Incidence and risk factors for early postoperative cognitive decline after coronary artery bypass grafting

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***Key words**: cognitive dysfunction; neurological complications; coronary artery bypass grafting.*

***Summary.** Background. The aim of our study was to evaluate the incidence of early postoperative cognitive decline (POCD) and determine perioperative risk factors as well as the impact of asymptomatic cerebral vascular lesion on the development of neurocognitive complications.*

Materials and methods. A total of 127 consecutive adult patients undergoing on-pump coronary artery bypass grafting were studied. Neuropsychological testing was performed the day before surgery and 7–9 days after operation. Stepwise logistic regression analysis determined independent predictors of POCD.

Results. The incidence of postoperative cognitive decline was 46% (n=59). Patients in the POCD group were older (P=0.04) and had an increased prevalence of asymptomatic carotid artery stenosis (P=0.0001). POCD was associated with longer time in surgery (P=0.018), inotropic support intraoperativelly (P=0.02) and during postoperative period (P=0.008). Patients in the POCD group had an increased incidence of postoperative bleeding (P=0.037), delirium (P=0.016) and stayed in hospital for a longer period (P=0.007). Age of more than 65 years (OR, 2.7), asymptomatic carotid artery stenosis of more than 50% (OR, 26.89), duration of surgery of more than 4 hours (OR, 4.08), postoperative mechanical ventilation of more than 6 hours (OR, 3.33), and stay in an intensive care unit for more than 3 days (OR, 3.38) were significant independent predictors of cognitive decline.

Conclusions. Increased age, preoperative prevalence of craniocervical atherosclerotic lesions, longer time in surgery, longer stay in an intensive care unit and mechanical ventilation time were found to be the risk factors for developing postoperative cognitive decline.

Introduction

During recent decades, success of the surgical treatment is defined not only by the absence of postoperative complications and mortality rates, but also by the quality of life of a patient after surgery. Extensive studies of neuropsychological disturbances following heart surgery showed that memory, concentration, language, and comprehension disturbances are frequent phenomena occurring early postoperatively, with an incidence varying from 30 to 60% (1, 2). It was noticed that early postoperative cognitive decline (POCD) was not only the sign of later neurological damage, manifesting years after surgery, but also a marker with important prognostic and clinical implications, related with increased morbidity and mortality rates (3). Nevertheless, neuropsychological complications are rarely detected and often taken into account as a natural part of postoperative course. Moreover, the number of investigators found that cognitive decline influences recovery process and strongly affects postoperative well-being of the patient (4, 5). The aim of our study was to evaluate the extent of early POCD in a low-risk patient group and to determine related perioperative risk factors as well as the impact of asymptomatic cerebral vascular lesion in the development of cognitive decline.

Materials and methods

Study population. Study population consisted of 127 consecutive adult patients undergoing on-pump coronary artery bypass grafting (CABG) at Vilnius University Hospital Santariškių Klinikos. The study was approved by regional Bioethics Committee, and the informed consent was obtained from all the patients. We applied the following exclusion criteria: age more than 70 years, preexisting neurological impairment or evident preoperative cognitive decline (MMSE <24), cardiac ejection fraction lower than 35%, diabetes requiring insulin therapy, renal failure, physical condition disabling the performance of neuropsychological tests, symptomatic peripheral vascular disease, and inability to read or speak Lithuanian. Baseline demographics,

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operative data, and postoperative outcomes were recorded using a standardized data entry form and were included in a computerized database. All patients underwent preoperative ultrasound examination of craniocervical arteries. There were no differences in anesthesia and surgical techniques between two groups.

Neuropsychological assessment. All patients underwent a battery of neuropsychological tests the day before surgery and at 7–9 days after the CABG, before the discharge from hospital. To optimize the reliability of the evaluation, cognitive test battery was done by the same physician. The neuropsychological testing followed the consensus statement on the assessment of disorders of the central nervous system after cardiac surgery (6). It included Mini-Mental State Examination, Rey Auditory Verbal Learning Test, Trail-Making Test (part A), Trail-Making test (part B), Digit span, Digit Symbol Substitution Test (DSST), Cube Drawing test. Preoperative emotional status was assessed using the Hospital Anxiety and Depression Scale (HADS) and Geriatric Depression Scale (GDS). Delirium was defined according to the Diagnostic and Statistical Manual for Mental Disorders (DSM IV). Cognitive decline was defined as a decrease of one standard deviation or more in performance of at least two neurocognitive tests.

Statistical analysis. Variables potentially related to cognitive dysfunction were considered in 3 categories: preoperative, intraoperative, and postoperative. Continuous data were expressed as the mean±SD. Multivariate logistic regression analysis was conducted to determine independent predictors of POCD. The criterion for a variable entry into logistic model was an unvaried probability level of $P<0.05$. A value of $P<0.05$ was considered statistically significant. Statistical analysis performed by using the Statistical Package for the Social Sciences program (SPSS 17).

