Brief Communications

Predictors of postoperative cognitive dysfunction in adult patients undergoing elective cardiac surgery

INTRODUCTION

Post-operative central nervous system dysfunctions persist as common complications with a significant impact on the patient's quality-of-life after cardiac surgery.[1] The incidence of post-operative cognitive dysfunction (POCD) ranges between 40% and 70% at the time of discharge from hospital., More than 20 risk factors have been identified for POCD, but it can occur even in the absence of these high-risk factors.

The aim of our current study was to evaluate the risk factors for the development of POCD in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) who were at low-risk of developing POCD.

METHODS

After obtaining institutional ethical committee approval, patients aged over 30 years undergoing elective cardiac surgery with Katz grading[2] of six were included in this prospective observational study, between May and December 2012. Exclusion criteria included previous cardiothoracic surgery, history of stroke or transient ischemic attack, carotid stenosis >50%, severe hypertension (>180/110 mm of Hg) at admission, renal dysfunction (serum creatinine >2 mg/dl), active hepatic disease, severe left ventricular dysfunction (ejection fraction <30%), pre-operative mini-mental state examination (MMSE) score <25, concomitant surgery on great vessels, pre-operative atrial fibrillation, pre-operative blood transfusions after admission, patients who remained intubated for >24 h after surgery and patients who died within 7 days post-operatively.

Mini-mental state examination[3] was performed on the day before surgery, 24 h after extubation and on the 7th post-operative day. MMSE score ≤24 was considered to be cognitive dysfunction. All patients were managed as per the institutional protocol. All patients were pre-medicated with ranitidine (150 mg PO), and alprazolam (0.5 mg PO). Anaesthesia was induced with midazolam (0.1 mg/kg), fentanyl (5 μg/kg), thiopentone sodium (2-4 mg/kg), and rocuronium (0.6 mg/kg). Anaesthesia was maintained with isoflurane (1-2 minimum alveolar concentration), midazolam (0.01 mg/kg/h as bolus-during CPB) and fentanyl (1.5 μg/kg/h as bolus). Intraoperative monitoring included electrocardiogram, invasive arterial pressure, central venous pressure, pulmonary arterial pressure (for coronary artery bypass grafting), pulseoximetry (SpO_2) temperature, end-tidal expiratory CO_2 and blood gas analysis.

On CPB, mean blood pressure was kept above 50 mm Hg for normotensive patients and above 60 mm Hg for hypertensive patients[4] throughout the procedure. Blood sugars were maintained at <200 mg/dl. All patients were cooled to 28-32°C. In-line arterial filter or bubble trap was used. Blood was added when haemoglobin (Hb) was <7 g/dl on CPB, and <10 g/dl after bypass. All patients were rewarmed to 36.5°C.

Statistical analyses were performed with SPSS version 17 (SPSS, Chicago, IL, USA). Univariate analyses were performed by comparing patients with and without POCD (MMSE ≤ 24) using $|_2$ test, Fisher exact test, Student's *t* test, the Mann–Whitney U-test wherever applicable. $P < 0.05$ was considered as significant. Multivariate analyses were performed by forward stepwise logistic regression using the variables that were found to be significant on univariate analysis to identify independent predictors for POCD. Receiver operated curve analysis was performed for the number of blood units transfused and POCD to identify the best cut-off of the number of blood transfusions for POCD.

RESULTS

Of 121 patients, 21 were excluded as they were having a MMSE score <25. Further 15 patients were excluded; due to death (5), non-fatal stroke (2), reoperation (4), and reintubation (4). The association of the patient characteristics, examined comorbidities, intra-operative and post-operative factors and peri-operative and risk factors and POCD are shown in Table 1.

Variables with significant association with POCD were considered for multivariate 'logistic regression model', which identified the number of blood transfusion, as

a single independent predictor for the development of POCD on the 7th post-operative day [Table 2].

