Intra-aortic Balloon Pump: Reviewing its Role in Cardiogenic Shock

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Abstract: Cardiogenic shock is a high-mortality condition caused, mostly, by ST-elevation myocardial infarction. When the adequate therapy is implemented in a timely fashion, recovery can be achieved. Treatment is based on intensive care measures, vasoactive drugs, early revascularization and the use of assist circulatory devices. In this review, the authors aim to discuss the available evidence on the use of intra-aortic balloon pump (IABP) in this clinical setting.

INTRODUCTION

Cardiogenic shock (CS) is a condition with a high mortality rate - around 50% [1] -, defined by a state of tissue malperfusion caused by heart failure (HF) and complicates up to 8% of cases of ST-elevation myocardial infarction (STEMI) [2,3]. Although a critical condition, it can be reversed if the proper set of therapies is instituted in time and the correct identification of in-risk patients is made. Therefore, some risk factors related to the development of CS in patients with an acute myocardial infarction (AMI) must be emphasized: older age, anterior MI, hypertension, diabetes, multivessel coronary heart disease, prior MI or HF and left bundle-branch block [4].

Treatment of CS is based, mainly, on coronary reperfusion; more specifically, on early revascularization (percutaneous coronary intervention – PCI – or coronary artery bypass graft – CABG). The survival benefit of non-delayed revascularization was clearly demonstrated in the randomized "Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock" (SHOCK) trial, with an absolute increase of 13% in 1-year survival compared to those assigned to initial clinical stabilization [5, 6].

However, mechanical circulatory support is, in a large proportion of cases, an important adjunctive therapy. In such cases, the most commonly used device is the intra-aortic balloon pump (IABP). There are evidence both demonstrating its benefits as well as showing no advantage in the setting of CS. [7-17].
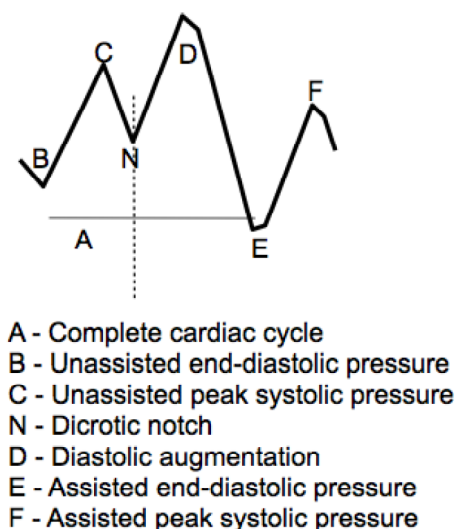
INTRA-AORTIC BALLOON PUMP

Intra-aortic balloon pump is the most commonly used mechanical support device to improve circulatory hemodynamics in cardiogenic shock. Based on the principle of counterpulsation, it was first clinically applied in the late 1960s, by Kantrowitz *et al*. [18]. In the early 1980s [19] its use became widespread since the development of a percutaneous approach for insertion

It is composed of a flexible catheter with a lumen that permits pressure monitoring, and a second one that allows the periodic in- and outflow of helium gas to a polyethylene balloon; also a console which contains the helium transfer system and an electronic control for the inflation-deflation cycle.

The catheter is inserted through the common femoral artery and advanced - either at the bedside or under fluoroscopic guidance in the cath lab - so the distal tip is positioned in the proximal descending aorta - 1-2 cm below the emergence of the left subclavian artery - and the proximal portion is placed above the renal arteries. The console controls the pumping using input from the aortic pressure and/or the electrocardiogram. Inflation occurs just after aortic

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valve closure, and deflation must happen immediately before aortic valve opening

A - Complete cardiac cycle
B - Unassisted end-diastolic pressure
C - Unassisted peak systolic pressure
N - Dicrotic notch
D - Diastolic augmentation
E - Assisted end-diastolic pressure
F - Assisted peak systolic pressure

Figure 1: Cardiac cycle and normal timing of IABP inflation - dotted line).

The hemodynamic effects depend on the appropriate balloon size and timing of the inflation-deflation cycle. When properly set, the use of IABP results in: decrease in systolic pressure (during balloon deflation, consequence of a reduction of left ventricle after load); increase in diastolic pressure (during balloon inflation, which raises coronary blood flow); reduction of heart rate (in nearly 10-20%); and elevation of cardiac output [20]. The net result is an improvement in cardiac energy balance, with a decrement in myocardial oxygen demand and augmentation of oxygen supply [21].

