Current use of preoperative intra-aortic balloon counterpulsation in high-risk cardiac surgery: a cohort study

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ABSTRACT

Objective: To determine whether preoperative introduction of intra-aortic balloon counterpulsation (IABC) reduced mortality in high-risk patients undergoing coronary artery bypass graft (CABG) surgery.

Methods: This was a retrospective cohort study of prospectively collected data on all patients who underwent cardiac surgery at a university hospital in Sydney, New South Wales, between 1 January 2002 and 20 August 2007. High risk was defined as the presence of two or more recognised risk factors. We compared the observed mortality to the mortality predicted by the EuroSCORE, and conducted a logistic regression analysis to determine the effect of preoperative IABC on mortality.

Results: Among 358 patients deemed high risk, 36 underwent preoperative IABC. This group had higher EuroSCORE-predicted mortality than the group that did not undergo IABC (38% v 18%, $P = 0.008$). Despite this, observed mortality was similar for those with and without preoperative IABC (both 2.8%) and was significantly lower than predicted in both groups. This equates to a risk-adjusted reduction in mortality associated with the use of preoperative IABC (hazard ratio, 0.47; 95% CI, 0.26–0.84; $P = 0.005$). This result was not confirmed in the logistic regression analysis, with an adjusted odds ratio for mortality of 0.85 (95% CI, 0.09–7.6; $P = 0.88$). Rates of postoperative complications, including limb ischaemia, were low and similar in both groups.

Conclusions: In this study of high-risk CABG patients, the use of preoperative IABC in the group with higher predicted mortality was associated with a relative reduction in observed mortality. These data provide cautious support for the use of preoperative IABC in selected high-risk patients.

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Intra-aortic balloon counterpulsation (IABC) has an established role in the short-term support of the failing heart, effecting both an increase in myocardial oxygen supply and a reduction in oxygen demand.[1,2] The most common indications for the use of IABC include weaning from cardiopulmonary bypass, management of cardiogenic shock, and support and stabilisation for angiography and angioplasty.[3] More controversial is the use of IABC preoperatively in patients undergoing high-risk coronary artery bypass graft (CABG) surgery. While the utility of prophylactic IABC in high-risk cases was suggested as long ago as 1977,[4] this indication has never been fully defined.

A recent meta-analysis concluded that preoperative use of IABC might be useful in selected high-risk cases.[5] High risk was defined as presence of at least two of the following: left ventricular ejection fraction (LVEF) < 30%, significant left main coronary artery stenosis, re-do surgery and unstable angina.[5,6] Concerns were raised that the studies included in the meta-analysis were conducted in a single centre, so the evidence may not be generalisable to other populations. Other studies have also raised doubts about the use of preoperative IABC,[7] and few have examined the potential for adverse effects related to its use.

