Predictors of adverse neurological outcome following cardiac surgery

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ABSTRACT

Introduction: Stroke is a debilitating complication of cardiac surgery. Many intraoperative and postoperative factors predict the likelihood of post-cardiac surgery stroke. We evaluated preoperative parameters, seeking correlations with adverse neurological outcome following cardiac surgery. We investigated the possibility of preoperative carotid ultrasonography to select patients for carotid endarterectomy pre- or intraoperatively.

Methods: We conducted a retrospective analysis of 61 patients who suffered stroke post-cardiac surgery from 2003 to 2006. Data was collected for patient and disease characteristics, preoperative status, intraoperative events and postoperative course. Postoperative neurological complications were subdivided into three groups: mild/temporary events, moderate events such as seizures, and severe events such as stroke. A mild/temporary event was defined as a focal neurological deficit of less than 24 hours in duration.

Results: A total of 2,226 cardiac cases were retrospectively evaluated. The frequency of stroke was 61 patients (2.7 percent). The mean age of these patients was 63.7 +/− 7.4 years, and 40 (65.6 percent) were males. Logistic EuroSCORE, left ventricular ejection fraction (as determined by two-dimensional echocardiogram) and aortic cross-clamp time were significantly correlated with postoperative neurological complications, with a p-value of less than 0.05 for all subgroups. There was a significant correlation between the presence of preoperative carotid disease (as proven by pre- and postoperative carotid ultrasonography) and postoperative neurological events (p-value equals 0.033). However, atrial fibrillation did not correlate with postoperative stroke.

Conclusion: The stage of cardiac disease (risk factor level, ejection fraction and presence of carotid stenosis) correlates with stroke and may predict an adverse neurological outcome.

Keywords: cardiac disease, cardiac surgery, carotid endarterectomy, carotid stenosis, postoperative neurological complications, stroke

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INTRODUCTION

Stroke is a debilitating complication of cardiac surgery. It is an important cause of mortality and morbidity as well as increasing healthcare costs, as elderly and sicker patients are undergoing cardiac surgery. Over the past 20 years, there has been a steady increase in the average age of patients undergoing cardiac surgery.[1] This increase has been accompanied by a rise in both the severity of cardiac disease at the time of surgery and the reoperation rate for recurrent disease.[2] The rate of complications from cardiac surgery varies widely, and depends heavily on the thoroughness of preoperative neurological evaluation. The rates of complications can range from 7% to 61% for transient neurological deficits, and 1.6% to 23% for permanent deficits.[3-5] Prospective series showed the complication rates to be between 16.8% and 61%.[5,6] As this brings devastating outcomes for both patient and family and has an enormous social and economic impact, studies have been performed to elucidate the risk factors for post-cardiac stroke. Hogue et al showed that the presence of significant carotid artery stenosis was an independent predictor of early stroke.[7] Other studies have shown that embolisation is a major factor in neurological injury. Through the use of transcranial ultrasonography and carotid ultrasonography (CUS), they were able to demonstrate high rates of cerebral emboli during aortic interventions, including cannulation, aortic cross-clamping or unclamping, use of partial occlusion clamps and other non-aortic cardiac manipulations.[8-10]

In a study done by Toumpoulis and Anagnostopoulos, the EuroSCORE showed a good discriminatory ability in predicting stroke over 24 hours with a C-statistic (receiver operating characteristic curve) value of 0.73 among patients with heart valve surgeries.[11] Charlesworth et al showed that the risk of postoperative stroke is 1.89 times in patients with preoperative ejection fraction of less than

40%.[12] In addition, in a study done by Svedjeholm et al, multivariate forward stepwise logistic regression analysis revealed that aortic cross-clamp time is an independent risk factor for cerebral complications after coronary artery bypass grafting (CABG) and CABG combined with valve procedures, with an odds ratio of 1.03 (95% confidence interval 1.01–1.06, p = 0.002).[13] In the present study, we investigated perioperative parameters in patients with postoperative adverse neurological outcome, and sought for potential correlations.

