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Incidence and risk factors of delirium in patients after cardiac surgery: *Modifiable* and *non-modifiable factors*

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ABSTRACT

Background: Post cardiac surgery delirium is a severe complication. This study tried to evaluate the early postoperative delirium risk factors and to identify which of them can be modified in order to optimize perioperative management.

Methods: It is a prospective observational study. 250 consecutive cardiac surgery patients took part in the study. Cardiac surgery, the anesthetic regiment and the postoperative management were standardized. The incidence and the risk factors of the postoperative delirium were analyzed by univariate and multivariate analysis. Delirium was assessed with screening scale – The Confusion Assessment Method for the intensive care unit every 12 h postoperatively.

Results: Delirium developed in 52 patients (20.8%). Univariate analysis of the variables confirmed that older age ($p = 0.0001$), the higher EuroSCORE II value ($p = 0.0001$), longer CPB time ($p = 0.0001$), longer ACC time ($p = 0.0001$), and the sufentanil dose ($p = 0.010$) were strongly independently associated with postoperative delirium. The benzodiazepine administration was shown to be an intermediate predictor for developing postoperative delirium ($p = 0.055$).

Conclusions: Advanced age, higher EuroSCORE II value, longer CPB and ACC times, and higher sufentanil doses during anesthesia were all predictors for the development of postoperative delirium. The only modifiable risk factor was the use of larger doses of sufentanil which is related with the duration of the operation. New preventive strategies and use of reduced dose of sufentanil intraoperatively, or the use of different opioid should be studied and applied in order to reduce the incidence of the postoperative delirium.

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Introduction

Post cardiac surgery delirium is a severe complication which can occur in any patient during the early postoperative period and is characterized by altered consciousness and global cognitive disturbances. The onset of symptoms is typically rapid, the course fluctuating and accompanied by a disturbance of the sleep–wake cycle. Delirium after cardiac surgery is associated with increased morbidity and mortality as well as prolonged length of stay in the intensive care unit (ICU) and the hospital [1,2]. Postoperative cognitive dysfunction occurs in 3–79% of patients [3] and the delirium has been reported to occur in 10–60% of surgical patients. However, the incidence of delirium in older surgical patients may be as high as 73% depending on the diagnosis method used. Moreover in ICU, up to 81% of patients manifest delirium [4,5]. Patients with decreased cognitive function after cardiac surgery are at increased risk for long-term cognitive decline with especially elderly patients being at the increased risk for both short and long-term cognitive dysfunction after cardiac surgery [6].

Previous publications described a large number of risk factors such as advanced age, dementia, depression, hearing and visual impairment, diabetes mellitus, impaired left ventricular function, electrolyte derangement, hypertension, high preoperative creatinine level, alcoholism, smoking, cerebrovascular disease, prolonged mechanical ventilation, prolonged cardiopulmonary bypass time, longer aortic cross-clamp times, fentanyl dose, high perioperative transfusion requirements, preoperative and postoperative atrial fibrillation, postoperative renal failure and perioperative use of intra-aortic balloon pressure (IABP) [1–3,7–16].

Complicated delirium diagnostics determine that the relationship between the preoperative condition of the patient and the intra-operative or postoperative factors affecting the cardiac surgery still remains quite unclear.

The aim of this study was to evaluate the preoperative and early postoperative delirium risk factors and their impact on the postoperative outcome by a risk factor analysis and to identify which of them can be modified in order to optimize perioperative management.

Materials and methods

250 consecutive patients, who had various types of cardiac surgery in our institution and were operated in an elective or urgent regime, were included in this prospective observational study. Patients who were operated on an emergency regime were excluded from the study. Of the patients who participated, medical history and preoperative characteristics (concomitant diseases or risk factors such as hypertension, diabetes mellitus, hypercholesterolemia, smoking, alcoholism, previous psychiatric disease), perioperative details (type of operation, duration of cardiopulmonary bypass and aortic cross-clamp, doses of opiates and benzodiazepines administered during the operation) and postoperative details (duration of mechanical ventilation >24 h, ICU and hospital stay) were recorded.

