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Risk factors for prolonged ICU stay in patients following coronary artery bypass grafting with a long duration of cardiopulmonary bypass

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Abstract
Purpose. Risk factors for prolonged stay in the intensive care unit (ICU) in patients following coronary artery bypass grafting (CABG) have been reported in many previous studies. However few have focused on circulatory and respiratory status as immediate postoperative risk factors. Therefore we examined immediate postoperative risk factors for prolonged ICU stay after CABG with a long duration of cardiopulmonary bypass (CPB).
Methods. We studied retrospectively 100 consecutive patients undergoing elective CABG with CPB. Patients were excluded from this study if the duration of aortic cross-clamping was less than 60 min. Patients were divided into three groups according to the duration of the ICU stay. Patients in group A ($n = 68$) were discharged from the ICU on the next morning after surgery, those in group B ($n = 19$) stayed for 3 days, and group C ($n = 13$) stayed for more than 3 days. Perioperative variables were compared among the three groups and we demonstrated risk factors for prolonged (more than 3 days) ICU stay.
Results. There were significant differences in duration of CPB (157 ± 34 versus 184 ± 48 minutes, $P < 0.05$) and aortic cross-clamping (119 ± 32 versus 141 ± 40 min) between groups A and B. On the other hand, there were significant differences in age (62.8 ± 7.8 versus 67.4 ± 6.2 years), mean pulmonary artery pressure (MPAP) (17 ± 2 versus 22 ± 3 mmHg), and Pa_{O_2}/FI_{O_2} (PF ratio) (409 ± 94 versus 303 ± 108 mmHg) on admission to the ICU between groups A and C. There were no significant differences in intraoperative fluid balance and duration of CPB. Multiple logistic regression analysis identified age (>65 years), MPAP (>21 mmHg), and PF ratio (<300 mmHg) as independent risk factors for more than a 3-day ICU stay.
Conclusion. Advanced age, increased MPAP, and decreased PF ratio on admission to the ICU were significant risk factors for a prolonged ICU stay of more than 3 days.

Key words CABG · Prolonged ICU stay · Mean pulmonary artery pressure · Pa_{O_2}/FI_{O_2}

Introduction

Perioperative management of patients undergoing coronary artery bypass grafting (CABG) has been improving recently, but the duration of stay in the intensive care unit (ICU) varies from one to several days for a variety of reasons. Prolonged ICU stay in such patients increases overall hospital costs as well as ICU costs [1] and reduces the availability of ICU beds for other critically unwell patients. Therefore, the ability to predict whether patients undergoing CABG will stay just one night or longer in the ICU would be useful.

Many studies [2–6] have reported perioperative risk factors for prolonged ICU stay, including prolonged mechanical ventilation, which is considered as one of the most important factors. The pre- and intraoperative risk factors described in these studies may be useful for short-duration cardiopulmonary bypass (CPB) because cardiac function is improved compared with that before surgery or does not change at least on admission to the ICU. In other words, CPB does not influence circulatory and respiratory status on admission to the ICU when its duration is short. However, cardiac function often deteriorates just after CPB for various reasons [7–11], especially in patients who have undergone long-duration aortic cross-clamping [12–13]. Therefore, circulatory and respiratory status on admission to the ICU may be useful for careful postoperative management and to predict the ICU stay when the duration of CPB is long. The aim of the present study was to identify risk factors, particularly on admission to the ICU, for prolonged ICU stay in patients after CABG with a long duration of CPB.

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Methods

Patients

After receiving approval from the Ethics Review Committee of Osaka City University and informed consent from the patients, we retrospectively investigated 100 consecutive patients who were scheduled to undergo elective CABG with CPB from January 1999 to June 2002 at the Osaka City University Hospital. Patients were excluded from this study if they required an intraaortic balloon pump (IABP) before surgery, if they had chronic renal failure, or if the duration of aortic cross-clamping was less than 60 min.

