**Abstract**

We evaluated the impact of immediate intra-aortic balloon pumping (IABP) on hospital and mid-term outcome of coronary artery bypass graft (CABG) whenever perioperative acute complications developed. We compared clinical, biochemical, echocardiographic in-hospital results and two-year follow-up outcome of 30 low-risk (EuroSCORE < 5) CABG (group A) who immediately received perioperative IABP when acute complications were suspected, to a contemporary, uncomplicated case-matched group (30 patients; Group B). Two in-hospital deaths were recorded in group A with no deaths in controls ($P = 0.492$). Group A showed significantly higher lactate only at ICU arrival ($P = 0.001$). Troponin I was always higher, but never reached values diagnostic for myocardial infarction ($P < 0.001$). Worse left ventricular ejection fraction ($P < 0.001$) and wall motion score index ($P = 0.008$) were recorded at ICU arrival in group A, although an almost complete recovery was registered at discharge. Two-year actuarial survival was similar between the two groups ($P = 0.598$). No differences were observed in freedom from acute myocardial infarction ($P = 0.503$) and from overall cardiac complications ($P = 0.410$). Early IABP should be established whenever cardiac complications are suspected, because of its beneficial impact on enzymatic leakage, myocardial recovery at echocardiography, hospital outcome, mid-term follow-up survival and freedom from cardiovascular events.

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**Keywords:** IABP; CABG; Cardiac complications

1. Introduction

Intra-aortic balloon pump (IABP) is today the most used ventricular assist device [1], either for preoperative and perioperative support in high-risk patients undergoing cardiac surgery [2–4]. On the other hand, preoperative insertion proved to reduce morbidity and mortality after cardiac surgery for high-risk patients, compared to intra- or postoperative support [2, 5, 6].

Anyway, guidelines do not suggest IABP when some complications are suspected (e.g. poor transit-time flowmetry, minor ECG changes and hemodynamic instability, etc.). However, despite few reports that proved the beneficial effects of immediate IABP support, the Benchmark registry still shows that IABP assistance is more often started when major ischemic events occur [7].

Therefore, the aim of the study was to determine if a precocious IABP support would be beneficial, even in case of ‘off-label’ indications, when an ischemic substrate is suspected. Therefore, we compared low-risk but complicated CABG to a contemporary group of patients similar for preoperative characteristics, but experiencing an uneventful postoperative course.

2. Materials and methods

2.1. Patients and study design

We retrospectively compared the hospital outcome of low-risk patients (EuroSCORE ≤ 5) who unexpectedly complicated and required IABP intraoperatively or in the immediate postoperative period (group A, $n = 30$) to a homogeneous contemporary case-matched group of uneventful low-risk patients (group B, $n = 30$). Patients with severe comorbidities or undergoing combined surgical procedures were excluded from the study. Institution’s Ethical Committee/Institutional Review Board approved the protocol, and informed consent was obtained from each patient.

2.2. Cardiac function and biochemical assay

Left ventricular ejection fraction (LVEF) and wall motion score index (WMSI) were recorded by echocardiography either at hospital admission, at ICU arrival and before discharge. Troponin I (TnI) and lactate release were recorded preoperatively, at ICU arrival, at 12 h, 24 h, 48 h and 72 h postoperatively.
2.3. Definition of perioperative data and events

Demographic data and intraoperative characteristics are reported in Tables 1 and 2, respectively. Criteria for perioperative AMI and myocardial damage has been previously described [8, 9]. Low output syndrome was diagnosed if the patient required IABP for hemodynamic compromise or if the patient required inotropes to maintain the systolic blood pressure > 90 mmHg and the cardiac index > 2.2 l/min·m⁻² after optimal medical therapy.

IABP-related complications were defined as any aortic dissection or perforation, limb or mesenteric ischemia, or infection or hemorrhage at the balloon entry point.

2.4. Surgery, cardiopulmonary bypass, and postoperative care

Cardiopulmonary bypass (CPB), surgical techniques and perioperative management were standardized and did not change during the study period [10]. Surgery was performed by the same senior surgeon in both groups through a median sternotomy.

Assessment of each graft function was performed with a transit-time flowmeter and the measurements were interpreted as previously reported [10].

2.5. IABP assistance

IABP was always inserted with the ‘sheatless’ technique via percutaneous femoral cannulation; 7.5 Fr 34 or 40 ml were connected to a Datascope pump (Datascope Corp, Fairfield, NJ). Assistance was maintained in 1:1 ratio. IABP was withdrawn when hemodynamic stability was restored.

2.6. Endpoints

The primary endpoints of the study were in-hospital and follow-up mortality. Secondary end-points were in-hospital morbidity, follow-up cardiac complications, ICU-stay and hospital-stay, changes in biochemical and echocardiographic findings.