Also the EuroSCORE II value was calculated for all patients and they were accordingly categorized into three groups as high, moderate and low risk of mortality after cardiac surgery (low risk <1.6%, moderate risk 1.6–6.7%, high risk >6.7%). Cut-off values of EuroSCORE II stratification come from literature [17].

The time frame for early post cardiac surgery delirium was defined 2–6 days after the operation.

Cardiac surgery, the anesthetic regiment and the postoperative management were standardized.

Ethics

Ethical approval for this study was provided by the local Ethical Committee of the Eastern Slovak Institute for Cardiovascular Diseases, Kosice, Slovakia (Chairman Juhas S., MD, PhD). All the study participants provided a written informed consent.

Anesthetic technique

All patients received premedication of 10 mg oxazepam the evening before surgery and 7.5 mg of midazolam 1–2 h before surgery. Anesthesia was induced by 2.5–5 mg midazolam, 2–2.5 mg/kg propofol, sufentanil 0.01–0.025 mg and isoflurane 4%. Tracheal intubation was facilitated by 0.6–1 mg/kg atracurium. Anesthesia was maintained with sufentanil infusion 0.0005 mg/kg/h and isoflurane 1–2%, while neuromuscular blockade was maintained with the administration of atracurium 50 mg every 40 min. No propofol was administered during anesthesia maintenance.

Surgery-conduct of cardiopulmonary bypass

All surgery procedures were performed through median sternotomy. For patients undergoing off-pump surgery, distal anastomoses were performed with the help of a tissue vacuum stabilizer (ACROBAT V, MAQUET Holding GmbH). No-touch aorta technique was used in off-pump surgery. Nasopharyngeal temperature was maintained above 35 °C and systolic blood pressure was kept at 80 mmHg or greater throughout the procedure.

For patients undergoing on-pump surgery anticoagulation was achieved with heparin to maintain an activated clotting time above 480 s and the cardiopulmonary bypass circuit was primed with 1 l of Ringer's Lactate and 250 ml of 20% mannitol. Mild hypothermia of 34–35 °C was induced during cardiopulmonary bypass, the pump flow rate was 2.4–2.8 l/min/m^2 and the mean perfusion pressure was between 70 and 75 mmHg. Hematocrit was kept between 25 and 35%. Myocardial protection was achieved with intermittent blood-enriched cold cardioplegic solution (3–6 °C of St. Thomas cardioplegic solution) using a blood to crystalloid ratio of 5:1. Fractional concentration of inspired oxygen was adjusted to keep arterial oxygen tension between 150 and 250 mmHg, and gas flow was adjusted to maintain arterial carbon dioxide tension between 35 and 40 mmHg without temperature correction (α-stat).

After all distal anastomoses were done, the aortic cross-clamp was removed and proximal anastomoses were then performed by means of a single side-clamp on the aorta.

Postoperative management

After surgery, all the patients were admitted to the cardiosurgical ICU, where a standard protocol was implemented for sedation, analgesia and management of mechanical ventilation. Patients initially were kept on mechanical ventilation until were stabilized and eligible for weaning. Patients were extubated according to the following criteria: responsive and cooperative, pO_2 of 10–11 kPa and oxygenation index of pO_2/FiO_2 >300. In the ICU patients were sedated with propofol until extubation. Analgesia was provided with intravenous morphine infusion at 2 mg/h, algifen (metamizole, pitofenone, fenpiverinium, Zentiva Group a.s., Czech Republic) 2.5 g every 8 h and intravenous tramadol 100 mg every 8 h.

Delirium assessment

Delirium was assessed with the CAM-ICU (The Confusion Assessment Method for the intensive care unit) [18] every 12 h postoperatively. The CAM-ICU allows the monitoring of delirium in both ventilated and extubated patients. It is based on the Diagnostic and Statistical Manual of Mental Disorders criteria and includes a 4-step algorithm assessing the following: (1) an acute onset of changes or fluctuations in the course of mental status, (2) inattention, (3) disorganized thinking, and (4) an altered level of consciousness. The patient is determined to be delirious (CAM-positive) if he or she manifests both features (1) and (2), plus either feature (3) or (4).

