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Predictors of Short-Term Neurocognitive Outcome Following Coronary Revascularisation (CABG) Depending on the Use of Cardiopulmonary Bypass

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A B S T R A C T

The purpose of our study was to investigate the association between perioperative cerebral microembolization, expressed as high-intensity transient signals (HITS) and postoperative dynamics of the neuromarker S100β in patients operated using cardiopulmonary bypass, and to assess their impact upon the neurocognitive function in the early postoperative stage. The study involved 62 consecutive male patients aged 60 or above, alls scheduled for elective aortocoronary bypass. The patients were recruited from two groups with respect to the use of CPB: on-pump group (CPB+, N=30) and off-pump group (CPB–, N=32). In all patients we performed intraoperative monitoring of cerebral haemodynamics using transcranial Doppler, with the goal of quantifying perioperative cerebral microembolization. The serum levels of the neuromarker S100β were measured immediately after surgery, and then 12, 24 and 48 hours after the surgery[1]. Neurocognitive status was assessed before and after the surgery and in three cognitive domains. Results of the study have shown that with respect to the short-term postoperative neurocognitive outcome there is no significant difference between the on-pump and off-pump surgical technique of coronary revascularization[1]. Perioperative cerebral microembolization was significantly more pronounced in the on-pump group yet it did not affect early postoperative neurocognitive function, while the increase in the neuromarker S100β serum level 48 hours after surgery may have prognostic value as a predictor of postoperative neurocognitive dysfunction.

Key words: *cerebral microembolization, high-intensity transients signals (HITS), neuromarker S100β, cardiopulmonary bypass (CPB), postoperative cognitive dysfunction (POCD)*

Introduction

Cardiac surgery using cardiopulmonary bypass (on--pump surgery) is the main cause of intraoperative microemboli and brain hypoperfusion. Although in the last two decades cardiac surgery has seen significant improvement, a substantial proportion of patients still experiences temporary or permanent postoperative neurological deficit[1]. Perioperative stroke is found in 2–3% adult patients who underwent cardiac surgery, while significant cognitive dysfunction appears in 40–60% of patients during the first postoperative week. A long-term cognitive dysfunction, lasting months and years, has been registered in 25–40% of patients and it has a significant negative impact upon their quality of life[1]. The clinical significance of diagnosed emboli in brain circulation is not entirely clear. While some patients remain asymptomatic, many studies have revealed association between cerebral microembolism and clinical symptoms[1,2]. The negative effect of microembolism upon short-term and long-term neurocognitive outcome is emphasized especially in the context of early and delayed post-operative cognitive dysfunction (POCD)[1,3]. Microembolic signals, also known as high-intensity transient signals (HITS), are detected using transcranial Doppler (TCD) as unidirectional signals of high intensity, having short duration

