

Review Article

Intra Aortic Balloon Counterpulsation in Coronary Artery Disease: Indications, Complications and Current Practice

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ABSTRACT

As the proportion of high risk patients with coronary artery disease, submitted for either interventional cardiology or surgical procedures increases, use of intra-aortic balloon counterpulsation (IABC) has increased, especially as preoperative therapy. Although the efficacy and cost-effectiveness of IABC have been demonstrated, historically higher complication rates have dissuaded some doctors from IABC use.

In this review indications, complications, outcomes as well as current and future IABC practices, in relation to coronary artery disease are high-lighted. Widened indications for IABC use, particularly as preoperative therapy in high-risk patients, have led to better patient outcomes and improved IABC technology. This has led to increased use of IABC with lower complication rates than previously reported in the literature.

KEY WORDS: complications, coronary artery bypass grafting, coronary artery disease, high-risk patients, intra-aortic balloon pump, prophylaxis.

Intra-Aortic Balloon Counterpulsation for Coronary Artery Disease

Experimental studies have shown the effectiveness of intra-aortic balloon counterpulsation (IABC) in decreasing the severity of myocardial ischemic injury from coronary artery occlusion^[1-4]. Clinically, the IABC has proved efficacious during acute episodes of cardiac ischemia associated with unstable angina^[5], early acute myocardial infarction (AMI)^[6], AMI with impending extension^[7], and malignant ventricular tachyarrhythmia. Presently, the primary indication for IABC in acute cardiac ischemia is before cardiac catheterization and interventional therapy by catheter or surgical techniques. IABC has been used extensively to stabilize surgical patients during anesthesia induction and after cardiac surgery, when acute myocardial dysfunction is suspected.

The rationale for the use of IABC in patients with acute myocardial ischemia is the evidence that it decreases myocardial oxygen demand^[8] and may improve coronary collateral blood flow to the area of ischemia and its surrounding zones^[9]. In support of this opinion are various hemodynamic improvements, such as an increase in cardiac index and a decrease in LV end-diastolic pressure and volume^[8], as well as amelioration of contraction in the ischemic myocardial zones using IABC^[10].

A number of investigators have shown that jeopardized, and especially hibernating myocardium, may be restored to satisfactory function by improving its blood supply with early and late revascularization and by diastolic augmentation^[11]. The combination of IABC with various pharmacological agents may influence the eventual size of the infarcted area, perhaps by preventing its extension^[12].

IABC may decrease the extent of hibernating myocardial segments, which are frequently seen in hearts with acute and chronic ischemia^[13]. Experimentally, IABC is effective in increasing coronary blood flow when mean arterial blood pressure is below 60 mmHg and coronary arteries are patent. In this setting, the coronary autoregulatory mechanisms are minimally functional while coronary blood flow decreases appreciably^[9]. During the episodes of ischemia and in the preinfarction phase, IABC significantly improves myocardial oxygen balance^[14].

Frequently, patients with severe myocardial ischemic symptoms, unresponsive to pharmacological therapy, require stabilization with elective IABC before interventional therapy^[15]. Similarly, for patients with early (less than 6 hours) acute myocardial infarction, pharmacological management, with beta-blockers, calcium channel blockers, and intravenous

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nitroglycerin, followed by thrombolytic therapy and angioplasty, should be routinely applied^[16]. These interventions frequently decrease the electrophysiologic extent of ST-segment changes and limit the eventual size of AMI. In these patients, the hospital and follow up mortality and re-infarction rate have declined significantly^[16].

IABC for Unstable Angina

Patients with acute cardiac ischemia (unstable angina), who do not respond to antianginal therapy, are candidates for urgent cardiac catheterization, followed by interventional therapy to achieve rapid myocardial reperfusion. These patients are candidates for IABC therapy. Clinically they may be regarded as having preinfarction angina, acute coronary ischemia, impending infarction, angina at rest, or intermediate coronary syndrome^[17]. In these patients, IABC allows for the safe performance of diagnostic studies followed by myocardial reperfusion. By using IABC, the incidence of transmural myocardial infarction and postreperfusion cardiac failure from myocardial stunning is decreased. Hospital mortality rate is low despite severe LV dysfunction^[18] and clearly, these patients harbor a large area of hibernating myocardium, which responds favorably to myocardial revascularization with minimal reperfusion injury^[19].

Patients with severe left main coronary artery disease with LV dysfunction, who are unstable before or during the course of cardiac catheterization studies or remain unstable thereafter (hypotension, ventricular arrhythmia, cardiac arrest), should have urgent placement of the IABC^[18]. IABC support maintains excellent hemodynamic stability until the operating room and the surgical team is ready.

Another group of patients with unstable angina that might benefit from IABC, in spite of apparently good cardiac function, are those who suffer from LV hypertrophy due to hypertension and coronary arteries of small size^[18]. These patients need IABC support because of a higher than normal incidence of AMI, when attempts at complete revascularization are made. Especially those who are obese and diabetic may have coronary arteries that could be hard to identify, which could result in an incomplete myocardial revascularization and intraoperative infarction.