Protocol

All patients were premedicated with 5–10 mg of morphine and 20 mg of famotidine intramuscularly. Monitoring consisted of electrocardiography, pulse oximetry, capnography, peripheral artery and pulmonary artery catheters, and bladder and peripheral temperatures. Anesthesia was induced with 5–10 $\mu g \cdot kg^{-1}$ of fentanyl, 0.1 $mg \cdot kg^{-1}$ of midazolam, and 0.1 $mg \cdot kg^{-1}$ of vecuronium and was maintained with 20–30 $\mu g \cdot kg^{-1}$ of fentanyl and 2–5 $mg \cdot kg^{-1} \cdot h^{-1}$ of propofol. Intravenous vecuronium was administered intermittently for muscle relaxation. Nitrous oxide was not used throughout the surgery. Acetate Ringer's solution was used as a crystalloid infusion. Intravenous nitroglycerine (0.3–1 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was infused continuously throughout the surgery and 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of diltiazem was infused after CPB in patients requiring the radial artery to be harvested as a conduit. Myocardial protection was achieved with both antegrade and retrograde intermittent cold blood cardioplegia infusion through the aortic and coronary sinus routes. CPB was performed at moderate systemic hypothermia (30°–32°C).

Continuous intravenous dopamine (3–5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was administered to all patients just after CPB. Continuous intravenous dobutamine was added when the cardiac index was less than 2.5 $l \cdot min^{-1} \cdot m^{-2}$ despite optimal filling pressures, and continuous intravenous noradrenaline was added when the systemic arterial blood pressure could not be maintained above 80 mmHg. All patients were transferred to the ICU before recovery from anesthesia and received mechanical ventilation under continuous intravenous infusion of propofol (1–3 $mg \cdot kg^{-1} \cdot h^{-1}$). Propofol infusion was discontinued and patients were weaned from the ventilator after confirming that, (1) postoperative bleeding from the drainage tube was less than 50 $ml \cdot h^{-1}$, (2) core (blood) temperature was higher than 36°C and patients were not suffering from shivering, and (3) the circulatory status was stable and arterial blood gas data matched our criteria ($Pa_{O_2}/FI_{O_2} > 350$ mmHg). Patients were discharged from the ICU the next morning if they matched our discharge criteria (alert and cooperative, already extubated, and stable hemodyamics with less than 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine or dubutamine without significant arrhythmia).

One hundred patients were divided into three groups according to the duration of the ICU stay. Group A consisted of patients who were discharged from the ICU on the next morning after surgery (duration of ICU stay, 2 days), group B consisted of patients who stayed in the ICU for 3 days, and group C consisted of patients who stayed for more than 3 days. We compared the following variables among the three groups: preoperative clinical characteristics, intraoperative surgical factors, intraoperative fluid balance, postoperative circulatory and respiratory status, and postoperative serum troponin T level. Intraoperative total fluid balance was defined as follows: urine output and blood loss were subtracted from infused crystalloid (except for the priming volume for CPB), blood products, and cardioplegia solution. We also evaluated perioperative independent risk factors for prolonged ICU stay.

Data processing and statistical analysis

All data were expressed as mean ± SD. As univariate analysis, the Dunnett method (group A defined as control group), chi-squared, and the Fisher exact tests were initially performed to identify perioperative risk factors associated with prolonged ICU stay in the three groups. Variables associated with prolonged ICU stay in these analyses and variables considered clinically significant between groups A and C, age, and circulatory and respiratory status on admission to the ICU [mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP), number of patients requiring continuous intravenous noradrenaline, and PF ratio (Pa_{O_2}/FI_{O_2})] were entered into multiple logistic regression models as multivariate analysis to identify independent risk factors for prolonged ICU stay (more than 3 days). The odds ratio, 95% confidence intervals, and *P* values were calculated for each risk factor in the final model. Repeated measures analysis of variance (ANOVA) was used for comparison of serum troponin T among the three groups. Differences were considered statistically significant if the *P* value was less than 0.05.