The CAM-ICU measurements were performed by the cardiovascular ICU nurses. All nurses were educated and well trained in the application of the CAM-ICU in both ventilated and non-ventilated patients.

The level of sedation (level of arousal) was assessed by means of the Richmond Agitation Sedation Scale (RASS) [19].

Statistical analysis

Data are given as mean value ± standard deviation (SD). Categorical variables are presented as numbers of patients (percentage). A univariate analysis was performed to identify perioperative risk factors associated with delirium using Chi-square analyses or Fisher's Exact Test. Different cut-off points for continuous variables were examined to determine the best association with delirium. Odds ratio (OR) was calculated to indicate the effect size of perioperative risk factors on delirium. Variables associated with outcome with a p value <0.05 in the univariate analyses and variables considered clinically significant were entered into multiple logistic regression model for delirium in order to identify independent risk factors. This was performed by using stepwise logistic regression technique.

Values of $p < 0.05$ were considered significant. For statistical analysis the SPSS software version (SPSS Inc., Chicago, IL, USA) was used.

Results

250 eligible patients were included in the study. The incidence of the postoperative delirium in our population was 20.8% (52 patients). The patients developed a hyperactive and mixed type of delirium with hyperactive and hypoactive activity. 171 (68.4%) patients were men and 79 (31.6%) were women. The mean age of the patients was 65.2 ± 10.3 years. The operative risk was evaluated by the EuroSCORE II. The mean EuroSCORE II value was 2.63 ± 2.65%.

The preoperative clinical patient's characteristics are shown in Table 1 and the perioperative and postoperative characteristics are shown in Table 2.

Patients with postoperative delirium had a longer stay in the ICU ($p < 0.0001$) and longer total duration of hospitalization ($p < 0.0001$); however, the ICU stay is not a predictor of postoperative delirium ($p = 0.534$).

Univariate analysis of the variables confirmed that older age ($p < 0.0001$), the higher EuroSCORE II value ($p < 0.0001$), longer CPB time ($p < 0.0001$), longer ACC time ($p < 0.0001$), and the sufentanil dose ($p = 0.010$) were strongly independently associated with postoperative delirium.

Concerning the EuroSCORE II value, patients with moderate risk score and high risk score compared with the low risk patients had a 4.5 and 14.5 times more increased risk of developing postoperative delirium respectively. Moreover, in patients where the CPB time was more than 120 min they had a 15 times higher risk for developing postoperative delirium. Also the longer the ACC time, the higher the risk for developing postoperative delirium. Finally, the higher the sufentanil dose (the patients were running a fixed dose per kg per minute), the higher the risk for developing postoperative delirium. From this analysis certain variables such as CPB time, ACC time and sufentanil dose are all linked to a common parameter the time so as a conclusion, the longer lasts the operation, the higher the risk for developing postoperative delirium.

Concerning the benzodiazepine administration, it was shown in our study to be an intermediate predictor for developing postoperative delirium ($p = 0.055$).

Table 1 – The preoperative clinical patient's characteristics.

	Total (n = 250)
Age, years mean ± SD	65.2 ± 10.3
<50 years	19 (7.6%)
50–70 years	146 (58.4%)
>70 years	85 (34.0%)
Men	171 (68.4%)
Women	79 (31.6%)
Diabetes mellitus	77 (30.8%)
Arterial hypertension	229 (91.6%)
Hypercholesterolemia	187 (74.8%)
Smoking	88 (35.2%)
Alcoholism	26 (10.2%)
Psychiatric disorder in the medical history	22 (8.8%)
EuroSCORE II, mean ± SD	2.63 ± 2.65%
Low risk <1.6%	106 (42.4%)
Moderate risk 1.6–6.7%	124 (49.6%)
High risk >6.7%	20 (8.0%)

Abbreviations: n = count, SD = standard deviation.

Table 2 – The intraoperative and postoperative characteristics.

