# Effect of a Perioperative Intra-Aortic Balloon Pump in High-Risk Cardiac Surgery Patients: A Randomized Clinical Trial

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**Objectives:** The aim of this study was to evaluate the efficacy of perioperative intra-aortic balloon pump use in high-risk cardiac surgery patients.

**Design:** A single-center randomized controlled trial and a meta-analysis of randomized controlled trials.

**Setting:** Heart Institute of São Paulo University.

**Patients:** High-risk patients undergoing elective coronary artery bypass surgery.

**Intervention:** Patients were randomized to receive preskin incision intra-aortic balloon pump insertion after anesthesia induction versus no intra-aortic balloon pump use.

**Measurements and Main Results:** The primary outcome was a composite endpoint of 30-day mortality and major morbidity (cardiogenic shock, stroke, acute renal failure, mediastinitis, prolonged mechanical ventilation, and a need for reoperation). A total of 181 patients (mean [SD] age 65.4 [9.4] yr; 32% female) were randomized. The primary outcome was observed in 43 patients (47.8%) in the intra-aortic balloon pump group and 42 patients (46.2%) in the control group ($p = 0.46$). The median duration of inotrope use (51 hr [interquartile range, 32–94 hr] vs 39 hr [interquartile range, 25–66 hr]; $p = 0.007$) and the ICU length of stay (5 d [interquartile range, 3–8 d] vs 4 d [interquartile range, 3–6 d]; $p = 0.035$) were longer in the intra-aortic balloon pump group than in the control group. A meta-analysis of 11 randomized controlled trials confirmed a lack of survival improvement in high-risk cardiac surgery patients with perioperative intra-aortic balloon pump use.

**Conclusions:** In high-risk patients undergoing cardiac surgery, the perioperative use of an intra-aortic balloon pump did not reduce the occurrence of a composite outcome of 30-day mortality and

major complications compared with usual care alone. (*Crit Care Med* 2018; XX:00–00)

**Key Words:** cardiac surgery; intra-aortic balloon pump; meta-analysis; morbidity; mortality; randomized controlled trial

Patients undergoing combined cardiac surgery procedures and those with comorbidities are considered high-risk patients (1–4).

The intra-aortic balloon pump (IABP) is widely used to optimize oxygen delivery and prevent complications (5–8). Even though recent randomized controlled trials (RCTs) have suggested that IABP insertion does not reduce complications in patients with cardiogenic shock after acute myocardial infarction (AMI) (9, 10), preoperative IABP use may prevent complications in high-risk patients undergoing cardiac surgery (11, 12).

Evidence is based mainly on retrospective data, and high-quality RCTs are lacking, resulting in inconclusive clarity (7, 8, 13–18). A recent meta-analysis suggested that preoperative IABP use is associated with mortality reduction (19), but these findings were mainly derived from small RCTs.

In the Intra-aortic Balloon Counterpulsation in Patients Undergoing Cardiac Surgery (IABCS) trial, we evaluated whether perioperative IABP insertion reduced the frequency of a composite endpoint of mortality and major postoperative complications in high-risk patients undergoing cardiac surgery. We also conducted an updated systematic review incorporating the findings of our trial.

## METHODS

### Study Design and Oversight

The IABCS study was a single-center, parallel RCT performed at the Heart Institute of the Sao Paulo University in Sao Paulo, Brazil, from May 2014 to June 2016. The protocol was approved by the ethics and research committee (Comitê de Ética para Análise de Projetos de Pesquisa 0352/08) and registered at ClinicalTrials.gov (NCT02143544). The trial was overseen by an independent data and safety monitoring board. All authors vouch for the fidelity of the study to the trial protocol and for the accuracy of the data and analyses.

### Patients

All patients greater than 18 years scheduled for coronary artery bypass graft (CABG) surgery or a combined procedure with CABG were eligible if they had a European System for Cardiac Operative Risk Evaluation (EuroSCORE) greater than 6 or left ventricular ejection fraction (LVEF) less than 40%. The exclusion criteria were cardiogenic shock, AMI less than 48 hours prior to enrollment, previous IABP use, AMI mechanical complications, peripheral vascular disease, severe aortic regurgitation, tachyarrhythmia, aortic procedures, and coagulopathy (full list in the **Supplemental Material**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

### Randomization

Patients scheduled for cardiac surgery were assessed for the inclusion/exclusion criteria, provided signed informed consent, and were randomly assigned to one of two treatments: IABP insertion before skin incision (IABP group) or no IABP insertion (control group).

Simple randomization was performed after patient enrollment with a computer-generated list in a 1:1 ratio that was generated online by a web-based program that ensured allocation concealment. The nature of the intervention precluded blinding of the patients and attending physicians. Outcome assessors were unaware of the assigned treatment.