IABC for Acute Myocardial Infarction

During the early phase of AMI, IABC is used with the hope of accomplishing four goals; a) limit the eventual size of AMI, b) maintain hemodynamic stability, c) prevent infarct expansion and d)

decrease the complications of AMI. In these situations, IABC is used as a temporary support measure before definitive interventional therapy to achieve myocardial perfusion, regardless of if that will be PTCA or surgery.

IABC for ventricular Tachyarrhythmia

Persistent ventricular tachyarrhythmia is frequently observed in the course of acute myocardial infarction. This complication has a poor prognosis. Their genesis is multifactorial. These include metabolic factors, such as myocardial ischemia, infarction and imbalance of oxygen/demand ratio, oxygen-derived free radicals, and mechanical factors, such as fiber stretch^[20]. Preload, after load, and wall tension further influence the latter. All these factors affect the excitation-contraction coupling, as well as the duration of action potential, which may evoke cardiac tachyarrhythmia^[20]. Malignant tachyarrhythmia usually results from abnormalities of ventricular activation. When persistent, they are due to early activation of ischemic areas that surround an infarcted segment^[21]. Revascularization of the ischemic area or improvement in blood flow or decrease in oxygen demand of the segment, with IABC, is frequently effective in diminishing the frequency or arrhythmic episodes^[22]. Since LV failure is an associated finding, IABC may be utilized as a temporizing measure^[23].

INDICATIONS FOR INTRA-AORTIC BALLOON COUNTERPULSATION

Trends in Current Uses of IABC

Although for many years IABC was implemented as a response to cardiogenic shock, a more enlightened, proactive approach is emerging, especially when performing percutaneous cardiac interventions (Interventional cardiology) or cardiomy (cardiac surgery) in high-risk patients. In the TAMI trial, 75% of IABCs were inserted either before or during cardiac catheterization in 810 consecutive patients initially treated with thrombolysis^[24].

Then why is early balloon insertion clinically important? Not only do the majority of patients in Killip class IV shock die within the first 48 hours, but available interventions to prevent or treat cardiogenic shock are insufficient without adjunctive IABC, compare results from the GISSI-1 trial^[25]. In a retrospective analysis of nearly 5000 patients of IABC support, it was determined that preoperative balloon counterpulsation reduced in-hospital mortality after cardiac surgery by nearly three times, from 35.7% to 13.6% for intra-operative placement^[26].

These results have been confirmed in a recent report, which shows even greater benefits on hospital survival when IABC is used as preoperative therapy^[27].

Another retrospective chart analysis demonstrated the survival benefits conferred by IABC support in the setting of cardiogenic shock, after thrombolysis for acute myocardial infarction. Patients who received IABC exhibited a 93% in-hospital survival rate compared to 37% for those patients who did not receive IABC^[28].

Despite these results and others, geographical and institutional variability in IABC use is marked. Even within the state of Massachusetts^[29], counterpulsation rates ranged from 7.8% to 20.8% of coronary bypass grafting (CABG). Apart from cardiogenic shock per se, independent risk factors for adjunctive IABC with CABG included same-admission PTCA, prior CABG, CHF, recent MI, and cardiac arrest. As compared with their European counterparts, US investigators in the GUSTO-trial^[30] were five times as likely to use IABC (35% versus 7%). The foregoing favorable pattern was consistent with an overall trend toward more aggressive percutaneous cardiac interventions in the US, including significantly higher rates of cardiac catheterization, CABG, and PTCA, as well as significantly more frequent use of beta-blockers and inotropic agents. Institution of IABC was among several independent risk factors significantly correlated (inversely) with 30-day mortality in patients with cardiogenic shock in the GUSTO-trial. Longer time to treatment was again a significant prognostic factor for mortality in

this study^[30]. Current indications for IABC in general are shown in Table 1.

Intra-aortic Balloon Pump Counterpulsation in Cardiac Surgery

One major indication for the use of the intra-aortic balloon counterpulsation has been during cardiac surgery and in the postoperative period. In the 70's reports, there have already been on the efficacy of IABC in reversing postoperative low cardiac output after cardiac surgery^[18]. Subsequently, other investigators, on a large series of patients confirmed these reports^[31]. Among the numerous factors that could lead to the development of postoperative low cardiac output, faulty myocardial preservation ranks first. In this situation, low cardiac output is frequently reversible and requires only a short period of IABC support^[32].

With improved methods for myocardial protection during surgery, other causes for development of postoperative cardiac failure are reperfusion injury (stunned myocardium), preoperative left ventricular dysfunction, and intra-operative myocardial infarction. This frequently results in protracted LV dysfunction with prolonged time to return to aerobic myocardial metabolism (increased lactate production), which frequently results in long IABC support together with massive doses of inotrope and vasoactive agents^[33]. Other causes of postoperative low cardiac output are prolonged ischemia (cross-clamping time) and cardiopulmonary bypass times, incomplete

Table 1. General Indications for IABC use.