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and appearing at irregular intervals[4]. They sound like »whistles«[1]. In cardiac surgery microemboli may come from air bubbles or solid particles (fat, atheromatous material, platelet conglomerates). Several studies examined which procedures during surgery increased the number of emboli: more than 60% of emboli were registered during heart or aorta manipulation, while more than 10% were recorded in the two minutes following the removal of clamps[3,4,6]. Yet over 1/3 of embolic signals were not associated with any specific period or surgical procedure[1,5]. Also, it was noted that patients with postoperative neurological deficit had more than twice as many embolic signals than patients who had no registered neurological deficit[2,3]. More recently, numerous studies have explored the possibility of using protein S100β as a marker of brain damage following cardiac surgery using cardiopulmonary bypass[7]. So far conclusions have been ambiguous. Under normal conditions, protein S100β is not found in circulation[3,4,6]. It is released from glia cells in response to stress or to the use of extracorporeal circulation (cardiopulmonary bypass) as well as after a neurological injury[4]. The biological halftime of S100β is two hours. As the $t^{1/2}$ of S100β is short, its serum concentration may only be maintained if continually released[3]. Thus the presence of S100β in peripheral blood for more than 24 hours probably indicates brain damage[2]. Although S100β is believed to be highly brain-specific, the main problem lies in the fact that its concentration is increased by the release from extra-cerebral tissues, in the first place traumatised fat tissue, skin and bone marrow[4,5]. It is precisely the extra(-)cerebral S100β that hinders elucidation of the increase of its serum concentration following cardiac surgery[8]. Thus its release in the early stage following cardiac surgery cannot be used to conclude with any certainty about potential neurological damage following cardiac surgery[9]. Late increase of S100β serum concentration, after 24 to 48 hours, is considered as a more reliable indicator of perioperative cerebral complications such as stroke, late awakening from anaesthesia or the appearance of confused and disoriented behaviour[2,8]. The goal of this article is to investigate whether there is a significant postoperative increase of the serum level of the neuromarker S100β. Furthermore, association between postoperative neurocognitive function and the dynamics of the neuromarker S100β is analyzed. The second important goal of this study is to quantify perioperative cerebral microembolization by registering high-intensity transient signals (HITS) using transcranial Doppler ultrasound (TCD) and establish if there is association between perioperative HITS and postoperative cognitive function.

Subjects and Methods

Subjects

We conducted a prospective study that involved 62 male coronary patients aged 60 or more years, scheduled for elective aortocoronary bypass procedure. Participants were recruited from two groups with respect to the use of cardiopulmonary bypass (CPB): (1) on-pump group (with the use of CPB, N=30, consecutive) and (2) off-pump group (no use of CPB, N=32, consecutive). Clinical exclusion criteria for this study were: occlusion or haemodynamically significant stenosis of carotid arteries (>70%), acute ischemic damage of myocardium, unstable angina, ejection fraction <30%, persistent atrial fibrillation, severe liver or kidney disease, malignancies, severe diabetic neuropathy, mental illness, alcohol and drug addiction.

Methods

Intraoperative monitoring of cerebral haemodynamics using transcranial Doppler was performed in all patients for the purpose of quantifying perioperative cerebral microembolization. Serum levels of the neuromarker S100β were measured before, immediately after, and 12, 24 and 48 hours after the surgery. The patient's neurocognitive status was assessed before and after surgery in three cognitive domains.

S100β analytical method

S100β analytical method is biochemical assessment of the marker S100β in peripheral blood samples[9]. Sampling was conducted in accordance to the set schedule, at five time points: one day before the surgery (T1), at admission in intensive care unit (T2), 12 hours after the surgery (T3), 24 hours after the surgery (T4) and 48 after the surgery (T5). The serum concentration of protein S100β was measured using immunoluminometric laboratory set that comprises monoclonal antibody for diagnosing S100β in dimeric isoforms and enables analytic sensitivity of 0.02 mg/L[9]. Concentration exceeding 0.12 mg/L is considered pathologically high[2].

Intraoperative monitoring using transcranial Doppler

To detect embolic signals, we used a 2-MHz pulse TCD system for continuous intraoperative measurement of blood flow in middle cerebral artery (*arteria cerebri media*, ACM) simultaneously at two depths between 50 and 55 mm[10]. The recording method assumes that ultrasound acts upon both middle cerebral arteries through temporal windows following fixation (with a rubber frame) of both probes transtemporally above right and left zygomatic arches.

Neurological and neurocognitive assessment

A neurologist conducted the initial examination 24–48 h following the hospital admission, 48 hours after the surgery, 5th day after the surgery and one day before the discharge. The first clinical psychological examination took place 24–48 hours following admission and then postoperatively 5th–7th day after the surgery. The following tests were used in the patient assessment: CPM (coloured progressive matrices) Raven – non-verbal test of general intelligence and WB II (Wechler-Bellevue Scale – second revision) intelligence test – four subtests were used for specific cognitive abilities from WB-II: Verbal (mechanical memory of numerical sequences and mathematical-logical thought) and Non-verbal (perceptual speed and oculomotor coordination and ability to organize abstract material)[10]. Test of verbal fluency (TVF) were also used.