Results

There were 68 patients in group A, 19 patients in group B, and 13 patients in group C. There were significant differences in age between groups A and C and in the duration of CPB and aortic cross-clamping between

Table 1. Clinical characteristics and intraoperative parameters of groups A, B, and C

	Group A (n = 68)	Group B (n = 19)	Group C (n = 13)
Preoperative patient characteristics			
Age (years)	62.8 ± 7.8	62.7 ± 9.8	67.4 ± 6.2*
Men/women	56/12	16/3	8/5
Weight (kg)	59.8 ± 7.7	62.0 ± 10.8	61.4 ± 9.4
LVEF (%)	56 ± 11	54 ± 13	63 ± 10
CTR (%)	49 ± 5	51 ± 5	50 ± 3
Pa_{O_2} (mmHg)	87 ± 10	87 ± 11	86 ± 6
Hb ($g \cdot dl^{-1}$)	13.1 ± 1.6	13.6 ± 1.3	13.5 ± 2.2
Serum creatinine ($mg \cdot dl^{-1}$)	0.8 ± 0.2	0.9 ± 0.2	0.8 ± 0.2
Hypertension (%)	42	47	61
Diabetes mellitus (%)	52	42	69
Chronic lung disease (%)	7	5	0
Smoking (%)	52	78	61
Beta-blocker (%)	66	57	76
ACE inhibitor (%)	26	26	46
Intraoperative factors			
Number of grafts	3.5 ± 1.1	3.7 ± 0.9	4.0 ± 0.8
CPB (min)	157 ± 34	184 ± 48*	165 ± 24
Aortic cross-clamping (min)	119 ± 32	141 ± 40*	129 ± 19
Use of radial artery (%)	77	89	92
Fentanyl ($\mu g \cdot kg^{-1}$)	26 ± 5	28 ± 7	29 ± 7
Fluid balance (l)	2.8 ± 1.5	3.4 ± 1.8	3.4 ± 1.2

All values are expressed as mean ± SD
Group A, 2-day stay in the ICU; group B, 3-day stay in the ICU; group C, more than 3-day stay in the ICU
LVEF, left ventricular ejection fraction; CTR, cardiothoracic ratio; Hb, hemoglobin; ACE, angiotensin converting enzyme; CPB, cardiopulmonary bypass
* $P < 0.05$ compared with group A

groups A and B. There were no significant differences in intraoperative fluid balance among the three groups (Table 1). There were significant differences in MPAP, PCWP, number of patients requiring continuous intravenous noradrenaline, and PF ratio on admission to the ICU between groups A and C (Table 2). We considered age (>65 year) as a preoperative risk factor and MPAP (>21 mmHg), PCWP (>12 mmHg), patients with or without continuous intravenous noradrenaline, and PF ratio (<300 mmHg) as immediate postoperative risk factors. Accordingly, these five risk factors were entered into multiple logistic regression models to identify independent risk factors for ICU stay of more than 3 days in the 81 patients of groups A and C. This analysis showed that age, MPAP, and PF ratio were independent risk factors. The odds ratio, 95% confidence intervals, and P values are shown in Table 3.

There were no significant differences among the three groups except for the proportion of patients extubated at 12 h after ICU admission. Extubation time after ICU admission was 7 ± 2 h in group A, 14 ± 6 h in group B, and 63 ± 47 h in group C. The duration of ICU stay in group C was 6 ± 2 days. There was a significant difference in the change of serum troponin T between groups A and B, but that in group C was quite similar to that in Group A (Fig. 1).

Discussion

Many studies have suggested perioperative risk factors for prolonged ICU stay in patients undergoing CABG [2–6]. The duration of aortic cross-clamping was generally short, less than 60 min on average, in these studies, and the duration of CPB was also short, less than 120 min. Pre- and intraoperative risk factors described in these studies may be useful for short-duration CPB because cardiac function is restored on admission to the ICU. Consequently, circulatory and respiratory status on admission to ICU was not considered as essential in these earlier studies. The longer the duration of aortic cross-clamping, the more cardiac function is depressed, even if the bypass graft is reconstructed completely [12]. Postoperative management should be arranged according to circulatory and respiratory status on admission to ICU in such patients to shorten the ICU stay. Therefore, we focused on circulatory and respiratory status on admission to ICU for patients with prolonged aortic cross-clamping.

