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Original Article

Patients and surgery-related factors that affect time to recovery of consciousness in adult patients undergoing elective cardiac surgery

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Abstract

Background: Central nervous system dysfunction is a serious complication following cardiac surgery. The prompt and predictable recovery of consciousness (ROC) from anesthesia is essential for neurological evaluations. This retrospective study aimed to determine the factors that were related to ROC time after elective cardiac surgery.
Methods: Patients receiving elective cardiac surgery under general anesthesia were included in the analysis. Patient and surgery-related factors were collected through chart review. Cox regression model was used to evaluate the associations between collected variables and ROC time. Backward model selection strategy was further applied to selecting independent factors from significant ones that affected ROC time in the univariate analysis.
Results: A total of 253 patients were recruited in our study. Among significant patient characteristics, higher body mass index (hazard ratio, HR = 1.06) and female gender (HR = 1.72) tended to shorten ROC time, but older age was inclined to prolong it (HR = 0.98). Higher preoperative blood urea nitrogen level also significantly delayed ROC after cardiac surgery (HR = 0.99). Among surgery-related factors, only longer duration of cardiopulmonary bypass significantly increased ROC time after the model selection processes (HR = 0.96). Other factors were not significant after adjustment for these five factors.
Conclusion: This study demonstrated that older age, male gender, lower body mass index, higher preoperative blood urea nitrogen level, and longer bypass duration were independent risk factors of delayed emergence after elective cardiac surgery. These findings provide insights into patient care and anesthetic management for clinicians in related fields.

Keywords: Cardiac surgery; Cardiopulmonary bypass; Cox regression model; General anesthesia; Recovery of consciousness

1. Introduction

Central nervous system dysfunction following cardiac surgery is a serious complication and results in postoperative morbidity and mortality.[1,2] Prompt and predictable recovery of consciousness (ROC) from anesthesia following cardiac surgery is essential for early diagnosis of central nervous system injury, which mainly relies on neurological evaluation after patients regain consciousness. It is also easier and more favorable to monitor the neurological status of a patient with clear consciousness.[3] On the other hand, ROC is a major criterion for tracheal extubation after cardiac surgery.[4,5] Therefore, timely awakening to facilitate early assessment of postoperative neurological function and tracheal extubation is of paramount importance among patients undergoing cardiac surgery.

Although some factors have been identified to affect ROC from general anesthesia in previous studies,[6−9] such as gender[6−8] and age,[9] few studies have ever investigated factors associated with ROC time after cardiac surgery. Previous reports have shown that patients receiving aortic valve or

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aortic aneurysm surgery, and with prolonged cardiopulmonary bypass (CPB) time, carry a higher risk of cerebral complications after cardiac surgery.[1,10,11] Nevertheless, it is not clear whether these factors were also associated with the ROC time among patients undergoing cardiac surgery. Therefore, we conducted this retrospective study to evaluate which factors, including patient characteristics and surgery-related factors, have significant effects on ROC time from general anesthesia among patients undergoing elective cardiac surgery. Independently influential factors of ROC time after elective cardiac surgery would also be identified with the aid of model selection processes.

2. Methods

After the approval of the Institutional Review Board of Mackay Memorial Hospital (10MMHIS084), data were collected from patients admitted to our hospital for elective cardiac surgery by chart review between January 2009 and April 2010. Patients aged between 20 years and 90 years, without conscious disturbance and receiving general anesthesia for elective cardiac surgery were included in the analysis. The exclusion criteria were those who presented neurological deficits at recovery, required postoperative sedation, or had re-operation because of surgical complications within 6 hours, postoperatively. All patients had routine monitoring for cardiac surgery, including electrocardiography, noninvasive blood pressure cuff, pulse oximetry, capnography, and arterial and pulmonary artery catheter. The anesthetic technique for cardiac surgery was standardized in our hospital; and consisted of induction with midazolam, fentanyl and etomidate, and neuromuscular blockade with rocuronium. Anesthesia was maintained with fentanyl (2 μg/kg/h), dormicum (0.05 mg/kg/h), atracurium infusion, and sevoflurane 0−1% in oxygen. Fentanyl and dormicum infusions were continued during the CPB. After completion of wound closure, the fentanyl/dormicum infusion and sevoflurane were discontinued. Other aspects of perioperative care were left to the discretion of attending anesthesiologists in charge.