Operative procedure and postoperative course

All patients received standard general anaesthesia and in all cases total median sternotomy was performed. Because systemic anticoagulation is a precondition of extracorporeal circulation, just before their connection to CPB, the patients received 3 mg/kg of their body mass of heparin to achieve activated coagulation time of 480 seconds. Following their separation from CPB, heparin was neutralized with protamine sulphate. In the off-pump group, patients received 1 mg/kg of body mass of heparin and the myocardial stabilization was achieved using vacuum stabilizer. Following the completion of all anastomoses, heparin was neutralized using protamine sulphate[2]. Details of the surgical procedure as well as cardiac surgery procedures that were performed using standardized methods and techniques are described in literature[2,3].

Statistical analysis

Data were analyzed using χ^2-test and Fisher's exact test for the comparison of categorical variable distributions as well as Student t-test and Mann-Whitney U-test for the comparison of quantitative variable distributions. Correlation analysis and multivariate regression analysis were conducted to establish association between quantitative variables. To determine if there is a difference in the dynamics of individual quantitative variables between groups, we used repeated-measures analysis of variance, Friedman ANOVA.

Results

The age distribution did not significantly differ between study groups (CPB+ *versus* CPB–, 66.7±5.9 *vs.* 66.6±6.2 years of age; t=–00906; p=0.928). As the age distribution in each of the two groups was almost entirely comparable, it was not necessary to conduct the standardization of neurocognitive tests with respect to age, also because when assessing the effect on neurocognitive functions patients were their own controls. In both groups prior to surgery (T1) S100β values were very low with the median value of 0 mg/L. Immediately after the surgery (T2) these values increased significantly to reach 1.2455 (CPB+) and 0.334 mg/L (CPB–) (p<0.001 for both groups). Twelve hours after the surgery S100β concentrations fell to 0.1035 and 0.0525 respectively (p<0.001 for both groups). Twenty-four hours after the surgery the values of S100β in CPB+ group decreased to 0.058 mg/L (t=0.89; p=0.3766), while in CPB– remained at the level recorded earlier (median value 0.063 mg/L, t=–0.36; p=0.7197). Forty-eight hours after the surgery in CPB+ group the value stayed at 0.0505 mg/L (t=0.13; p=0.9008), while in group CPB– they exhibited a significant decrease (median 0 mg/L; t=2.49; p=0.0185). Perioperative cerebral microembolization was assessed by measuring high-intensity transient signals (HITS)[11]. As expected, the CPB+ group had significantly higher values ($\bar{X}$±SD, 771±221.5 HITS) than CPB– group ($\bar{X}$±SD, 135±109.4 HITS; z=–6.7049; p<0.001). When comparing two study groups, it was noticed that there was a statistically significant difference in the value of the measured neuromarker S100β at T2, that is just after admission in intensive care unit (z=–5.9161; p<0.001) with CPB+ showing a higher number of HITS and a higher level of S100β (median CPB+ 1.2455 mg/L *vs.* CPB– 0.334 mg/L). At the same time, CPB+ group also had a higher increase of S100β ($\bar{X}$±SD, 1.3249±0.6781 mg/L) when compared to the initial (preoperative) value, and the equivalent increase in CPB– group ($\bar{X}$±SD, 0.4006± 0.3117 mg/L; z=–5.9019, p<0.001). When comparing the entire dynamics of the neuromarker S100β in two study groups, despite of the differences described above, the difference in the time dynamics failed to reach statistical significance (χ^2=7.600; df=4; p=0.1074; Friedman ANOVA; Figure 1). We found no statistically significant difference between groups for any of the parameters used to measure neurocognitive function initially (preoperatively) (CPM, t=0.7549, p=0.453; WBP, t=0.4749, p=0.637; WBR, t=1.1841, p=0.241; WBK, t=1.5569, p=0.125; WBS, t=–0.6548, p=0.515; TVF, t=0.7153, p=0,477). Furthermore, no statistically significant difference between groups was found for any of the neurocognitive function parameters at postoperative measurements (CPM, t=0.8760, p=0.385; WBP, t=0.8598, p=0.394; WBR, t=–0.2307, p=0.818; WBK, t=0.8386, p=0.405; WBS, t=–0.7419, p=0.461; TVF, t=–0.2714, p=0.787). Also no statistically significant differences were found between groups for most differences between initial and postoperative measurement of neurocognitive function parameters (CPM, z=0.3804, p=0.704; WBP, z=1.3541, p=0.176; WBK, t=–0.8806,

