Neuropsychological Alterations After Coronary Artery Bypass Graft Surgery

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Abstract

Objective : To evaluate neuropsychological dysfunction in patients following elective coronary artery bypass graft surgery at Siriraj Hospital.

Patients and Method : One hundred and ten patients who were scheduled for elective coronary artery bypass graft surgery were included in this study. We used the Thai Mental State Examination (TMSE) in order to detect the presence of cognitive impairment after coronary artery bypass graft surgery. The examinations were conducted on two consecutive occasions; first preoperatively, the day before surgery, secondly on the third - fifth postoperative day. The patients' clinical characteristics were assessed perioperatively.

Results : The overall occurrence of neuropsychological deficit was 18.18 per cent. Predictors of neuropsychological dysfunction were older age and preexisting disease such as hypertension, hypercholesterolemia and renal insufficiency. Other risk factors such as gender, history of congestive heart failure, myocardial infarction, diabetes mellitus, dysrhythmia, cardiopulmonary bypass time, hemoglobin during cardiopulmonary bypass <7 g/dl, hemoglobin on admission to surgical cardiac care unit <10 g/dl, and atrial fibrillation arising after surgery were not significant.

Conclusion : Neuropsychological impairments after coronary artery bypass graft surgery are relatively common. This study did not find an increased incidence with respect to gender as other studies have done. However, long-term follow-up of these patients would be very valuable.

Key word : Neuropsychological Alterations, Coronary Artery Bypass Graft Surgery, Risk Factors

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Coronary artery bypass graft (CABG) surgery is used to treat angina pectoris and coronary artery disease. In Thailand approximately 500 patients undergo myocardial revascularization each year. At Siriraj hospital, this procedure is quite successful with a mortality rate of only 3 per cent. However after CABG surgery, patients may show cerebral complications which will increase the length of hospitalization and the cost of the treatment[1]. The most serious complication is stroke which has an incidence of approximately 3 per cent[1,2]. Other changes in cerebral function are neuropsychological dysfunction that occurs in 3-70 per cent of patients[1,3-6]. Patients with adverse cerebral outcomes had a mortality rate of 10-21 per cent which is increased 5-10 fold compared with patients who had no complications[1,7]. Microembolization and cerebral ischemia as a result of cardiopulmonary bypass and hypoperfusion are the presumed etiology of the cerebral dysfunction after cardiac operation[5,6]. Postoperative atrial fibrillation may also increase the incidence of neuropsychologic dysfunction due to cerebral ischemia from either hypoperfusion or microemboli[7].

Age, diabetes mellitus, history of excessive alcohol consumption pre-existing cardiac, cerebrovascular disease and cognitive impairment have all been identified as preoperative risk factors[1,4,8-12]. Intraoperative risk factors include prolonged cardiopulmonary bypass time, low body temperature during CPB, and an arterial line filter in the extracorporeal circuit[6,12,13].

We prospectively assessed the frequency of neurological alteration after CABG surgery at Siriraj Hospital. Possible preoperative and operative risk factors were also evaluated.

PATIENTS AND METHOD

The study was approved by the ethical clearance committee on human rights related to research involving human subjects of our institute. One hundred and ten patients who underwent elective CABG surgery at Siriraj Hospital between May 1997 and April 2000 were included in the study by systematic random sampling. Informed consent was obtained from every patient. The exclusion criteria were patients who had pre-existing cerebrovascular, neurological or psychological disease.

The neuropsychological assessments were performed using the Thai Mental State Exam (TMSE). This questionnaire is composed tests of orientation, registration, attention and calculation, language, recall and visual-motor integrity[14]. The patients were tested by the first author on two consecutive occasions; preoperatively and 3-5 days postoperatively. A patient whose postoperative score had dropped further than one standard deviation from the average preoperative score was defined as having neuropsychological deterioration.

Every patient was anesthetized by one of the first two authors and was operated on by either of the two surgeons. All patients received a standard anesthetic technique of a narcotic supplemented as necessary with a volatile agent to maintain hemodynamic stability. They were premedicated with an oral benzodiazepine, either midazolam or diazepam one hour before anesthesia. After premedication, supplementary oxygen was given until induction. On arriving at the theater the patients' pulse and blood pressure were monitored, and 2 peripheral intravenous catheters were inserted under local anesthesia.