2.7. Statistical analysis

Statistical analysis was performed using SPSS program for Windows, release 15.0.0 (SPSS Inc, Chicago, IL). Continuous variables are presented as mean ± S.D.; categorical variables are presented as absolute numbers and percentages. Comparison between and within groups was made using two-way analysis of variance for repeated measures to test the effect of group and time on the levels of Troponin I and Lactate. Unpaired t-test was used to compare other continuous variables. 95% confidence interval of mean were computed for the most significant differences. Categorical data were analyzed using the chi²-test or Fisher’s exact test when appropriate.

Estimates of survival, freedom from acute myocardial infarction and from cardiac-related complications during follow-up were determined with the method of Kaplan–Meier life-table analysis. The log-rank test was performed to ascertain differences between the two groups.

Statistical significance was assumed at a probability level of < 0.05.

3. Results

Fourteen patients in group A (57%) required intraoperative IABP insertion for: difficult weaning from CPB because of intraoperative LOS in 5 (36%), minor ECG changes (defined as right bundle branch block and/or new ST depression in at least two leads, inversion of polarity of T waves, depression of R wave in antero-lateral leads) together with poor TTF findings (systolic pattern of the waveform, pulsatility index > 4.0) – as expected by intraoperative finding of a diffuse and severely calcified coronary bed – in 4 (29%), ST elevation > 2 mm in at least two leads in 3 (21%), refractory ventricular arrhythmias in 2 (14%). Nine of the remainder 16 patients (56%) required IABP insertion postoperatively for minor changes at 12-lead ECG despite stable hemodynamic at ICU admission, whereas 6 (38%) needed IABP for LOS at ICU arrival and only one for unexpected electromechanical dissociation during the first postoperative day. Mean length of IABP support was 57.2 ± 11.8 h (95% confidence interval 36–73 h).

Mean intubation time (group A: 17.98 ± 4.84 h vs. group B: 18.53 ± 3.11 h; P = 0.48), mean ICU stay (18.53 ± 3.31 days vs. group B: 2.67 ± 2.54; P = 0.16) and mean in-hospital stay (group A: 10.13 ± 5.24 days vs. group B: 9.50 ± 4.35 days; P = 0.61) were similar between the two groups.

TnI leakage was similar in the two groups at hospital admission and differed from ICU admission, to 72 h. However, TnI never peaked > 3.1 µg/l at 12 h or 3.7 µg/l at any sampling time [8].

Blood lactate concentrations were similar preoperatively, differed significantly at ICU admission and were similar again from 12 h postoperatively.

Table 1
Patient demographics and preoperative functional characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
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<tbody>
<tr>
<td>Mean age (years)</td>
<td>62.83 ± 9.45</td>
<td>60.83 ± 7.32</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>21/9</td>
<td>21/9</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (23.3%)</td>
<td>7 (23.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>6 (20.0%)</td>
<td>6 (20.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (60.0%)</td>
<td>18 (60.0%)</td>
<td>NS</td>
</tr>
<tr>
<td>Left main stem disease</td>
<td>5 (16.6%)</td>
<td>5 (16.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>19 (63.3%)</td>
<td>19 (63.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>4.1 ± 0.76</td>
<td>4.03 ± 1.03</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2
Patient intraoperative and postoperative characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB time</td>
<td>89.73 ± 23.89</td>
<td>101.37 ± 30.81</td>
<td>0.108</td>
</tr>
<tr>
<td>Aortic cross-clamp time</td>
<td>54.57 ± 16.36</td>
<td>53.90 ± 16.72</td>
<td>0.895</td>
</tr>
<tr>
<td>n. of CABG</td>
<td>3.40 ± 1.10</td>
<td>3.67 ± 0.61</td>
<td>0.250</td>
</tr>
<tr>
<td>Ventilation time</td>
<td>17.98 ± 4.84</td>
<td>18.53 ± 1.31</td>
<td>0.482</td>
</tr>
<tr>
<td>ICU stay</td>
<td>3.97 ± 4.26</td>
<td>2.67 ± 2.54</td>
<td>0.157</td>
</tr>
<tr>
<td>In-hospital stay</td>
<td>10.13 ± 5.24</td>
<td>9.50 ± 4.35</td>
<td>0.612</td>
</tr>
</tbody>
</table>

CPB, cardiopulmonary bypass; CABG, coronary artery bypass graft; ICU, intensive care unit.
However, serum markers proved to be statistically different at unpaired t-test in terms of within- and between-groups comparison (Fig. 1). The same trends of biochemical markers were confirmed when 95% confidence intervals of means were computed (Table 3).

