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The risk factors for delayed recovery in patients with cardiopulmonary bypass

Why should we care?

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Abstract

Cardiopulmonary bypass (CPB) is very commonly performed among the cardiovascular surgeries, and delayed recovery (DR) is a kind of serious complications in patients with CPB. It is necessary to assess the risk factors for DR in patients with CPB, to provide evidence into the management of CPB patients.

Patients undergoing CPB in our hospital from January 2018 to March 2020 were included. Cases that consciousness has not recovered 12 hours after anesthesia were considered as DR. The preoperative and intraoperative variables of CPB patients were collected and analyzed. Logistic regressions were conducted to analyze the potential influencing factor.

A total of 756 CPB patients were included, and the incidence of DR was 9.79%. There were significant differences on the age, aspartate aminotransferase (AST), glutamic pvruvic transaminase (ALT), blood urea nitrogen (BUN), and serum creatinine (SCr) between patients with and without DR (all $P < .05$); there were no significant differences in the types of surgical procedure (all $P > .05$); there were significant differences on the duration of CPB, duration of aortic cross clamp (ACC), duration of surgery, minimum nasopharyngeal temperature, and transfusion of packed red blood cells between patients with and without DR (all $P < .05$). Logistic regression analysis indicated that duration of CPB ≥132 minutes (odds ratio [OR] 4.12, 1.02–8.33), BUN ≥9 mmol/L (OR 4.05, 1.37–8.41), infusion of red blood cell suspension (OR 3.93, 1.25–7.63), duration of surgery ≥350 minutes (OR 3.17, 1.24–5.20), age ≥6 (OR 3.01, 1.38–6.84) were the independent risk factors for DR in patients with CPB (all $P < .05$).

Extra attention and care are needed for those CPB patients with duration of CPB ≥132 minutes, BUN ≥9 mmol/L, infusion of red blood cell suspension, duration of surgery ≥350 minutes, and age ≥60.

Abbreviations: ACC = aortic cross clamp, ALT = glutamic pvruvic transaminase, AST = aspartate aminotransferase, BMI = body mass index, BUN = blood urea nitrogen, CPB = cardiopulmonary bypass, DR = delayed recovery, ICU = intensive care unit, LVEF = left ventricular ejection fraction, SCr = serum creatinine.

Keywords: cardiopulmonary bypass, cardiovascular, care, delayed recovery, factors, risk

1. Introduction

Over the past decades, the incidence of cardiovascular diseases has been continuously increasing, and it has become one of the leading causes of death worldwide.[1] With the improvement of people's living conditions and lifestyle changes, the incidence of aortic and cardiac diseases related with hypertension and atherosclerosis has also increased accordingly.[2] Although the medical conservative treatment of aortic and cardiac diseases has made great progress, surgery is the preferred treatment for those diseases.[3] Cardiopulmonary bypass (CPB) has laid the foundation

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for the development of cardiovascular surgery, and it plays a pivotal role in the cardiac and macrovascular surgery.[4] However, it may also lead to several complications such as delayed recovery, pulmonary, or kidney damage, etc.[5] The prevention of complications associated with CPB is essential to the prognosis of patients.

The patient's anesthesia recovery is not only one of the main evaluation indicators for tracheal extubation after surgery, but also one of the most convenient and important observation indicators for the early diagnosis of central nervous injury after cardiovascular surgery.[6] Delayed recovery (DR) often leads to prolonged mechanical ventilation duration and longer stay of intensive care unit (ICU).[7] Increasing the incidence of other systemic complications and even causing the death of patients also puts a huge financial burden on patients and their families.[8] Therefore, it is very important for patients undergoing cardiac surgery to clearly identify the risk factors that affect patients' DR and to help them wake up in time. Therefore, we performed this retrospective analysis to explore the incidence of recovery delay and related risk factors in patients with CPB to prevent and early recognition of DR after cardiovascular surgery.

2. Methods

2.1. Ethical consideration

Our study has been approved by the ethical committee of Second People's Hospital of Liaocheng (approval number: 201800184-3c) and written informed consents have been obtained from all the included patients.

2.2. Participants

Patients undergoing CPB in the department of cardiothoracic surgery in our hospital from January 2018 to March 2020 were identified. The patients were included if: adult patients with age ≥18 years old; patients underwent the cardiovascular surgery and CPB in the status of general anesthesia; patients' preoperative consciousness was normal, and they could communicate with people normally; patients agreed to participant in this study. And the patients were excluded if: the patients had mental illness or poor preoperative consciousness; the patients disagreed to participant in this study.