	Total (n = 250)
Operation type	
CABG	104 (41.6%)
AVR	50 (20.0%)
MVR	20 (8.0%)
CABG + AVR	27 (10.8%)
CABG + MVR	8 (3.2%)
AVR + MVR	4 (1.6%)
AVR + MVR + CABG	3 (1.2%)
OPCAB	32 (12.8%)
Other (ASD, Myxoma)	2 (0.8%)
ACC time, mean ± SD	55.11 ± 38.61 min
≤60 min	101 (40.4%)
>60 min	149 (59.6%)
CPB time, mean ± SD	72.90 ± 45.46 min
≤120 min	232 (92.8%)
>120 min	18 (7.2%)
Total sufentanil dose, mean ± SD	0.15 ± 0.03 mg
≤0.15 mg	178 (71.2%)
>0.15 mg	72 (28.8%)
Total benzodiazepines dose, mean ± SD	4.73 ± 2.86 mg
≤5 mg	217 (86.8%)
>5 mg	33 (13.2%)
Mechanical ventilation time, mean ± SD	3.70 ± 2.39 h
ICU stay, mean ± SD	4.62 ± 3.47 days
≤3 days	126 (50.4%)
>3 days	124 (49.6%)
Hospitalization time, mean ± SD	10.84 ± 6.85 days
≤10 days	180 (72.0%)
>10 days	70 (28.0%)

Abbreviations: n = count, SD = standard deviation, CABG = coronary artery bypass grafting, AVR = aortic valve replacement, MVR = mitral valve replacement, OPCAB = off-pump coronary artery bypass, ASD = atrial septal defect, ACC = aortic cross-clamping, min = minute, CPB = cardiopulmonary bypass, mg = milligram, ICU = intensive care unit.

Concerning the type of surgery only CABG showed to be associated with the incidence of the postoperative delirium ($p = 0.010$).

In multivariate analysis of the variables age ($p < 0.001$), EuroSCORE II value ($p < 0.001$), CPB time and ACC time ($p < 0.05$), sufentanil dose ($p < 0.001$), benzodiazepine administration ($p < 0.05$) and the CABG type of operation ($p < 0.001$) are all predictors of postoperative delirium development.

Table 3 shows the univariate analysis of the variables and Table 4 shows the multivariate analysis of the variables.

Concerning the different postoperative complications, 82 patients (32.8%) suffered from postoperative atrial fibrillation. 5 patients (2.0%) had a pacemaker implantation, 5 patients (2.0%) suffered from sternal wound infection, 5 patients (2.0%) had re-exploration due to severe postoperative bleeding and 4 patients (1.6%) died during their hospitalization. Two patients died due to severe bradycardia accompanied by hypotension without ECHO signs of cardiac tamponade. Despite the efforts cardiopulmonary resuscitation was unsuccessful. In another two patients respiratory insufficiency developed along with alterations of renal parameters. In both patients despite intensive treatment the death was caused by fully developed MODS.

Discussion

The incidence of postoperative delirium in this study is 20.8% compared with the incidence rate of 3–50% reported in the literature [3,20–22].

The results of this research indicate that older age ($p < 0.0001$), the higher EuroSCORE II value ($p < 0.0001$), longer CPB time ($p < 0.0001$), longer ACC time ($p < 0.0001$), and the sufentanil dose ($p = 0.010$) were strongly independently associated with postoperative delirium.

Concerning the benzodiazepine dose, it was also shown in our study to be an intermediate predictor for developing postoperative delirium.

Advanced age has consistently been reported as a predictor of postoperative delirium [8,14,20,23]. Moreover, Osse et al. [17] showed also that in individuals aged 70 and older undergoing elective cardiac surgery high preoperative levels of pterin are associated with postoperative delirium and the authors suggested that plasma neopterin may be a candidate biomarker for delirium after cardiac surgery in these older adults.

In this study the EuroSCORE II value was calculated to evaluate the operative risk. The higher EuroSCORE II values were found to be associated with the incidence of postoperative delirium. The higher the EuroSCORE II value, the higher the risk for developing delirium. Also, Osse et al. [17] showed that EuroSCORE greater than 6 was associated with postoperative delirium. Concerning the left ventricular ejection fraction which is a variable in the calculation of the EuroSCORE II, Bucerius et al. [1] found an impaired left ventricular ejection fraction <30% to be an independent predictor of delirium. In contrast, in a study by Santos et al. [9] using a cut-off value of 50% for impaired left ventricular function, an impaired ejection fraction was not a predictor of delirium.