<p>Pump failure or cardiogenic shock (as indicated by hemodynamic instability refractory to volume optimization and inotropic support (BP less than 90 mmHg, cardiac index less than 2 L/min/m², pulmonary capillary wedge pressure greater than 18 mmHg, and ST elevation)</p> <p>Hemodynamic or ECG instability in the catheterization laboratory</p> <p>Ventricular arrhythmia unresponsive to conventional treatment.</p> <p>Cardiac failure due to coronary artery disease complications resistant to inotropes and diuretics</p> <p>Cardiac surgical patients at risk for hemodynamic decompensation</p> <p>Severe left main disease, stenosis greater than 70%</p> <p>Ischemic changes during hypotensive episodes (e.g. anesthesia induction)</p> <p>LV aneurysm</p> <p>Acute mitral valve insufficiency</p> <p>Post-infarction ventricular septal rupture</p> <p>Hemodynamic/ECG instability pre-cardiopulmonary bypass</p> <p>Failure to wean from cardiopulmonary bypass</p> <p>Instability during OPCAB myocardial revascularization (beating heart)</p> <p>Bridge to cardiac transplantation</p>
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surgical revascularization or repair, as well as technical problems with the conduct of the operation. In recent years, hemodynamic instability during the course of off-CPB, beating heart surgery can be added to the list^[34] (Table 2).

Table 2. Predominant causes of postoperative low cardiac output.

A. Preoperative factors
Preoperative cardiac dysfunction
Severe left main stenosis
Re- and re-re-operations
Unstable angina despite optimal medical therapy
B. Intra-operative factors
Faulty myocardial preservation
Intra-operative myocardial infarction
Incomplete surgical revascularization
Prolonged ischemia time (aortic cross-clamping)
Prolonged cardiopulmonary bypass time
Hemodynamic instability during OPCAB surgery
Technical problems, e.g. anastomosis
C. Postoperative factors
Prolonged anaerobic myocardial metabolism
Hypovolemia
Arrhythmia
Vascular constriction (arterial conduits)

Postoperative low cardiac output also frequently results in splanchnic hypoperfusion with an increased frequency of gastro-intestinal complications as well as renal failure^[35]. The goals of intra-operative use of IABC are the maintenance of hemodynamic stability, adequate organ perfusion, and metabolism during weaning from cardiopulmonary bypass^[36]. For these reasons, IABC, at times, has been used electively (preoperatively) as a prophylactic measure in critically ill patients and in patients prone to intra-operative myocardial ischemic injury^[36].

In recent years, as the number of patients with severe LV dysfunction and less ideal coronary anatomy who require both primary and repeat myocardial revascularization has increased, the frequency of use of IABC in the course of cardiac surgery has proportionally increased^[37-39].

Simultaneous with the improvements in myocardial preservation and in anaesthetic management of patients with LV failure or with acute cardiac ischemia, IABC has played a significant role in decreasing operative mortality and morbidity^[37,38].

PREOPERATIVE IABC THERAPY IN RELATION TO CORONARY BYPASS GRAFTING (CABG)

Patient Selection for Preoperative IABC Therapy

In order to identify those patients at high risk, who would most likely benefit from preoperative IABC therapy, an in-depth, retrospective analysis of 1,811 patients who had undergone CABG surgery between January 1, 1990 and June 30, 1994, was performed. Of the overall patient group, a total of 1,538 underwent primary CABG while 273 were re-operations^[27]. Careful review of patient's records revealed that intra/postoperative IABC support proved necessary in 80 patients (4.4%), as a result of failure to be successfully weaned from cardiopulmonary bypass (CPB), despite maximum-dose pharmacological support with inotropic and vasoactive agents. Thirty-five of those patients, who ultimately required postoperative IABC, had undergone redo CABG (12.8% of the total), while the remaining 45 had received primary CABG (2.9% of the primary surgery Group; $p < 0.001$). As a whole, the subgroup of patients requiring postoperative IABC was at a greatly increased risk, with overall mortality of 46.3% compared with only 3.6% for those CABG surgery patients who did not require postoperative support. These findings correspond to earlier reports^[26].

Through multivariate analysis, a number of specific clinical characteristics that were related to increased mortality in this high-risk patient population were identified. The one independent risk factor for mortality, which proved to be statistically significant, was preoperative unstable angina ($p < 0.001$). However, it was found that the presence of a combination of any two of four other identified risk factors - redo CABG, Left Ventricular Ejection Fraction (LVEF) equal or less than 0.40, diffuse coronary artery disease (requiring more than four distal anastomoses for complete revascularization), and left main stenosis equal or greater than 70% - also reached a level of statistical significance for increased mortality^[27] (Table 3).

Table 3. Criteria for determination of high-risk CABG patients. At least two factors are required.