DISCUSSION

During cardiac surgery blood loss occurs from the surgical site, haemodilution and as the blood volume left in venous reservoir at the end of surgery, which necessitates blood transfusion. Cerebral embolization of the micro particulates (MPs) present in the stored blood is the main reason for cerebral injury. Red blood cells stored in the blood bank undergo a series of changes and release many potentially hazardous products, resulting in the so-called 'storage lesion.'[5] Studies has shown that, micro particulates released from blood cells exhibited strong procoagulant and proinflammatory activities.[6-9] The proinflammatory property of microparticulates (MP) causes cognitive dysfunction after CPB. MPs also contain Hb, which is a potent scavenger of nitric oxide (NO), which has been shown to modulate vascular contractility through NO pathway.[10]

In this study, we also identified that, patients with POCD had low peri-operative Hb, higher post-operative lactate values (24 h after surgery), and more than 2 blood transfusions. Even though blood loss and transfusions are not completely avoidable during cardiac surgery, measures, which will reduce the blood transfusion like use of antifibrinolytics and cell salvage techniques are advisable to reduce the incidence of POCD.

Limitations of this study are a small sample size, absence of intraoperative neurological monitoring, use of MMSE alone as neuropsychological test and cognitive function assessed only in the immediate post-operative period. The MMSE test was chosen because it is easy to perform and can be done even in patients with low educational standards.

Table 1: Prevalence of risk factors in cardiac patients with post-operative delirium (univariate analysis)

Variable	Mean (SD)		*P* value
	Patients with POCD	Patients without POCD	
n=85	*n*=32	*n*=53	
Age (years)	54.53 (9.83)	47.81 (12.24)	0.01
Pre-operative MMSE	26.91 (1.71)	28.02 (1.57)	0.003
ICU MMSE	22.0 (2.14)	25.26 (2.35)	0.004
CPB duration (mins)	148.63 (46.98)	136.34 (56.69)	0.30
IO Hb (g%)	7.27 (1.01)	8.09 (1.36)	0.004
PO Hb (g%)	10.64 (1.86)	11.50 (1.90)	0.04
Total blood transfusion (units)	4.71 (4.97)	2.47 (1.55)	0.003
BT on CPB			
Yes	26 9 (44.1%)	33 (55.9%)	0.06
No	6 (23.1%)	20 (76.9%)	
LOS ICU (days)	4.63 (1.77)	3.60 (0.94)	0.01
Sex			
Male	24 (38.1)	39 (61.9)	0.54
Female	8 (36.4)	14 (63.6)	
Surgery			
CABG	25 (54.3)	21 (45.7)	0.001
AVR	2 (12.5)	14 (87.5)	0.90
Other	5 (21.7)	18 (78.3)	0.002
DM			
No	15 (28.8)	37 (71.2)	0.036
Yes	17 (51.5)	16 (48.5)	
HTN			
No	16 (30.2)	37 (69.8)	0.56
Yes	16 (50)	16 (50)	
ICU MMSE≤24	30 (54.5)	2 (6.7)	0.00
Lactates at 24 h in ICU (mmol/l)	2.54 (1.52)	1.87 (1.22)	0.04

Data are presented as mean±SD or number of patients (percentage).
MMSE – Mini-mental state examination; ICU – Intensive Care Unit;
CPB – Cardio pulmonary bypass; IO – Intraoperative; PO – Post-operative;
Hb – Haemoglobin; LOS ICU – Length of stay in Intensive Care Unit;
CABG – Coronary artery bypass grafting; AVR – Aortic valve replacement;
DM – Diabetes mellitus; HTN – Hypertension; BT – Blood transfusion;
SD – Standard deviation; POCD – Post-operative cognitive dysfunction

Table 2: Multivariate, stepwise logistic regression analysis for predictors of POCD after cardiac surgery

Parameter	Exp (B)	95% CI for Exp (B)		Significance (*P* value)
		Lower	Upper	
Blood transfusion>2 units	4.315	1.592	11.701	0.004

CI – Confidence interval; POCD – Post-operative cognitive dysfunction

CONCLUSION

We conclude that POCD is a known, but less emphasised complication of blood transfusion. Multiple blood transfusions can predispose to POCD even in the absence of clinical conditions known to produce POCD. It is important to understand the burden of the POCD and reduce the need for transfusion in cardiac surgery.

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