In our study other risk factors such as hypertension, diabetes mellitus, hypercholesterolemia, and smoking history were not predictors of delirium. Concerning these factors the evidence is conflicting in cardiac surgery. A history of hypertension and diabetes mellitus were independent predictors of postoperative delirium in the study by McKhann et al. [2] and Dong-Liang et al. [24] whereas in other studies they were not [3,8]. Also in studies by Nikolic et al. [13] and Lin et al. [16] diabetes mellitus, cerebrovascular and peripheral vascular diseases were associated with postoperative delirium.

Moreover, in our study alcoholism (a chronic, progressive disease that includes problems controlling of alcohol consumption) and previous psychiatric disease (most commonly manifesting as depression, occasionally like bipolar affective disorder or schizophrenia) were not associated with delirium. On the contrary, studies by Lin et al. [16], Kazmierski et al. [8] and Katznelson et al. [25] showed that depression diagnosis is associated with postoperative delirium.

Furthermore, in our study it was shown that the higher the sufentanil dose (the patients in our study were running a fixed dose per kg per minute), the higher the risk for developing

Table 3 – Univariate analysis of the variables.

S. no.	Variable	T. no.	Delirium no. (%)	No delirium no. (%)	Sig. *p* value	Exp(B) OR	95% C.I. for exp (B) OR	
							Lower	Upper
1.	Age, years	250	52 (20.8%)	198 (79.2%)	<0.0001	1.090	1.048	1.133
	<50	19	0 (0%)	19 (100%)				
	50–70	146	18 (12.4%)	128 (87.6%)				
	>70	85	34 (40.0%)	41 (60.0%)				
2.	Gender	250	52	198	0.616	0.842	0.431	1.646
	Men	171	37 (21.8%)	134 (78.2%)				
	Women	79	15 (19.0%)	64 (81.0%)				
3.	EuroSCORE II	250	52 (20.8%)	198 (79.2%)	<0.0001	1.348	1.187	1.153
	LR <1.6%	106	8 (7.5%)	98 (92.5%)	<0.0001			
	MR 1.6–6.7%	124	33 (26.8%)	90 (73.2%)	<0.0001	4.492	1.971	10.236
	HR >6.7%	20	11 (55.0%)	9 (45.0%)	<0.0001	14.972	4.797	46.729
4.	D. mellitus	77	21 (27.3%)	56 (72.7%)	0.99	1.706	0.904	3.217
5.	Hypertension	229	49 (21.4%)	180 (78.6%)	0.441	1.642	0.465	5.805
6.	Hypercholest.	187	36 (19.3%)	151 (80.7%)	0.309	0.705	0.359	1.383
7.	Smoking	88	13 (14.4%)	75 (85.6%)	0.082	0.542	0.272	1.082
8.	Alcoholism	26	5 (19.3%)	21 (80.7%)	0.827	0.892	0.319	2.490
9.	Psych. disease	22	2 (9.1%)	20 (90.9%)	0.171	0.354	0.080	1.566
10.	ACC time, min	250			0.003	1.010	1.003	1.017
	ACC time cat.	250	52 (20.8%)	198 (79.2%)	0.108	1.708	0.889	3.280
	≤60 min	101	16 (15.8%)	85 (84.2%)	0.4133			
	>60 min	149	36 (24.2%)	113 (75.8%)	<0.001			
11.	CPB time, min							
	≤120 min	232	42 (18.1%)	190 (81.9%)	0.015	1.010	1.002	1.017
	>120 min	18	10 (55.6%)	8 (44.4%)	<0.0001	15.188	3.749	61.626
12.	Sufentanil d., mg	250	52 (20.8%)	198 (79.2%)	<0.0101	12.419	16.649	92.644
13.	Benzodiaz. d. mg	250	52 (20.8%)	198 (79.2%)	0.055	1.120	0.998	1.257
	≤5 mg	217	46 (21.3%)	171 (86.3%)				
	>5 mg	33	6 (18.2%)	27 (81.8%)				
14.	M. vent. >24 h	0	0	0	n/a	n/a	n/a	n/a
15.	ICU stay	250	52 (20.8%)	198 (79.2%)	0.534	1.225	0.646	2.320
	ICU stay, days	250	52 (20.8%)	198 (79.2%)	<0.0001	1.256	1.137	1.387
16.	Hosp. stay, days	250	52 (20.8%)	198 (79.2%)	<0.0001	1.112	1.056	1.172
17.	Operation type	250	52 (20.8%)	198 (79.2%)				
	OPCAB	32	6 (18.7%)	26 (81.3%)	0.823	0.897	0.348	2.317
	CABG	104	20 (19.3%)	84 (80.7%)	0.010	2.427	1.238	4.760
18.	Valve comb., OS	114	26 (29.6%)	88 (70.4%)	0.460	1.269	0.674	2.390