Unstable angina, despite optimal medical treatment
Left ventricular Ejection Fraction equal to or less than 0.30
Redo or re-redo CABG
Left Main Stenosis greater than 70%
Diffuse Coronary Artery Disease requiring more than four distal
Anastomoses for complete revascularization

Evolving Myocardial Infarction
Cardiogenic Shock

Using these multiple risk factors, it was determined that 93 of the original, overall Group of 1,811 patients could be identified as having been at high-risk; of these, 80 (86%) ultimately required intra/postoperative IABC support in addition to massive pharmacological support. This categorization process was then applied to a second Group of 188 CABG surgery patients, treated between July 1 and December 31, 1994, in order to select out those at high risk, who would be most likely to benefit from preoperative IABC therapy. A total of 19 patients were found to have at least two of the previously-noted risk factors, thus fulfilling the selection criteria.

Preoperative IABC was initiated in the operating room at induction of anesthesia, 1-1.5 hours before aortic cross-clamping. No balloon-related complications were reported. Overall hospital mortality in this high-risk group was 21% (4/19) and only six of the patients had low postoperative cardiac output that required further IABC support for more than one day. Weaning from CPB did not prove difficult, and 30% of these high-risk patients required no postoperative IABC. Finally, the intra-aortic balloon was removed within 24 hours postoperatively in 90% of the patients^[27]. Length of stay in the intensive care unit (ICU) was also significantly shorter for the patients who received preoperative IABC therapy (2.1 ± 0.9 days) than for those in the original group, who had required postoperative IABC due to difficulty in weaning from CPB (5.4 ± 1.8 days).

In summary, in selected CABG patients determined to be at increased risk of death due to presence of at least two of four identified risk factors, preoperative IABC therapy led to a substantial reduction in hospital mortality, fewer patients with low cardiac output postoperatively, and a reduced stay in the ICU. It was demonstrated that with preoperative IABC therapy, the intra-aortic balloon could be removed more quickly following revascularization, as the patients generally no longer suffered from myocardial ischemia. It was also concluded that the fact that the balloon was already in place during weaning from CPB might well have played an important role in the improved results seen with preoperative IABC therapy. This study has identified high-risk factors and the results correspond well with those reported elsewhere in the literature^[40-45].

Criteria for Initiation and Termination of IABC Therapy

In all prospective randomized studies from the Geneva Group of investigators, definitions for intra/postoperative intra-aortic balloon pump counterpulsation initiation, as well as when IABC

support should be terminated, were clearly stated and did not change during the study.

Intra/postoperative IABC was initiated when a cardiac index more than 2.0 L/min/m² could not be maintained postoperatively, despite pharmacological support (dopamine more than 15 µg/kg/min, dobutamine more than 5-10 µg/Kg/min, amrinone at 0.5 mg/kg bolus dose, or a combination of drugs).

The intra-aortic balloon catheter used was a 9.5-F and as soon as it became available a 8-F, either 30 or 40 ml balloon Percor STAT-DL catheter (Datascope Corp, Fairfield, NJ) connected to a Datascope pump unit (Datascope, Fairfield, NJ). The balloon catheter was usually placed percutaneously via the femoral artery using local analgesia, and with the aid of guide-wire, before induction of anesthesia.

All patients received prophylactic antibiotics (cephalosporin). Thyroid hormones were not used. Patients who had preoperative catheter insertion received anticoagulation with intravenous heparin after catheter placement, with a target partial thromboplastin time greater than 40 seconds. Patients returning from the operating room with an IABC-catheter in place were anticoagulated with calciparine after the mediastinal drainage subsided (usually within 24 hours). The IABC support was terminated once hemodynamic stability was restored (i.e., a cardiac index greater than or equal to 2 L/min/m²) with only minimal pharmacological inotrope support, dopamine at 5 µg/kg/minute.

Surgical and Cardiopulmonary Bypass Techniques

Anesthesia, CPB, and surgical techniques were standardized and were not changed during the study period. Myocardial revascularization was done during normothermic CPB (35 °C to 37 °C). For myocardial protection, intermittent crystalloid cardioplegia (St Thomas' II, with addition of 100 mg allopurinol) along with topical hypothermia with iced slush was used. Initially, 1,000 ml of cardioplegia solution was infused into the aortic root under low pressure. Cardioplegia (500 ml, with 20 mmol/L potassium chloride at 4 °C to 8 °C), was repeated every 30 minutes or whenever electrical activity resumed. Just before aortic declamping, an infusion of 1,000 ml of warm blood cardioplegia (50% venous blood) was given into the aortic root.

All operations were done through a median sternotomy. A cell-saver device was used routinely. The internal thoracic artery was harvested as a pediculated graft whenever used as conduit. No other arterial conduits were used in these series. The sequential bypass grafting

technique was used routinely, as described elsewhere^[46].

