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# PROGNOSTIC ROLE OF EEG INDICATORS FOR CHANGES IN COGNITIVE PERFORMANCE IN PATIENTS IN THE EARLY AND LONG-TERM POSTOPERATIVE PERIODS OF CORONARY ARTERY BYPASS GRAFTING

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**Aim** To study the prognostic role of background EEG activity indicators recorded in patients in the preoperative period of coronary artery bypass grafting (CABG) for the development of cognitive impairment in the early and late postoperative periods.

**Methods** A total of 85 patients with coronary artery disease (CAD) who underwent CABG were included in the study. Before CABG (3-5 days) all neuropsychological testing and EEG studies were performed, at the 7-10th days and 1 year after CABG - only neuropsychological testing. EEG predictors of early (n = 85) and long-term (n = 65) postoperative cognitive dysfunction were detected using the method of multiple linear regression.

**Results** EEG predictors of deterioration of cognitive status in the early postoperative period of CABG were basic higher values of theta-rhythm power in the posterior regions of the cortex of both hemispheres with closed and open eyes. Whereas higher preoperative parameters of beta2-rhythm biopotentials in the left frontal areas with eyes open and lower alpha-rhythm power in the left occipital parts of the cerebral cortex with eyes closed were associated with long-term postoperative cognitive dysfunction.

**Conclusion** Associations of preoperative EEG indicators with deteriorations of cognitive status in the early and long-term postoperative periods of CABG were revealed.

**Keywords** Postoperative cognitive dysfunction • EEG rhythms • Coronary artery bypass grafting

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**Abbreviations**

| | | | | | |
|---|---|---|---|---|---|
| CABG | – | coronary artery bypass grafting | MMSE | – | Mini-Mental State Examination |
| CAD | – | coronary artery disease | FAB | – | Frontal Assessment Battery |
| EEG | – | electroencephalography | BDI-II | – | Beck Depression Inventory-II |

## Introduction

Postoperative cognitive dysfunction is common after coronary artery bypass grafting (CABG) and is associated with reduced effectiveness of surgical treatment, increased length of in-hospital stays, as well as their prolonged rehabilitation period. Moreover, it results in patients' disability and poor quality of life [1, 2]. Researchers believe there are several factors that might contribute to the decline in cognitive performance during on-pump coronary artery bypass grafting, such as the release of micro-emboli during the cardiopulmonary bypass, hypoperfusion, the onset of systemic inflammatory response syndrome, which result in neuronal damage [1, 3]. Therefore, there is a need for using informative and sensitive methods that might be potentially beneficial for prediction of postoperative brain damage and cognitive impairment after cardiac surgeries.

Electroencephalography (EEG) monitoring is worthwhile diagnostic tool for detecting ischemic brain damage with high sensitivity and temporal resolution and moderate specificity [4, 5]. Previous studies have shown the prognostic significance of EEG changes for the progression of the neurodegenerative type of cognitive impairment [6, 7]. Thus, it is relevant to assess the prognostic role of preoperative background EEG activity in patients referred to elective CABG for the development of cognitive impairment in the early and long-term postoperative periods.

## Methods

*Study Population*

Written informed consent was obtained from all study participants. The study design was approved by the Local Ethics Committee of the Research Institution. Only those patients who did not have organic lesions in the central nervous system based on neurologic examination and CT scan of the brain were enrolled in the study. The inclusion criteria for patients with coronary artery disease were as follows:

1. Age of patients from 45 to 69 years old
2. Elective CABG
3. Written informed consent

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4. Male gender
5. Right-handers

Patients over 70 years who have significant carotid artery stenosis (over 50%), life-threatening rhythm disturbances, chronic heart failure II B and III stages according to the Vasilenko-Strazhesko classification, severe comorbidities (chronic obstructive pulmonary disease, hepatic failure, neoplastic disease), suffers from alcohol abuse, takes psychoactive substances, have central nervous system diseases and prior cerebrovascular accidents were excluded from the study. We also excluded subjects with the sum-score on the Mini-Mental State Examination (MMSE) ≤24, the Frontal Assessment Battery (FAB) score ≤11 and the Beck Depression Inventory (BDI-II) ≤8, as well as those who refused to participate in the study.

A total of 85 patients were included in the study. Table 1 presents the preoperative clinical and demographic data of the study population.