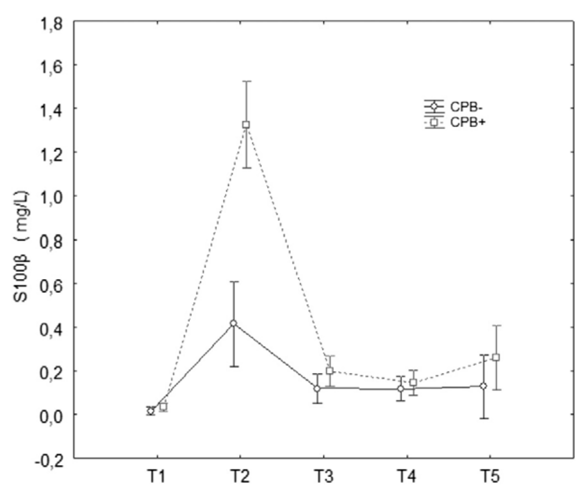

Fig. 1. Time dynamics of the neuromarker S100β values in two study groups, depending on the use of cardiopulmonary bypass (CPB). The graph shows arithmetic mean ±95% confidence interval of the arithmetic mean, T1: one day before the surgery; T2: at admission in intensive care unit; T3: 12 hours after the surgery; T4: 24 hours after the surgery and T5: 48 after the surgery.

p=0.382; WBS, t=–0.1287, p=0.898; TVF, t=–1.3338, p=0.188). The only exception was WBR for which statistically significant difference was found (t=–2.2852, p= 0.026) characterized by an increase of the values in CPB+ after surgery ($\overline{X}$±SD; 0.4±1.0) and a decrease of the values in CPB– ($\overline{X}$±SD; –0.3±1.3). Correlation analysis of association between the number of HITS and the level of the neuromarker S100β found a statistically significant difference between the level of S100β immediately after surgery as well as 48 hours after the surgery and the number of HITS (Spearman R=0.708, p<0.0001; Spearman R=0.269, p= 0.0359; consequently) when both groups were analysed together (Figure 2 and 3). When the same association was studied for the group CPB– no statistically significant association of the number of HITS with the level of S100β was found for any of the time points (p>0.25 for all time points). Only in the CPB+ group we found statistically significant correlation between the number of HITS and the level of S100β at all-time points (p<0.05 for all time points). When analysing the association between postoperative cognitive function and time dynamics of the level of the neuromarker S100β we found a statistically significant association only for the postoperative value of nonverbal test of general intelligence (CPM) and the postoperative level of S100β 48 hours after the surgery (Spear- man R=–0.337; p=0.0098) as well as the level of increase of S100β in comparison to the preoperative measurement (Spearman R=–0.366; p=0.0048; Figure 4). At the same time, no statistically significant association between the number of HITS and any of the parameters used to assess postoperatively neurocognitive function (p>0.05 for all). Multivariate regression analysis (forward stepwise) used postoperative values of neurocognitive parameters and their change with respect to initial measurement as dependent variables, while age, levels of neuromarker S100β, its dynamics and the number of perioperative HITS were used independent variables[11,12]. The analysis showed a statistically significant association for a large number of neurocognitive parameters with independent variables. Thus the postoperative value CPM is statistically significantly associated with the increase of S100β at T3 and T5 time points (r=0.4203; p=0.0058). A change in CPM is statistically significantly associated with an increase in S100β at T2 and T3 tie points (r=0.3431; p=0.0300). Postoperative value of WBP is statistically significantly associated with age and the increase of S100β at T5 (r=0.4284; p=0.0046) while the change in WBP has not shown such association. Postoperative value of WBR is statistically significantly associated with the same two variables (age and the increase of S100β at T5; r=0.3440; p=0.0355). Yet its change was not statistically significantly associated with independent variables. Postoperative value of WBK was statistically significantly associated with age r=0.4608; p= 0.0002) and its change with increase of S100β at T5 (r=0.2875; p=0.0286). Postoperative value of WBS was statistically significantly associated with age and the increase of S100β at T4 (r=0.4736; p=0.0012). Its change was not statistically significantly associated with independent variables. Postoperative value of TVF and its change were not statistically significantly associated with independent variables.

