Intra-aortic balloon counterpulsation to support percutaneous coronary intervention: what do the trials tell us?

"Intra-aortic balloon counterpulsation simultaneously increases coronary blood flow … and decreases myocardial oxygen demand … making it an attractive means of ameliorating ischemia and consequently enhancing cardiac output."

KEYWORDS: cardiogenic shock ■ circulatory support ■ counterpulsation ■ high risk ■ intra-aortic balloon ■ percutaneous coronary intervention

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Percutaneous coronary intervention (PCI) in the presence of impaired left ventricular function is associated with significant mortality and morbidity, particularly when a large proportion of the remaining viable myocardium is affected by the burden of coronary disease [1]. The consequences of the ischemic cascade are particularly marked in these patients, whose diminished physiological reserve renders them less able to withstand the consequences of ischemia or arrhythmias occurring during a PCI procedure. This may result in a deleterious downward spiral of hemodynamic compromise, culminating in cardiogenic shock or death. Intra-aortic balloon counterpulsation simultaneously increases coronary blood flow (by augmentation of the diastolic aorto–coronary pressure gradient) and decreases myocardial oxygen demand (by reducing the end-diastolic pressure, and therefore the afterload), making it an attractive means of ameliorating ischemia and consequently enhancing cardiac output.

When first introduced four decades ago, intra-aortic balloon pumps (IABPs) were used to support patients undergoing coronary artery bypass grafting. However, the Benchmark Registry demonstrated that cardiogenic shock and high-risk angiography or PCI procedures have become the most common indications for their use [2]. The American College of Cardiology/American Heart Association have classified cardiogenic shock as a 1B indication for IABP insertion while the European Society of Cardiology have awarded this a 1C recommendation [3,4]. At present, international guidelines do not offer formal recommendations for the use of IABP outside the setting of shock, but recommend counterpulsation "in patients at the extreme end of the spectrum of hemodynamic compromise". IABPs entered routine clinical practice in an era when medical devices were not always subject to the scrutiny of randomized controlled investigation and were not as judiciously governed by the principles of evidence-based medicine as therapies that have been introduced more recently. The paucity of evidence reflects, in part, the difficulty of evaluating established therapies in randomized trials and also the high-risk nature of the patients receiving IABPs, making them harder to enroll in such trials.

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The recently published Balloon Pump-Assisted Coronary Intervention Study (BCIS)-1 is the first adequately powered multicenter randomized trial of elective IABP use in patients who were hemodynamically stable at the outset, but at increased risk of major complications during PCI [1]. A total of 301 patients with severe impairment of left ventricular function (mean ejection fraction [EF]: 23.6%) and extensive coronary disease (mean Jeopardy score: 10.4; maximum possible score: 12) were randomized to receive elective IABP support during PCI, or to undergo PCI without planned IABP insertion [5]. In total, 16% of those who underwent unsupported PCI suffered major adverse cardiac or cerebrovascular complications at hospital discharge and it was not possible to reduce the incidence of these complications by elective IABP insertion. On the other hand, elective IABP insertion was associated with an increased rate of bleeding and access-site complications. These results do not support a strategy of routine insertion of IABP in all patients undergoing high-risk PCI. The trial provides definitive randomized

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trial evidence that should allow the international cardiology committees to issue formal guidelines regarding IABP use in this setting. However, there is an important caveat: one in eight patients who were randomized to receive unsupported PCI suffered hemodynamic compromise sufficient to warrant rescue IABP insertion. These patients were more likely to suffer periprocedural infarction than those who did not need IABP insertion and required a longer duration of IABP support than those who received an IABP before PCI. There is a signal that those requiring bailout may be patients at the extreme end of the spectrum of coronary disease, but the trial was not powered for subgroup analysis and did not attempt to generate a model to predict this risk. As such, it is important to acknowledge that some of these high-risk patients will require bailout IABP insertion during PCI and a standby approach should be adopted when undertaking such cases. The standby strategy is likely to vary between centers, from priming the catheter laboratory staff for IABP insertion to gaining contralateral femoral access, to allow timely insertion of a balloon catheter if required.