All the patients were treated with basic, symptomatic therapy for coronary artery disease, chronic heart failure (CHF) and arterial hypertension according to the National guidelines (2013, 2014). All patients were recommended a low-salt (<1.5 g/day) and low-cholesterol diet. Patients commonly received beta-blockers (bisoprolol fumarate 5-10 mg per day), statins (rosuvastatin 20 mg per day), angiotensin converting enzyme inhibitors (enalapril maleate 5-40 mg per day or perindopril 5-10 mg per day) and antiplatelet agents (aspirin). If indicated, patients received indirect anticoagulants (unfractionated heparin 20,000 IU monitored by the activated partial thromboplastin time (aPTT) or clexane 0.8 mg per day by subcutaneous injection), calcium antagonists (amlodipine 2.5-10 mg per day), nitrates (isosorbide dinitrate 40- 80 mg per day) and angiotensin II receptor blockers (losartan 12.5-50 mg or candesartan 150-300 mg per day). All patients underwent routine preoperative management, including estimation of fluid and electrolyte balance, measurement of body weight, blood pressure and diuresis, as well as serial electrocardiography and echocardiography.

**Table 1. Preoperative clinical and demographic data of patients undergoing on-pump CABG**

| Parameters | Patients (n = 85) |
|---|---|
| Age, M±σ, years | 56.5±5.11 |
| Duration of CAD, M±σ, years | 3.9±4.92 |
| SYNTAX, M±σ, score | 23.3±8.04 |
| MMSE, M±σ, score | 27.8±1.31 |
| Trait anxiety, M±σ, score | 38.1±6.01 |
| Beck Depression Inventory-II, M±σ, score | 2.65±1.67 |
| Education, n (%) | |
| secondary | 59 (69) |
| higher | 26 (31) |
| Arterial hypertension, n (%) | 74 (87) |
| Carotid artery stenosis <50%, n (%) | 30 (35) |
| Diabetes mellitus, n (%) | 23 (27) |
| NYHA functional class, n (%) | |
| II | 53 (62) |
| III | 32 (38) |
| Angina functional class, n (%) | |
| I-II | 71 (84) |
| III | 14 (16) |

All patients underwent elective normothermic CABG with extracorporeal circulation performed according the standard perfusion protocol. The anesthesia (diprivan, fentanyl, sevoflurane) and endotracheal intubation was used in all cases. Intraoperative invasive monitoring of hemodynamics and cerebral cortex oxygenation (rSO2) was performed. There were no cases of hypotension and cerebral hypoxia observed.

*Neuropsychological testing*

Neuropsychological examination was performed in 2 stages. First, all patients underwent primary neuropsychological screening using the MMSE and FAB scales for the further patient enrollment into the study.

Cognitive performance was preoperatively assessed in all recruited patients using the software package "Status PF". The assessment protocol and detailed description of the neuropsychological battery are presented in [8, 9].

Neuropsychological examination was performed on days 3-5 before surgery, days 7-10 and 1 year after CABG. The integral index of cognitive status was calculated according to the procedure described by O.L. Barbarash and O.A. Trubnikova [8]. This index allowed assessing the initial neuropsychological status of patients using computerized tests and comparing it with the MMSE scores.

*EEG Recording*

High-resolution monopolar EEG recordings in relaxed wakefulness with eyes closed and open were made in patients 3-5 days before elective CABG. All recordings were made in the first half of the day in light- and sound-proof rooms. The Scan 4.5 software and Neuvo SynAmps2 System amplifier (Compumedics, Charlotte, NC, USA) were used (more details were previously described in [10]).

The total power specified in each frequency band was recorded as well as the power for each frequency band with eyes closed and open. EEG power data were performed on five clusters in each hemisphere, such as frontal (Fp1/2, AF3/4, F1/2, Fp3/4, Fp5/6, F7/8), fronto-central (FC1/2, FC3/4, FC5/6, C1/2, C3/4, C5/6), temporal (FT7/8, T7/8, TP7/8), centro-parietal (CP1/2, CP3/4, CP5/6, P1/2, P3/4, P5/6, P7/8) and occipital (PO3/4, PO5/6, PO7/8, O1/2) in each frequency range. The midline sites were excluded from the further analysis.