METHODS

This is a retrospective analysis of a 61-patient population from January 2003 through December 2006 and who subsequently suffered stroke post-cardiac surgery. A total of 2,226 consecutive patients underwent cardiac surgery at the National University Hospital in this period. 1,671 (75.1%) patients underwent isolated CABG; 266 (11.9%) valvular surgery; 105 (4.7%) combined CABG and valvular surgery; 101 (4.5%) other types of cardiac surgery; 46 (2.1%) combined CABG and other types; 32 (1.4%) had combined valvular surgery and other cardiac procedures; and five (0.2%) combined CABG, valvular surgery and additional concurrent procedures.

We collected preoperative demographical, clinical and laboratory data using a standardised document for all patients, addressing the period from hospital entry to discharge. Preoperative variables include patient age, gender, ethnicity, body mass index (BMI), body surface area (BSA), status of surgery, EuroSCORE, New York Heart Association classification of angina, American Society of Anesthesiology classification, comorbidities, medications, smoking and alcohol, left ventricular ejection fraction (LVEF), serum creatinine level and use of intra-aortic balloon pump (IABP). Emphasis is placed on the presence of preoperative carotid disease, evidenced by pre- or postoperative CUS.

We examined intraoperative variables which included the type of surgery done, presence of carotid endarterectomy, number of diseased vessels, presence of aortic calcification, aortic cross-clamp time, cardiopulmonary bypass time, presence of intraoperative atrial fibrillation and use of intraoperative IABP. The presence of aortic calcification is a subjective assessment being done by the surgeon and is recorded as being present (severe) or absent. In addition, we evaluated postoperative outcomes that included mortality, neurological complications, low cardiac output syndrome, arrhythmia, acute myocardial infarction (AMI), congestive heart failure, serum creatinine for the first, second and third postoperative days, use of postoperative IABP and duration of stay in the hospital, use of intensive care unit and use of ventilation and intubation. Neurological complications were classified into three subgroups for the purpose of analysis; viz. stroke, seizures and mild/temporary deficits. Stroke was defined as a permanent, focal neurological deficit that persisted beyond one week, while mild/temporary neurological deficit was defined as a reversible neurological deficit that resolved within 24 hours. We used the Statistical Package for Social Sciences version 13.0 (SPSS Inc, Chicago, IL, USA) for statistic analysis. For patient demographics, comorbidities and outcome, we utilised descriptive analysis tools. We used the *t*-test for independent variables to compare between groups of numerical data, and the chi-square test to assess correlations between perioperative parameters on the ordinal scale and stroke. Statistical significance was assumed at $p < 0.05$.

RESULTS

There were a total of 61 (2.7%) patients who suffered neurological complications post-cardiac surgery. The mean age of the patients was 63.7 ± 9.4 years. 21 (34.4%) were females and 40 (65.6%) were males. There were 44 (72.1%) Chinese, 13 (21.3%) Malays, three (4.9%) Indians and one (1.6%) Eurasian (Table I). A sizeable number of them had comorbidities that included hypertension (78.7%), diabetes mellitus (55.7%), hyperlipidemia (75.4%) and AMI (60.7%). The incidence of cardiogenic shock, congestive cardiac failure (CCF), AMI, atrial fibrillation, hyperlipidaemia, hypertension, diabetes mellitus, cerebrovascular event and peripheral vascular disease were higher in patients with postoperative neurological complications (Table I). 39 (63.9%) patients were on beta blockers, 38 (62.3%) were on ACE inhibitors/AT II antagonists, 18 (29.5%) were on diuretics, 15 (24.6%) were on calcium channel blockers, 38 (62.3%) were on statins, and 32 (52.5%) were on aspirin and glyceryl trinitrate. 27 (44.3%) patients were smokers and 13 (21.3%) exhibited chronic alcohol abuse.

As for their preoperative status, five (8.2%) patients had preoperative atrial fibrillation. 27 (44.3%) patients belonged to New York Heart Association (NYHA) Class 3, 18 (29.5%) to NYHA Class 2, 14 (23.0%) to NYHA Class 4, and two (3.3%) to NYHA Class 1. There is a higher incidence of NYHA > 2 in patients with postoperative neurological complication (67.3%), when compared to patients without neurological complications (26.5%) (Table I).