### Study Treatments

The IABP was inserted percutaneously through the femoral artery (Sensation 7F; Maquet Cardiopulmonary AG, Mahwah, NJ) after anesthesia induction and immediately before skin incision. Positioning of the IABP was guided by radioscopy. The balloon size was based on the patient's height. Transesophageal echocardiography was used to confirm correct IABP placement before and after cardiopulmonary bypass (CPB).

Electrocardiographically triggered 1:1 support was interrupted only during CPB. In the control group, an IABP could be inserted if CPB weaning failed because of poor cardiac performance or during the ICU stay if the patient developed cardiogenic shock.

Details of surgical and anesthetic techniques are given in the Supplemental Material (Supplemental Digital Content 1, http://links.lww.com/CCM/D562) and **supplemental data** (Supplemental Digital Content 2, http://links.lww.com/CCM/D563). All patients stayed in the ICU for postoperative care and for 24 hours of standardized hemodynamic monitoring (Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). All patients had a pulmonary artery catheter with continuous monitoring of cardiac output. Fluids and vasoactive drugs were administered during surgery and for the first 24 hours of ICU admission in both groups to maintain adequate cardiac index and tissue perfusion markers (Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). Dobutamine 5–20 μg/kg/min was given if patients had signs of low cardiac output and norepinephrine 0.01–1 μg/kg/min if patients had hypotension despite fluid administration. The hemoglobin trigger for transfusion was individualized according to hemodynamic variables. Weaning from mechanical ventilation was performed in normothermic, hemodynamically stable, nonbleeding patients with adequate levels of consciousness and pain control irrespective of the presence of an IABP.

Based on the experience of our center in high-risk patient management, we kept the IABP in place for the first 24 hours in the ICU to stabilize the patients and then performed IABP weaning by reducing the frequency of assistance (1:1–1:2–1:3), based on hemodynamic evaluation (cardiac index ≥ 2.2 L/min/$m^2$, no clinical signs of poor tissue perfusion, no evidence of markers of tissue hypoxia, and ≤ 5 μg/kg/min of dobutamine). After reaching an IABP frequency of assistance of 1:3 in a hemodynamically stable patient, the IABP catheter was removed. In

patients developing signs of tissue hypoperfusion during IABP trial weaning (altered mental status, oliguria, mottled clammy skin, tachycardia, hypotension, lactic acidosis, or reduced mixed venous oxygen saturation [$Svo_2$]), the IABP was not removed. For patients who required an IABP for longer than 48 hours after surgery, systemic anticoagulation was initiated with IV sodium heparin. Independent study monitors verified adherence to the required clinical trial procedures and confirmed accurate collection of data according to Good Clinical Practice.

### Outcomes

The primary outcome was a composite endpoint of 30-day mortality and major postoperative complications (cardiogenic shock, stroke, acute renal failure, requirement of mechanical ventilation for longer than 24 hr, deep sternal wound infection, and a need for reoperation) (20).

Secondary outcomes included the 30-day occurrence rate of septic shock, arrhythmias (atrial fibrillation and ventricular arrhythmias), myocardial ischemia, delirium, seizures, acute kidney injury (AKI), need for renal replacement therapy (RRT), 60-day mortality, ICU and hospital length of stay, duration of use of inotropes and vasopressors, and adverse effects related to the IABP. We also assessed hemodynamic variables, markers of tissue hypoxia, and biomarkers during the ICU stay (details in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

### Data Collection

After randomization, we recorded the demographic, hemodynamic, and clinical data of patients (details in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). Data were collected by three blinded assessors. Patients were discharged from the ICU if their physiologic status was stable with no need for monitoring and no active interventions planned. Follow-up after hospital discharge was performed by telephone until the 30th postoperative day.

### Sample Size and Data Analysis

To detect a decrease in the primary combined outcome of mortality and major postoperative complications from 40% in the control group to 20% in the IABP group, we enrolled 181 patients (details in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). All data analyses were performed according to a pre-established intention-to-treat analysis plan, and we also performed per-protocol analyses (including participants who completed the protocol for the treatment that they were originally allocated to) for the primary outcome.

Dichotomous data were compared using a two-tailed chi-square test with Yates' correction or Fisher exact test when appropriate. Continuous measurements were compared using the Mann-Whitney *U* test. Two-sided significance tests were used throughout. Data are presented as medians (25–75th percentiles) or as means (± SD). Further details on statistics are available in the Supplemental Material (Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

A two-sided $p$ value of less than 0.05 was considered statistically significant. The statistical analysis was performed using SPSS Version 18.0 (SPSS, Chicago, IL).