*Statistical analysis*

Statistical analysis was carried out using commercially available software package STATISTICA 8 (StatSoft, USA). The analysis of the EEG predictors of postoperative cognitive dysfunction was performed using the multiple linear regression and stepwise approach.

## Results

There were no significant adverse cardiovascular events, such as death, stroke, myocardial infarction and redo myocardial revascularization among the recruited patients in the early and long-term postoperative period of CABG. No cases of repeated hospitalizations due to cardiovascular causes were observed.

**Table 2. Regression model for cognitive decline in patients on days 7-10 after on-pump CABG**

| | Beta | St.Er. - beta | B | St.Er. - B | t | p |
|---|---|---|---|---|---|---|
| Intercept | | | 0,526 | 0,047 | 11,14 | 0,0000001 |
| FR_L_01_T1 | 0,456 | 0,178 | 0,488 | 0,190 | 2,56 | 0,01 |
| O_R_01_T2 | -0,383 | 0,148 | -0,384 | 0,149 | -2,58 | 0,012 |
| FC_R_Z1_A1 | 0,282 | 0,126 | 0,102 | 0,046 | 2,24 | 0,028 |
| CP_L_01_T1 | -0,203 | 0,196 | -0,248 | 0,239 | -1,04 | 0,30 |

Multiple regression models were constructed to determine the predictive role of baseline EEG parameters for the decline cognitive performance in the early (7-10 days after CABG) and long-term (1 year after surgery) postoperative periods. The integral index of cognitive status on days 7-10 and 1 year after CABG was used as the dependent variable. The independent variable included the mean EEG power data for five cortex regions located symmetrically in the left and right hemispheres in theta-1,2, alpha -1,2 and beta-1,2 frequency bands.

Previously, exploratory data analysis was performed to identify the most significant indicators in each frequency band, which were subsequently used for the general regression models to predict the development of cognitive dysfunction in patients in the early and long-term postoperative periods.

Data of 85 patients were used to construct prediction model for early cognitive decline. We have found that theta and alpha power has the greatest prognostic weight. Estimated regression standardized coefficients of the model were $R = 0.47$; $R2 = 0.22$; adjusted $R2 = 0.17$; $F\ (4.65) = 4.59$; $p = 0.0025$. The standard estimation error was 0.153.

Table 2 shows the EEG indicators included in the regression model.

EEG predictors of cognitive decline in patients on days 7-10 after on-pump CABG were low baseline theta-1 power in the frontal lobe of the left hemisphere with eyes open (FR_L_01_T1) and alpha-1 power in the front-central section of the right hemisphere with eyes closed (FC_R_Z1_A1). In addition, increased theta-power in the posterior regions of the cortex of both hemispheres (CP_L_01_T1 and O_R_01_T2) at baseline was also accompanied by the decline in cognitive performance in the postoperative period.

Prediction models for persistent cognitive decline, depending on the baseline power, were constructed using the data of 65 patients. The analysis has shown alpha and beta powers has the greatest prognostic significance. Estimated regression standardized coefficients of the model were: $R = 0.37$; $R2 = 0.14$; adjusted $R2 = 0.11$; $F\ (4.61) = 0.79$; $p = 0.011$. The standard estimation error: 0.179. Table 3 shows the EEG indicators included in the final regression model.

We have found that increased alpha-2 power in the left occipital regions of the cerebral cortex with eyes closed at baseline (O_L_Z1_A2) is associated with good cognitive status in patients 1 year after traditional CABG, whereas increased beta-2 power in the left frontal regions of the cortex with open eyes at baseline (FR_L_01_B2) suggests persistent decline in cognitive performance.

Thus, we have determined the associations between preoperative EEG activity and the decline in cognitive performance in the early and long-term postoperative periods.

## Discussion

According to the results of our study, EEG predictors of cognitive decline in the early postoperative period of CABG are increased theta power in the posterior cortex regions of the left and right hemispheres with eyes open and closed, as well as reduced theta-1 power with eyes open and alpha-1 power with eyes closed in the frontal lobes of both hemispheres at baseline.

Recent studies have found that the transformations of functional connections in the cerebral cortex, i.e. the pre-set of functional cortical associations, are critical for successful processing of information [11, 12]. In the present study, increased theta power in the posterior cortex prior to cardiac surgery has a negative association with the integral index of cognitive status measured on days 7-10 after CABG. Cognitive decline has also been shown to be accompanied by an increase in slow EEG power in the parietal and occipital cortex, which reflects the involvement of neural oscillators in information processing reducing its effectiveness [6]. We can presuppose that several patients have already had pathological changes in the functional systems of the brain which contributes to the development of postoperative cognitive dysfunction.