After fentanyl 25 μg was given intravenously, radial and pulmonary artery catheter were placed respectively. Other intraoperative monitoring included an ECG lead II and V_5, oxygen saturation, capnograph, nasopharyngeal temperature, urine output, arterial blood gases, and potassium levels were measured at intervals during CPB. Anesthesia was induced with midazolam 1.5-3 mg, fentanyl 5 μg/kg, and thiopental 25-100 mg intravenously. Tracheal intubation was facilitated and neuromuscular blockade maintained by bolus doses of atracurium. If the patient had a history of asthma or allergy, vecuronium would be used instead. Anesthesia was maintained with nitrous oxide, oxygen, a continuous intravenous drip of fentanyl and 0.2-1 per cent isoflurane. Before going on to CPB, 300 heparin units/kg were given in order to maintain the ACT over 400 seconds during CPB. The bypass system consists of a membrane oxygenator and an arterial line filter. The mean arterial blood pressure during CPB was maintained at 50-70 mmHg. The patients were cooled to a nasopharyngeal temperature between 30-33°C. Protamine was given after coming off bypass to reverse the effect of the heparin. At the end of the operation, all patients were transferred to the surgical cardiac care unit for continued care and ventilatory support.

Statistical analysis

The descriptive data are presented as mean ± standard deviation and compared using paired sample *t*-test and independent sample *t*-test.

Chi-square test was used to compare differences in the groups with respect to neuropsychological deficit. Predictors of the presence of were performed using Stepwise logistic regression. Results were reported as odds ratios with an associated 95 per cent confidence interval. A p-value less than 0.05 was considered statistically significant.

RESULTS

One hundred and ten patients at Siriraj Hospital were enrolled in this study. There were 84 men and 26 women. The mean ages of the men and women were 61.49 ± 8.02 and 63.45 ± 6.10 years respectively which were statistically significantly different. The mean total scores on neuropsychological testing before and after surgery were 26.6 ± 8.02 and 25.31 ± 4.14 respectively which were statistically significantly different (Table 1). These results were the same as in older patients. But for patients aged under 65 years, there was no statistically significant difference between the pre-and postoperative mean total scores.

There were 20 (18.18%) patients who showed a difference between pre-and post-CABG scores ≥1 SD. There was no difference in the number of male and female patients who showed neuropsychological changes (Table 2). But there was a significant difference between patients aged <65 and ≥65 years. Postoperatively, twenty-three CABG surgery (20.91%) patients had an abnormal score for attention and calculation (Table 3).

Using univariate analysis, older patients were significantly at risk of neuropsychological deficit after CABG surgery (Table 4). Other factors that were found to be significant included a history of hypertension and hyperlipidemia. Recent congestive heart failure, myocardial infarction, and stroke were not found to be significant factors in this study. Intraoperative and postoperative factors including a hemoglobin less than 7 g/dl during cardiopulmonary bypass or less than 10 g/dl on admission to the surgical cardiac care unit, cardiopulmonary bypass time, new atrial fibrillation, and creatinine level were evaluated and revealed no significant differences in neuropsychological testing postoperatively.

A preoperative history of renal insufficiency was found to be a significant predictor of neuropsychological deterioration. (p=0.057, adds ratio (OR) =4.2, 95% CI, 1.02-17.36)

Table 1. Total TMSE scores as mean ± SD for preoperative and three-five day postoperative assessments in the group aged <65 years and the elderly group (≥65 years).

Groups of patient	Preoperative day	Postoperative day 3-5	P-value age	P-value pre- and postoperative
All age	26.60 ± 3.12	25.31 ± 4.14		0.00*
Age<65	26.85 ± 3.27	25.97 ± 3.65	0.38	0.01*
Age≥65	26.62 ± 3.19	24.57 ± 4.60	0.005*	0.004*

TMSE = Thai Mental State Exam.

Table 2. Patient characteristics.

Characteristics	Abnormal patients	%	Normal patients	%	P-value
Gender					
Men	15	75	69	76.7	1.0
Women	5	25	21	23.3	
Age (Y)					
<65	7	35	61	67.8	0.01*
≥65	13	65	29	32.2	
Total	20	100	90	100	

Abnormal patients = patients with a decrease of ≥1 SD on the Thai Mental State Exam (TMSE) scores between pre-and post-CABG.

Table 3. Number of patients with abnormal Thai Mental State Exam (TMSE) scores.