Role of Preoperative IABC Therapy in High-Risk Patients Undergoing Redo CABG Surgery

The development of invasive and non-invasive cardiology has extensively influenced the indications for primary and re-operative (redo) myocardial revascularization. In the past, patients undergoing redo CABG were generally younger than those accepted for primary CABG^[47], but because of the acceptance of a larger number of elderly patients for a primary operation, the average age of patients requiring redo CABG is gradually increasing. This is an added risk to the other well-recognized challenges of redo CABG. Consequently, both hospital mortality and morbidity rates are reported to be higher after redo CABG compared with those of primary CABG^[47]. This is particularly true for those patients whose condition is complicated by specific factors known to compromise overall clinical outcome. These include LVEF equal or less than 0.40, unstable angina (requiring urgent surgical intervention), presence of severe (greater than 70%) left main stem stenosis as well as a short interval between the first operation and the reoperation (less than 1 year)^[45-46].

In view of the favorable results of the previous study by Christenson et al, confirming the clinical benefits of preoperative IABC therapy in high-risk CABG surgery, 48 redo CABG patients presenting with two or more of the above-noted risk factors were randomized either to IABC therapy an average of 2 hours prior to CPB, or to no preoperative IABC therapy. The mean patient age was 65 years, and 90% of the study patients were male^[48].

It was reported that virtually all physiological parameters were more favorable in those patients who had received preoperative IABC therapy. As with prior studies, the time on CPB was significantly ($p = 0.006$) shorter (86 minutes versus 110 minutes in the control group). Cardiac index was significantly higher during the first 48 hours postoperatively, with only 16.7% of the treatment Group experiencing a low postoperative cardiac index compared with 54.2% of the controls. Only two patients (8.3%) in the preoperative IABC group also required counterpulsation support postoperatively, and in each of these instances, the intra-aortic balloon was successfully removed on the first postoperative day. This contrasted with a total of nine (37.5%) of the control patients requiring postoperative IABC support, for an average of 4.1 days (ranging from 2 to 8 days)^[48].

The improvement in post-surgical cardiac index was highly significant, as severely disturbed cardiac performance can often lead to difficulty in weaning the patient from CPB, resulting in a high rate of postoperative mortality. This was clearly reflected in the absence of any hospital mortality among the 24 patients who received preoperative IABC therapy, while four control patients (16.7%) died ($p < 0.049$), all between the first and fourth postoperative days^[48].

Mean length of stay in the ICU was also significantly reduced in the postoperative IABC group, 2.4 ± 0.8 days versus 4.5 ± 2.2 days for the controls ($p = 0.007$). Finally, total hospital expenditures were reported lower for those patients who received preoperative IABC therapy^[48]. Only two (4.2%) IABC-related complications (both instances of leg ischemia) occurred, one each preoperatively and postoperatively.

It was concluded that preoperative IABC therapy significantly improved cardiac index, leading to a less ischemic, or even non-ischemic, myocardium at the time of aortic cross-clamping, and thus overall improvement in patient outcome. An additional benefit of the improved cardiac performance observed in this study was a reduced requirement for pharmacological inotropic support during the first 24 hours following CPB.

Preoperative IABP-Efficacy

To further evaluate the efficacy of preoperative IABC therapy in high-risk patients undergoing CABG, a randomized controlled trial was performed which compared clinical outcomes in two groups of patients receiving preoperative IABC therapy, either 24 hours or 1-2 hours prior to CPB, with those of a non-preoperatively-treated control group^[49]. Over a period of nearly two years, all of the 52 high-risk patients who underwent CABG surgery were entered into the study. Patients were considered to be at high risk if they met two or more of the following criteria - LVEF equal or less than 0.40, left main stem stenosis greater than 70%, reoperative CABG, or unstable angina. The latter was defined as a worsening of angina class, in spite of appropriate drug therapy, or angina at rest and/or signs of evolving myocardial infarction. Among the study population, 56% of the patients were undergoing redo CABG surgery, 59% had unstable angina, 87% had LVEF values equal to or less than 0.40, and 30% had left main stem stenosis. It was reported that ischemia time did not differ between the three study groups to an appreciable extent. However, the average CPB time was significantly ($p < 0.001$) shorter in those who received preoperative IABC,

(83.7 ± 20.3 minutes versus 105.5 ± 26.8 minutes) in the control group. The time difference between cardiac reperfusion and termination of the extracorporeal circulation was also significantly shorter in the preoperative IABC patients (19.9 ± 7.8 minutes versus 31.1 ± 14.7 minutes for the controls; $p = 0.002$).

As would be expected, it was reported that cardiac index increased significantly following initiation of IABC support in the preoperative treatment groups. However, cardiac index continued to rise in these patients between five and 30 minutes after revascularization and termination of CPB, while mean postoperative cardiac index values deteriorated somewhat in the controls during this period.

Postoperatively, low cardiac output requiring IABC support was frequently observed in the group that did not receive preoperative counterpulsation therapy. While 60% of these patients experienced this postoperative complication, only 13% of those patients receiving preoperative support did so. Moreover, in those cases where postoperative IABC proved necessary, the intra-aortic balloon remained in place for an average of only 1.3 days in preoperatively treated patients versus 3.1 days in the control group ($p < 0.001$)^[49]. Hospital mortality was dramatically lower in the preoperative IABC treated patients (60% reduction in mortality in the IABC therapy Group, $p < 0.05$), as was the time required in the ICU (2.3 versus 3.5 days, $p < 0.004$).