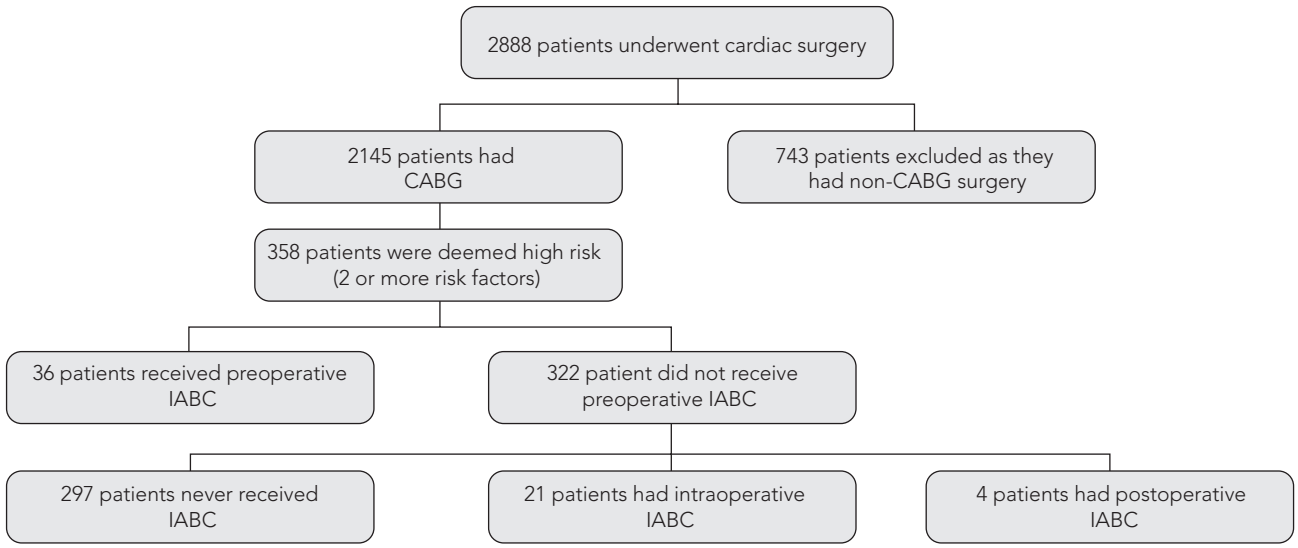
Accordingly, we conducted a retrospective, cohort study to investigate these issues. In particular, we sought to determine whether, in patients undergoing CABG and deemed at high risk of adverse outcomes based on the presence of two or more known risk factors, the preoperative introduction of IABC was associated with differences in mortality and morbidity.

Methods

The study was conducted at the Royal North Shore Hospital, a university-affiliated referral hospital in Sydney, New South Wales. It serves a local population of about 300 000 and provides specialist referral services to a population of 1.3 million. The study was approved by the Northern Sydney and Central Coast Area Health Service Human Research Ethics Committee.

It is hospital practice to collect data prospectively for all patients undergoing cardiac surgical procedures, using standardised forms. Data were extracted from this database for all patients who underwent a cardiac surgical procedure between 1 January 2002 and 20 August 2007. We identified from the database all patients who underwent CABG and had at least one risk factor for preoperative IABC (LVEF < 30%, unstable angina at time of surgery, re-do operation, or left main coronary artery stenosis > 50%), and all patients who underwent IABC at any time. High-risk

Figure 1. Derivation of the patient groups



CABG = coronary artery bypass graft. IABC = intra-aortic balloon counterpulsation.

patients were defined as those with two or more risk factors.[5,8] Preoperative IABC was defined as the introduction of an IABC catheter before the induction of anaesthesia. Patients who had an IABC catheter inserted during the surgical procedure when weaning from cardiopulmonary bypass, or postoperatively were not included in the preoperative IABC group.

We used standard definitions for patient clinical characteristics. Renal impairment was defined as a documented history of renal failure or a fasting serum creatinine level > 0.2 mmol/L. Peripheral vascular disease was defined as a history of claudication, amputation for arterial insufficiency, peripheral vascular surgery, angioplasty or stent, or a documented abdominal aortic aneurysm. Pulmonary disease was defined by the long-term use of bronchodilators or corticosteroids with a forced expiratory volume (FEV_1) ⩽ 75% predicted. Neurological dysfunction was defined as unresponsive coma for > 24 hours, or a history of a recent stroke or transient ischaemic attack. Previous cardiac surgery was defined as any previous CABG or valve surgery. We used the EuroSCORE definition of a critical preoperative state: a requirement for preoperative cardiac massage, mechanical ventilation, inotropic support or IABC, or presence before surgery of malignant ventricular arrhythmias or acute renal failure.

Baseline factors likely to affect prognosis, including those in EuroSCORE, were extracted from the database. Missing variables were assumed to be absent. Outcomes measured included 30-day all-cause mortality, intensive care unit and hospital length of stay (LOS), and IABC-related complications.