2.3. Surgery management

All patients underwent routine monitoring of cardiac surgery, including monitoring of electrocardiogram, pulse oximetry, end-expiratory carbon dioxide, radial artery blood pressure, central venous pressure, transesophageal echocardiography, and cardiac output. Induction medications included midazolam, sufentanil, etomidate, and cis-atracurium. Sufentanil, midazolam, propofol, cis-atracurium, and sevoflurane were used for anesthesia maintenance. After the incision was closed, the infusion of anesthesia related drugs was stopped. After surgery, all patients were transferred to the cardiac ICU with endotracheal intubation, and then further supported by mechanical ventilation.

2.4. DR definitions

The nurse regularly recorded the patient's consciousness and neurological status. Patients who could cooperate and respond to verbal instructions were considered to have recovered their state of consciousness. Cases where consciousness has not recovered 12 hours after anesthesia were considered as DR.[9,10]

2.5. Data collection

Two authors independently evaluated and collected the related information. The following preoperative and intraoperative variables were collected and analyzed: age, sex, height, weight, body mass index (BMI), related complications such as hypertension, diabetes mellitus, hyperlipidemia and anemia, left ventricular ejection fraction (LVEF), blood urea nitrogen (BUN), serum creatinine (SCr), aspartate aminotransferase (AST), glutamic pvruvic transaminase (ALT), duration of CPB, duration of aortic cross clamp (ACC), duration of surgery, minimum nasopharyngeal temperature, infusion of red blood cell suspension.

2.6. Statistical methods

We used SPSS 23.0 version statistical software for data processing. All the continuous data were presented by mean and standard deviation. The binary data were expressed as cases and percentage. The comparison of continuous data adopted student t test. Chi-square test or Fisher exact test was used for comparison of binary data. Logistic regressions were conducted to analyze the potential influencing factors. $P < .05$ was considered statistically significant.

3. Results

3.1. The basic characteristics of included patients

As Table 1 presented, a total of 756 patients were included in this present study, and 74 patients had the attack of DR, the incidence of DR was 9.79%. There were significant differences on the age, AST, ALT, BUN, and SCr between patients with and without DR (all $P < .05$), no significant differences on the sex, BMI, hypertension, diabetes mellitus, hyperlipidemia, anemia, hypoalbuminemia, and LVEF were found (all $P > .05$).

3.2. The type of surgical procedure of 2 groups

As showed in Table 2, there were no significant differences on the type of surgical procedure of 2 groups (all $P > .05$).

3.3. The surgical characteristics of 2 groups

As presented in Table 3, there were significant differences on the duration of CPB, duration of ACC, duration of surgery, minimum nasopharyngeal temperature, and transfusion of packed red blood cells between patients with and without DR (all $P < .05$).

3.4. Logistic regression analysis

As presented in Table 4, logistic regression analysis indicated that duration of CPB ≥132 minutes (OR 4.12, 1.02–8.33), BUN ≥9 mmol/L (OR 4.05, 1.37–8.41), infusion of red blood cell suspension (OR 3.93, 1.25–7.63), duration of surgery ≥350 minutes (OR 3.17, 1.24–5.20), age ≥6 (OR 3.01, 1.38–6.84) were the independent risk factors for DR in patients with CPB (all $P < .05$).

Table 1

The basic characteristics of included patients.

Variables	DR group (n=74)	Normal group (n=682)	χ^2/t	*P*
Male/female	48/26	455/227	1.194	.088
Age, y	67.4±5.25	59.4±4.77	10.420	.019
BMI, kg/m^2	24.3±3.18	24.2±3.07	3.284	.068
Hypertension	36 (48.65%)	324 (47.51%)	1.043	.137
Diabetes mellitus	28 (37.84%)	205 (30.06%)	1.235	.053
Hyperlipidemia	22 (29.73%)	194 (28.45%)	1.401	.129
Anemia	14 (18.92%)	118 (17.30%)	1.108	.142
Hypoalbuminemia	13 (17.57%)	101 (14.81%)	1.220	.066
AST, U/L	39.4±13.18	28.2±12.09	12.184	.037
ALT, U/L	36.1±10.85	27.1±13.64	10.755	.043
BUN, mmol/L	9.2±2.04	6.7±2.17	1.406	.009
Cr, μmol/L	101.8±14.18	79.3±11.97	9.073	.006
LVEF (%)	54.2±8.19	59.6±10.30	7.175	.192

ALT=glutamic pvruvic transaminase, AST=aspartate aminotransferase, BMI=body mass index, BUN=blood urea nitrogen, LVEF=left ventricular ejection fraction.