Reduced theta-1 power with eyes open and alpha-1 power with eyes closed in the frontal cortex at baseline established as another factor associated with decline in cognitive performance in the early postoperative period.

The increase in theta power in the left frontal region at rest is associated with cognitive processing of emotional information, as well as with increased anxiety [13, 14]. In addition, hypoactivation of the anterior regions of the left hemispheric cortex may suggest

**Table 3. Regression model for decline in cognitive performance in patients 1 year after traditional CABG**

| | Beta | St.Er. - beta | B | St.Er. - B | t | p |
|---|---|---|---|---|---|---|
| Intercept | | | 0,442 | 0,06 | 7,76 | 0,000001 |
| FR_L_01_B2 | -0,254 | 0,119 | -0,188 | 0,09 | -2,12 | 0,03 |
| O_L_Z1_A2 | 0,243 | 0,120 | 0,117 | 0,06 | 2,03 | 0,04 |

the violation of analytical strategies for information perception [15]. At the same time, a decrease in alpha power in the right frontal lobe is associated with experiencing negative emotions [16, 17]. Emotional component is known to determine the effectiveness of brain functions [11, 18]. Negative emotions are suggested to interfere with the formation of functional brain systems optimal for cognitive performance [11].

Thus, decline in cognitive status in the early postoperative period of traditional CABG is triggered by the baseline specific dysfunction pattern of EEG activity that reflects the involvement of stem structures and the disruption of the activity of the anterior cortical regions responsible for analytical and emotional strategies for processing of incoming information.

Based on our results, low alpha-2 power in the left occipital regions with eyes closed and high beta-2 power in the left frontal cortical regions with eyes open at baseline are associated with the long-term (1 year after CABG) decline in cognitive performance.

Importantly, the established relationships are associated with the left hemisphere. Previously we have hypothesized that changes in neural activity in the posterior cortex of the left hemisphere are an early sign of oppression of its functional state and one of the possible mechanisms responsible for decline in cognitive performance. In addition, any changes, both functional and pathological, in right-handers are more pronounced in the left hemisphere than in the right hemisphere [19, 20].

The preservation of cognitive status in patients with neurodegenerative type of cognitive impairment within the 1-year follow-up was assessed by C. Babiloni et al. [6], who reported the presence of the positive correlation between the amplitude of cortical alpha rhythms in the posterior cortical regions in EEG at rest and cognitive performance evaluated with the MMSE scale. We have found that preoperative alpha-2 power has prognostic potential to predict the long-term cognitive outcomes.

The associations between increased beta-2 power in the left frontal cortical regions with eyes open at baseline and reduced cognitive status 1 year after surgery should be interpreted within the following framework - increased beta power reflects high excitation of the central nervous system ("hyperarousal") [ 21]. Several other studies have found that such changes might occur under ischemia [4, 22, 23]. The anterior regions of the left hemispheric cortex are actively involved in the higher-order cognitive processes associated with targeted behavior, the processing of conflict information, the recognition of emotions. The hyperarousal may affect the cognitive status.

Thus, different oscillatory components of preoperative EEG activity are associated with postoperative cognitive dysfunction. The decline in cognitive performance on days 7-10 after on-pump CABG is associated with baseline theta power, which could indicate that ischemic brain changes has already been in these patients. The intraoperative factors, directly or indirectly coupled with acute episodes of cerebral ischemia, worsen the status of the initially compromised regions of the cortex, resulting in cognitive dysfunction.

As for the decline in cognitive performance 1 year after CABG, the associated frequency-topographic characteristics of baseline EEG activity (low alpha-2 and high beta-2 power) suggest the decline of cerebral functions related to targeted behavior, selection of information and monitoring of the environment in the long-term postoperative period.

## Conclusion

This neurophysiological study demonstrated the presence of the associations between baseline EEG activity in CAD patients and severe decline in cognitive performance in the early and long-term postoperative period of on-pump CABG. The obtained data confirms the rationale for preoperative EEG recording and interpretation in patients referred to elective cardiac surgeries.

**Conflict of interest:** The authors have no conflict of interest to declare.

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