Abbreviations: S. = subject, T. = total, no. = count, sig. = significant, exp(B) = coefficient, OR = odds ratio, C.I. = confidence interval, LR = low risk, MR = moderate risk, HR = high risk, D. = diabetes, Hypercholest. = hypercholesterolemia, Psych. = psychiatric, ACC = aortic cross-clamping, min = minute, cat. = categories, CPB = cardiopulmonary bypass, d. = dose, mg = milligram, Benzodiaz. = benzodiazepine, M. vent. = mechanical ventilation, h = hours, n/a = not available, ICU = intensive care unit, Hosp. = hospitalization, OPCAB = off-pump coronary artery bypass, CABG = coronary artery bypass grafting, comb. = combined, OS = other surgery.

postoperative delirium. The sufentanil dose is linked with time, so the longer the duration of the operation, the higher the sufentanil dose, and the higher the risk for developing postoperative delirium. This association was also investigated by other authors. Burkart et al. [26] showed that an increasing dose of fentanyl administered intraoperatively appeared to be a risk factor for postoperative delirium.

Gunaydin et al. [27] found a higher rate of delirium in patients after high dose fentanyl anesthesia compared with barbiturate anesthesia without the use of fentanyl. Comparing remifentanil with fentanyl in cardiac surgery Cheng et al. [28] found a significantly lower rate of confusion in the remifentanil group. Alternative use of remifentanil should be considered in strategies focusing on the prevention of delirium.

Concerning the benzodiazepine dose, it was also shown in our study to be an intermediate predictor for developing postoperative delirium. Pandharipande et al. [29] also showed that exposure to benzodiazepines is one of the strongest modifiable risk factors for postoperative delirium development. In our study the patients developed a hyperactive and mixed type of delirium. McPherson et al. [30] showed that patients who received benzodiazepines and are restrained after heart surgery had hypoactive type of delirium. Avoiding

Table 4 – Multivariate analysis of the variables.

Variable	OR (95% C.I.)	*p* value
Age	1.106 (1.061–1.155)	<0.001
EuroSCORE II	1.331 (1.171–1.514)	<0.001
CPB time	1.009 (1.002–1.016)	<0.050
ACC time	1.010 (1.002–1.019)	<0.050
Sufentanil dose	5.657 (2.159–14.821)	<0.001
Benzodiaz. admin.	2.056 (1.036–4.081)	<0.050
CABG	6.142 (2.248–16.782)	<0.001

Abbreviations: OR = odds ratio, C.I. = confidence interval, CPB = cardiopulmonary bypass, ACC = aortic cross-clamping, Bezodiaz. = benzodiazepine, admin. = administration, CABG = coronary artery bypass grafting.

chemicals restrains via use of benzodiazepines or the use of physical restraining devices and as much as possible early mobilization could be an effective preventive strategy in order to decrease the development of the postoperative delirium. In our department a patient with an uncomplicated postoperative course is usually mobilized on postoperative day 4, so there is room for improvement in this issue.

