Subsyndromal Delirium in Cardiac Surgery Patients: Risk Factors and Outcomes of the Different Trajectories

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Acknowledgement: This manuscript was supported by funding via the Quebec Nursing Intervention Research Network, the Montreal Heart Institute and a postdoctoral fellowship grant from the Quebec Research Funds.

Conflict of Interest: None to declare.

Word count: Abstract 250 words; Main text 3387 words; Tables 3.

ABSTRACT

Background: Subsyndromal delirium (SSD), a subthreshold form of delirium, is related to poor outcomes of longer length of stay and increased mortality rate among older adults. Risk factors and outcomes of SSD in cardiac surgery patients are misunderstood. **Objective**: To assess and describe the characteristics and outcomes related to trajectories of SSD and delirium in cardiac surgery patients. **Methods.** In this secondary analysis of a retrospective case-control (1:1) cohort study, SSD was defined as a score between 1 and 3 on the Intensive Care Delirium Screening Checklist paired with an absence of diagnosis of delirium on the day of assessment. Potential risk factors (e.g. age) and outcomes (e.g. mortality) were identified from existing literature. Patients were grouped in four trajectories: 1) without SSD or delirium; 2) SSD only; 3) both; and 4) delirium only. These trajectories were contrasted using analysis of variance or Chi-square. **Results.** Among the cohort of 346 patients, 110 patients did not present SSD or delirium, 62 presented only SSD, 69 presented both, and 105 presented only delirium. In comparison to patients without SSD or delirium, SSD patients presented preoperative risk factors known for delirium (i.e. older age, higher EuroSCORE), but underwent less complicated surgical procedures, received less transfusions postoperatively and had a lower positive fluid balance postoperatively than patients who presented delirium. Patients with both SSD and delirium had worsened outcomes in comparison to those with delirium only. **Conclusion.** This study stresses the importance for nurses to identify SSD and prevent its the progression to delirium.

Keywords: Delirium, Cardiac surgery, Length of stay, Mortality.

INTRODUCTION

Subsyndromal delirium (SSD), a subthreshold form of delirium, is frequent in older hospitalized patients and is associated with poor outcomes. Subsyndromal delirium refers to patients presenting with one or more core diagnostic characteristic of delirium, without meeting all the diagnostic criteria defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)[1]. It is accepted that SSD represents an intermediate state between full-syndromal delirium, defined by the DSM-5, and normal mental state [2-4]. In the intensive care unit (ICU), SSD occurs in one-third of patients and is related to an increased length of stay and mortality rate [2,5-8]. Systematic reviews and meta-analysis on SSD highlight the need for further research to increase our understanding of the risk factors and outcomes related to SSD, and the risk factors and outcomes that differentiate patients who will present SSD and delirium from those who will present only delirium [2,9].

Risk factors and outcomes related to SSD among post-cardiac surgery patients have been the focus of three cohort studies. Aside from older age and comorbidity, these studies either did not look at similar risk factors or concluded with conflicting results on SSD risk factors and related outcomes, thereby impeding the identification of targeted preventive measures [10-12]. For example, Li et al found perioperative hypotension to be a risk factor for SSD, while Breu et al did not. Thus, risk factors that differentiate post-cardiac surgery patients who will present SSD from those who will not and from those who will present delirium remain unclear. Risk factors associated with SSD transition into delirium among post-cardiac surgery patients have been explored in a single study [12]. The authors observed that history of cerebrovascular disease, left ventricular dysfunction and diabetes were predictive of SSD transition into delirium [12].

Therefore, the aim of this study is to assess and describe the differences in risk factors and outcomes related to the different trajectories relative to SSD and delirium among patients hospitalized in a cardiac surgery intensive care unit.

MATERIALS AND METHODS

Study Design and Setting

This is a secondary analysis of a retrospective case-control (1:1) cohort study approved by the ethics and scientific committee (#2017-2139) of the tertiary cardiac hospital in Canada where the study took place. The aim of the main cohort study was to describe the association between the cumulative fluid balance and delirium occurrence among cardiac surgery patients [13]. The aim of this secondary analysis is to report on SSD among this cohort. Precisely, we focus on the risk factors and patient outcomes related to different postoperative trajectories of SSD and delirium. Reporting was done in accordance with the STROBE statement extension for case-control studies and was adjusted according to the Reporting of studies Conducted using Observational Routinely collected Data [14,15]. Data was collected using an electronic medical chart review.