Results

Preoperative characteristics. Of the 127 patients enrolled in this study, postoperative cognitive dysfunction was detected in 46% (n=59) of patients. Subjects in the POCD group were significantly older (mean age, 62.3±6.7 vs. 59.8±7.8 years; $P=0.04$). No statistically significant differences were found in the prevalence of hypertension, previous myocardial infarction, cardiac arrhythmia, left main disease, NYHA, ejection fraction, or diabetes mellitus comparing the groups (Table 1). Although patients of both groups were at low risk evaluated by EuroSCORE, overall comorbidity level was significantly higher in patients with postoperative cognitive impairment (3.5±2.3 vs. 2.5±2, $P=0.009$).

Prevalence of carotid artery stenosis. Almost half of the study population (n=64, 50.3%) undergoing CABG had alterations of carotid and intracerebral arteries of various degree, detected by ultrasound. The frequency of carotid artery lesions of various

Table 1. Comparison of preoperative patient characteristics

Characteristic	POCD N=59, 46%	Without POCD N=68, 54%	*P* value
Age, mean±SD, years	62.2±6.7	59.8±7.7	0.04
Male, n (%)	49 (79.7)	54 (79.4)	NS
Smoking history, n (%)	18 (30.5)	14 (20.6)	NS
Body mass index, mean±SD, kg/m^2	27.7±10.3	28.7±9.1	NS
NYHA, mean±SD	3±0.1	3±0.4	NS
Left main disease, n (%)	16 (32.4)	22 (27.1)	NS
Previous myocardial infarction, n (%)	23 (39)	32 (47)	NS
Myocardial infarction <90 days, n (%)	8 (13.6)	6 (8.8)	NS
Ejection fraction, mean±SD, %	48.5±8	50.5±8.4	NS
Arterial hypertension, n (%)	54 (91.5)	61 (89.7)	NS
History of cardiac arrhythmia, n (%)	6 (10.2)	6 (8.8)	NS
Diabetes mellitus, n (%)	8 (13.6)	7 (10.3)	NS
Hb preoperatively, mean±SD, g/L	142.3±13.2	138 ±12.1	NS
EuroSCORE, mean±SD	3.5±2.3	2.5±2	0.009

POCD, postoperative cognitive decline; NS, not significant; NYHA, New York Heart Association; EuroSCORE, European System for Cardiac Operative Risk Evaluation.

Table 2. Prevalence of carotid artery stenosis

	POCD	Without POCD	*P* value
Without carotid artery lesion (n=63, 49.6%)	18 (28.6%)	45 (71.4%)	0.0001
Carotid artery stenosis <50% (n=38, 30%)	18 (47.4%)	20 (52.6%)	0.007
Carotid artery stenosis >50% (n=26, 21%)	23 (88.5%)	3 (11.5%)	0.0001

POCD, postoperative cognitive decline.

degrees in both the groups is presented in Table 2. Half of the patients in the POCD group (n=18, 47.4%) had asymptomatic carotid artery stenosis less than 50% (P=0.007). In cases, when carotid stenosis of more than >50% was detected, POCD occurred with an incidence of 88.5% (P<0.0001). The incidence of POCD in patients without any atherosclerotic alterations in craniocervical arteries was 28.6% (n=18).

Operative and postoperative variables. Operative and postoperative data are presented in Table 3. Patients experiencing postoperative cognitive dysfunction had a significantly longer inhospital waiting period for surgery (7.0±5.0 vs. 5.3±3.7min, P=0.03). Duration of operation (220.9±47.2 vs. 202.6±38.6 min, P=0.018) and reperfusion time (37.5±17.3 vs. 30.9±11 min, P=0.012) were significantly longer in POCD group. Meanwhile, the comparison of CPB and aortic cross-clamp time did not show any difference. Patients with postoperative cognitive decline experienced intraoperative and postoperative hemodynamic instability with the need of inotropic support significantly more often (P<0.05). Comparing other postoperative variables, the POCD group more often experienced increased bleeding, comparing chest tube drainage during the first 48 hours (802.4±521.2 vs. 620.7±334.3 mL, P=0.037), atrial fibrillation (7.8% vs. 3.1%, P=0.01), postoperative delirium (11.9% vs. 1.5%, P=0.016), and finally had longer postoperative hospital stay (20.3±15.9 vs. 14.8±5.4 days, P=0.007). Multivariate stepwise regression analysis (Table 4) showed that preoperative independent risk factors for cognitive decline were age more than 65 years (OR, 2.78; CI, 1.13–6.85) and asymptomatic carotid artery stenosis of more than 50% (OR, 26.89; CI, 6.44–112.34). Development of POCD was influenced by time in surgery; surgery lasting more than 6 hours (OR, 4.08; CI, 1.26–13.20) was an independent risk factor of cognitive deterioration. From all postoperative variables, controlled mechanical ventilation lasting more than 6 hours and stay in an intensive care unit (ICU) more than 3 days were the strongest predictors of POCD (OR, 3.33; CI, 1.22–9.10, and OR, 3.83; CI, 1.3–11.29).