Table 2

The comparisons on the surgery distributions of 2 groups.

Surgery	DR group (n=74)	Normal group (n=682)	χ^2	*P*
VR	39 (52.70%)	364 (53.37%)	1.190	.148
CABG	17 (22.97%)	155 (22.73%)	1.083	.110
VR+CABG	4 (5.41%)	39 (5.72%)	1.511	.271
ASDR	8 (10.81%)	74 (10.85%)	1.948	.192
VSDR	6 (8.11%)	50 (7.33%)	1.657	.089

ASDR=atrial septal defect, CABG=coronary artery bypass grafting, VR=valve replacement, VSDR=ventricular septal defect repair.

4. Discussion

Consciousness recovery is a continuous process, yet currently there is no uniform definition on the DR after general anesthesia. We have referred to relevant reports,[9,10] and we considered cases where consciousness had not recovered 12 hours after the end of anesthesia as delayed recovery. There are many factors involved in the delayed recovery after CPB cardiovascular surgery, but the exact mechanism is not yet clear.[11] The results of this present study have found that the duration of CPB, duration of ACC, duration of surgery, minimum nasopharyngeal temperature and infusion of red blood cell suspension may influence the occurrence of DR, and particular attention and care are needed to those patients with duration of CPB ≥132 minutes, BUN ≥9 mmol/L, infusion of red blood cell suspension, duration of surgery ≥350 minutes, and age ≥60.

During the CPB process, the occurrence of inflammation can cause brain tissue edema, and the rolling of the artificial tube by the rolling pump during artificial blood vessel placement and

Table 3

The comparisons on the surgical characteristics of 2 groups.

Items	DR group (n=74)	Normal group (n=682)	χ^2/t	*P*
Duration of CPB, min	143.2±38.41	120.1±37.29	13.747	.005
Duration of ACC, min	96.8±22.17	81.2±19.96	12.103	.041
Duration of surgery, min	288.3±52.14	268.4±51.30	20.184	.042
Minimum nasopharyngeal temperature, °C	27.4±3.18	28.9±4.05	7.199	.047
Infusion of red blood cell suspension	48 (64.86%)	105 (15.40%)	1.185	.002

ACC=aortic cross clamp, CPB=cardiopulmonary bypass.

Table 4

Logistic regression analysis on the risk factors for DR in patients with CPB.

Variables	β	SE	OR	95% CI	*P*	Rank
Duration of CPB ≥132 min	0.85	0.28	4.12	1.02–8.33	.041	1
BUN ≥9 mmol/L	0.90	0.32	4.05	1.37–8.41	.032	2
Infusion of red blood cell suspension	1.05	0.46	3.93	1.25–7.63	.045	3
Duration of surgery ≥350 min	0.94	0.31	3.17	1.24–5.20	.018	4
Age ≥60	1.44	0.28	3.01	1.38–6.84	.044	5

BUN=blood urea nitrogen, CI=confidence interval, CPB=cardiopulmonary bypass, DR=delayed recovery, OR=odds ratio.

removal process may lead to foreign micro-embolism.[12] And if the water temperature and blood temperature differ by >10°C during rewarming, it may lead to the occurrence of air embolism, and lead to cerebral vascular embolism, which in turn damages brain tissue.[13] The reason for the abnormal metabolism of narcotic drugs may be due to the changes in the pharmacokinetics of the patient's basic conditions such as age, sex, liver, and kidney function.[14] On the one hand, elderly patients have increased sensitivity to general anesthetics such as opioids and benzodiazepines. On the other hand, the function of central nervous system gradually declines, and consciousness recovery is prone to be slow.[15] The intense stress is derived from surgical trauma, the inflammatory response, endocrine changes, low temperature, blood thinning, application of cardioplegia.[16] Therefore, understanding the potential risk factors for DR is vital to the prognosis of patients with CPB.