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The BCIS-1 study excluded patients with acute ST-segment elevation myocardial infarction (STEMI) and those in cardiogenic shock. The latter are broadly accepted indications for counterpulsation, but lack evidence from randomized controlled trials. In the Primary Angioplasty in Myocardial Infarction (PAMI)-II trial, Stone *et al.* demonstrated that patients presenting with STEMI did not seem to benefit from routine use of IABP [6]. Major cardiovascular mortality and morbidity end points and left ventricular ejection fraction at 6 months in the IABP arm were no different to those treated conservatively. Furthermore, Sjauw *et al.* provided a meta-analysis of the 1009 patients studied across seven randomized trials of IABP use in STEMI [7]. These collective data reaffirmed the initial findings that no significant benefit was apparent with the routine use of IABP in this setting. However, the majority of these studies were performed during an era of outdated PCI techniques [8,9] with limited use of stents and are unlikely to accurately portray the advancement in angioplasty techniques along with the recent progress made in adjunctive pharmacotherapy. Furthermore, the lack of benefit of counterpulsation may reflect the fact that IABPs were inserted after primary PCI, which is arguably beyond the window of opportunity to influence infarct size and its subsequent sequelae. The ongoing, contemporary, randomized trial, Counterpulsation Reduces Infarct Size Pre-PCI for Acute Myocardial Infarction (CRISP-AMI) is attempting to revaluate and determine whether elective insertion of an IABP before PCI in patients presenting with anterior STEMI, corresponds with a reduced infarct size [101]. It may also provide mechanistic insights into the effect of counterpulsation on microvascular obstruction, an important determinant of long-term myocardial recovery. However, until the results of this and other randomized trials are made available, the jury remains out on the utility of IABP in hemodynamically stable STEMI.

By contrast, balloon counterpulsation is often considered an integral therapy when managing cardiogenic shock, which continues to be associated with mortality rates in excess of 50% [10], despite advances in PCI techniques and management algorithms aimed at rapid revascularization of STEMI. However, to date, there are no robust randomized trial data on IABP therapy in cardiogenic shock, and current practice and recommendations are based upon relatively small, somewhat dated, registries. Sjauw and colleagues recently reported a meta-analysis of nine such registries, including over 10000 shock patients [7]. This analysis showed an impressive synergistic effect of IABP therapy and thrombolysis on survival but interestingly, no clear benefit of IABP therapy was found in the primary PCI registries. Interpretation of these data is hampered by the selection bias that is inherent in registries, as exemplified by higher revascularization rates in patients receiving thrombolysis as well as IABP, compared with those who were treated conservatively. Notwithstanding the difficulties of studying this group of patients, there is a clear need for a randomized trial of IABP therapy in cardiogenic shock. The IABP in cardiogenic shock (IABP-SHOCK)-2 trial seeks to fulfill this requirement and hopes to randomize 600 patients in cardiogenic shock to receive primary PCI with or without elective IABP support [102]. This ambitious and important trial has made an encouraging start, having randomized more than 150 patients to date.

Intra-aortic balloon pumps remain an important adjunct to PCI in patients who have an increased risk of death or major cardiac complications. The findings of BCIS-1 mean that

there is no longer a role for routine IABP placement when undertaking PCI in patients with severe left ventricular impairment and extensive coronary disease, although a standby approach should be adopted, as an important minority may require bail-out IABP insertion in the event of hemodynamic compromise. The available evidence suggests that a similar approach would be justifiable during primary PCI when the patient is hemodynamically stable at the outset. In light of the data from the thrombolysis era, coupled with persistently high mortality in patients with cardiogenic shock, we feel that IABP therapy should be considered in this scenario, until more definitive data are available. Ongoing randomized controlled trials are expected to strengthen the evidence base relating to IABP therapy, but there is considerable heterogeneity within each of these groups, and translation of guidelines to individual care will continue to be based on estimation of risk and benefit in each case.

Future perspective

The complexity of coronary revascularization has increased markedly over the last two decades and this trend is likely to continue. This has partly been made possible owing to improved mechanical and pharmacological adjunctive therapies available to the interventional cardiologist. Intra-aortic balloon pumps will continue to be an important device, with a clearly defined mandate, guided by BCIS-1 and ongoing trial data. Mechanical supportive devices in general are likely to play a vital role in treating critically ill or high-risk patients, but the stringent assessment of these devices through randomized trial investigation is paramount to their safe introduction to mainstream practice, in order to allow maximal benefit to the patients being treated.

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