Subtest of TMSE	Number of abnormal patient	%
Orientation	18	16.36
Registration	10	9.09
Attention and calculation	23	20.91
Recall	20	18.18
Language	5	4.55
Visual-motor integrity	20	18.18
Total	20	18.18

Abnormal patients = patients with a decrease of ≥ 1 SD on each TMSE subtest between pre-and post-CABG scores.

DISCUSSION

Adverse cerebral outcome after cardiac surgery using cardiopulmonary bypass have been a concern for more than 50 years[15], because they are associated with prolonged hospitalization and increased cost of treatment. Family members may also report that patient is more short-tempered and has problems with mental arithmetic after CABG surgery.

In this prospective study, a total 110 patients undergoing CABG surgery were studied. The incidence of neuropsychological alteration at 3-5 postoperative days was 18.18 per cent. Our incidence was lower than Harrison MJG, et al. who reported an incidence as high as 77 per cent[5]. But a study reported by Hammon JW, et al. had an incidence of only 21 per cent[16]. In the past, studies were from a single institute. In 1996, Roach GW, et al. reported a prospective study involving 2108 patients from 24 U.S. institutions between 1991-1993[1]. They found that the incidence of patients who showed deterioration in intellectual function, memory deficit or seizures was 3 per cent (range 0-9.3%, varying from institute to institute). Patients who were at risk of neuropsychological alteration included those who were older, prior CABG surgery, a history of excessive alcohol consumption, dysrhythmia, a history of perivascular disease, pulmonary disease or a history of hypertension[1]. Our study also found that patients who were 65 years or older, or who had a history of hypertension or hypercholesterolemia were at risk of neuropsychological deterioration. Di Carlo A, et al. reported that age, sex, educational level, and the use of beta-adrenergic blockers were associated with neuropsychological alteration[17].

Table 4. Adjusted odds ratios for neuropsychological alteration associated with selected risk factors.

Factor	P-value	OR (95% CI)
Age : <65 yr/≥65 yr*	0.01	3.91 (1.41, 10.83)
Gender : Male/Female	1.0	1.09 (0.36, 3.37)
Preoperative history of		
Congestive heart failure	0.59	1.53 (0.52, 4.53)
Myocardial infarction	1.0	1.03 (0.35, 2.99)
Angina pectoris	1.0	1.9 (0.23, 16.12)
Diabetes mellitus	0.8	1.26 (0.48, 3.32)
Hypercholesterolemia	0.008	4.73 (1.56, 14.40)*
Renal disease	0.057	4.2 (1.02, 17.36)*
Dysrhythmia	1.0	1.09 (0.22, 5.61)
Valvular heart disease	0.42	1.77 (0.42, 7.35)
Hypertension	0.04	3.75 (1.10, 11.53)*
Recent congestive heart failure (<4 wk)	1.0	0.72 (0.15, 3.51)
Recent myocardial infarction (<4 wk)	0.76	0.75 (0.24, 2.34)
Recent stroke (<4 wk)	0.33	2.11 (0.37, 11.89)
Intraoperative factors		
During bypass hemoglobin	0.76	0.88 (0.26, 2.98)
Post-bypass hemoglobin	0.62	1.36 (0.49, 3.73)
CPB duration : <180/≥180 min	1.0	10.9 (0.41, 2.94)
Postoperative factors		
New atrial fibrillation	1.0	0.87 (0.22, 3.43)
Creatinine level >2 mg/dl	0.83	0.39 (0.14, 1.08)

CI = confidential interval.

The attention and calculation subtest gave the highest number of patients with abnormal scores. In order to performed calculation, one needs to memorize using the frontal lobe before doing the calculation which needs the temporal lobe[18]. Studies on experimental ischemia in amimals have shown that the hippocampal neurons are vulnerable to transient hypoxia[19]. Tufo HM, et al. reported that the hippocampal formation was the most common area showing anoxic changes in patients who died immediately after cardiac surgery[20]. So transient perioperative cerebral hypoxia is likely to be responsible for the neuropsychological deterioration that was observed in the postoperative period.

One of the problems involving in neuropsychological dysfunction after CABG surgery is increasing age. Generally elderly people tend to have brain dysfunction as well as after cardiac surgery [21,22]. Gender difference and educational level may have their effects on the study too. According to within-group variables, the study should have different subgroups eg. male, female, aged <65 year and aged ≥65 years. These four subgroups should each have their own control groups. The investigator may choose the control group from the spouse, a friend or senior citizen groups. However our study did not have enough patients to categorize in that way. The other problem was the practice effect. It may lead to a false positive showing neuropsychological improvement after surgery. Also boredom or sleepiness may result in a poor performance of test. Slade P, et al. has suggested that in approximately half of the patients the effect of brain dysfunction was greater than the practice effects, while the practice effect was greater for the other half of these patients[23].