Table 3
95% confidence intervals for biochemical assays and echocardiographic findings

<table>
<thead>
<tr>
<th>Troponin I</th>
<th>Preop</th>
<th>ICU</th>
<th>12 h postop</th>
<th>24 h postop</th>
<th>48 h postop</th>
<th>72 h postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n = 30)</td>
<td>0.02 (0.0–0.04)</td>
<td>0.37 (0.34–0.40)</td>
<td>0.78 (0.73–0.83)</td>
<td>1.59 (1.53–1.64)</td>
<td>1.83 (1.78–1.88)</td>
<td>0.94 (0.82–1.07)</td>
</tr>
<tr>
<td>Group B (n = 30)</td>
<td>0.03 (0.02–0.04)</td>
<td>0.23 (0.20–0.26)</td>
<td>0.35 (0.30–0.40)</td>
<td>1.33 (1.25–1.42)</td>
<td>0.80 (0.74–0.85)</td>
<td>0.41 (0.37–0.46)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lactate</th>
<th>Preop</th>
<th>ICU</th>
<th>12 h postop</th>
<th>24 h postop</th>
<th>48 h postop</th>
<th>72 h postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n = 30)</td>
<td>0.97 (0.79–1.16)</td>
<td>4.73 (4.50–4.96)</td>
<td>2.37 (2.67–3.07)</td>
<td>2.35 (2.20–2.50)</td>
<td>1.64 (1.55–1.73)</td>
<td>1.17 (1.09–1.26)</td>
</tr>
<tr>
<td>Group B (n = 30)</td>
<td>0.83 (0.77–0.89)</td>
<td>4.22 (4.03–4.40)</td>
<td>2.74 (2.53–2.95)</td>
<td>2.31 (2.15–2.47)</td>
<td>1.51 (1.54–1.69)</td>
<td>1.06 (0.98–1.14)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Echocardiographic findings</th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative LVEF</td>
<td>56 (52–59)</td>
<td>59 (57–62)</td>
</tr>
<tr>
<td>ICU LVEF</td>
<td>42 (40–44)</td>
<td>54 (52–56)</td>
</tr>
<tr>
<td>Postoperative LVEF</td>
<td>58 (56–61)</td>
<td>60 (57–62)</td>
</tr>
<tr>
<td>Preoperative WMSI</td>
<td>1.63 (1.47–1.80)</td>
<td>1.60 (1.46–1.75)</td>
</tr>
<tr>
<td>ICU WMSI</td>
<td>2.03 (1.86–2.21)</td>
<td>1.73 (1.59–1.89)</td>
</tr>
<tr>
<td>Postoperative WMSI</td>
<td>1.55 (1.40–1.70)</td>
<td>1.61 (1.50–1.73)</td>
</tr>
</tbody>
</table>

LVEF, left ventricular ejection fraction; ICU, intensive care unit; WMSI, wall motion score index. Data are expressed as mean (95% confidence intervals).
between the two groups (Fig. 2). Such echocardiographic improvements were also recorded at 95% confidence intervals of means (Table 3).

Two in-hospital deaths occurred in group A: one for sepsis and another one for low cardiac output syndrome. Both patients received IABP at ICU admission (in-hospital mortality group A: 2 (7%) vs. group B: 0 (0%); P=0.49).

Two-year follow-up was completed for all the 58 survivors. Both groups were comparable in terms of actuarial survival rate (group A: 96% vs. group B: 93%; P=0.60), freedom from AMI (group A: 93% vs. group B: 97%; P=0.50) and freedom from cardiac complications (group A: 79% vs. group B: 87%; P=0.41) (Fig. 3).

When patients in group A receiving IABP in consequence of minor changes at 12-lead ECG (minor indication group, n=9) were compared to the rest of patients in group A (major indication group, n=21), in terms of serum markers, echocardiographic findings, in-hospital and follow-up outcomes, we found higher TnI leakage at 12 h and length of IABP support in the subgroup of patients who met criteria suggestive for major myocardial damage, whereas all the other variables were comparable (Table 5).

4. Discussion

Incorrect myocardial protection during CPB, incomplete revascularization, reperfusion damage all can contribute to temporary myocardial stunning after CABG [9], with consequent myocardial and peripheral hypoperfusion, that increase myocardial injury and hospital mortality [9].
In the past, IABP support became part of the armamentarium of surgeons, anesthesiologists and cardiologists to treat unexpected cardiac complications. However, the role of aggressive postoperative IABP is still debated, especially when off-label indications are considered [7, 11, 12].

Intraoperative need for aortic counterpulsation is predictor of poor outcome [7, 13] being the witness of intraoperative troubles that can result in temporary or long-lasting ischemia [9].