Age ≥60 years old is an independent risk factor for DR. The clearance rate, and plasma protein binding rate of anesthetic drugs in elderly patients have decreased to varying degrees.[17] This leads to an increase in the free concentration of the drug in the plasm.[18] Therefore, compared with young people, to achieve the same depth of anesthesia, the amount of intravenous or inhaled anesthetic drugs required by the elderly has decreased to varying degrees.[19] Besides, as the age of the patient grows, the anatomical and functional areas that affect the recovery of brain consciousness will change accordingly.[20,21] Moreover, the elderly population will not only have more basic diseases with reduced organ function, but also changes in pharmacokinetic properties and response to anesthetic drugs.[22] In addition, the vascular compliance of the elderly is reduced, the tolerance to advection and hypoperfusion in CPB is poor, and neurological damage is more likely to occur under the same conditions.[23] All those factors increase the risk of DR in elder patents, more evaluation and nursing care are highlighted in patients with age ≥60 years old.

Preoperative BUN ≥9 mmol/L is an independent risk factor for DR. Previous studies[24–26] suggest that the BUN test is more sensitive to renal perfusion, related hemodynamic changes, and neurohormonal activation, and it may have a strong predictive effect on the risk of death in patients with heart failure and acute myocardial infarction. Furthermore, related studies[27,28] have found that elevated BUN levels are also associated with adverse outcomes after aortic and cardiac surgery. Although BUN is only a routine examination, it can reflect the clinical status related to the heart and kidney function of the patient. CPB, CP, hypothermia, and hypotension during the surgery may further reduce the renal function of patients with abnormal BUN levels before surgery, resulting in the change of patient's pharmacodynamics and pharmacokinetics of narcotic drugs.[29] This also explains why higher BUN levels may, to a certain extent, increase the risk of DR for patients undergoing cardiovascular surgery.

Several studies[30,31] have reported that the risk of neurological complications will increase with the duration of CPB, which is related to increased inflammatory factor release, blood damage and increased ischemia-reperfusion injury of related organs. But there are studies[32,33] have showed that CPB and the duration of CPB time don't affect the recovery process of patients' consciousness after cardiac surgery. The effect of longer CPB duration on DR may come from the anesthetic drugs given to patients during CPB.[34] In this study, patients with longer CPB and surgery durations had an increased risk of DR, and CPB ≥132 minutes, duration of surgery ≥350 minutes is the independent risk factor for DR in patients with CPB, indicating that the clinical surgeon should complete the operation as soon as possible to shorten the duration of CPB and surgery.

The results of this study have suggested that red blood cell transfusion is an independent risk factor for DR. Although there is blood loss during the operation, but the level of hemoglobin after diuresis and ultrafiltration is sufficient to maintain the oxygen supply of tissues and organs, there is no need to red blood cell transfusion regularly.[35] Transfusion of red blood cells pose a great impact on the body, and transfusion of red blood cells cannot only trigger the formation of various microemboli, but also a large number of rapid blood transfusions can lead to internal environment disturbances and a decrease in central body temperature, which affects the blood supply and metabolism of the brain.[36,37] Studies[38,39] have shown that intraoperative red blood cell transfusions can adversely affect the prognosis of patients with CABG surgery. In addition, patients who require a large amount of blood transfusion during the perioperative period are often patients with severe lesions, long CPB time, heavy intraoperative bleeding and difficulty in hemostasis.[40] The chance of hypoperfusion and embolism of brain tissue in these patients is significantly increased compared with those patients without transfusions.[41] Therefore, we should put more attentions on those patients with red blood cell transfusion during the surgery, closer monitoring, and nursing care may be helpful to the early recovery of consciousness.

5. Conclusions

In conclusions, duration of CPB ≥132 minutes, BUN ≥9 mmol/L, infusion of red blood cell suspension, duration of surgery ≥350 minutes, and age ≥60 are the independent risk factors that affect the DR in patients with CPB. Those who are older, have longer CPB, surgery duration and elevated BUN levels, and red blood cell transfusions are at greater risk of DR. Active treatment to improve kidney function before surgery, select appropriate surgical methods and improve surgical strategies to shorten the operation time, reduce intraoperative bleeding are beneficial to the prognosis of patients with CPB.

Author contributions

Conceptualization: Baozeng Chen, Mingjing Feng, Chen Sheng.
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