Participant Selection and Eligibility Criteria

The cohort was selected from a screening log, generated in a previous prospective clinical trial of consecutive patients who were scheduled for a surgical procedure between 2013 and 2015 in a tertiary cardiac hospital (#ISRCTN95736036). Patients who underwent any type of cardiac surgery and who had a medical chart available electronically were eligible to be included in the cohort. However, patients who received procedures of transcatheter valve implantation or who presented with a congenital disease were excluded from the cohort as their clinical profiles differ from other post-cardiac surgery patients [16]. A flow chart of patients included in the final cohort has been previously published [13].

Variables and Data Measurement

A structured case report form was used to extract data by trained research assistants and accuracy of data was verified for a random sample of 10% of the cohort, which was reviewed by a third research assistant blinded to allocation and the study hypotheses [13]. All variables were treated

as continuous unless specified otherwise. Categorical distribution of the variables and units of measurements are reported directly in result tables.

Subsyndromal delirium. The majority of studies on SSD have used a score between one and three on the Intensive Care Delirium Screening Checklist (ICDSC) or the presence of two items out of four on the Confusion Assessment Method (CAM), without a diagnosis of delirium on the day of assessment, to define SSD. In our cohort, the ICDSC was used to define SSD. The ICDSC consists of an eight-item scale based on the DSM-IV-TR [17]. The items include altered level of consciousness, inattention, disorientation, hallucinations, psychomotor agitation or retardation, inappropriate speech or mood, sleep-wake cycle disturbance, and symptom fluctuations. The score ranges from 0 to 8 and a score of 4 or more is considered as high suspicion of delirium [17]. In the research setting, the ICDSC is completed by trained bedside nurses three times daily, when the patient's level of consciousness allows for assessment. For this secondary analysis, we retained one score per 24 hours. The highest ICDSC score over a 24-hour period was retained for the day. Scores between 1 and 3 and not matched with a diagnosis of delirium were considered as indicative of SSD, as defined in previous literature [2].

Delirium. Delirium was defined as a diagnosis of delirium or a mention of acute confusion or encephalopathy in the electronic medical chart completed by the trained attending physicians.

Clinical data for potential risk factors. Relevant clinical data for potential preoperative, intraoperative, and postoperative risk factors of SSD were collected from electronic medical records. These potential risk factors were identified following a literature search on SSD among cardiac surgery patients and other population [2,4,6,8,10-12,18-38]. Potential preoperative risk factors consisted of age, gender, tobacco and alcohol consumption, auditory and visual impairment, needing help with activities of daily living, walking aid, EuroSCORE, history of neurological disorders, history of psychiatric disorders, left ventricular dysfunction, diabetes, previous cardiac surgery, cerebral oximetry, hemoglobin and creatinine levels, type of admission before cardiac surgery. Clinical data for potential perioperative risk factors included the type of procedure, length

of procedure, length of cardiopulmonary bypass (CPB), cerebral oximetry desaturation of 20% or more from baseline, and lowest regional cerebral oxygen saturation. Clinical data for the postoperative factors included the total amount of fluid balance daily, and the amount of red blood cells product received daily.

Clinical data for patient outcomes. Collected from the medical charts were amount of time (in hours) before the first extubation and the first mobilization following surgery, returning to the operating room following the initial procedure, length of hospital stay, discharge location (home, other hospital, rehabilitation center or long-term care) and death within 12 months.

Patient trajectories relative to SSD and delirium. Trajectories for SSD and delirium were described using the SSD and delirium assessments described above in the first four days following the procedure. Trajectories were identified from previous literature and are presented in Table 1.

Study Size

The cohort sample size was 346 patients. No power calculations were performed for this secondary analysis.

Statistical Analysis

Continuous variables are presented as means ± standard deviations and categorical variables are presented as frequencies and percentages. The alpha significance level was set at 0.05 for all tests. The normality of the distribution was assessed using the Kolmogorov-Smirnov and the Shapiro-Wilk tests. Continuous variables were contrasted between the different trajectories using analysis of variance (ANOVA). Equality of variances was assessed with the Levene's test and, when equality could not be assumed, the Welch's statistic was used to determine statistical significance. When statistical significance was achieved, post hoc tests were performed to identify which trajectories differed from one-another using Bonferroni (or Games-Howell post hoc test when homogeneity of variance could not be assumed). Categorical variables were contrasted

between the different trajectories using Chi-Square test. Fisher's exact test was used when cell counts in the crosstabs were less than five. All statistical analyses were performed using SPSS, version 25.0 (SPSS Inc., Chicago, USA).

