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Association between serum biomarkers and postoperative delirium after cardiac surgery

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Background. In cardiac surgery, patients face an increased risk of developing postoperative delirium (POD) that is associated with poor outcomes. Neuron-specific enolase (NSE) and glial fibrillary acidic protein (GFAP) have shown some promising results as potential tools for POD risk stratification, diagnosis, monitoring, and prognosis.

Methods. Prospective single-centre study enrolled 44 patients undergoing elective coronary artery bypass grafting (CABG) and/or valve procedures using cardiopulmonary bypass (CPB). The patients were assessed and monitored preoperatively, during surgery, and in the early postoperative period. The blood levels of NSE and GFAP were measured before and after surgery. The early POD was assessed by CAM-ICU criteria and patients were assigned to the POD group (with POD) or to the NPOD group (without POD) retrospectively.

Results. The incidence of POD was 18.2%. After surgery, NSE significantly increased in the whole sample ($p = 0.002$). Comparing between groups, NSE significantly increased in the POD group after surgery ($p = 0.042$). ΔGFAP (before/after operation) for the whole sample was statistically significant ($p = 0.022$). There was a significant correlation between ΔGFAP and the lowest MAP during surgery in the POD group ($p = 0.033$).

Conclusions. Our study demonstrated that NSE and GFAP are associated with early POD. An increase in NSE level during the perioperative period may be associated with subclinical neuronal damage. Serum GFAP levels show the damage of glial cells. Further studies are needed to find the factors influencing the individual limits of optimal MAP during surgery.

Keywords: cardiac surgery, cardiopulmonary bypass, postoperative delirium, neuron specific enolase, glial fibrillary acidic protein

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INTRODUCTION

In cardiac surgery, patients run an increased risk of developing postoperative delirium (POD) that is associated with poor outcomes (1). POD is a common but underdiagnosed complication: many studies have confirmed this in occurrence from 3% to 72% (2). Neuron-specific enolase (NSE) and glial fibrillary acidic protein (GFAP) have shown some promising results as potential tools for POD risk stratification, diagnosis, monitoring, and prognosis (3, 4). Our study aims to examine the association between serum biomarkers and POD after cardiopulmonary bypass (CPB).

MATERIALS AND METHODS

The study protocol was approved by Kaunas Regional Biomedical Research Ethics Committee**.** Prospective single-centre study enrolled 44 patients (nine female and 35 male) undergoing elective coronary artery bypass grafting (CABG) and/or valve procedures using CPB in the Kauno Klinikos Hospital of the Lithuanian University of Health Sciences. Patients without preoperative neurological disorders were included. The patients were assessed and monitored preoperatively (day before surgery), during surgery, and in the early postoperative period. The blood levels of NSE and GFAP were measured before and after surgery. The early POD was assessed by CAM-ICU criteria and the patients were assigned to the POD group (with POD) or to the NPOD group (without POD) retrospectively. All statistical analysis was made with IBM SPSS Statistics platform.

RESULTS

The incidence of POD was 18.2% (8 of 44 patients). After surgery, NSE significantly increased in the whole sample (6.98 (4.831) vs. 9.19 (5.14) μg/L, $p = 0.002$). Comparing between groups (Table), NSE significantly increased in the POD group after surgery (8.48 (4.66) vs. 12.42 (6.35) μg/L, $p = 0.042$). ΔGFAP (before/after operation) for the whole sample was statistically significant (0.0032 (0.0081) μg/L, $p = 0.022$). The lowest mean arterial pressure (MAP) was kept within empirically acceptable ranges (63.50 (4.6) mmHg; median 65 (min. 56, max 68)). There was a significant correlation between ΔGFAP and the lowest MAP during surgery in the POD group ($r = 0.794$, $p = 0.033$).

CONCLUSIONS

Our study demonstrated that NSE and GFAP are associated with early POD. An increase in NSE level during the perioperative period may be associated with subclinical neuronal damage due to recurring causes such as diffuse microembolism or increased permeability of the blood-brain barrier. Serum GFAP levels show the damage to glial cells. Our results suggest that further studies are needed to find the factors influencing the individual limits of the optimal MAP during surgery.

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Table. Frequency of postoperative delirium

	NPOD	POD	*p*
Age, years	67(8.4)	65 (8.9)	*n*
Sex (male/female) %	57/43	67/33	*n*
MAP, mmHg	62.5 (3.45)	62.9(4.61)	*n*
NSE, mg/l	8.48(4.66)	12.42 (6.35)	0.042
GFAP, mg/l	0.0432 (0.005)	0.046(0.007)	0.022

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SĄSAJA TARP SERUMO BIOMARKERIŲ IR POOPERACINIO DELYRO IŠSIVYSTYMO PO ŠIRDIES OPERACIJŲ

Santrauka

Įvadas. Pacientams po kardiochirurginių operacijų padidėja pooperacinio delyro (PD) išsivystymo rizika, kuris yra susijęs su blogesnėmis perspektyvomis. Atliktų tyrimų duomenimis, neuronų specifinė enolazė (NSE) ir glialinis fibrilinis rūgšties baltymas (GFRB) gali būti potencialūs rodikliai pooperacinio delyro rizikai nustatyti, jį diagnozuoti ir monitoruoti bei įvertinti tolimesnę prognozę.

Metodika. Perspektyviniame tyrime dalyvavo 44 pacientai, kuriems buvo atlikta planinė aortokoronarinių jungčių suformavimo operacija ir / ar vožtuvų procedūros naudojant dirbtinę kraujo apytaką. Pacientų būklė buvo įvertinta ir stebima prieš operaciją, operacijos metu ir ankstyvuoju pooperaciniu laikotarpiu. NSE ir GFRB koncentracija kraujyje buvo tiriama prieš ir po operacijos. PD buvo įvertintas pagal CAM-ICU skalės kriterijus. Pacientai retrospektyviai buvo priskirti PD grupei (su delyru) arba NPD grupei (be delyro).

Rezultatai. PD dažnis buvo 18,2 %. Po operacijos NSE žymiai padidėjo (p = 0,002). Palyginus grupes, NSE aktyvumas po operacijos labiau padidėjo PD grupėje (p = 0,042). GFRB pokytis (prieš / po operacijos) buvo statistiškai reikšmingas visai imčiai (p = 0,022). Per operaciją PD grupėje nustatyta reikšminga koreliacija tarp ΔGFRB ir mažiausio vidurinio arterinio spaudimo (VAS) (p = 0,033).

Išvada. Atliktas tyrimas parodė, kad NSE ir GFRB yra susiję su ankstyvuoju pooperaciniu delyru. NSE aktyvumo padidėjimas perioperaciniu laikotarpiu gali būti susijęs su subklinikiniu neuronų pažeidimu. Serumo GFRB lygiai rodo glialinių ląstelių pažaidą. Siekiant rasti veiksnius, kurie daro įtaką individualiai optimaliai VAS ribai per operaciją, reikalingi tolimesni tyrimai.

Raktažodžiai: kardiochirurgija, dirbtinė kraujo apytaka, pooperacinis delyras, neurono specifinė enolazė, glialinis fibrilinės rūgšties baltymas