Preoperative coronary angiography (Table I) showed that 47 (77.0%) patients had triple vessel disease, seven (11.5%) had double vessel disease, and two (3.3%)

Table 1. Patient characteristics.

Characteristics	Patients with neurological complications (n = 61)	All patients with cardiac surgery in 2003–2006 (n = 2,226)
Age* (years)	63.7 ± 9.4	59.2 ± 11.8
Body mass index* (kg/m^2)	19.4 ± 10.1	24.7 ± 4.3
Body surface area* (m^2)	1.6 ± 0.2	1.7 ± 0.2
Ethnicity (%)		
Chinese	72.1	68
Malay	21.3	16.1
Indian	4.9	10.8
Eurasian	1.6	0.9
Others	0	3.9
Risk factors (%)		
Female gender	34.4	23.0
Non-elective	44.3	36.5
NYHA > 2	67.3	26.5
Smoker	44.3	50.4
Preoperative IABP insertion	8.2	15.7
Cardiogenic shock	6.6	3.9
Congestive cardiac failure	24.6	10.2
Acute myocardial infarction	60.7	42.5
Atrial fibrillation	8.2	5.7
Hyperlipidaemia	75.4	69.1
Hypertension	78.7	68.9
Diabetes mellitus	55.7	46.2
Cerebrovascular event	24.6	8.4
Peripheral vascular disease	4.9	2.5
Pulmonary disease	8.2	11.9
Renal insufficiency	21.3	7.4
Coronary artery disease (%)		
Triple vessel disease	77.0	66.8
Double vessel disease	11.5	13.7
Single vessel disease	3.3	3.7
Intraoperative characteristics		
Type of surgery done (%)		
CABG	85.2	78.1
Valve	6.6	12.1
Combined CABG and valve	8.2	5.2
Aortic calcification		
Severe	3.3	–
None/mild	96.7	–
Intraoperative atrial fibrillation	6.6	–
Intraoperative IABP insertion	11.5	4.6

* data is expressed as mean ± standard deviation

CABG: coronary artery bypass grafting; IABP: intra-aortic balloon pump

had single vessel disease. The mean LVEF assessed by two-dimensional (2D) echocardiogram was 47.2 ± 16.7 %. IABP insertion was required pre-, intra- and postoperatively in five (8.2%), seven (11.5%) and five (8.2%) patients, respectively. 34 (55.7%) surgeries were performed electively; and 13 (21.3%) and 14 (23.0%) were performed as emergent and urgent cases, respectively. In these patients who suffered neurological complications post-cardiac surgery, 52 (85.2%) underwent isolated CABG, four (6.6%) underwent valvular surgery and five (8.2%) underwent combined CABG and valvular surgery. The mean cross-clamp time and cardiopulmonary bypass time were found to be 85.7 ± 39.8 minutes and 146 ± 67 minutes, respectively. Four (6.6%) patients developed atrial fibrillation intraoperatively.

In the 61 patients who suffered post-cardiac surgery neurological complications, mortality rate was 18.0%. 29 (47.5%) suffered stroke, another 29 (47.5%) suffered mild/temporary neurological events, and three (4.9%) suffered generalised tonic-clonic seizures. Other postoperative complications included low-cardiac output syndrome (3.3%), supraventricular arrhythmia (49.2%), AMI (1.6%) and CCF (1.6%) (Table II).

Postoperative CUS indicating carotid disease significantly correlated with postoperative neurological events (p = 0.033). Out of the 61 patients who suffered post-cardiac surgery neurological complications, a total of 15 (24.6%) postoperative CUS scans were performed

Table II. Carotid ultrasonographic findings in patients with neurological complications post-cardiac surgery and other postoperative events.