RESULTS

Descriptive data on the characteristics of patients in the different trajectories.

As presented in Table 1, four different trajectories were identified among the cohort of 346 patients: Trajectory A: no SSD or delirium, Trajectory B: SSD without developing delirium, Trajectory C: SSD followed by delirium, Trajectory D: delirium without presenting SSD. All descriptive characteristics of patients in the different trajectories are presented in Table 2. Below, we describe the patient characteristics for each trajectory.

Trajectory A consisted of 110 patients who did not present SSD or delirium in the first four postoperative days. As presented in Table 2, patients were mostly males, had few comorbidities, and had a low cardiac operative risk as reflected by the EuroSCORES [39]. About half of these patients had preoperative left ventricular dysfunction but no differences in left ventricular dysfunction between the four groups. The majority underwent isolated CABG procedures. The majority were discharged home and one patient died in the 12 months following the surgery.

Trajectory B consisted of 62 patients who had SSD following cardiac surgery without developing delirium in the first four postoperative days. The majority presented SSD for one day, while the rest presented SSD for two or three days. Patients were mostly males and presented with a medium cardiac operative risk as reflected by the EuroSCORES [39]. Approximately a third had preoperative left ventricular dysfunction. Preoperative hemoglobin levels were low and creatinine levels were in the normal values. The majority underwent isolated CABG procedures. The majority were discharged home and one third were discharged to another hospital. Four patients died in the 12 months following surgery.

Trajectory C consisted of 69 patients who presented both SSD and delirium in the first

four postoperative days. The majority (n=45) presented SSD before the onset of delirium, while the rest presented SSD symptoms after the delirium episode. Subsyndromal delirium was generally present for one day before delirium was diagnosed. The majority (n=48) of patients presented SSD symptoms for 1 day, while the rest presented SSD for two (n=6) or three days (n=8). As presented in Table 2, the patients in trajectory C were the eldest patients over all trajectories, where mostly males, and a third had auditory and visual impairment. Around the fifth needed help with activities of daily living or had a walking aid. These patients presented with a medium cardiac operative risk as reflected by the EuroSCORES [39]. About 40% percent of these patients had preoperative left ventricular dysfunction. Preoperative hemoglobin levels and creatinine levels were in the high range of normal values (mean: 126.7, SD: 112.56). About one third underwent isolated CABG procedures, isolated valve procedure, or two or more procedures. In terms of postoperative outcomes, the majority were discharged to another hospital or home. Mortality rate was triple that of patients in trajectory B with 16 patients (23%) dying in the 12 months following surgery.

Trajectory D consisted of 105 patients who presented delirium without SSD in the first four postoperative days. Most patients presented delirium for two or three days. Patients were mostly males. close to a quarter had auditory and visual impairment preoperatively, around the third needed help with activities of daily living. Patients presented with a medium cardiac operative risk as reflected by a the EuroSCORES [39]. Preoperative hemoglobin levels were low and creatinine levels were in the high range of normal values. About one third underwent isolated CABG procedures, isolated valve procedure, or two or more procedures. In terms of postoperative outcomes, about half were discharged either home or to another hospital. The mortality rate was 11.4% with twelve patients dying in the 12 months following surgery.

Out of the patients who presented delirium (either classified in Trajectory C or D), 245 (71%) had resolved their delirium on day 4 following surgery.

Differences in the risk factors and outcomes of SSD and delirium

As presented in Table 2, in comparison to patients without SSD or delirium, patients who presented SSD were statistically older, needed more help with activities of daily living, had higher EuroSCORE, lower preoperative hemoglobin, had lower baseline cerebral oximetry values, had similar surgical procedures and received more liquids following surgery. In comparison to patients who developed delirium following surgery (trajectories C and D), patients who presented SSD had similar preoperative characteristics (age, euroSCORE, low cerebral oximetry values and hemoglobin values, help with ADLS), but underwent less complicated procedures that were shorter, presented lower decrease in cerebral oximetry during surgery, and received less fluids and less red blood cells in the first 2 days following surgery.