A systematic review and meta-analysis of RCTs studying IABP use in cardiac surgery was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (21), with mortality as the primary outcome (details in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). Two authors assessed the risk of bias using the Cochrane Risk of Bias tool (The Cochrane Collaboration, Copenhagen: The Nordic Cochrane Centre, 2014) (22).

## RESULTS

### Study Patients

Of the 1,116 assessed patients, 181 (16.2%) fulfilled the inclusion criteria and were randomized (90 patients to the IABP group and 91 to the control group) and analyzed according to the intention-to-treat principle (**Fig. 1**). Seventy-four patients (41%) underwent randomization because of a LVEF less than or equal to 40%, 66 (36%) had a EuroSCORE greater than or equal to 6, and 41 (23%) had both criteria.

### Interventions

All patients completed the 30-day follow-up. Among the patients in the control group, 14 (15%) had an IABP inserted: five for CPB weaning and nine because of cardiogenic shock during the first 48 hours of the ICU stay. Nine patients assigned to the IABP group (10%) did not have an IABP inserted because of technical difficulties. Irrespective of IABP insertion, all patients were analyzed according to random group allocation (intention-to-treat principle). The baseline and intraoperative characteristics were similar between the two groups (**Tables 1** and **2**).

### Outcomes

The primary composite outcome occurred in 43 patients (47.8%) in the IABP group and 42 patients (46.2%) in the control group (absolute risk difference, 1.6%; 95% CI, –12.7% to 15.8%; $p = 0.46$) (**Table 3** and **Fig. 2**).

No differences were observed between the IABP and control groups in prolonged mechanical ventilation (5.6% vs 7.7%; $p = 0.70$), deep sternal wound infection (7.8% vs 14.3%; $p = 0.25$), surgical re-exploration (3% vs 4%; $p > 0.99$), reoperation (14.4% vs 12.1%; $p = 0.60$), cardiogenic shock (18% vs 19%; $p = 0.98$), acute renal failure (22% vs 14%; $p = 0.12$), or stroke (2% vs 2%; $p > 0.99$) (Table 3).

The per-protocol analysis confirmed no differences in the composite endpoint between the IABP and control groups (43 patients (47.8%) vs 42 patients (46.2%); $p = 0.46$) (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). The results were also consistent across all prespecified subgroup analyses (**Supplemental Fig. 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562) and when selectively removing mechanical ventilation or AKI from the composite endpoint (**Supplemental Tables 2**