Furthermore, the correct timing for IABP insertion is a relevant issue [2, 7, 13], with better outcome reported after preoperative IABP insertion compared to intra- or postoperative support for high-risk patients [2, 11, 14]. Probably preoperative IABP results in better hemodynamic stability and myocardial perfusion [1], thus preventing progressive myocardial dysfunction [14]. Therefore, IABP should be inserted as soon as the minimum suspect of myocardial hypoperfusion occurs [5].

In the setting of an early diagnosis of myocardial injury, ECG or echocardiography can only suggest transmural infarction, whereas only troponins can detect minimal myocardial damage [8, 9]. In this study, TnI in group A never reached the peak of 3.7 μg/l or 3.1 μg/l at 12 h postoperatively [8, 9], even if TnI was higher than patients in group B, who experienced an uncomplicated course.

Furthermore, despite higher lactate concentrations in group A at ICU arrival (\(P=0.001\)), both groups showed comparable lactate leakage from 12 h postoperatively, as a result of a better organ perfusion. Furthermore, mean values of serum markers were homogeneous within groups at each sampling time at 95% confidence intervals (Table 3). We argued that the earlier IABP assistance whenever myocardial damage is suspected, the better the myocardial recovery and the peripheral perfusion.

Accordingly, LVEF and WMSI in group A significantly worsened at ICU admission, being witnesses of perioperative myocardial injury that recovered at hospital discharge. Again, 95% confidence intervals of mean showed that mean LVEF and WMSI within each group were homogeneous at each evaluation time (Table 3).

Probably IABP assistance results in a better perfusion of ischemic areas of viable myocardium before frank necrosis established [1, 2, 15].

The comparable ICU stay, need for mechanical ventilation and inotropic support between the two groups support the efficacy of early IABP in restoring hemodynamic stability when complications develop. It could be possible that immediate ‘early’ IABP could lower the risk of complications by diminishing the need for high doses of vasoactive (vasoconstricting) medications.

The low incidence of IABP-related complications reported in this study are likely explained by the effects of newer technologies (such as small 7.5- or even 7-Fr catheters), increased experience of the surgical teams, better education and surveillance of patients supported with IABP, and more focused attention to IABP-related complications.

Despite general agreement existing on the beneficial effects of IABP on cardiac performance after complication.
occurred, which complications really need IABP support are still a debated issue [6].

As a matter of fact, it can be questioned that the Group A cannot be considered uniform. Indeed, when patients in group A were further subdivided into two subgroups according to the indications for IABP support, troponin I leakage and length of IABP support proved to be higher in patients with major indications to IABP (Table 5). Probably a longer IABP support was needed to heal a more injured myocardium. However, such policy proved to be effective for myocardial recovery, as was shown by echocardiographic and follow-up results, either at subgroup analysis.

Authors agree that survival at follow-up is better for patients who received preoperative IABP compared to intra- or postoperative emergent support [1, 5, 11, 13]. Therefore, an earlier IABP assistance should be a routine surgical strategy to improve the outcome of high-risk or complicated CABG [5].

Our data suggest an early IABP insertion whenever unexpected cardiac complications develop intraoperatively or during ICU stay, also in stable hemodynamic conditions. These results are further confirmed by the comparable follow-up survival trends between the two groups (Fig. 3). Again, it can be speculated that an early IABP insertion could be effective in salvaging viable myocardium before irreversible damage developed [5, 13].

Our study suggests a novel role to early IABP support for complicated low-risk CABG. Whenever cardiac complications are even suspected (e.g. expected poor TTF findings together with even minor ECG changes, unexpected major ECG changes, difficulties in wean-off bypass, etc), early IABP should be established even if stable hemodynamic is achieved, because of the beneficial impact on enzymatic leakage, echocardiographic myocardial recovery, hospital outcome, short-term follow-up survival and freedom from cardiovascular events. In these patients, early IABP reverses myocardial ischemia and allows similar hospital and follow-up outcome of uncomplicated low-risk CABG.

5. Limitation of the study

General agreement exists in the literature about the positive effects of IABP in case of cardiac complications [1–5]. Therefore, it was not ethical to exclude complicated patients from IABP assistance. Even if larger studies are needed to definitely prove this topic, we reported here our institutional experience during the last three years showing us that an early and more aggressive IABP support saves viable myocardium whenever ischemic complications are suspected, also in patients with stable hemodynamics.

Although the single-center design of the study limits the conclusions, on the other hand, it guarantees uniformity of the perioperative management of the patient population throughout the experimentation. Moreover, on an intention-to-treat basis, we enrolled patients with the most similar risk profile to avoid misleading results.

References