It was noted that improved cardiac performance, which was observed 5 minutes after the conclusion of CPB, in patients who received preoperative IABC therapy, continued to increase thereafter. This progressive improvement was in sharp contrast to the condition of the control patients, who exhibited no change or a slight deterioration in cardiac index, which in many cases required massive pharmacological support as well as postoperative IABC support.

The study patients who received 24 hours of preoperative IABC therapy demonstrated a greater improvement in cardiac performance than did those in whom IABC was administered 1-2 hours preoperatively. However, no significant differences were noted between these two groups in hospital mortality, postoperative complications or length of ICU stay. Therefore, it was concluded that a brief, 1- to 2-hour period of preoperative IABC might be sufficient for high-risk patients undergoing CABG surgery.

Optimal Timing for Preoperative IABP

To further assess the most effective timing for use of preoperative IABC therapy, between 1997

and mid-1998, 60 high-risk CABG surgical patients were randomized to one of three preoperative treatment time periods - 2 hours, 12 hours or 24 hours, respectively^[50]. As with the previous non-randomized study, differences in terms of postoperative mortality and major morbidity were not found to be statistically significant between the three groups, in which varying durations of preoperative IABP were employed. It was concluded that a 2-hour period of preoperative IABC therapy is most cost-effective in providing optimal therapeutic benefit for these high-risk patients^[50], and this treatment approach has therefore been formally established for use in all such patients undergoing CABG surgery.

Economic Impact of Preoperative IABC Therapy

The efficacy of preoperative IABC therapy in high-risk coronary patients has been demonstrated earlier. However, in the health care profession's increasingly restrained economic situation, the introduction of any new therapeutic modality should have not only proven efficacy but also a demonstrable impact on the total procedural cost. Preoperative IABC therapy has been suggested to be cost beneficial in previous reports^[6,14]. To further shed light on the economic aspect of preoperative IABC therapy, a detailed cost analysis of pooled information from two earlier published randomized studies^[49-50] and 144 consecutive low-risk CABG operations was undertaken^[51].

Costs for patients receiving preoperative IABC therapy before aortic cross-clamping ($n = 62$) were compared to those in a control group not receiving preoperative IABC ($n = 50$). Detailed cost analysis was based on data provided by the hospital finance department. Comparing costs within various categories of standard hospital commodities revealed other striking differences: the cost of pharmaceuticals was markedly significantly higher in the control group compared to the preoperative IABC therapy group. Additionally, intensive care costs were lower in the preoperative IABC group.

It was concluded that preoperative IABC therapy in high-risk coronary patients undergoing CABG surgery is significantly cost-beneficial, with an average saving of 24,000 Swiss francs (\$16,000) on the total hospital cost, which corresponds to a 36% reduction^[51].

Preoperative IABC Therapy for High-Risk Coronary Patients in Routine Clinical Practice

During the time when controlled trials concerning a certain therapy modality is ongoing, results tend to be better than when trials

are not on-going. In order to evaluate post-study effectiveness, a post-study evaluation was undertaken. Between July 1, 1998 and December 31, 1999 (18 months), patient data were analyzed to evaluate the effectiveness of preoperative IABC therapy, beyond a formal study protocol, only following routine guidelines for management of high-risk coronary patients undergoing CABG surgery^[52]. It was found that IABC was used in 12.9% of all patients undergoing CABG (39/103). During the post-study period, all but one high-risk coronary patient received preoperative IABC therapy (n = 38), 97.5%. The only high-risk patient who did not benefit from preoperative IABC subsequently developed postoperative low cardiac output, which required massive doses of inotropic agents as well as postoperative IABC support. Despite this management, the patient succumbed due to multiple organ failure.

It should be stressed that due to encouraging results of the preoperative IABC therapy on outcome parameters after high-risk CABG surgery, sicker patients were accepted for surgery during the post-study period, still with excellent results. One third of the patients presented with four of the above described high-risk criteria.

Utilization rate of arterial conduits, internal thoracic artery, increased during the study period, because preoperative IABC therapy led to hemodynamic stability which allowed time to harvest arterial bypass conduits. This is an important point, because ITA grafts have a lot better long-term patency rate than vein grafts^[53].

From a combined analysis of all high-risk patients who received preoperative IABC therapy it was moreover found that postoperative intubation time was reduced by 68% (Fig. 1), incidence of postoperative acute renal failure was reduced by 85% and length of hospital stay was significantly shortened, $p < 0.0001$, compared to control patients.

It was concluded that the effectiveness of preoperative IABC therapy in high-risk patients undergoing surgical myocardial revascularization continued to show excellent outcome during the post-study period, despite acceptance of sicker patients for surgery^[53].