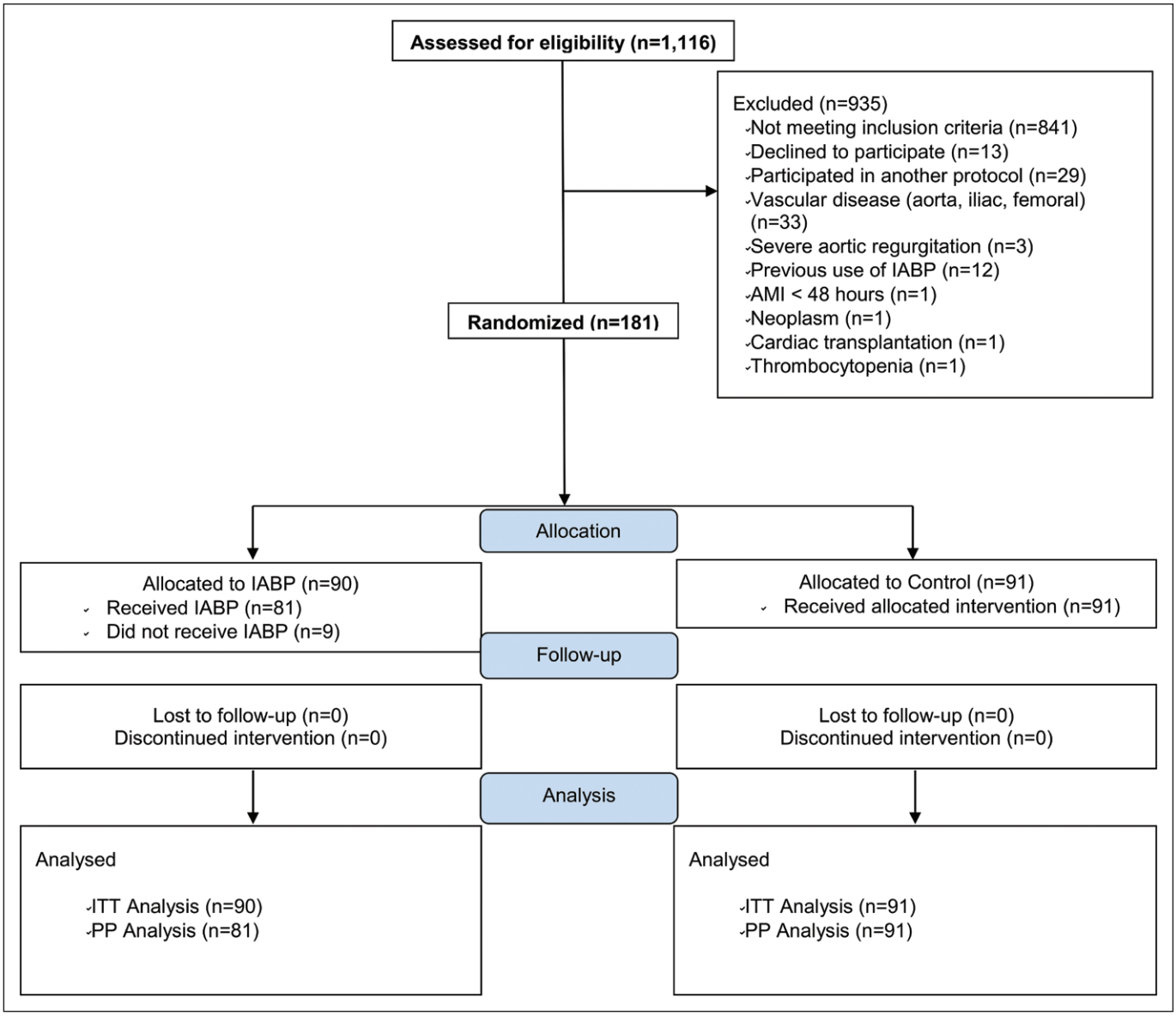


**Figure 1.** Flowchart of the study. AMI = acute myocardial infarction, IABP = intra-aortic balloon pump, ITT = intention-to-treat, PP = per-protocol.

and **3**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

No differences were found between the study groups in the duration of mechanical ventilation, duration on vasopressors, occurrence rate of AKI, use of RRT, arrhythmias, septic shock, myocardial ischemia, delirium, seizure, bleeding, length of hospital stay, length of ICU stay, or safety endpoints (Table 3 and **Supplemental Table 4**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). Patients assigned to IABP insertion had a longer duration of inotropic therapy than the control group (51 vs 39 hr; absolute difference, 12 hr; 95% CI, –0.1 to 24.1; $p = 0.007$). Patients in the IABP group had a longer ICU stay (5 vs 4 d; absolute difference, 1 d; 95% CI, –0.3 to 2.3; $p = 0.035$). No significant differences were observed in the rate of life-threatening bleeding, vascular complications, or the ICU or hospital readmission rates (Table 3 and Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

## Physiologic and Laboratory Values

Hemodynamic variables were not different between the groups at any time point (**Supplemental Figs. 2–10**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). Blood lactate, base excess, $Svo_2$, and venous-arterial $CO_2$ tension gap values were similar between groups (**Supplemental Figs. 11–14**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562), as were N-terminal pro b-type natriuretic peptide, creatine-kinase muscle/brain, troponin I, and heart-type fatty acid–binding protein levels (**Supplemental Figs. 15–18**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). The neutrophil gelatinase-associated lipocalin (NGAL) level was higher in the IABP group than in the control group (**Supplemental Fig. 19**, Supplemental