After the operation, all patients were transferred to the cardiovascular intensive care unit with endotracheal tube in place and received mechanical ventilation support. Patients' consciousness and neurological status expressed in Glasgow coma scale were regularly recorded by nurses in charge. Patients who could be cooperative and follow verbal commands or had Glasgow coma score of 15 were considered to be conscious.

The ROC time was defined as the duration from the completion of the surgery to the time the patient recovered clear consciousness. Miscellaneous preoperative and intraoperative variables were collected as follows. Preoperative variables collected includes age, gender, height, weight, body mass index (BMI), and ejection fraction of left ventricle (%). Baseline laboratory data consisted of hemoglobin, blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (GFR), albumin, aspartate transaminase (AST), and alanine transaminase were also collected. The collected surgery-related factors included undergoing the CPB or not, the duration of the CPB, cross-clamp time, surgical types [including coronary arterial bypass (CABG) surgery, valve surgery, CABG plus valve surgery, and others], and body temperature during the CPB (in °C).

2.1. Statistical analysis

Parametric variables were presented as mean with standard deviation, and categorical data were expressed as count and percentage. The proportion of patients remaining unconscious was plotted against time. Cox proportional hazards regression model was used to assess the relationship between potentially influential variables and ROC time. Significant factors on univariate analysis ($p < 0.05$) were considered for inclusion in the following main-effect model, and a backward selection strategy (α-to-stay was set to 0.1) was used to select factors with significant effects in the multivariable Cox regression analysis. The hazard ratio (HR) with its 95% confidence interval (CI) was estimated for each variable that is included in univariate and multivariable Cox regression analyses. The proportional hazards assumption of the Cox model was assessed for each covariate included in the selected model using a graphical approach (log-log survival curves).[12,13] The significance level for each main-effect hypothesis was set at 0.05. SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA) was used for all analyses.

3. Results

There were 253 patients recruited in our study. Table 1 describes the patient baseline characteristics. Most patients were male (70.8%), underwent the CABG (63.6%), and received cardiopulmonary bypass (69.6%) during operations. Fig. 1 illustrates the unconditional survival curve of the ROC time in our study. Only 17.4% of patients regained their consciousness in 1 hour. Nearly half (49%) of our study population recovered their consciousness within 2 hours postoperatively, and about 80% of recruited patients had emergence time from general anesthesia less than 3 hours.

Table 2 presents the results of univariate analysis, which assessed the association between miscellaneous factors and the ROC time. The HR greater than 1 favors early emergence. Among patient baseline characteristics, only age, gender, and the BMI had statistically significant effects on the ROC time. Female gender and higher BMI exerted positive effects on the ROC time (HR = 1.33 and 1.07, respectively), which means that female patients and those with higher BMI tended to have shorter ROC time than their counterparts. Furthermore, older patients were inclined to have longer ROC time than younger ones (HR = 0.99). For laboratory data, the effects of hemoglobin level, BUN, estimated GFR, and AST on ROC time were statistically significant. The higher hemoglobin level and the estimated GFR favored early emergence (HR = 1.1 and 1.01, respectively). In contrast, the higher BUN and the AST values tended to prolong the emergence time from anesthesia. Serum creatinine level and preoperative ejection fraction of