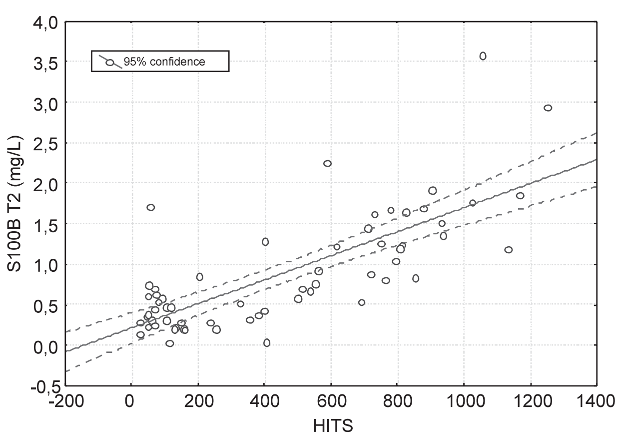

Fig. 2. Diagram of dispersion function for the association between the number of high-intensity transients signals (HITS) and the level of S100β at admission in intensive care after the surgery (N=62).

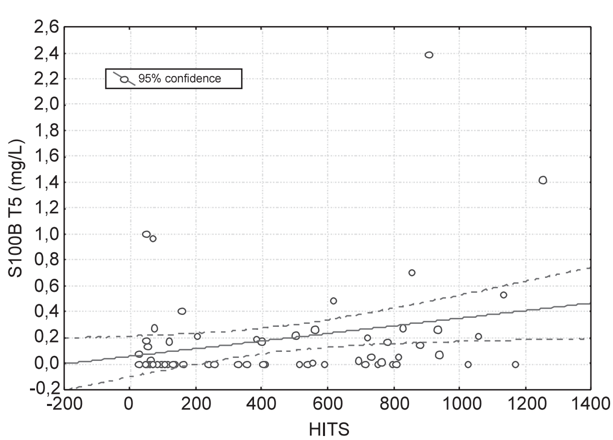

Fig. 3. Diagram of dispersion function for the association between the number of high-intensity transients signals (HITS) and the level of S100β 48 hours after the surgery (N=61).

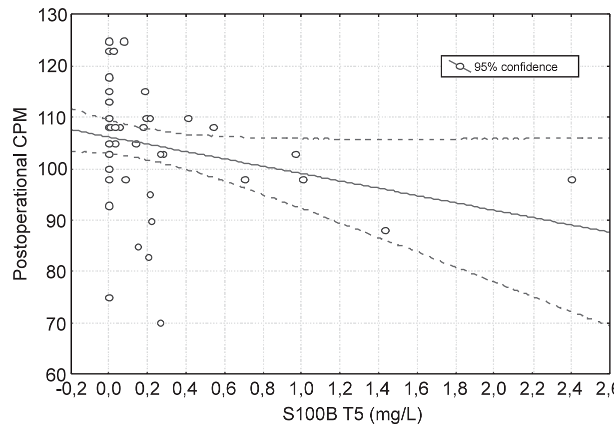

Fig. 4. Diagram of the dispersion function for the association between the level of S100β 48 hours after surgery and the postoperative values in coloured progressive matrices (CPM) test (N=61).