**TABLE 1. Baseline Patients Characteristics**

| Variables | Intra-Aortic Balloon Pump (*n* = 90) | Control (*n* = 91) |
|---|---|---|
| Men, *n* (%) | 65 (72) | 58 (64) |
| Age (yr), mean ± SD | 64.4 ± 8.3 | 66.4 ± 10.5 |
| Body mass index (kg/m$^2$), median (IQR) | 27 (24–29) | 26 (23–30) |
| Left ventricular ejection fraction (%), median (IQR) | 40 (30–45) | 40 (35–55) |
| Heart failure, *n* (%) | 70 (78) | 60 (66) |
| New York Heart Association functional classification, *n* (%) | | |
| 1 | 10 (14) | 14 (23) |
| 2 | 40 (57) | 30 (50) |
| 3 | 18 (26) | 16 (26) |
| 4 | 2 (3) | 0 (0) |
| Previous cardiac surgery, *n* (%) | 2 (2) | 2 (2) |
| Right ventricular dysfunction, *n* (%) | 6 (7) | 2 (2) |
| Pulmonary hypertension, *n* (%) | 15 (17) | 11 (12) |
| Arterial hypertension, *n* (%) | 71 (79) | 81 (89) |
| Peripheral vascular disease, *n* (%) | 9 (10) | 15 (16) |
| Chronic obstructive pulmonary disease, *n* (%) | 3 (3) | 3 (3) |
| Dyslipidemia, *n* (%) | 53 (59) | 64 (70) |
| Current smoker, *n* (%) | 16 (18) | 13 (14) |
| Atrial fibrillation, *n* (%) | 4 (4) | 8 (9) |
| Diabetes, *n* (%) | 45 (50) | 48 (53) |
| Liver disease, *n* (%) | 0 (0) | 1 (1) |
| Previous stroke, *n* (%) | 13 (14) | 8 (9) |
| Dialysis, *n* (%) | 4 (4) | 5 (6) |
| Obesity, *n* (%) | 15 (17) | 22 (24) |
| Chronic renal failure, *n* (%) | 18 (20) | 14 (15) |
| Previous acute myocardial infarction, *n* (%) | 72 (80) | 68 (75) |
| Stable angina, *n* (%) | 57 (63) | 61 (67) |
| Unstable angina, *n* (%) | 33 (37) | 29 (32) |
| Left main coronary artery disease > 50%, *n* (%) | 32 (36) | 31 (34) |
| Coronary artery disease triple vessel, *n* (%) | 73 (81) | 79 (87) |
| Valvular disease, *n* (%) | 19 (21) | 17 (19) |
| Mitral | 17 (90) | 14 (82) |
| Mitral and aortic | 1 (5) | 0 (0) |
| Aortic | 1 (5) | 1 (6) |
| Angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker, *n* (%) | 68 (76) | 75 (82) |
| Betablocker, *n* (%) | 74 (82) | 76 (84) |
| Antiplatelet drugs, *n* (%) | 75 (83) | 83 (91) |
| Drug, *n* (%) | | |
| Aspirin | 58 (77) | 66 (80) |
| Aspirin and clopidogrel | 15 (20) | 17 (21) |
| Clopidogrel | 2 (3) | 0 (0) |
| Warfarin, *n* (%) | 4 (4) | 2 (2) |
| European System for Cardiac Operative Risk Evaluation, median (IQR) | 6 (4–7) | 6 (4–7) |

IQR = interquartile range.

Body mass index calculated as weight in kilograms divided by height in meters squared.

Digital Content 1, http://links.lww.com/CCM/D562) at 24 hours after ICU admission. Hemoglobin and serum creatinine levels were not different (**Supplemental Figs. 20** and **21**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

Eleven RCTs (**Supplemental Fig. 22**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562) were included in the meta-analysis (7, 8, 13–18, 23, 24); their key characteristics are presented in **Supplemental Table 5** (Supplemental Digital Content 1, http://links.lww.com/CCM/D562). All were single-center RCTs. The combined mortality was lower in the IABP group than in the control group (risk ratio [RR], 0.59; 95% CI, 0.37–0.94; $p = 0.03$; $I^2 = 21\%$) (**Supplemental Fig. 23**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). On visual examination, the funnel plot was asymmetrical. Egger's regression test showed significant evidence of publication bias ($p = 0.018$) (**Supplemental Fig. 24**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). The trim and fill method estimated that at least four "negative" studies were unpublished, which when added to the pooled estimation would result in a nonsignificant adjusted RR for mortality of 0.76; 95% CI, 0.46–1.27; *p* value equals to 0.29 (**Supplemental Fig. 25**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). A meta-regression showed that mortality differences were present in older studies but not in those performed in recent years ($p = 0.011$) (**Supplemental Fig. 26**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). A subgroup analysis based on the year of publication revealed lower mortality in the IABP group than in the control group in RCTs performed before 2010 but not in those performed after 2010, including the present trial (**Supplemental Fig. 27**, Supplemental Digital Content 1, http://links.lww.com/CCM/D562). The risk