Table 1
Baseline characteristics of patients receiving elective cardiac surgery

	Mean ± SD	*n* (%)
Age (y/o)	63.8 ± 13.48	
Gender (male)		179 (70.8)
Height (cm)	161.8 ± 8.3	
Weight (kg)	64.3 ± 12.6	
BMI (kg/m^2)	24.5 ± 3.9	
Hemoglobin (g/dL)	11.9 ± 2.1	
BUN (mg/dL)	25.8 ± 17.6	
Creatinine (mg/dL)	2.2 ± 2.7	
Estimated GFR (mL/min/1.73 m^2)	61.2 ± 36.3	
Albumin (g/dL)	4.1 ± 4.6	
AST (IU/L)	46.2 ± 141.7	
ALT (IU/L)	43.5 ± 137.7	
Ejection fraction of left ventricle (%)	56.1 ± 12.0	
Surgical type		
CABG		161 (63.6)
Valve surgery		53 (20.9)
CABG + valve surgery		18 (7.1)
Others		21 (8.3)
Cardiopulmonary bypass		176 (69.6)
Cardiopulmonary bypass time (min)	76.7 ± 72.7	
Cross-clamp time (min)	36.4 ± 54.7	
Body temperature during CPB (°C)	32.6 ± 4.6	
Operation time (min)	360.1 ± 76.1	
ROC time (min)	148.8 ± 136.1	

ALT = alanine transaminase; AST = aspartate transaminase; BMI = body mass index; BUN = blood urea nitrogen; CABG = coronary artery bypass graft surgery; CPB = cardiopulmonary bypass; GFR = glomerular filtration rate; ROC = recovery of consciousness; SD = standard deviation.

Table 2
Univariate analysis of factors potentially influencing time to recovery of consciousness after elective cardiac surgery

	HR	95% CI	*p*
Age (y/o)	0.99	0.98−1.00	0.003
Gender (female *vs.* male)	1.33	1.01−1.74	0.042
Height (cm)	1.00	0.99−1.00	0.433
Weight (kg)	1.00	1.00−1.01	0.307
BMI (kg/m^2)	1.07	1.03−1.10	0.000
Hemoglobin (g/dL)	1.10	1.03−1.16	0.002
BUN (mg/dL)	0.99	0.98−0.99	0.001
Creatinine (mg/dL)	0.96	0.91−1.01	0.113
Estimated GFR (mL/min/1.73 m^2)	1.01	1.00−1.01	0.002
Albumin (g/dL)	1.01	0.99−1.04	0.321
AST (IU/L)	1.00	1.00−1.00	0.024
ALT (IU/L)	1.00	1.00−1.00	0.107
Ejection fraction of left ventricle (%)	1.00	0.99−1.02	0.384
Surgical type			0.056
Valve surgery versus CABG	0.75	0.55−1.02	0.066
Combined surgery versus CABG	0.57	0.34−0.93	0.026
Others versus CABG	0.78	0.48−1.25	0.305
Cardiopulmonary bypass	0.68	0.52−0.89	0.006
Cardiopulmonary bypass time (per 10 min)	0.97	0.96−0.99	0.001
Cross-clamp time (per 10 min)	0.96	0.94−0.99	0.001
Body temperature during CPB (°C)	1.05	1.02−1.08	0.001
Operation time (per 10 min)	0.99	0.97−1.00	0.135

ALT = alanine transaminase; AST = aspartate transaminase; BMI = body mass index; BUN = blood urea nitrogen; CABG = coronary artery bypass graft surgery; CI = confidence interval; CPB = cardiopulmonary bypass; GFR = glomerular filtration rate; HR = hazard ratio.

left ventricle were not significantly associated with ROC time ($p = 0.11$ and 0.38, respectively).

Regarding the surgery-related factors, patients receiving cardiopulmonary bypass during elective cardiac surgery were predisposed to delayed emergence (HR = 0.68, 95% confidence interval = 0.52−0.89). Lower body temperature during the CPB and longer bypass time or cross-clamp time also significantly prolonged the ROC time. However, surgical types and total operation time were not predictors of the ROC time ($p = 0.06$ and 0.14, respectively).