Trends in IABC Related Complications

Intra-aortic balloon counterpulsation is the most widely used circulatory assist device in cardiac surgery and provides circulatory support for patients experiencing preoperative and postoperative hemodynamic instability, or for high-risk patients undergoing angioplasty or coronary artery bypass graft surgery^[31,54-55]. As the proportion of high-risk patients presenting for

cardiac surgery increases, use of IABC has also increased, especially for preoperative therapy^[50]. Although the efficacy and cost-effectiveness of preoperative IABC therapy have been demonstrated^[50], historically higher IABC-related complication rates have dissuaded some surgeons and cardiologists from IABC use^[27,56]. Of course, IABC treatment is associated with certain risks for complications, as all other treatment modalities. However, reports on IABC complications have all been retrospective in nature and often cover an extensive time period, during which medical therapy, anesthesia, extracorporeal circulation techniques and surgical techniques have improved, together with improved balloon catheters and driving units, as well as greater experience in intra-aortic balloon counterpulsation.

- a) **Technical complications.** Most of the technically related complications such as balloon rupture and gas escape, catheter fracture, balloon entrapment, interference with balloon function, and interference with hemodynamic measurements. These complications occur very rarely and most are overcome by better quality equipment. Problems with balloon catheter insertion can be avoided by using guide wires and sheathless percutaneous catheter insertion. Incorrect positioning of the balloon catheter can lead to complications. However, this can be avoided by better markers on the catheter and X-ray control of catheter position.
- b) **Infection and septic complications.** Balloon catheter insertion site infection and bacteremia can occur but the risk can be lowered by applying appropriate sterile techniques at insertion and during therapy, with additional antibiotic prophylactic treatment.
- c) **Hematologic complications.** Thrombocytopenia frequently develops. Red cell destruction with an increase in plasma hemoglobin may be seen in prolonged (> 5 days) balloon counterpulsation.
- d) **Vascular complications.** By far the most frequently encountered IABC related complications are arterial injury and limb ischemia. A variety of vascular complications, including arterial injury, interference with peripheral circulation, and leg ischemia, limb loss, and aortic dissection, has been associated with the use of IABC. The most important factors that significantly affect the occurrence of vascular complications are; method of balloon catheter insertion, preexisting peripheral vascular disease, urgency of the procedure, female sex, diabetes, obesity, the need for large doses of

vasopressor agents, and patients of short stature. In two reported studies the incidence of complications related to balloon pumping increased as a direct result of duration of IABC assist^[57,58].

Leg Ischemia is the most frequent early complication of balloon pumping^[37,59]. Factors that contribute to leg ischemia include balloon catheter/femoral artery mismatch, method of insertion, preexisting peripheral vascular disease, female gender, hypertension, urgency of balloon catheter insertion, and duration of balloon assist. The overall incidence of this complication in surviving patients ranges between 7% and 11%^[40,55]. More than 90% of ischemic legs present with loss of distal pulse, cold leg, and rest pain which may subside upon diagnosis, and immediate withdrawal of the balloon catheter. Leg ischemia leading to major complications such as limb loss (amputation), and requirement for surgical interventions to relieve the ischemia (thrombectomy), fasciotomy or cross-femoral graft, range between 0.75 to 2.2%^[37,60]. The incidence of limb loss varies and is about 0.5% to 0.7%.

Acute Aortic Dissection occurs in less than 1% of patients and may depend on two factors: the method of catheter insertion and extent of aortoiliac disease

Other Vascular Complications include injury to aorta, iliac and mesenteric arteries, peripheral embolization and thrombosis of the abdominal aorta. However, these complications are rare.

Access site bleeding is a frequent complication in the interventional cardiology practice due to thrombolysis therapy and less of a problem in cardiac surgery.

Neurologic Complications in relation to IABC has been reported to vary between 1.7% to 0.3%^[55,61] and are most frequently paraplegia.

In order to evaluate the **trends in IABC related complications** over time a comparative study of data from two major registries [the Benchmark® Counterpulsation Outcomes Registry with 7,101 IABC in cardiac surgery 1997-2000^[62] and the Society of Thoracic Surgeons (STS) National Database], 41,150 IABC in cardiac surgery 1996 and 1997, and a meta-analysis from literature survey was undertaken, 8,505 surgical IABC and 8,902 medical IABC. The literature survey clearly demonstrated a diminishing incidence of IABC related complications from 22.2% (1980-1990) to 14.1% (1991-2000). The same trend was true for vascular complications decreasing from 16.9% (1980-1990) to 5.1% (1991-2000). A comparison between IABC related complications when used in cardiac surgery and cardiology revealed a

steady decline in both groups regarding vascular complications, while bleeding complications were slightly increased in the medical group in recent years, probably due to more aggressive use of thrombolysis. There was a good correlation between the incidence of major vascular complications using comparable years between the literature survey, the benchmark registry and the STS database (Table 4).

Table 4. Comparison of major vascular complications (requiring surgical intervention or blood transfusions) in relation to intra-aortic balloon counterpulsation as reported in the literature from 1996 to 2000, the benchmark registry 1997-2000, and the STS National database 1996-1997.

	Literature	Benchmark	STS
N	1,876	7,101	41,150
Major Vascular Complications	95	255	2,219
% of Major Vascular Complications	5.1	3.6	5.4*

* likely overestimation due to data specificity.