**TABLE 2. Surgical and Other Intraoperative Characteristics**

| Variables | Intra-Aortic Balloon Pump (*n* = 90) | Control (*n* = 91) | *p* |
|---|---|---|---|
| Surgery type, *n* (%) | | | 0.38[a] |
| Isolated CABG | 82 (91) | 86 (95) | |
| CABG combined with valve procedure | 8 (9) | 5 (6) | |
| CABG reoperation | 2 (2) | 1 (1) | 0.62[b] |
| Number of grafts, *n* (%) | | | 0.19[d] |
| 1 | 0 (0) | 4 (4) | |
| 2 | 22 (24) | 24 (26) | |
| 3 | 44 (49) | 39 (43) | |
| 4 | 21 (23) | 22 (24) | |
| 5 | 3 (3) | 2 (2) | |
| Graft type, *n* (%) | | | 0.35 |
| LIMA | 1 (1) | 4 (4) | |
| LIMA, saphenous vein, radial artery | 3 (3) | 1 (1) | |
| LIMA, saphenous vein | 79 (88) | 79 (87) | |
| LIMA, radial artery | 1 (1) | 0 (0) | |
| Saphenous vein | 6 (7) | 7 (8) | |
| Duration of surgery, hr, median (IQR) | 5.1 (4.8–5.7) | 5.0 (4.3–5.7) | 0.056[c] |
| On pump surgery, *n* (%) | 81 (90) | 73 (80) | 0.06[a] |
| Duration of cardiopulmonary bypass, min, median (IQR) | 90 (72–107) | 86 (57–106) | 0.21[c] |
| Aortic cross-clamp time, min, median (IQR) | 72 (57–85) | 69 (56–85) | 0.44[c] |
| RBC transfusion, *n* (%) | 37 (41) | 33 (36) | 0.50[a] |
| Antifibrinolytic, *n* (%) | 81 (90) | 74 (81) | 0.096[a] |
| Crystalloid, mL, median (IQR) | 2,000 (1,500–2,500) | 2,000 (1,500–3,000) | 0.38[c] |

CABG = coronary artery bypass grafting, IQR = interquartile range, LIMA = left internal mammary artery.
[a]Pearson $\chi^2$.
[b]Fisher exact test.
[c]Mann-Whitney *U* test.
[d]Likelihood ratio.

of bias is presented in **Supplemental Fig. 28** (Supplemental Digital Content 1, http://links.lww.com/CCM/D562) and **Supplemental Table 6** (Supplemental Digital Content 1, http://links.lww.com/CCM/D562).

## DISCUSSION

The main finding of the present RCT performed on high-risk patients undergoing cardiac surgery was that perioperative IABP use did not reduce a composite endpoint of 30-day mortality and major complications. Additionally, no between-group differences were found in the primary outcome in any subgroups. Patients assigned to IABP insertion had a longer ICU stay and needed inotropes for a longer period. We observed that the IABP did not improve hemodynamic variables or markers of tissue oxygenation. Biomarkers of myocardial reserve were not changed by the perioperative use of an IABP.

Previous RCTs suggested a higher survival rate with IABP use in patients undergoing cardiac surgery (7, 8, 13–16), but our updated meta-analysis showed a publication bias (small studies showing no beneficial effects were likely not published). Recent studies have argued that the hemodynamic effects of the IABP are modest and do not result in a significant increase in cardiac output, left ventricular stroke work index, or systemic vascular resistance (25, 26). We may also postulate that in patients already receiving an optimized hemodynamic protocol based on fluids, inotropes, and vasopressors, IABP use may not provide additional hemodynamic benefit in cardiac surgery.

Recently published evidence in randomized patients with cardiogenic shock after AMI has demonstrated no benefit of IABP use on mortality or complications (9, 10). Cardiac surgery is the ideal scenario for IABP use because this device does not increase oxygen consumption and may result in temporary hemodynamic improvement. However, in our study,