Carotid ultrasonographic (CUS) findings	Percentage of patients
Preoperative CUS done	21.3
Preoperative carotid disease picked up by preoperative CUS	19.7
Postoperative CUS done	24.6
Postoperative CUS indicating carotid disease	19.7
Postoperative characteristics (%)	
Neurological complications	2.7
Stroke	47.5
Seizures	4.9
Mild/temporary	47.5
Other postoperative complications	
Low cardiac output syndrome	3.3
Supraventricular arrhythmia	49.2
Acute myocardial infarction	1.6
Congestive cardiac failure	1.6
Postoperative IABP insertion	8.2
Death	18.0

and 12 (80%) indicated the presence of significant carotid artery disease, i.e. stenosis greater than 70% (Table II).

The logistic EuroSCORE of our 61 patients was found to be significantly correlated with stroke and seizures ($p = 0.025$) and with seizures and mild/temporary neurological events ($p = 0.044$). In addition, there was a significant correlation between LVEF and stroke and seizures ($p = 0.035$) and with seizures and mild/temporary neurological events ($p = 0.036$). Aortic cross-clamp time correlated significantly with stroke and seizures ($p = 0.004$) and with seizures and mild/temporary neurological events ($p = 0.001$). However, only a trend is found between NYHA grade and postoperative neurological events ($p = 0.053$). It is also noted that preoperative CCF and the presence of aortic calcification are both significantly correlated with the development of postoperative neurological events with p-values of 0.040 and 0.041, respectively.

In addition, there was an independent significant correlation between BMI and LVEF ($p = 0.022$) and between BMI and the use of intraoperative IABP ($p = 0.063$). BSA correlated with LVEF ($p = 0.004$) significantly. Besides correlations with neurological events, aortic cross-clamp time is found to significantly correlate with postoperative supraventricular arrhythmia ($p = 0.018$). Our analysis revealed that preoperative serum creatinine level and cardiopulmonary bypass time are both independently correlated with postoperative death with p-values of 0.018 and 0.022, respectively. Status of surgery did not correlate significantly with development of postoperative neurological outcome ($p = 0.618$).

DISCUSSION

Our analysis revealed that postoperative CUS indicating carotid disease significantly correlates with the occurrence of post-cardiac surgery neurological complications. This suggests that a preoperative CUS scan of high-risk patients will be useful in selecting patients for pre- or intraoperative carotid endarterectomy. Hogue et al demonstrated that severe left carotid artery stenosis correlates with the development of early stroke after cardiac surgery ($p = 0.0001$).[7] Furthermore, current knowledge that postoperative stroke is usually embolic in origin supports the observation that carotid artery stenosis is a significant contributor to post-cardiac surgery neurological complications. We found that logistic EuroSCORE and LVEF of the patients significantly correlate with the development of postoperative neurological events, and hence can be used clinically to predict the neurological outcomes of patients undergoing cardiac surgery. This is in keeping with current knowledge of this scoring system as it considers factors such as age, gender, neurological dysfunction and LVEF. These factors in turn have been cited to be significant predictors of post-cardiac surgery neurological complications. Roach et al demonstrated that age (per additional decade) increased the risk of a Type I cerebral outcome by 1.75 times and that of a Type II cerebral outcome (a new deterioration in intellectual function, confusion, agitation, disorientation, memory deficit, or seizure without evidence of focal injury) by 2.20 times. In addition, a history of neurological disease increased the risk of a Type I cerebral outcome (death due to stroke or hypoxic encephalopathy, non-fatal stroke, transient ischaemic attack, or stupor or coma at the time of discharge) by 3.19 times.[1]

Hogue et al also showed that the history of stroke was the strongest independent predictor of perioperative stroke and that the female gender is an independent risk factor for stroke.[7] In addition, Bucerius et al noted that

history of cerebrovascular disease (i.e. transient ischaemic attack, prolonged reversible ischaemic neurological deficit, stroke) was the strongest preoperative predictor of stroke with an odds ratio of 3.55. His patients with cerebrovascular disease had a 16.8% incidence of stroke, demonstrating the high risk associated with this variable.[14] Other investigators have demonstrated a 7%–13% incidence of postoperative stroke for patients with a history of previous neurological events.[15,16] This is in accordance with the current knowledge that a history of cerebrovascular disease denotes the existence of pathological conditions within the cerebrovascular system or an underlying stenosis of one or both carotid arteries, leading to embolisation into the internal carotid artery and subsequently into the cerebral circulation. A poor LVEF will result in poor cerebral perfusion which subsequently can lead to cerebral ischaemia and hence neurological deficits.