The overall complication rate in the Benchmark Registry was 6.5% (460/7101) and the rate of major complications (those requiring surgery or blood transfusion) was only 2.1% (148/7101). By far, vascular complications and bleeding are the most frequently encountered complications, representing more than 90% of all complications, while the incidence of limb loss was only 0.5%. Furthermore, the Benchmark data demonstrated that preoperative IABC therapy did not increase the risk for IABC-related complications compared to intra/postoperative IABC treatment. On the contrary, major limb ischemia was significantly lower for preoperative IABC, most likely due to shorter treatment times. Moreover, it was again confirmed from the two registries that preoperative IABC therapy significantly reduced hospital mortality rate, despite the high-risk status of most of these patients.

In conclusion, better patient outcomes plus improved IABC technology has led to increased use and lower complication rate in relation to IABC. Preoperative IABC therapy leads to dramatic increases in survival. Although selection bias is inherent in retrospective studies, the benchmark Registry outcomes are in close concordance to prospective randomized studies previously reported^[63].

DISCUSSION, CONCLUSIONS AND THE FUTURE

Over thirty years of clinical use of IABC has placed this circulatory assist device as the most extensively researched device of all circulatory assist devices, as is evident by the large body of

literature on the topic available. Numerous indications for the use of IABC have been established over the years, and yet others are rapidly emerging in close association with the rapid development of interventional cardiology and surgical techniques. The role of IABC for intra-operative and postoperative support relative to the use of ventricular assist devices needs to be defined, possibly in the setting of multi-center trials. There is some evidence that the IABC can be used to support primarily right ventricular failure, particular in the transplant population. The reason for effectiveness of IABC is presumably due to the interdependence of the right and left ventricular function together with enhanced coronary perfusion^[64]. More research into this interesting aspect of counterpulsation is required. The IABC has also been found to be an effective adjuvant to off pump coronary artery bypass grafting particularly in high-risk patients^[34,65], a venue that requires more studies since the number of OPCAB procedures is steadily increasing, so to avoid the negative effects of cardiopulmonary bypass and lower the procedural cost.

Longer-term IABC use has been effectively employed, as a bridge to transplant, although its role in the era of long-term ventricular assists devices may be more limited. In this concept, perhaps powered pneumatically implantable intra-aortic counterpulsation would pave the way^[66]. The implantable IABC consists of the balloon pump, skin connector, and an external drive unit. Permanent counterpulsation devices are sutured to the wall of the thoracic aorta in the same anatomical position as the traditional device. In pre-clinical experience, the device becomes pseudoendothelialized, essentially removing it from exposure to the circulation, and thus poses a lower risk as source for embolization. In clinical trial, permanent implantable IABC exhibited the familiar hemodynamic benefits conferred by traditional counterpulsation devices, increasing cardiac output and decreasing both LV-end-diastolic pressure and pulmonary capillary wedge pressure. The advantages of implantable IABC include non-obligatory use (the device can be turned on and off at the physician's discretion), the permanent device is non-thrombogenic, and many patients, including those in heart failure, can be maintained without inotropic drugs, which may compromise their peripheral circulation^[66]. The present challenges of permanent implantable counterpulsation device include infection complications and the prospect of leakage from the device.

The use of IABC has continued to increase dramatically, particularly over the past decade

with the expansion of interventional cardiology, and the increasing age and acuity of cardiac surgery patients.

The use of the balloon pump has been extended with good results to the increasing population of elderly.

Over the past five years there has been an increased use of preoperative IABC's^[26,44,50]. This has been associated with a decrease in hospital mortality and post-therapeutic morbidity. Better identification of those patients that will benefit the most is perhaps required. There is a definite move towards prophylactic use to avoid rather than to treat myocardial ischemia in surgery^[51]. For interventional cardiologist confronted with low-output cardiogenic shock, which can severely compromise prognosis in the setting of acute myocardial infarction, unstable angina, heart failure, and other cardiovascular diseases, intra-aortic balloon counterpulsation represents a sound clinical option.

Early insertion of IABC to diminish severe myocardial ischemia already at local community hospitals for safe transportation to cardiac centers may be beneficial^[28], and should be explored further.

Further development of smaller sized catheters and better driving units is one way of lowering the incidence of IABC related complications, but proactive, prophylactic use also leads to shorter IABC treatment times which in turn diminishes the risk for complications. Better education of the team dealing with patients with IABC is needed. Surveillance protocols, including continuous oxymetric measurements etc., will identify ischemic limb complications early, and early intervention will diminish major complications.

Contemporary trends towards more frequent percutaneous placement in the cardiac catheterization laboratory, on a proactive basis, rather than in the operating room as a last resort response to cardiogenic shock, reflect the numerous potential hemodynamic and clinical benefits associated with counterpulsation, particularly among high-risk patients undergoing percutaneous cardiac interventions or surgical procedures. Counterpulsation remains the mechanical circulatory support modality of first choice.

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