Of patients who presented delirium in trajectories C and D, those who presented SSD before delirium were more at risk with more often both auditory and visual impairment and higher preoperative risk, as reflected by higher EuroSCORE II scores (Table 2). Patients who presented both SSD and delirium, were aged an average of 74 years old versus an average of 71 for patients with only delirium (Table 2). The postoperative stay did not differ between patients in trajectories C and D.

As reported in Table 3, patients who presented SSD (trajectory B) had similar intubation duration postoperatively and discharge location than patients from trajectory A (who do not present with SSD or delirium), but had longer lengths of stay and higher mortality rate than patients who did not present SSD or delirium. Patients who presented delirium (either trajectory C or D) were intubated longer and had higher lengths of stay and mortality rates than patients who did not develop delirium (trajectory A or B). Among patients who presented delirium in trajectories C or D, patients who presented both SSD and delirium (trajectory C), had worsened outcomes in terms of discharge location and mortality rates than patients who only presented delirium (trajectory D).

DISCUSSION

The aim of this study was to assess and describe the differences in the risk factors and outcomes related to the different trajectories of SSD and delirium in cardiac surgery patients. We considered four different trajectories with regard to SSD and delirium over the first four postoperative days. In comparison to patients without SSD or delirium, patients who developed only SSD following surgery were those who had preoperative characteristics that correspond to the risk factors known for delirium, such as older age and higher operative risk score, but who underwent less complicated surgical procedures, received less transfusions postoperatively and had a lower positive fluid balance postoperatively than those who develop delirium. In this cohort, we observed that the increased amount of perioperative and postoperative risk factors seems to correlate with an increased gravity of the delirium syndrome –from SSD to delirium. We observed that patients who presented with both SSD and delirium were sicker preoperatively and underwent surgeries as complicated as patients with only delirium while also presenting a postoperative stay as complicated as patients with only delirium.

Our study underlines the impact of SSD on the prognosis of cardiac surgery patients. In terms of outcomes, patients with SSD were worst off in comparison to those without both SSD and delirium, as reflected by longer lengths of stay and higher mortality. More importantly, patients with SSD and delirium had worsened outcomes in comparison to those with only delirium; i.e. mortality rate was higher when SSD was combined with delirium in comparison to delirium alone. This finding shows the crucial importance of preventing the progression of SSD to delirium.

In terms of risk factors for SSD, previous studies among cardiac surgery patients found similar but also conflicting results to our observations. Risk factors highlighted in previous studies include older age, higher EuroSCORE values, pulmonary bypass duration, receiving blood transfusions, and an incidence of emergency surgeries [10-13]. History of cerebrovascular disease, diabetes and left ventricular dysfunction have been related to SSD converting into delirium in a small cohort study of 53 cardiac surgery patients [12]. A recent cohort study with a focus on post-cardiac surgery delirium has reported 31.2 % rate of incident SSD and, contrarily to previous cohort

studies, has not observed a relation between SSD and bad patient outcomes [28]. Finally, SSD has been the focus of one randomized controlled trial in which it has been recognized a major risk factor for developing delirium [26].

Results regarding risk factors of SSD correspond to that of previous studies in terms of older age, comorbidities (as reflected by EuroSCORE), blood transfusion, complicated procedures with longer duration of cardiopulmonary bypass, and a complicated postoperative period [10,11]. Contrarily to Breu et al.'s observations, we did not find a history of cerebrovascular disease, diabetes, left ventricular dysfunction, the incidence of emergency operations or duration of procedure to be risk factors specific for SSD, but rather risk factors for SSD converting into delirium or for delirium. In our cohort, half of patients presenting with SSD eventually converted to delirium while in Breu et al's cohort, only 2% of patients with SSD converted into delirium. Methodological differences can explain this. We used the reference standard in terms of delirium assessment, i.e. the medical diagnosis, while Breu et al used the ICDSC to define delirium.

Previous studies have found conflicting results in terms of patient outcomes related to SSD in a cardiac surgery context. Both Breu et al and Li et al found SSD to be related to longer lengths of stay and discharge locations other than home. Sanson et al [28], found diverging results regarding these outcomes and Breu did not observe mortality being related to SSD. We observed SSD to be related to longer lengths of stay and higher mortality. Moreover, patients with SSD and delirium had worsened outcomes in comparison to those with only delirium. These results are consistent with previous studies among the critical care populations [2,6,8,19].