Baseline variables and postoperative complications were compared using Student's *t* test, the Mann–Whitney test, or Fisher's exact test, as appropriate. Predicted mortality was calculated from the logistic EuroSCORE[9] and compared with observed mortality using Fisher's exact test. The ratio of observed to predicted mortality for high-risk patients undergoing IABC compared with those who did not undergo IABC was used to estimate the hazard ratio.[10]

The other method used to allow for differences in baseline risk of mortality was backwards, stepwise logistic regression. ICU and hospital LOS were log (ln) transformed, as these variables were not normally distributed. Backwards stepwise linear regression was used to examine the effect of use of preoperative IABC on ln(LOS), while allowing for differences in baseline characteristics between the two groups of high-risk patients. Coefficients of ln(LOS) were exponentiated to give estimates of the factor by which LOS was increased in those undergoing preoperative IABC. All analyses were conducted using Stata 10.0 (Stata Corp, College Station, Tex, USA).

Results

A total of 2698 patient records were available in the cardiothoracic database for patients who underwent cardiac surgery between 1 January 2002 and 20 August 2007. We identified 2145 records of patients who underwent CABG, with 358 of these patients deemed high-risk. Of these, 36 underwent preoperative IABC. Of the high-risk patients who did not undergo preoperative IABC, 297 did

Table 1. Characteristics of high-risk cardiac surgery patients, by treatment group*

	IABC ($n = 36$)	No IABC ($n = 322$)	*P*
Age: mean (SD)	67.1 (12)	67.7 (10)	0.75
Women	5 (14%)	85 (26%)	0.11
Renal impairment	1 (3%)	15 (5%)	0.99
Peripheral vascular disease	4 (13%)	36 (13%)	0.99
Pulmonary disease	4 (15%)	33 (12%)	0.76
Neurological dysfunction	0	8 (3%)	0.99
Previous cardiac surgery	2 (6%)	69 (21%)	0.03
Recent AMI	22 (61%)	149 (46%)	0.11
LVEF 30%–50%	11 (31%)	94 (29%)	0.85
LVEF < 30%	21 (58%)	94 (29%)	0.001
LVEF score: median (IQR)†	4 (3–4)	3 (1–3)	< 0.001
Systolic pulmonary pressure > 60 mmHg	5 (14%)	11 (3%)	0.02
Active endocarditis	0	2 (0.6%)	0.99
Unstable angina	36 (100%)	301 (94%)	0.25
Emergency operation	36 (100%)	267 (83%)	0.003
Critical preoperative state	36 (100%)	15 (5%)	< 0.001
Ventricular septal rupture	0	0	0.99
Surgery other than isolated CABG	7 (19%)	26 (8%)	0.04
Thoracic aortic surgery	0	0	0.99
LMCA stenosis > 50%	24 (67%)	219 (68%)	0.85
Diabetes	7 (19%)	89 (28%)	0.33
Hypertension	21 (58%)	210 (65%)	0.46
Smoking	20 (56%)	192 (60%)	0.72
Additive EuroSCORE: mean (SD)	14.8 (3.2)	10.5 (2.2)	< 0.001

AMI = acute myocardial infarction. CABG = coronary artery bypass graft. IABC = intra-aortic balloon counterpulsation. IQR = interquartile range. LMCA = left main coronary artery. LVEF = left ventricular ejection fraction.
* Values are frequencies (percentage) unless otherwise stated.
† LVEF score: 1 = > 60%, 2 = 51%–60%, 3 = 30%–50%, 4 = < 30%.

not receive IABC at any time, 21 had an IABC catheter inserted intraoperatively, and four had IABC begun postoperatively (Figure 1).

Baseline characteristics

Patient baseline characteristics are compared between high-risk patients who underwent preoperative IABC and those who did not in Table 1. The groups showed clinically important differences in sex distribution, LVEF, and rates of emergency surgery, pulmonary hypertension, previous cardiac surgery, surgery other than CABG, critical preoperative state, and recent acute myocardial infarction.