Discussion

Although literature[2,6,7,11,12] indicates that cognitive dysfunction appears in 4–79% of cardiac surgery cases, steps necessary for diagnosing this condition are rarely undertaken. The wide range of the published rate of postoperative cognitive dysfunction (POCD) is probably the consequence of several factors: differences in surgical procedures used to perform coronary artery bypass graft (CABG) surgery; differences in methods used to assess neurocognitive dysfunction, varying duration of the patient follow-up, as well as lack of studies with control groups[2,13,14]. The gold standard for the confirmation of cognitive dysfunction is neuropsychological testing, which is complex and difficult to carry out[15]. Recently, protein S100β has been suggested as a simple method for diagnosing cognitive dysfunction following cardiac surgery[15]. This protein is believed to be the serum marker of brain damage in patients that underwent cardiac surgery[2,3,16]. This protein belongs to the large group of S100 proteins and it is one of the two isoforms of this protein, believed to be brain-specific[2,4,16]. Recently, many studies have raised the question if S100β could be used as a marker of cognitive dysfunction following cardiac surgery. So far conclusions have been far from unambiguous[17]. One of the main reasons is the fact that S100β is present at high concentrations in mediastinal blood that is returned to the patient using cardiotomy suction or autotransfusion, which in turn thwarts accurate measurements of S100β levels in the early postoperative stage[18]. To the present day only one published study has taken into account this type of »contamination«[2,19]. Anderson et al. have shown that blood that leaks into mediastinum during surgery contains high levels of S100β[2,20]. When this blood is returned into circulation directly using cardiotomy suction or later during postoperative care using autotransfusion, it affects the level of S100β in the systemic circulation[21]. This S100β is not of cerebral but extracerebral origin and it probably comes from S100β-containinig tissues, probably fat tissue, skin and bone marrow. The reabsorption of S100β from damaged fat tissue undoubtedly contributes to the levels of S100β measured in the serum. A study by Jönsson et al. has shown that protein S100β has complex dynamics with the pattern of early and late release[21]. The study has also demonstrated association between the serum level of protein S100β in the hours immediately following the surgery and the neurocognitive outcome[21,22]. Yet it did not offer a definitive conclusion concerning the time point that would provide most information for the prediction of POCD[21]. Therefore the authors emphasize the importance of multiple measurements of the postoperative serum levels of S100β and argue that a single measurement of S100β during postoperative follow-up is not useful for clinical prediction of neurocognitive outcome, because it is not sufficiently sensitive[2,3,20–23]. Our study has found an increase of the serum S100β levels in the early stage immediately after the surgery with a statistically significant difference between two groups. Increase in the concentration of S100β was much more pronounced in the on-pump group. In the late stage, 48 hours after surgery, a small increase of the serum S100β level was found in the on-pump group only. Although the difference between two groups is not statistically significant, it is still evident. So if we take into account the result of correlation analysis that found statistically significant association between the S100β serum levels 48 hours after surgery and one of the postoperative cognitive function parameters, then we reach one of the most important conclusions of this study. This conclusion is that the late increase of serum S100β found in the on-pump group may have a prognostic value in patients with no clinical signs of brain damage. Cardiovascular surgery with the use of cardiopulmonary bypass machine (on-pump) is probably the main cause of intraoperative microemboli and cerebral hypoperfusion. A study by Bowles et al. has shown that stroke and neurocognitive dysfunction are correlated with cerebral microembolism generated by cardiopulmonary bypass machine[23]. That study was based on a retrospective analysis of the results collected from 137 patients who underwent elective CABG. While 70 patients underwent traditional CABG, 67 underwent OPCABG (off-pump CABG)[23,24]. Significantly lower number of cerebral microemboli and better clinical results (fewer strokes and deaths) were found in the off-pump group. These results speak in favour of the off-pump surgical strategy as a both sustainable and potentially harmless alternative to the traditional CABG[2,6,11,12,24]. Results of our study demonstrate that perioperative cerebral microembolization is statistically significantly more frequent in the on-pump group in comparison with the off-pump group ($z=-6.7049$; $p<0.001$). Yet we found no statistically significant association between early postoperative neurocognitive function and the number of microemboli (HITS) ($p>0.05$ for all). It is surprising that in spite of the strong association between the number of microemboli and S100β level in the on-pump group, which was found in all postoperative measurements, there was no statistically significant association between the number of microemboli and any of the parameters used for the postoperative