According to the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of STEMI, the use of IABP can be useful for those with CS in this setting who do not quickly stabilize with pharmacological therapy [22], receiving a Class II a recommendation. Noteworthy is the fact that IABP use in CS was downgraded in relation to the earlier edition of those guidelines [23], where it used to receive a Class IB recommendation.

Data regarding complications associated with IABP are difficult to be summarized as a general topic because of the heterogeneity of studies - not only regarding study population, but also in the definitions of such complications. However, it is known that vascular complications - arterial laceration with need of surgical repair, limb ischemia (with eventual amputation) and

major bleeding - are the most common IABP-related complications. Embolization, infection and IABP rupture may also occur. In the Benchmark Registry, the authors evaluated 22,663 consecutive patients in whom an IABP was inserted at 250 centers worldwide from 1996 to 2001, and Stone *et al*. [24] analyzed the 5,495 of those subjects who had an MI. In their study, one or more complications of IABP use occurred in 8.1% of patients, although major complications (severe limb ischemia - requiring surgical therapy -, severe bleeding - need of blood transfusion/surgical intervention or associated with hemodynamic compromise -, balloon leak or death directly due to IABP insertion or failure) occurred in only 2.7% of cases. Regarding those patients in whom IABP was used for CS, the rate of major complications was 2.9%. Ferguson *et al*. [25], in a previous publication of the same Registry, performed a multivariate logistic regression analysis to identify independent predictors of a major IABP-related complication. The results showed that female gender (OR 1.968; CI 1.557 - 2.487), peripheral vascular disease (OR 1.737; CI 1.414 - 2.134), small body surface area (BSA; <1.65 m^2) (OR 1.453; CI 1.095 - 1.926) and higher age ($\geqq$75 years) (OR 1.289; CI 1.048 - 1.585) were significantly related to an increased risk of such events.

INTRA-AORTIC BALLOON PUMP IN CARDIOGENIC SHOCK

Data regarding the use of IABP in patients with cardiogenic shock complicating an MI are controversial and the majority of positive results come from observational non-controlled studies. This was thought to be the reason for the low (<40%) use of IABP in this clinical scenario [26].

O`Rourke *et al*. [7], in 1981, studied the value of IABP in patients with early MI complicated by acute heart failure. Thirty patients were randomized to IABP or standard therapy, and no significant difference between groups was seen in infarct size, morbidity or mortality during a mean follow-up of 15 months.

In the analysis of 200 consecutive patients at Duke University with MI-related CS, between 1987 and 1988, 99 subjects used IABP [8]; the in-hospital mortality was lower (48% x 57%; p=0.23) in those who used IABP than in those who did not. Stomel *et al*. [9] examined 64 consecutive patients with MI and CS dividing the patients in three groups: thrombolytic therapy, IABP and combined thrombolysis plus IABP. The groups were similar in regard to age, sex, medical history,

hemodynamic data and extent of coronary artery disease. Survival was improved in patients treated with combined thrombolytic therapy and IABP support (23% x 28% x 68%, respectively; p=0.0049).

More than 40,000 subjects were enrolled in the "Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries" (GUSTO I) trial, and all were eligible for thrombolytic therapy. A small percentage (7%; n=2,972) developed CS after STEMI [10]. Therapy included the use of IABP in 734 patients. The results showed that early insertion of IABP in these patients was related to a non-significant decrease in mortality compared to those cases in which it was used with delay or not inserted (47% x 60%; p=0.06). In the same year, Hochman *et al*. reported data from the SHOCK Registry [11] analyzing 251 patients from 19 American and Belgian centers where both thrombolysis and mechanical revascularization were used. Patients in whom IABP was used were significantly younger, more often underwent coronary angiography and had no benefit in adjusted mortality compared to those in whom IABP was not used (p=0.66). This lack of benefit in mortality also occurred in those who underwent coronary angioplasty (62% with IABP x 54% without IABP; p=0.743).