Table 2. Observed versus predicted mortality of high-risk patients

	Mortality		
	Observed	Predicted	*P*
All patients ($n = 358$)	10 (2.8%)	73 (20.4%)	< 0.001
No preop IABC ($n = 322$)	9 (2.8%)	59 (18.3%)	< 0.001
Preop IABC ($n = 36$)	1 (2.8%)	14 (38.3%)	< 0.001

Preop IABC = preoperative intra-aortic balloon counterpulsation.

Table 3. Postoperative complications and length of stay*

Complications	IABC ($n = 36$)	No IABC ($n = 322$)	*P*
Postoperative AMI	0	0	0.99
Limb ischaemia	0	1 (0.3%)	0.99
Stroke	0	5 (2%)	0.99
Acute renal failure	1 (3%)	2 (0.6%)	0.27
Pneumonia	3 (8%)	8 (2%)	0.09
Deep sternal infection	0	3 (0.9%)	0.99
Hospital LOS (days): median (IQR)	13 (10–16)	7 (6–9)	< 0.001
Intensive care LOS (h): median (IQR)	120 (72–219)	48 (46–72)	< 0.001

AMI = acute myocardial infarction. IABC = intra-aortic balloon counterpulsation. IQR = interquartile range. LOS=length of stay.
* Values are frequencies (percentage) unless otherwise stated.

Mortality

Observed and predicted mortality are shown in Table 2. Observed mortality was significantly lower than predicted in all high-risk patients, both those who underwent preoperative IABC and those who did not. The unadjusted odds ratio for mortality associated with use of preoperative IABC was 0.99 (95% CI, 0.12–8.08; $P = 0.99$). However, patients who underwent preoperative IABC were at higher risk of mortality than those who did not undergo IABC (EuroSCORE-predicted mortality, 38% v 18%; $P = 0.008$). The increase in baseline risk was accounted for by two methods. Using logistic regression to adjust for differences in baseline characteristics, we obtained an odds ratio for mortality with the use of preoperative IABC of 0.85 (95% CI, 0.09–7.6; $P = 0.88$; pseudo $R^2 = 0.06$). Using comparison of the ratio of observed to expected mortality based on EuroSCORE results in the two groups, we obtained an estimated hazard ratio associated with preoperative use of IABC of 0.47 (95% CI, 0.26–0.84; $P = 0.005$), indicating that the use of preopera-

tive IABC in high-risk patients is associated with a significant reduction in mortality.

Complications and length of stay

Complications and length of stay are shown in Table 3. Multiple linear regression indicated that the use of preoperative IABC was associated with a significant 1.46 times increase in average hospital LOS (95% CI, 1.26–1.70; $P < 0.001$; $R^2 = 0.20$). ICU length of stay was also significantly increased, by 1.80 times, with the use of preoperative IABC (95% CI, 1.43–2.27; $P < 0.001$; $R^2 = 0.20$).

Discussion

This retrospective cohort study of 358 high-risk cardiac surgical patients compared outcomes between those who had preoperative initiation of IABC and those who did not. We found that overall mortality was similar whether or not preoperative IABC was used, even though patients who underwent preoperative IABC were at higher risk of mortality. The hazard ratio for mortality was less than half for the latter group, suggesting a protective effect of preoperative IABC, although this result was not confirmed with logistic regression analysis. Importantly, we also found a significantly lower observed mortality than predicted by the EuroSCORE in all patients. Despite a low rate of complications in those who received preoperative IABC, they had a significant increase in both ICU and hospital LOS.

The study had several strengths. The data were collected prospectively by trained data collection personnel using standardised forms. The focus on clear, well-defined endpoints, such as 30-day all-cause mortality, minimised ascertainment bias. However, the study also had limitations. First, it was an observational study, and not a randomised comparison. It is highly likely that unmeasured confounding variables could account for some of the differences found. Second, it is possible that missing data could have resulted in some patients being falsely classified as not at high risk, influencing the estimate of treatment effect. Third, it is difficult to control for confounding in a study such as this. Logistic regression is the most common method used to control for confounding, but can be unreliable when there are fewer than 10 events per predictor variable.[11] As there were few events in this study, we attempted to control for confounding by comparing the observed mortality with that expected from the EuroSCORE, in keeping with previous research in this area.[8]