The deterioration of neuropsychological function in the early postoperative period usually improves after a period of time[21,24]. Newman MF, et al. followed up 261 patients for 5 years and found that 53 per cent of patients had a cognitive decline at discharge[25]. At six weeks and six months, the incidences decreased to 36 per cent and 24 per cent respectively. The incidence of cognitive decline at five years post-CABG surgery increased to 42 per cent and found that it was predicted by the presence of cognitive decline at discharge.

There is still much to learn about the effect of neuropsychological alteration in patients undergoing CABG surgery on their daily life. Several interventions have been investigated in order to decrease the incidence of these complications such as off-pump CABG surgery[26] or the use of remacemide to protect the brain during cardiopulmonary bypass [27] are promising.

SUMMARY

This study is the first report involving neuropsychological alterations in Thai patients undergoing CABG surgery. An incidence of 18.18 per cent of neuropsychological deficits was found. Preoperative risk factors that were identified from this study were older age (≥65 years), a history of hypertension, hypercholesterolemia, and renal insufficiency. But we did not find that intraoperative and postoperative factors such as cardiopulmonary bypass time, hemoglobin less than 7 g/dl during cardiopulmonary bypass or less than 10 g/dl on admission to surgical cardiac care unit, new atrial fibrillation, and blood creatinine >2 g/dl were risk factors.

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การเปลี่ยนแปลงทางประสาทจิตวิทยาของผู้ป่วยที่มารับการผ่าตัดหลอดเลือดหัวใจโคโรนารีย์

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วัตถุประสงค์ : เพื่อศึกษาอุบัติการณ์การเกิดการเปลี่ยนแปลงทาง neuropsychology ในผู้ป่วยที่มารับการผ่าตัดหลอดเลือดหัวใจโคโรนารีย์ที่โรงพยาบาลศิริราชคณะแพทยศาสตร์ศิริราชพยาบาล รวมทั้งศึกษาถึงปัจจัยเสี่ยงด้วย

วิธีการศึกษา : ทำการศึกษาผู้ป่วยที่มารับการผ่าตัดหลอดเลือดหัวใจแบบไม่เร่งด่วนจำนวน 110 ราย โดยให้ผู้ป่วยทำแบบทดสอบ Thai Mental State Examination (TMSE) หนึ่งวันก่อนผ่าตัด และครั้งที่ 2 ในระยะ 3–5 วันหลังผ่าตัด

ผลการศึกษา : พบอุบัติการณ์การเกิดการเปลี่ยนแปลงทาง neuropsychology ร้อยละ 18.18 ปัจจัยเสี่ยงที่พบได้แก่ ผู้ป่วยอายุตั้งแต่ 65 ปีขึ้นไป ประวัติโรคความดันโลหิตสูง โรคไขมันในเลือดสูงและโรคไต ปัจจัยอื่นที่พบว่าไม่เป็นปัจจัยเสี่ยงของปัญหาทางระบบประสาทหลังการผ่าตัดหลอดเลือดหัวใจ ได้แก่ เพศ ระยะเวลาการใช้เครื่องปอดและหัวใจเทียม ค่าฮีโมโกลบินในระหว่างการใช้เครื่องปอดหัวใจเทียมน้อยกว่า 7 กรัม/ดล หรือน้อยกว่า 10 กรัม/ดล เมื่อแรกรับเข้าหออภิบาล รวมถึงภาวะ atrial fibrillation ที่เกิดใหม่หลังผ่าตัด และระดับ creatinine ในเลือดหลังผ่าตัด >2 กรัม/ดล

สรุป : ภายหลังการผ่าตัดหลอดเลือดหัวใจอาจเกิดภาวะแทรกซ้อนทางระบบประสาทได้ การศึกษาครั้งนี้ไม่พบว่าเพศเป็นปัจจัยเสี่ยงต่อการเกิดภาวะแทรกซ้อนนี้ อย่างไรก็ตามควรจะได้มีการติดตามศึกษาการดำเนินโรคต่อไป

คำสำคัญ : การเปลี่ยนแปลง neuropsychology, การผ่าตัดหลอดเลือดหัวใจ, ปัจจัยเสี่ยง

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