Another two intraoperative predictors found in our study to be associated with postoperative delirium are longer CPB and ACC times. Other reports published in the literature have similar results. Andrejaitiene et al. [11] found that ACC time >68 min is associated with the development of delirium. Similar results are reported by other authors [14,15,25] reporting that increased CPB times are associated with the development of postoperative delirium. It has been hypothesized that cerebral atherosclerosis combined with postsurgical inflammatory changes may inhibit cerebral blood flow which may be exacerbated by the non-pulsatility of CPB [31]. Longer duration of surgery is correlated with longer CPB and Brown et al. [32] showed that increased duration of CPB was associated with increased gaseous embolic load to the brain. Also, longer surgical duration may also mean a more complex procedure, perhaps requiring more heart and major vascular manipulation, with resultant embolic phenomena.

In our study the duration of the mechanical ventilation was less than 24 h and it was not shown to be a predictor for development of delirium. Other authors showed that the duration of ventilation (prolonged ventilation >24 h) is as independent predictor of postoperative delirium [8,10,12,13,16,23].

Concerning the type of the operation in our study only CABG operation was associated with the development of postoperative delirium. On the contrary a higher incidence of delirium in patients undergoing valve replacement and combined surgery with valve replacement and CABG has been described compared with patients undergoing isolated coronary artery bypass graft surgery [1,25,33–36]. The reason for this according the authors may be the embolization of air which is trapped within the cardiac chambers during the valve replacement surgery. Concerning our study, the relatively small sample size of valve replacement patients compared with the CABG patients sample could be responsible for the fact that in our patient's population CABG surgery and not valve surgery is associated with the development of the postoperative delirium.

According to the data available in the literature postoperative delirium occurs most often during the first 5 days [1,3,8,10]. Any delirium diagnosed during the first or after the sixth postoperative day, it might not be directly related to the surgery, but it might be related with the presence of any respiratory or urogenital infections, the use of any psychotropic substances, acidosis or various other electrolyte disturbances [37]. Therefore, in our study the time frame for early post cardiac surgery delirium was defined between 2 and 6 days after the operation.

The study has some limitations. First, we did not perform baseline psychiatric and cognitive screening tests as preoperative mental disorders are strong predictors of postoperative delirium. Any psychiatric disorders that were examined in our study were obtained from the medical history of the patient and their incidence could be underestimated. Secondly, the CAM-ICU assessment was performed in the cardiovascular ICU and was not extended to the cardiac surgical floor. As a result, our findings can only be applied to early postoperative delirium. Thirdly, delirium has a multifactorial etiology, so in each type of the cardiac operations a different factor may have a predominant role in the development of the postoperative delirium (e.g. in CABG aortic manipulation and atherosclerotic microembolization during cannulation and cross-clamping, whereas in valve surgery air bubbles trapped in the cardiac chambers may play a significant role in the development of delirium). For definite results future studies should be focused on more homogenous groups, for example, on-pump CABG. Moreover, we did not examine the association of the various perioperative medications (e.g. inotropic support) with the development of the postoperative delirium. Lastly, our study mainly focused on preoperative and perioperative predictors of delirium and did not include postoperative variables.

Conclusion

In our study advanced age, higher EuroSCORE II value, longer CPB and ACC times, higher sufentanil doses during anesthesia were all predictors for the development of postoperative delirium. The only modifiable risk factor was the use of larger doses of sufentanil which is related with the duration of the operation. The identification of potentially modifiable risk factors for delirium in the management of elderly patients undergoing cardiac surgery may be important to design randomized controlled trials to test whether modifications of these factors reduce the incidence of postoperative delirium (to test the hypotheses that a reduced dose of intraoperative sufentanil or the use of different opioid prevent delirium). However, typically most of the above risk factors in our study were non-modifiable, so new preventive strategies such as the preoperative use of melatonin [38] and perioperative use of dexmedetomidine [39] in the cardiac surgery patients should be studied and applied in order to reduce the incidence of the postoperative delirium.

Conflict of interest

All authors declare no conflict of interest.

Ethical statement

The clinical research was done according to ethical standards.

Informed consent

The patients agreed to participate in the clinical research.

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