Several studies have suggested that a longer duration of CPB is associated with prolonged postoperative mechanical ventilation [4,14–15]. Therefore, the duration of CPB was considered to be one of the risk factors for prolonged ICU stay [3–5]. Our findings were

Table 2. Differences in cardiopulmonary parameters and drugs used postoperatively among the three groups

	On admission	6 h	12 h
MAP (mmHg)			
Group A	95 ± 12	86 ± 11	84 ± 9
Group B	94 ± 15	81 ± 9	80 ± 8
Group C	90 ± 10	84 ± 8	81 ± 7
HR (bpm)			
Group A	94 ± 12	92 ± 10	86 ± 9
Group B	96 ± 12	94 ± 12	90 ± 9
Group C	93 ± 15	94 ± 11	81 ± 7
MPAP (mmHg)			
Group A	17 ± 2	18 ± 3	17 ± 2
Group B	19 ± 4	19 ± 2	18 ± 3
Group C	22 ± 3*	20 ± 3	18 ± 2
PCWP (mmHg)			
Group A	9 ± 2	10 ± 2	9 ± 2
Group B	9 ± 2	1 ± 3	10 ± 2
Group C	13 ± 3*	10 ± 7	10 ± 2
CVP (mmHg)			
Group A	8 ± 2	8 ± 2	8 ± 2
Group B	8 ± 2	9 ± 1	9 ± 2
Group C	10 ± 2	9 ± 2	9 ± 2
CI ($l \cdot min^{-1} \cdot m^{-2}$)			
Group A	3.3 ± 0.7	3.4 ± 0.6	3.1 ± 0.6
Group B	3.2 ± 0.5	3.3 ± 0.4	2.9 ± 0.4
Group C	2.9 ± 0.4	3.2 ± 0.4	3.1 ± 0.5
Noradrenaline (%)			
Group A	3	7	4
Group B	5	5	10
Group C	31*	23	23
Pa_{O_2}/F_{IO_2} (mmHg)			
Group A	409 ± 94		
Group B	377 ± 109		
Group C	303 ± 108*		
Patients extubated (%)			
Group A	0	38	97
Group B	0	15	36*
Group C	0	0	30*

All values are expressed as mean ± SD
Group A, 2-day stay in the ICU; group B, 3-day stay in the ICU; group C, more than 3-day stay in the ICU
MAP, mean arterial blood pressure; HR, heart rate; MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CVP, central venous pressure; CI, cardiac index
* $P < 0.05$ compared with group A

Table 3. Risk factors for prolonged ICU stay (more than 3 days)

	Univariate analysis			Multivariate analysis		
Factor	Group A (%)	Group C (%)	*P* value	Odds ratio	95% CI	*P* value
Preoperative						
Age > 65 years	31	69	0.0207	9.6	1.02–89.89	0.0471
On admission to the ICU						
MPAP > 21 mmHg	10	54	0.0007	19.7	1.80–214.89	0.0145
PCWP > 12 mmHg	15	46	0.0255	3.8	0.59–25.02	0.1576
Continuous noradrenaline	3	31	0.0033	11.2	0.72–176.00	0.0842
Pa_{O_2}/F_{IO_2} < 300 mmHg	12	62	0.0002	9.1	1.29–64.32	0.0267

Group A, 2-day stay in the ICU; group C, more than 3-day stay in the ICU
MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CI, confidence interval