Table 3. Comparison of intraoperative and postoperative variables

Variable	POCD N=59, 46%	Without POCD N=68, 54%	P value
Days in hospital waiting for surgery, mean±SD	7.0±5.0	5.3±3.7	0.03
Operative variables			
Operation time, mean±SD, min	220.9±47.2	202.6±38.6	0.018
CPB time, mean±SD, min	99.2±28.9	93.2±21.3	NS
Aortic clamp time, mean±SD, min	60.8±15.5	56.8±14.7	NS
Reperfusion time, mean±SD, min	37.5±17.3	30.9±11	0.012
Number of distal anastomosis, mean±SD	3.8±1.1	3.5±1.1	NS
Minimal nasopharyngeal temperature, mean±SD, C°	33.7±1.4	33.4±4.2	NS
Lowest intraoperative Hb, mean±SD, g/L	96.4±16.5	100.6±17.7	NS
Intraoperative fluid balance, mean±SD, mL	2969.8±1012.8	2342.13±717	0.0001
Inotropic support intraoperativelly, n (%)	13 (22)	5 (7.4)	0.02
Postoperative variables			
Postoperative inotropic support, n (%)	24 (64.9)	13 (35.1)	0.008
Lowest intraoperative Hb, mean±SD, g/L	104.2±17.6	110.1±18	0.06
Lowest hematocrit, mean±SD	27.8±7.7	31.4±13.0	NS
CMV duration, mean±SD, min	583.9±564.6	459.0±456.4	NS
Chest tube drainage, mean±SD, mL	802.0±519.8	620.7±334.3	0.037
Atrial fibrillation, n (%)	10 (7.8)	4 (3.1)	0.01
Delirium, n (%)	7 (11.9)	1 (1.5)	0.016
ICU stay, mean±SD, days	2.3±1.5	1.7±0.9	0.01
Inhospital stay, mean±SD, days	20.3±15.9	14.8±5.4	0.007

NS, not significant; POCD, postoperative cognitive decline; CPB, cardiopulmonary bypass; CMV, controlled mechanical ventilation; ICU, intensive care unit.

Table 4. Multivariate logistic regression analysis of risk factors associated with postoperative cognitive decline

Factor	Odds ratio	95% confidence interval	P value
Age >65 years	2.78	1.13–6.85	0.025
Carotid artery stenosis >50%	26.89	6.44–112.34	<0.001
Operation time >240 min	4.08	1.26–13.20	0.019
CMV ⩾360 min	3.33	1.22–9.10	0.019
ICU stay ⩾3 days	3.83	1.3–11.29	0.015

CMV, controlled mechanical ventilation; ICU, intensive care unit.

Discussion

Cardiac surgery is associated with cognitive decline in a substantial proportion of population undergoing coronary artery bypass grafting. In our study, all patients were attributed to low risk group for developing adverse neurological events (7); therefore, the incidence of early POCD (46%) was lower comparing with the data of previous studies (1, 2). In contemporary medical literature, the occurrence of postoperative cognitive decline is explained mainly by three mechanisms: intraoperative cerebral microembolism, hypoperfusion and systemic inflammatory response, and ischemic injury (8).

First of all, according to our data, susceptibility to cognitive decline was significantly higher in patients subjected to asymptomatic, hemodynamically significant alterations of carotid arteries. This is an important finding supported by data of previous studies, indicating the relationship between cerebral vascular lesion and cognitive function (9, 10). Authors hypothesize that deterioration of cognitive function in patients with chronic hypoperfusion of the brain might be a result of decreased cerebral reserve and increased vulnerability to perioperative fluctuations of hemodynamics, or microembolism (11, 12).