Table 3 shows the final model after the model selection processes. The effects of the AST, the hemoglobin level, the estimated GFR, the cardiopulmonary bypass, the cross-clamp time, and the body temperature during the CPB were no longer statistically significant after further adjustment for the first five factors in the table. Five independent factors were identified to have significant effects on the ROC time. Among these

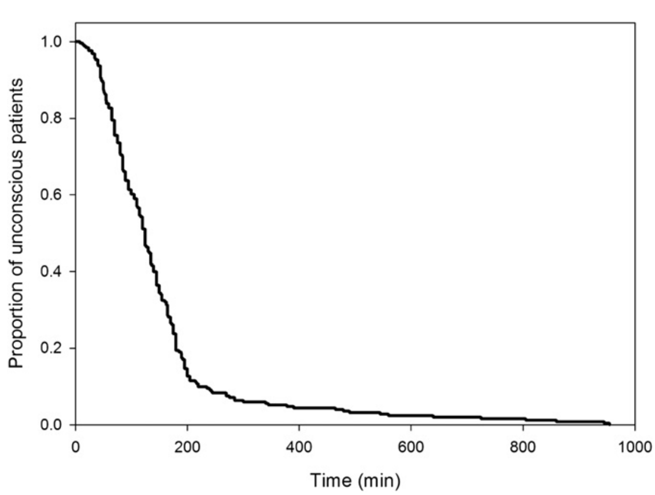

Fig. 1. The proportion of patients remaining unconscious with time after elective cardiac surgery. The percentage of unconscious patients decreased gradually with time. Only 17.4% of patients regained their consciousness in 1 hour, and nearly half (49%) of patients recovered their consciousness within 2 hours. Less than 20% of patients had emergence time from general anesthesia longer than 3 hours.

Table 3
Multivariate analysis of factors potentially influencing recovery of consciousness time after elective cardiac surgery using backward model selection strategy

	HR	95% CI	*p*
Age (y/o)	0.98	0.97−0.99	0.001
Gender (female *vs.* male)	1.72	1.29−2.29	0.000
BMI (kg/m^2)	1.06	1.03−1.10	0.000
BUN (mg/dL)	0.99	0.98−0.99	0.000
Cardiopulmonary bypass time (per 10 min)	0.96	0.95−0.98	0.000
AST (IU/L)	1.00	1.00−1.00	0.088
Hemoglobin (g/dL)	1.05	0.98−1.13	0.182
Estimated GFR (mL/min/1.73 m^2)	1.00	0.99−1.01	0.850
Cardiopulmonary bypass	1.24	0.83−1.86	0.294
Cross-clamp time (per 10 min)	0.98	0.91−1.06	0.652
Body temperature during CPB (°C)	0.99	0.91−1.08	0.824

AST = aspartate transaminase; BMI = body mass index; BUN = blood urea nitrogen; CI = confidence interval; GFR = glomerular filtration rate; HR = hazard ratio.

significant factors, older age, higher BUN, and longer bypass time were inclined to prolong the ROC time (HR = 0.98, 0.99, and 0.96, respectively). Female gender and higher BMI tended to shorten it (HR = 1.72 and 1.06, respectively). The effects of other significant factors in the univariate analysis vanished after further adjustment for these five factors.

4. Discussion

In this retrospective study, we found that old age, male gender, longer CPB time, higher preoperative BUN level, and lower BMI were independent risk factors of the prolonged ROC time after elective cardiac surgery. Few previous studies have ever investigated factors influencing the ROC time after the cardiac surgery. Our findings provided valuable information for further investigations and potential clinical implications for physicians. The mechanisms of relationships between the ROC time and these factors are also interesting topics deserving more explorations. These issues will be further discussed in the following sections.

Age was associated with the ROC time after elective cardiac surgery, and older patients had slower ROC. The mechanisms behind this finding are multiple. During the aging process, the anatomic and functional areas of the brain participating in consciousness change progressively.[14–16] The alteration in pharmacokinetic property and response to anesthetics in the geriatric population also play some role. The volume of distribution, clearance rate, and plasma protein binding decreased and resulted in an increase in the free plasma concentration of drugs.[9] Furthermore, compared with young people, the concentration required to attain the similar anesthetic depth, either intravenous or inhaled anesthetics, is decreased in elderly patients.[17,18]

Similar to other investigators,[6–8] we also found women wakened faster from general anesthesia than men, even in cardiac surgery, which belongs to the more complex procedures. Gan et al discovered that gender appeared to be an independent predictor for recovery time.[6] In a study of 1079 patients, Buchanan et al demonstrated similar findings and proposed that lower sensitivity to the hypnotic effect of anesthetics in women may account for their faster recovery.[7] The female sex hormone that affected pharmacokinetics and pharmacodynamics of anesthetics was postulated to play a role in the gender differences in recovery time.[19] Further investigations are needed to elucidate the relationship between sex hormone and recovery from anesthesia.