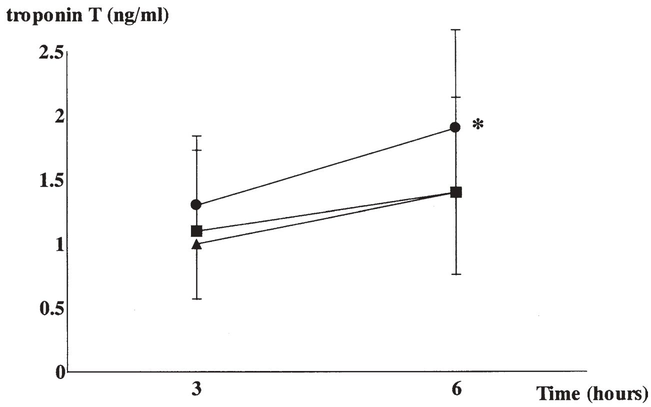

Fig. 1. Time course of serum troponin T after release of the aortic clamp. *Squares*, group A; *circles*, group B; *triangles*, group C. All values represent mean ± SD. Differences were considered statistically significant when the *P* value was less than 0.05 by repeated measures analysis of variance (ANOVA). *The serum troponin T level in group B was significantly higher than that in group A. There was no significant difference between groups A and C

consistent with these studies. In our study, an ICU stay of 2 or 3 days depended on the duration of aortic cross-clamping and CPB times, as reflected by the significant differences between groups A and B.

There were no significant differences in duration of CPB or aortic cross-clamping between groups A and C. This demonstrated that a longer stay in ICU depended on factors other than CPB. Circulatory status in group C was not stable on admission to the ICU, as reflected by the significantly higher values of PCWP and MPAP. The MAP in group C was lower (not significant) than that in group A and this was the reason why more patients required intravenous noradrenaline despite optimal filling pressures. Slight congestion of the lung as a result of high values of MPAP and PCWP probably reduced gas exchange. Therefore, the PF ratio in group C was significantly lower than that in group A on admission to the ICU, despite the absence of significant differences in preoperative Pa_{O_2}, history of chronic lung disease, smoking, and intraoperative fluid balance. The high values of MPAP and PCWP on admission to the ICU were probably a result of slight deterioration of cardiac function after CPB. The causes of the deterioration are unknown. Preoperative left ventricular ejection fraction was not different between the two groups. No patients of group C had new Q waves on the postoperative ECG, defined as an essential factor for diagnosis of perioperative transmural myocardial infarction [16]. In addition, the serum troponin T level, which is considered more accurate than creatine kinase-MB for detecting myocardial infarction after CABG [17] and which is closely related to the duration of aortic cross-clamping [18], was similar to that in patients of group A after release of the aortic clamp. Therefore, perioperative transmural myocardial infarction was not considered to be the cause of the deterioration of cardiac function after CPB in group C. Given the circulatory restoration at 6h and 12h after admission to the ICU in group C, myocardial stunning could be related to deterioration of cardiac function after CPB [19]. In general, cardiac reserve decreases with age [20], and our finding that age is a preoperative risk factor for prolonged ICU stay is consistent with previous studies [3–6]. The most relevant age-related changes in cardiovascular performance for perioperative management are stiffened myocardium and vasculature, blunted β-adrenoceptor responsiveness, and impaired autonomic reflex control of heart rate [21]. These changes are of little relevance at rest, but the increased oxygen demand on undergoing major surgery is met primarily by activation of the preload reserve in the elderly, in contrast to heart rate in the young, which may result in cardiopulmonary insufficiency. Because the preoperative left ventricular ejection fraction in each group was not significantly different, cardiac reserve could be related to the deteriorated cardiac function on admission to the ICU.

Reich et al. [22] suggested that intraoperative pulmonary artery pressure was independently associated with mortality and perioperative transmural myocardial infarction in patients undergoing CABG. High pulmonary artery pressure can be caused by left ventricular dysfunction after CPB. PAP may also increase in patients with high pulmonary vascular resistance caused by lung disease. Therefore, continuous MPAP measurement in combination with the PF ratio might be a useful marker for assessing the circulatory and respiratory status after CPB and might help to accurately evaluate patients with unstable hemodynamics.

In summary, we retrospectively studied 100 patients who underwent elective CABG and had prolonged aortic cross-clamping during CPB to identify risk factors for prolonged ICU stay. Our results indicates that a longer stay in the ICU depends on advanced age, increased MPAP, and decreased PF ration on admission to the ICU.

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