Impact of cardiopulmonary bypass on postoperative neurological outcomes is still controversial. We did not find any associations between cognitive decline and duration cardiopulmonary bypass time. On the other hand, the duration of surgery appeared to be an independent predictor of cognitive impairment. As well as previous investigators, we assume that this finding could be related with increased exposition to anesthesia and embolic load during surgery (12). Although both the groups of patients, evaluated by EuroScore, were at low risk for developing unfavorable outcomes, patients with cognitive decline had a higher risk score and more stressful postoperative period. Our data confirmed that hypotension and inotropic support, even in the absence of cardiovascular events, might contribute to cognitive abnormalities (13). Another important finding is that cognitive damage was independently predicted by duration of mechanical ventilation and ICU stay. Therefore, we agree with previous studies confirming the negative impact of prolonged sedation on mental status and furthermore postoperative cognition (14). Application of early CMV weaning protocols could benefit for the patients, which are at increased risk for development of postoperative neuropsychological damage. In the present study, we were exploring the influence of perioperative factors on cognitive performance in subjects without any evidence of ischemic cerebral lesions. The presence of a direct relationship between carotid artery stenosis and cognitive performance was the main finding. Therefore, our data confirm previous reports that cognitive failure is a prognostic symptom of underlying cerebrovascular pathology, becoming evident due to decreased cerebral reserve and enhanced by hemodynamic instability (15). Due to low number of patients included in our study, it is not possible to make far-reaching conclusions; nevertheless, we state that identification of patients with preoperative atherosclerotic lesion of the cerebral vasculature and increased risk of postoperative neurocognitive impairment might provide a rational basis for recommendations toward its prevention.

Conclusions

Demographic aging and progress in cardiac surgery techniques, allowing operating on patients at higher surgical risk, will result in an increasing number of neurological complications after heart surgery in the nearest future. Postoperative cognitive disorder is a frequent complication, detected almost in every second patient after CABG at our institution during early postoperative period. Increased age, preoperative prevalence of craniocervical atherosclerotic lesions, longer operation and mechanical ventilation time were found to be the risk factors for developing postoperative cognitive dysfunction.

Pažinimo funkcijų sutrikimai po miokardo apeinamųjų jungčių suformavimo operacijų: dažnis ir rizikos veiksniai

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Raktažodžiai: pažinimo funkcijų sutrikimai, neurologinės komplikacijos, miokardo apeinamųjų jungčių suformavimo operacijos.

Santrauka. *Tyrimo tikslas.* Nustatyti pažinimo funkcijų pažeidimo dažnį po miokardo apeinamųjų jungčių suformavimo operacijų, išaiškinti rizikos veiksnius, turinčius įtakos šiai komplikacijai rastis, bei įvertinti sąsajas tarp besimptomės miego arterijos stenozės ir pažinimo funkcijų disfunkcijos sutrikimų.

Tyrimo medžiaga ir metodai. Į tyrimą įtraukti 127 pacientai, kuriems atliktos apeinamųjų jungčių suformavimo operacijos su dirbtine kraujo apytaka. Pažinimo funkcijų ištyrimas buvo atliekamas vieną dieną prieš ir 7–8 dienas po operacijos devynių neuropsichologinių testų rinkiniu.

Rezultatai. Pažinimo funkcijų sutrikimų nustatyta 59 pacientams (46 proc.). Šie pacientai buvo vyresnio amžiaus (p=0,04), jiems dažniau nustatytas besimptomis miego arterijos pažeidimas (p=0,0001). Pažinimo funkcijų sutrikimai buvo susiję su ilgesne operacijos trukme (p=0,018) ir nestabilia hemodinamika, kuriai koreguoti prireikė inotropinių vaistų infuzijos: operacijos metu (p=0,02) bei pooperaciniu laikotarpiu (p=0,008). Pažinimo funkcijų sutrikimų grupėje dažniau pasireiškė padidėjęs kraujavimas (p=0,037) ir delyras (p=0,016). Šie pacientai buvo ilgiau gydomi reanimacijoje bei ligoninėje (p=0,007). Multivariacinės analizės metu nustatyta, kad amžius daugiau nei 65 metai (GS (galimybių santykis) 2,7), hemodinamiškai reikšmingas miego arterijos susiaurėjimas (GS 26,89), ilgesnė nei 4 valandų operacijos trukmė (GS 4,08), mechaninė plaučių ventiliacija, trukusi ilgiau kaip 6 valandas (GS 3,33), bei paciento gydymas intensyviosios terapijos skyriuje ilgiau kaip tris dienas (GS 3,38) yra veiksniai, turintys tiesioginę įtaką pooperaciniams pažinimo funkcijų sutrikimams.

Išvados. Vyresnis amžius, besimptomė miego arterijos stenozė, operacijos, dirbtinės plaučių ventiliacijos bei gydymo intensyviosios terapijos skyriuje trukmė yra pažinimo funkcijų sutrikimo, atsirandančio ankstyvuoju pooperaciniu laikotarpiu, rizikos veiksniai.

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Received 11 November 2009, accepted 8 July 2010
Straipsnis gautas 2009 11 11, priimtas 2010 07 08