**TABLE 3. Primary and Secondary Outcomes**

| Outcomes | IABP ($n = 90$) | Control ($n = 91$) | Absolute Difference (95% CI) | $p$ |
|---|---|---|---|---|
| Primary, *n* (%) | | | | |
| Composite 30-d mortality or major morbidity | 43 (47.8) | 42 (46.2) | 1.6 (−12.7 to 15.8) | 0.46[a] |
| Mechanical ventilation > 24 hr | 5 (5.6) | 7 (7.7) | −2.1 (−10.1 to 5.7) | 0.70[a] |
| Wound infection | 7 (7.8) | 13 (14.3) | −6.5 (−16.1 to 2.9) | 0.25[a] |
| Surgical re-exploration | 3 (3.4) | 4 (4.4) | −1.1 (−7.8 to 5.5) | > 0.99[b] |
| Stroke | 2 (2.2) | 2 (2.2) | 0.02 (−5.7 to 5.8) | > 0.99[b] |
| Cardiogenic shock | 16 (18.0) | 17 (18.9) | −0.9 (−12.2 to 10.4) | 0.98[a] |
| Acute renal failure (Society of Thoracic Surgeons definition) | 20 (22.2) | 13 (14.3) | 7.9 (−3.4 to 19.1) | 0.12[a] |
| Mortality | 13 (14.4) | 11 (12.1) | 2.4 (−7.8 to 12.5) | 0.60[a] |
| Secondary | | | | |
| Duration of mechanical ventilation, hr, median (IQR) | 11 (7–19) | 10 (7–13) | 0.8 (−1.2 to 2.8) | 0.13[c] |
| Use of vasopressor, hr, median (IQR) | 61 (21–104) | 58 (3–88) | 2.4 (−24.1 to 28.8) | 0.22[c] |
| Use of inotropic, hr, median (IQR) | 51 (32–94) | 39 (25–66) | 12 (−0.1 to 24.1) | 0.007[c] |
| 60-d mortality, *n* (%) | 17 (19) | 13 (14) | 4.6 (−6.4 to 15.5) | 0.41[a] |
| AKI, *n* (%) | | | | 0.67[a] |
| Without AKI | 55 (61.8) | 62 (68.9) | −7.0 (−20.5 to 6.8) | |
| AKIN 1 | 19 (21.3) | 14 (15.6) | | |
| AKIN 2 | 8 (9) | 9 (10) | | |
| AKIN 3 | 7 (7.9) | 5 (5.6) | | |
| Renal replacement therapy, *n* (%) | 6 (6.7) | 1 (1.1) | 5.6 (−0.5 to 12.7) | 0.064[b] |
| Tachyarrhythmia, *n* (%) | 43 (48.3) | 35 (38.9) | 9.3 (−5.0 to 23.1) | 0.20[a] |
| Bradyarrhythmia, *n* (%) | 7 (7.9) | 5 (5.6) | 2.3 (−5.5 to 10.3) | 0.54[a] |
| Low cardiac output, *n* (%) | 21 (23.6) | 25 (27.8) | −4.1 (−16.6 to 8.5) | 0.52[a] |
| Septic shock, *n* (%) | 16 (17.8) | 10 (11.0) | 6.8 (−3.6 to 17.2) | 0.19[a] |
| Myocardial ischemia, *n* (%) | 9 (10.1) | 11 (12.2) | −2.1 (−11.6 to 7.4) | 0.65[a] |
| Delirium, *n* (%) | 26 (29.2) | 23 (25.6) | 3.6 (−9.3 to 16.4) | 0.58[a] |
| Bleeding, *n* (%) | 10 (11.2) | 12 (13.3) | −2.1 (−11.9 to 7.7) | 0.67[a] |
| Adverse events, *n* (%) | | | | |
| IABP complications | 7 (7.8) | 3 (3.3) | 4.5 (−2.7 to 12.2) | 0.21[b] |
| Fistula | 1 (1.1) | 0 (0) | 1.1 (−3.0 to 6.0) | 0.50[b] |
| Pseudoaneurysm | 3 (3.3) | 1 (1.1) | 2.2 (−3.1 to 8.3) | 0.37[b] |
| Limb ischemia | 2 (2.2) | 2 (2.2) | 0.02 (−5.7 to 5.8) | > 0.99[b] |
| Bleeding at insertion site | 1 (1.1) | 0 (0) | 1.1 (−3.0 to 6.0) | 0.50[b] |
| Amputation | 1 (1.1) | 0 (0) | 1.1 (−3.0 to 6.0) | 0.50[b] |
| ICU length of stay, d, median (IQR) | 5 (3–8) | 4 (3–6) | 1 (−0.3 to 2.3) | 0.035[c] |
| Hospital length of stay, d, median (IQR) | 13 (9–18) | 11 (8–17) | 1.5 (−1.2 to 4.2) | 0.30[c] |

AKI = acute kidney injury, AKIN = AKI network, IABP = intra-aortic balloon pump, IQR = interquartile range.

[a]Pearson $\chi^2$.

[b]Fisher exact test.

[c]Mann-Whitney *U* test.