assessment of neurocognitive function[25]. This finding may be explained in many ways, and possibly the most acceptable explanation is that in these cases cerebral microemboli were asymptomatic and did not have the expected clinical significance in the early postoperative stage[3,11,25]. Yet delayed cognitive dysfunction may still develop in these patients, caused by the phenomenon of the cumulative effect of embolism[6,25]. It is important to stress that emboli rarely cause immediate neurological symptoms[12,23,26]. Rather, it seems that the cumulative effect of cerebral microembolism with a resulting long-term cognitive dysfunction is more clinically significant[2,6,7,12,21,27]. One of the issues in cardiac surgery that causes the most heated debates is the question whether the surgical technique of direct revascularization of myocardium (off-pump) has advantage over the conventional procedure that uses cardiopulmonary bypass (on-pump) with regard to neurocognitive surgical outcome[10,11,15,21]. Although more procedures are performed on a beating heart, so far research has failed to produce definite proof of the superiority of the off-pump over the on-pump surgical procedure[12,19,28]. This study shows that with respect to the short-term neurocognitive outcome there is no significant difference between on--pump and off-pump surgical technique of coronary revascularization. It is obvious that the use of cardiopulmonary bypass is not the only factor contributing to the postoperative cognitive dysfunction; the latter owes its emergence to a multifactorial mechanism. Results of our study match the results of the latest multicentric study, named ROOBY (Randomized On/Off Bypass trial) by Shroyer and al, published in 2009[25]. They go against all the other published studies with respect to the advantage of »on/off« approach[25]. This prospective multicentric study lasted for six years (2002–2008) and included as many as 2203 patients, almost exclusively men, who were scheduled for either emergency or elective CABG and randomized to on-pump or off-pump procedure[2,25]. ROOBY study did not find significant differences between the groups with respect to the neuropsychological outcome, and its results did not show weakening of cognition within a year of the surgery in either of the groups[25]. Instead, it found a consistent trend towards better outcome in patients who had had conventional on-pump CABG procedure, including a better complex outcome indicator after one year and better rate of bypass patency after one year[25,26]. This is an important outcome as numerous previous studies indicated that on-pump surgical technique results in permanent neurological dysfunction or worsening of cognitive and motor abilities[2,3,5,27]. The meta-analysis by Marasco et al. also compared on- and off-pump surgical technique from the perspective of neurocognitive outcome[28]. This 2008 study comprised eight prospective randomized studies with a total of 892 patients[28]. Results of this comprehensive analysis have shown that there is no convincing difference in the neurocognitive outcome between off- and on-pump groups[28,29]. Thus the authors conclude that, for the neurocognitive function, there is no significant advantage of off-pump in comparison to the on-pump cardiac surgical technique[28]. Results of our study, together with literature data coming from a variety of randomized and non-randomized studies that explored this problem, have shown that there is as yet no definitive recommendation concerning the relative value of on-pump *vs.* off--pump procedure. Although in the last several years much data have been collected about neuropsychological dysfunction following coronary artery bypass graft surgery using cardiopulmonary bypass machine, both the aetiology and mechanism of this phenomenon remain unclear and probably are multifactorial[14,19,21]. The relatively old age of patients who undergo CABG and the widely distributed atherosclerotic disease are probable reasons for the sequence of vascular events leading to neurological dysfunction[2,6,10,13,27]. Regardless of etiological factors of postoperative cognitive dysfunction, it seems that results of most studies indicate current trends. This is confirmed by the scientific statement of the Council on Cardiovascular Surgery and Anaesthesia of the American Heart Association, in cooperation with the Quality of Care and Outcomes Research Interdisciplinary Working Group[2,5,7,12,30]. The current trend is that more operations are performed using off-pump procedure than the standard CABP yet the length of the hospital stay, mortality rate, long-term neurological function and cardiac outcome seem similar for both methods. A thorough preoperative preparation of the patient who has a risk of poor neurocognitive outcome may help clinician choose the method of revascularization as well as inform the patient about risks and benefits from the operation in comparison with conservative treatments[30]. Furthermore, monitoring cerebral haemodynamics during surgery is extremely useful as it provides the surgeon with an insight into the number of cerebral microemboli[11,12,21,28]. The surgeon may then decide to switch the surgical technique or to manipulate instruments and devices in a more careful manner. Yet to provide definitive answers to the question if either of the method is truly superior and in which cases, large prospective randomized studies will be necessary.

