showed less intraprocedural events, better procedural results, and lower risk of mortality compared with patients without elective IABP insertion.[11,12] The Balloon Pump-Assisted Coronary Intervention Study (BCIS-1) randomized 301 patients scheduled to undergo high-risk single-vessel or multivessel PCI to either IABP insertion prior to PCI or no planned IABP insertion and showed no difference in major adverse cardiac and cardiovascular events (the primary endpoint).[13]

Prophylactic insertion of an IABP seemed to be associated with fewer events in all high-risk patients presenting with AMI.[14] However, the prospective CRISP-AMI study that investigated whether routine IABP therapy prior to primary PCI in patients with anterior ST-segment elevation myocardial infarction would reduce infarct size did not corroborate these results.[15] In cardiogenic shock complicating AMI, most trials favoring IABP use were performed in the thrombolytic era.[16] Registries and retrospective studies in the era of primary PCI showed little or no difference in outcome with the use of IABP. The IABP-SHOCK II trial, which prospectively randomized 600 patients with AMI (with or without ST-segment elevation) complicated by cardiogenic shock to primary PCI with adjunctive IABP support or PCI alone, showed no reduction in short- or long-term mortality.[17,18]

When thinking about these trials and their outcomes, it is important to emphasize that the status of coronary autoregulation was not yet sufficiently understood. In patients undergoing high-risk PCI, further follow-up showed that IABP support resulted in a long-term mortality benefit, possibly explained by the periprocedural salvage of myocardium with IABP counterpulsation in the case of periprocedural ischemia (with exhausted autoregulation).[19] Use of IABP resulted in a significant survival benefit at 6 months in patients who presented with AMI without shock, when focusing solely on the patients with large myocardial infarction and persistent ischemia (ie, the population at high risk for future events) (Figure 2).[20] Finally, in patients who presented with cardiogenic shock, there was no apparent benefit of IABP therapy.

Several comments can be made regarding the study design.[21] For instance, patients with cardiogenic shock for up to 24 hours and patients who were resuscitated were eligible for inclusion, the depth of cardiogenic shock was questionable, and usage of other assist devices was allowed in the control group. All of these choices led to rapid enrollment of 600 patients but also yielded a very heterogenous study population, making it hard to draw adequate conclusions. For patients who presented too late in their AMI, no salvage of myocardium by IABP was to be expected, and the choice of a more potent assist device might have been better. For

patients who were easily stabilized by inotropics, there was no need for any assist device, and inclusion of these patients diluted the possible treatment effect. In resuscitated patients, outcome is primarily determined by neurologic recovery and not in any way influenced by IABP support. Finally, by using other assist devices and allowing crossover in the control group, adverse events in the control group might have been prevented. If the assumption is that all patients receiving any assist device in the control group would otherwise have died, then this study may have shown a benefit for IABP therapy.

UTILITY IN CURRENT PRACTICE

Although IABP therapy has been the first choice in left ventricular assist devices over the past 4 decades, its benefit is not undisputable, especially today, when AMI is almost exclusively treated by primary PCI, which immediately relieves myocardial ischemia in most cases. The hemodynamic effects of IABP counterpulsation are almost completely dependent on the status of coronary autoregulation. Therefore, IABP should not be used in every patient presenting in the catheterization laboratory. There are certain clinical situations in which IABP counterpulsation is expected to be beneficial based on pathophysiologic considerations, animal studies, and substudies of large randomized trials.

The SEMPER FI study is an ongoing, randomized, dual-center trial investigating the effect of IABP counterpulsation in patients who present in the catheterization laboratory with a large AMI (defined as ST-segment deviation 15 mm before PCI) complicated by persistent ischemia (defined as ST-segment resolution < 50%) after successful epicardial reperfusion. The SEMPER FI trial aims to include 100 patients. The primary endpoint is defined as the combination of all-cause mortality, necessity of implantation of a left ventricular assist device, or admission with heart failure within 6 months. Crossover from the control group is not allowed. In this clinical setting of persistent ischemia after PCI, the investigators hypothesize that the IABP will increase coronary blood flow and thereby reduce ischemia, while not being counteracted by coronary autoregulation.[22]

CONCLUSION

The rationale for effective IABP therapy is the combination of exhausted autoregulation, persistent ischemia, and still viable myocardium. We should be careful not to abandon such a potentially life-saving treatment. Future randomized studies that adequately recognize the importance of coronary autoregulation will show whether IABP is beneficial. ■

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