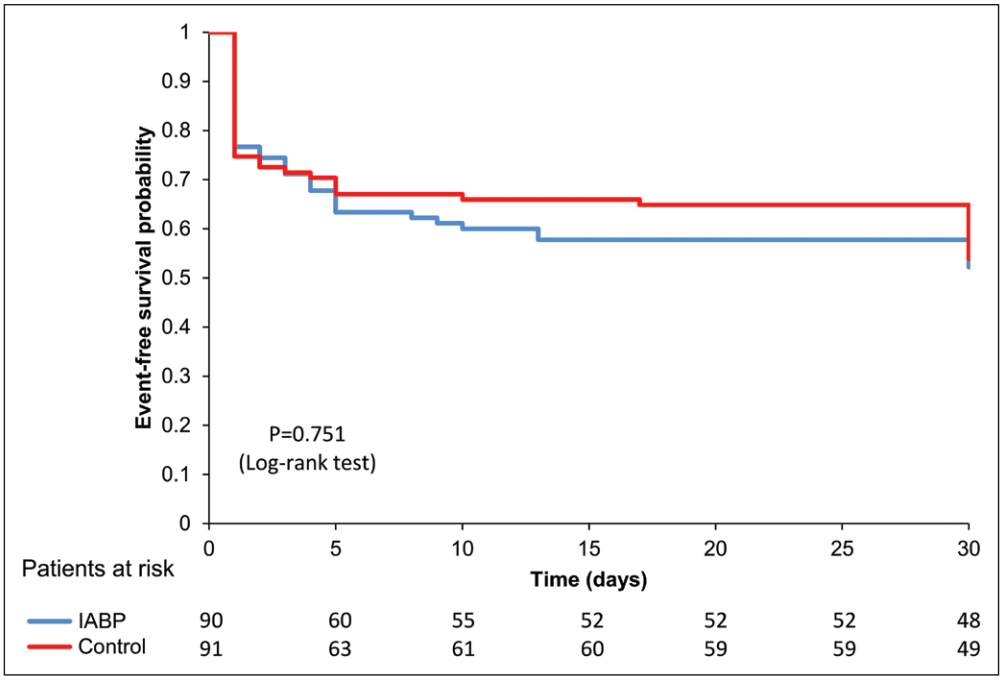


**Figure 2.** Kaplan-Meier event-free survival probability for 30 d after surgery. Unadjusted Kaplan-Meier survival curves showing 30-d probabilities of the primary outcome for each group were compared using the log-rank test. IABP = intra-aortic balloon pump.

perioperative IABP use did not improve postoperative outcomes compared with the control group.

A recent meta-analysis showed a 6.7% mortality reduction in patients with preoperative IABP use (19). However, the results were driven by small trials performed more than 10 years ago by a single group of researchers. In those studies, no predefined hemodynamic protocol was used, the duration of IABP therapy was unknown, balloon insertion was performed at different times, and few data regarding vasoactive drugs, transfusion rates, and balloon weaning were reported. The most recent high-quality RCT showed no benefit of preoperative IABP insertion on clinical outcomes in CABG patients with an LVEF less than 35% (18).

The main strength of our trial was that we strictly followed the hemodynamic optimization, IABP management, and weaning protocol while performing the trial in actual everyday practice, which significantly increased the validity of the trial results. In our study, the eligibility rate for preoperative IABP insertion was 16.2%, similar to the data of a 10-center prospective cohort of 29,961 CABG patients (27). Furthermore, the IABP group mortality rate of our trial coincided with data of 455 high-risk patients with preoperative IABP use in the above-mentioned cohort (28). In addition, the rate of mortality and major morbidity in our trial was the same as that in a large RCT on preoperative IABP use in high-risk CABG patients (18). The primary outcome of our study was a composite endpoint modified from the Society of Thoracic Surgeons risk model outcomes, as in the RCT by Ranucci et al (18) However, we added cardiogenic shock, allowing us to better demonstrate the actual postoperative morbidity in high-risk cardiac surgery patients. Another strength is that we studied high-risk patients undergoing cardiac surgery defined by low LVEF and/or a high EuroSCORE, whereas recent studies have not included patients based on preoperative risk scores (16, 17). We also included patients undergoing combined procedures (CABG plus valve surgery), who are considered a high-risk subgroup and have been excluded from most previous RCTs (7, 8, 13–17, 23). To our knowledge, this is the first RCT of perioperative IABP use in cardiac surgery that followed a strict protocol of hemodynamic therapy, with cardiac output optimization based on Swan-Ganz monitoring, evaluation of tissue perfusion markers, and measurement of biomarkers. This design could have contributed to the between-group similarities in hemodynamic variables, markers of tissue perfusion, and biomarkers. The only difference we observed was the higher NGAL level at 24 hours after ICU admission in the IABP group, but this was not clinically significant, and no difference was observed in the AKI rate between groups. In addition, the IABP weaning protocol was started only after hemodynamic stability was achieved with low doses of inotropes and after evaluation of signs and symptoms of low cardiac output. Previous RCTs showing a benefit of preoperative IABP had no defined protocol of perioperative care and enrolled patients over long time frames that could significantly have influenced the obtained positive results (16, 23).

The addition of an updated meta-analysis showing that the perioperative use of an IABP does not change outcomes after cardiac surgery in high-risk patients confirmed the validity of our findings.

Another strength of the trial was the intention-to-treat analysis, which allowed us to avoid potential overoptimistic estimation of treatment efficacy and reflected the actual practical effectiveness of the treatment care program of perioperative IABP use. Finally, per-protocol analysis confirmed the intention-to-treat principle of the data analysis.

Our study is limited by its single-center design, but this may also increase the intrinsic value of the study by reducing noise.

In conclusion, in high-risk patients undergoing cardiac surgery, the perioperative use of an IABP did not reduce the occurrence of a composite outcome of 30-day mortality and major complications compared with usual care alone.

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