Conclusion

The conclusion of our study is that from the perspective of short-term neurocognitive outcome there is no significant difference between on-pump and off-pump surgical techniques. The increase in the serum level of the neuromarker S100β 48 hours after the surgery may have prognostic value in patients without clinical signs of brain damage.

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PREDIKTORI KRATKOROČNOG NEUROKOGNITIVNOG ISHODA NAKON KORONARNE REVASKULARIZACIJE (CABG) OVISNO O UPOTREBI IZVANTJELESNOG KRVOTOKA

SAŽETAK

Istraživanje je provedeno sa svrhom ispitivanja povezanosti perioperacijske cerebralne mikroembolizacije (HITS) i poslijeoperacijske dinamike neurobiljega S100β s primjenom izvantjelesnog krvotoka (CPB), te utvrđivanjem njihovog učinka na neurokognitivnu funkciju u ranom poslijeoperacijskom razdoblju. U ispitivanje su uključena 62 konsekutivna muška bolesnika starija od 60 godina predviđena za elektivnu operaciju aortokoronarnog premoštenja. Bolesnici su regrutirani iz dvije skupine s obzirom na uporabu CPB: on-pump skupina (CPB+, N=30) i off-pump skupina (CPB–, N=32). Kod svih ispitanika provedeno je intraoperacijsko monitoriranje cerebralne hemodinamike transkranijskim doplerom u cilju kvantificiranja perioperacijske cerebralne mikroembolizacije. Serumske razine neurobiljega S100β mjerene su prije operacije, neposredno nakon operacije te 12, 24 i 48 sati od operacije. Neurokognitivni status se ocjenjivao prije i poslijeoperacijski u tri kognitivne domene. Rezultati istraživanja pokazuju da nema značajne razlike između on-pump i off-pump kirurške tehnike koronarne revaskularizacije s aspekta kratkoročnog poslijeoperacijskog neurokognitivnog ishoda. Perioperacijska cerebralna mikroembolizacija značajno je izraženija uz primjenu izvantjelesnog krovotoka ali ne utječe na ranu poslijeoperacijsku neurokognitivnu funkciju, dok porast serumske razine neurobiljega S100β 48 sati nakon operacije može imati prognostičku vrijednost kao mogući prediktor poslijeoperacijske neurokognitivne disfunkcije.