Some have questioned the use of preoperative IABC for high-risk patients on the grounds that IABC is an established therapy for patients with acute myocardial infarction and cardiogenic shock, and thus its use in these patients represents therapy rather than prophylaxis.[12] As most of the patients in this group underwent urgent CABG for unstable angina, our study cannot address this question. However, it does not seem important whether the benefit derives from therapy or prophylaxis under these circumstances. This study is of particular interest to intensive care clinicians as these critically ill patients are those most likely to be referred to an intensive care physician for preoperative resuscitation and stabilisation.

Previous studies have suggested a reduction in mortality with the use of preoperative IABC in selected, high-risk patients. A meta-analysis of five randomised controlled trials found a significant reduction in mortality associated with the use of preoperative IABC in patients at high risk.[5] However, these trials were all performed in the same institution, with a total of 193 participants, and some have questioned the external validity of their results.[7] The results of our cohort study add cautious support for the apparent mortality benefit of preoperative IABC in high-risk patients.

It is of interest that preoperative IABC was associated with significantly longer ICU and hospital LOS. The increased LOS is likely related to the more severe illness of this group, but might also have resulted from the use of IABC itself. There are plausible reasons: the requirement for patients to remain largely recumbent during IABC could predispose to pneumonia, a possibility supported by the higher (albeit not statistically significant) rate of pneumonia in the preoperative IABC group. The increase in ICU and hospital LOS has potential economic implications. Of note, this finding is at odds with previous reports, which have suggested that use of preoperative IABC in high-risk cases is associated with reduced LOS and reduced costs.[13] Different patient selection criteria in the two studies may well account for these differences.

Patient selection is obviously of paramount importance when clinicians are faced preoperatively with high-risk cardiac surgical candidates. Intensive care clinicians are often called to review these critically ill patients, and the decision to initiate preoperative IABC is not taken lightly, given the associated risks.[14,15] It is clear from this study that factors in addition to the established risk factors were being used to guide the use of IABC in this group of patients: only about 10% of the patients who met "standard" criteria for preoperative IABC actually received the therapy. The experience of the clinician at the bedside is likely, at least in part, to account for the unmeasured confounding seen in this group. Previous studies have attempted to account for this type of confounding by use of propensity scores.[7,12] However, it is likely that the clinical judgement of experienced clinicians, while not measurable, is critical to the selection process. The importance of this judgement can be seen in the results of our study, with an additional reduction in mortality in the group who were judged to require preoperative IABC.

The question of how to select patients remains a problem. Some authors have suggested using the EuroSCORE to guide preoperative use of IABC,[16] but IABC use contributes to, and thus invalidates, the score. Another problem is the poor calibration of the EuroSCORE in this particular population. While the EuroSCORE has been validated in a number of populations,[17,18] its calibration is not consistent across populations, and it has been shown to consistently overestimate mortality in Australian cardiac surgical populations.[19,20] This may in part be due to the fact that the EuroSCORE[18] was derived from data collected more than 10 years ago.[21] Efforts are currently underway to refine the scoring system;[22] a refined system might provide a better means of determining which patients are truly likely to benefit from preoperative IABC.

Further studies to delineate groups of patients most likely to benefit from the use of preoperative IABC may assist clinicians in decision-making. Given that all the high-level evidence reporting benefit from this therapy comes from a single centre, and given the conflicting evidence from observational studies from other centres, an adequately powered, methodologically rigorous, randomised trial appears warranted. Our data clearly support the further evaluation of this highly invasive but potentially beneficial treatment.

Conclusions

The use of IABC preoperatively in this group of high-risk patients was associated with a relative reduction in the observed mortality compared with the predicted mortality. This reduction in observed mortality was associated with increased resource utilisation, as measured by increased ICU and hospital LOS. These data provide cautious support for the use of preoperative IABC in selected high-risk patients.

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