Limits

The large sample of this cardiac surgery cohort is a strength of this study. Independent assessment of SSD and delirium during usual care by the trained healthcare team limited the possibility of bias regarding their assessment about study hypothesis. However, as delirium and SSD are often underrecognized, it is possible that patients who presented delirium or SSD were not identified by the healthcare team. As such, we considered both the nursing and the medical

assessment and also chose to consider terms such as “confusion” and “encephalopathy” in the medical charts as indicative of delirium. Limitations are relative to its retrospective nature, which limited the possibility of assessing with certainty the type of delirium and then being able to report on types for trajectories C and D. Patients in this cohort were recruited from a single center thereby limiting the generalizability of our observations. Our analyses were also limited by the current state of knowledge regarding the definition of SSD and known risk factors. The lack of consensus on the definition of SSD matched with the known under-recognition of SSD by nursing staff may have resulted in the misclassification of patients in the different trajectories of the cohort. Furthermore, as we assessed for risk factors identified in previous albeit scarce literature and for risk factors known to contribute to delirium, there may be other existing risk factors that were not considered in this study.

Implication for Practice

Our results shed light on the serious condition that is SSD among cardiac surgery patients. Our observations on the increased mortality rates when SSD develops into delirium stresses the importance of quickly identifying SSD to prevent its progression. In our cohort, half of patients presenting with SSD eventually progressed to developing delirium. A deeper understanding of key characteristics of patients presenting with SSD who are susceptible to developing delirium will support nursing practice. Specifically, findings such as the results of our study, can help nurses target high-risk patients and focus their efforts on non-pharmacological interventions that will prevent the progression of the syndrome. In our study, we highlight characteristics that are modifiable, such as the postoperative fluid balance. Future studies should focus on such characteristics to support nursing practice in terms of the identification of SSD and the prevention of its progression to delirium.

Conclusion

To this day and to our knowledge, SSD has been the subject of very few studies among post-cardiac surgery patients. This study identified characteristics of patients with SSD as well as their increased mortality rate when compared to patients who do not develop SSD or delirium. Our results highlight the urgent need for early identification of SSD and the implementation of preventive measures. The characteristics identified could help healthcare teams in prospectively targeting patients at risk of SSD and who may develop delirium. This represents a crucial first step towards improving the outcomes post-cardiac surgery in patients presenting SSD.

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WHAT'S NEW?

- Patients with both subsyndromal delirium that progressed to delirium had worsened outcomes in terms of length of stay and mortality in comparison to those with delirium only.
- It is important for nurses to identify SSD and prevent its the progression to delirium.

Tables

Table 1. Trajectories observed in the cohort.

Trajectories	Definition	Conditions defined for this cohort
A	Absence of both SSD and delirium	1) Never a score other than 0 on the ICDSC AND 2) Never a diagnosis of delirium, on each day of the first four postoperative days
B	SSD only and never delirium	1) A score between 1 and 3 on the ICDC on one of the first four postoperative days AND 2) Never a diagnosis of delirium during the first four postoperative days
C	SSD followed by delirium	1) A score between 1 and 3 on the ICDC, without a diagnosis of delirium on one of the first four postoperative days FOLLOWED BY 2) Diagnosis of delirium on one or more of the following days
D	Delirium only and never SSD	1) A diagnosis of delirium on one or more of the first four postoperative days AND 2) Never a score other than 0 on the ICDSC on days without a diagnosis of delirium

SSD: subsyndromal delirium. The Trajectories variable was treated as categorical.

Table 2. Patient characteristics per trajectories.