In our study, the duration of CPB had a negative effect on the ROC time, and patients undergoing longer duration of CPB needed more time to recover consciousness after cardiac surgery. The longer CPB time had been considered as a risk factor for delirium and neurological complications after cardiac surgery.[20,21] However, a study about the relationship between the duration of CPB and the consciousness recovery after cardiac anesthesia was not found. The institution of CPB has profound effects on the pharmacokinetics and pharmacodynamics of anesthetic drugs.[22] Barbosa et al reported pharmacokinetics of propofol modified by the CPB, may contribute to an increase in hypnotic effects after cardiac surgery.[23] In our clinical practice, fentanyl and dormicum infusion continued to be administrated during the CPB and we speculate that the effects of the CPB on these anesthetic drugs may be related to our finding.

BMI is a widely used tool for the measurement of obesity. In the present study, we analyzed the effects of varying BMI on the ROC time in patients undergoing elective cardiac surgery. We found that the patients with higher BMI awaked faster than those with lower BMI. The underlying cause of this finding is not clear and awaits further investigation. Obesity had been considered to be a risk factor of postoperative morbidity and mortality following cardiac surgery.[24] However, some recent investigations revealed that underweight patients had even higher risk of mortality and complications and recovered more slowly after the CABG or vascular surgery.[25–27] Furthermore, mildly obese patients ($25 < BMI \leq 35$) might have less mortality than those with normal weight after cardiac and vascular surgery.[25] The mean and maximum BMI values of our study population were 24.5 and 34, respectively. No severely or morbidly obese patient was enrolled in our study. Although we could not evaluate the effect of BMI higher than 34 based on our data, our findings still provided promising evidence on the relationship between the BMI and the ROC time after cardiac surgery.

Although BUN, creatinine and estimated GFR were all considered as markers of renal function, only BUN was found to be an independent factor to have a significant effect on the ROC time after elective cardiac surgery in our study. Recent studies regarded BUN as a marker related to renal perfusion, hemodynamic alternation, and neurohormonal activation; and appeared to be a strong predictor of mortality in patients with heart failure and acute myocardial infarction.[28,29] Elevated BUN level was also positively associated with poor outcome and adverse effects after aortic and cardiac surgery.[30–32] According to our results and previous reports,[28,29] BUN, a routine laboratory test, seemed to reflect the general clinical status related to cardio-renal alteration, which might affect pharmacokinetics and pharmacodynamics of anesthetic drugs. It could also explain why patients with higher BUN level were inclined to prolonged ROC time from anesthesia in patients undergoing cardiac surgery to some degree.

There are some limitations to this retrospective study. First, we did not include dosage of anesthetics in the analysis because standardized anesthetic protocols for elective cardiac surgery were adopted in our hospital. Second, the ROC time recorded by nurses in charge may not be very precise because of individual nursing habits and care protocols. This may only increase the random error of the ROC time recording to some degree, yet systematic bias is less likely because nurse rotation tends to average out errors in the ROC time recording. Third, our data were collected retrospectively based on medical chart review, and the selected factors only partially account for the ROC time after elective cardiac surgeries. More variables should be considered in future research.

In conclusion, in this retrospective study, we found that age, gender, BMI, preoperative BUN level, and duration of CPB were independent factors which affected the ROC time from general anesthesia in patients undergoing elective cardiac surgery. Patients with older age, higher BUN, and longer CPB time tended to recover consciousness slowly, but female patients and those with higher BMI were inclined to have faster emergence. These findings provided valuable information on patient care following cardiac surgery for clinician and assist anesthesiologists to adjust their anesthetic management based on patients' condition.

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