A later analysis of 856 subjects from 36 participating centers in the SHOCK Trial Registry showed lower mortality rates in those who used IABP compared to those who did not (50% x 72%; p< 0.0001), and in the group treated with the combination of thrombolytic plus IABP compared to the one who did not receive nor thrombolytic nor IABP (47% x 77%; p< 0.0001) [12]. Similarly, in a retrospective analysis of data from the SHOCK trial, French *et al*. [13] observed a reduction in 1-year mortality, yet not statistically significant, in those patients assigned to initial medical stabilization who received the combination of thrombolysis and IABP compared to those who did not use IABP (41% x 64%; p=0.07).

One crucial aspect when performing invasive procedures is the level of expertise presented by hospitals and their staff. This point was addressed by Chen *et al*. [14] using data from over 12,000 patients enrolled in the National Registry of Myocardial Infarction (NRMI) in the mid 1990`s. In their paper, the authors demonstrated that patients treated in hospitals with a high IABP volume had lower mortality (OR 0.71; 95% CI 0.56-0.90) regardless of other factors.

In the TACTICS trial [15], 57 subjects were randomized to fibrinolytic therapy alone or the combination of fibrinolysis plus IABP. The primary endpoint was all-cause mortality in 6 months and the results showed no significant difference between groups (34% for combination x 43% for fibrinolysis alone; p=0.23) but a trend toward significant benefit in this same outcome when combination therapy was used in those with more severe conditions (Killip III/IV) - 39% x 80% 6-month mortality, respectively; p=0.05). In 2009, Sjauw *et al*. [16] performed two different analyses with previous studies in patients with CS following STEMI: the first one was restricted to data from randomized trials, in a total of seven trials and 1,009 patients; the other included nine cohorts with more than 10,000 subjects. The results from the first analysis showed no advantage of IABP in 1-month survival - but higher rates of stroke and bleeding. In the second analysis, the use of IABP in patients treated with thrombolysis was related to an 18% lower mortality in 30 days (95% CI 16-20; p<0.0001); however, in those treated with primary PCI, IABP was associated with a 6% increase in the same endpoint (95% 3-10; p<0.0008). The authors concluded the article challenging the available guideline recommendations at that time.

More recently, the IABP-SHOCK II trial was published with the aim to answer the question if IABP was capable of reduce mortality in patients with CS following MI for whom early revascularization was planned [17]. It was a multicenter, open-label, randomized study where 600 patients were randomly assigned (1:1 ratio) to IABP or non-IABP and were expected to be treated with early revascularization (primary PCI with treatment of the target lesion only, PCI of the target lesion plus additional immediate or staged PCI of nontarget lesions, or CABG at the discretion of the operator). There was no difference in the primary outcome (30-day mortality) among groups (39.7% IABP x 41.3% non-IABP; RR with IABP 0.96, 95% CI 0.79-1.17; p=0.69). In terms of safety, there was no significant difference between groups with respect to the rates of stroke, bleeding, sepsis or vascular complications requiring intervention.

CONCLUSIONS

When faced with such condition, one must keep in mind the considerable severity inherent to it, where pump failure is the primary derangement but other parts of the circulatory system play a role with inadequate compensation or additional defects [27]. Another point to be remembered is that the cornerstone in the treatment of such cases is early

revascularization; the use of assist circulatory devices is an adjunctive therapy - and nothing more.

Compared to other devices, *e.g.* TandemHeart and Impella, IABP does not need a surgeon to be inserted. It can be inserted either under fluoroscopic guidance or at the bedside by the interventional cardiologist, clinical cardiologist or intensive care physician. Studies in which patients were randomly assigned to treatment with IABP or TandemHeart showed that latter was related to an increase risk – significantly [28] and non-significantly [29] – of severe bleeding. When it comes to the comparison between Impella and IABP, Seyfath *et al*. [30] found similar results. Noteworthy is the fact that both TandemHeart and Impella had better hemodynamic data than IABP, although this was not translated into significantly lower mortality.

Considering the high costs involved in the treatment of patients with myocardial infarction complicated by cardiogenic shock, and the net results demonstrated so far by newer, more expensive devices, IABP might still be the most cost-effective option in this clinical setting.

Although the recent downgrade in the recommendation for its use in this setting, IABP may be the assist circulatory device with the best combination of ease of insertion and handling, lower complication rates, potential benefits in terms of hemodynamics and outcomes and cost-effectiveness.

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