In view of the significant correlation between the length of aortic cross-clamp time and the development of postoperative neurological complications, reduction of the former will result in lower risk of developing postoperative neurological deficits. This is in accordance with Hogue et al, who showed that cross-clamp time significantly correlated with the occurrence of early and delayed postoperative stroke ($p = 0.046$).[7] In addition, Bucerius et al demonstrated that aortic cross-clamp time ≥ 1 hour was more prevalent in patients with stroke (35.1%) compared to only 21.5% of patients without stroke ($p < 0.0001$).[14]

We found a trend between NYHA classification of angina and the occurrence of postoperative neurological events, which suggests that a higher NYHA classification increases the risk of postoperative neurological complications, so the timing of surgery and optimisation of NYHA status are important. This is likely because patients with a reduced cardiac reserve are less able to tolerate the stresses of cardiac surgery, resulting in an increased risk of cerebral ischaemia as a result of reduced cerebral perfusion.

In addition, we found that preoperative CCF significantly correlates with postoperative neurological events. This is supported by Roach et al who found that CCF on the day of surgery increases the risk of Type II cerebral outcome by 2.46 (0.85–7.09) times.[1] However, Wolmen et al did not show any significant correlation between CCF and development of post-cardiac surgery neurological events.[17]

Aortic calcification was also found to significantly correlate with postoperative neurological events. This is supported by Hogue et al who showed that ascending aorta atherosclerosis is associated with increased risk of all strokes (odds ratio [OR] 1.1, $p = 0.007$), early strokes (OR 2.0, $p = 0.004$) and delayed strokes (OR 1.4, $p = 0.047$).[7] Our results are in accordance with current knowledge that embolic strokes can originate from atherosclerotic plaques in the ascending aorta.

We also found a significant correlation between BMI and LVEF, indicating that a higher BMI predicts reduced cardiac function. In addition, BMI was found to significantly correlate with the use of intraoperative IABP, suggesting that patients with increased BMI have lower cardiac reserves which require augmentation. This was shown by Wong et al who demonstrated that BMI correlated with the left ventricular ass and wall thickness, and severely-obese subjects ($BMI > 35\ kg/m^2$) had reduced LV systolic and diastolic function.[18] Ferraro et al also showed that a subclinical impairment of the LV systolic and diastolic functions occurred at rest and during exercise in asymptomatic severely-obese ($BMI > 31\ kg/m^2$) but otherwise healthy subjects.[19] However, studies were not conducted on moderately-obese individuals. There was also a significant correlation between BSA and LVEF.

Our analysis revealed that preoperative serum creatinine and cardiopulmonary bypass time are in compliance with the current general knowledge,[20-22] and is beyond the scope of our paper to comment on. In addition, we noted that aortic cross-clamp time correlated significantly with postoperative supraventricular arrhythmia. However, Nurözler et al found that there was no significant relationship between the development of atrial fibrillation and aortic cross-clamp time.[23] Tchervenkov et al observed a strong correlation between the duration of atrial activity during cardioplegic arrest and the incidence of postoperative supraventricular tachyarrhythmias,[24] suggesting the possibility that these arrhythmias may be a manifestation of inadequate atrial protection during global myocardial ischaemia.

There were several limitations to our study. First, our sample size might be too small to discern several trends between predictors and outcomes, especially borderline findings. Hence, certain parameters which could be significant in other studies appeared to be non-significant in ours. Second, there was significant heterogeneity in our study population with respect to the surgery performed. Also, neurocognitive decline after cardiac surgery was not included in our analyses. In summary, the neurological outcome correlated with a series of perioperative parameters that ought to be considered. These are preoperative carotid artery disease, preoperative CCF, logistic EuroSCORE, LVEF, aortic cross-clamp time and aortic calcification.

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