Variables		Trajectories				*P* value
	All cohort	A *Absence of SSD and of delirium*	B *SSD only*	C *SSD and delirium*	D *Delirium only*	
	N=346	N=110	N=62	N=69	N=105	
Preoperative characteristics						
Age, *years*	70.17 (9.09)	66.46 (8.1)	71.02 (9.9)	74.03 (8.8)	71 (8.47)	<0.001[c]
Gender, *male*	259 (74.5)	84 (76.4)	47 (75.8)	49 (71)	79 (75.2)	0.87
Tobacco and alcohol consumption, *yes*	11 (3.2)	1 (0.9)	1 (1.6)	3 (4.3)	6 (5.7)	0.164
Auditory and visual impairment, *yes*	68 (19.7)	15 (13.6)	9 (14.5)	21 (30.4)	23 (21.9)	0.006[b]
Need help with ADL, *yes*	62 (17.9)	11 (10)	9 (14.5)	14 (20.3)	28 (26.7)	0.005
Walking aid, *yes*	48 (13.9)	4 (3.6)	11 (17.7)	16 (23.2)	17 (16.2)	0.001
EuroSCORE II	3.74 (4.46)	2.41 (2.21)	3.60 (3)	5.01 (6.84)	4.45 (4.68)	<0.001[¥b*]
History of neurological disorders, *yes*	64 (18.5)	14 (12.7)	6 (9.7)	18 (26.1)	26 (24.8)	0.009
History of psychiatric disorders, *yes*	30 (8.7)	8 (7.3)	6 (9.7)	5 (7.2)	11 (10.5)	0.76
Left ventricular dysfunction, *yes*	152 (43.9)	51 (46.4)	22 (35.5)	27 (39.1)	52 (49.5)	0.39
Diabetes, *yes*	121 (35)	37 (33.6)	19 (30.6)	21 (30.4)	44 (41.9)	0.25
Previous cardiac surgery, *yes*	25 (7.2)	6 (5.5)	3 (4.8)	7 (10.1)	9 (8.6)	0.54
Cerebral oximetry, *%*	66.18 (8.27)	69.30 (7.3)	65.58 (9.18)	64,27 (8.19)	64,86 (7.95)	<0.001[c]
Hemoglobin	126.05 (29.26)	132.44 (16.87)	127.39 (27.26)	125,57 (47.66)	117,57 (23.99)	<0.001[¥c*]
Creatinine	106.31 (61.24)	90.36 (31.93)	94.15 (41.18)	126,7 (112.56)	119,3 (46.74)	<0.001[e]
Type of admission, *urgent*	45 (13)	11 (10)	9 (14.5)	13 (18.8)	12 (11.4)	0.39

Variables		**Trajectories**				***P* value**
	All cohort	**A** *Absence of SSD and of delirium*	**B** *SSD only*	**C** *SSD and delirium*	**D** *Delirium only*	
	N=346	**N=110**	**N=62**	**N=69**	**N=105**	
Perioperative characteristics						
Type of procedure, *yes*						<0.001
Isolated CABG	166 (48)	66 (60)	36 (58.1)	27 (39.1)	37 (35.2)	
Isolated valve	94 (27.2)	32 (29.1)	17 (27.4)	16 (23.2)	29 (27.6)	
Two or more combined procedures	86 (24.9)	12 (10.9)	9 (14.5)	26 (37.7)	39 (37.1)	
Length of procedure, *hh:mm*	3:48 (3:03)	2:59 (0:51)	2:54 (0:59)	4:36 (3:59)	4:41 (4:09)	<0.001¥e*
Length of CPB, *hh:mm*	1:24 (0:38)	1:21 (0:36)	1:19 (35:06)	1:24 (0:36)	1:28 (43:40)	.501
Cerebral oximetry desaturation of at least 20% from baseline, *yes*	39 (11.3)	11 (10)	4 (6.5)	10 (14.5)	14 (13.3)	0.53
Lowest rSO2 value, *%*	59.03 (8.98)	62.21 (7.13)	60.36 (8.88)	56.5 (8.64)	57 (9.86)	<0.001[e]
Postoperative characteristics						
Fluid balance, *ml*						
Day 1	2849,45 (2056.74)	1746,74 (1675.98)	2154,29 (1891.12)	3904,45 (1866.85)	3695,98 (1916.09)	<0.001¥e*
Day 2	3016,17 (2334.23)	1702,12 (2047.71)	2487,04 (2094.46)	3765,22 (2144.73)	3687,39 (2328.04)	<0.001¥e*
Day 3	2873,14 (2598.6)	1712,88 (1946.29)	2452,63 (3014.42)	3534,4 (2625.61)	3033,51 (2482.88)	0.033[c]
Red blood cells, *ml*						
Day 1	176,42 (457.25)	28,55 (132.07)	157,65 (566.16)	221,88 (309.99)	312,54 (617.28)	<0.001¥e*
Day 2	217,38	52,51 (181.06)	190,98 (589.31)	278,87 (352.46)	365,28 (631.77)	<0.001¥e*

Variables		**Trajectories**				***P* value**
	All cohort	**A** *Absence of SSD and of delirium*	**B** *SSD only*	**C** *SSD and delirium*	**D** *Delirium only*	
	N=346 (482.46)	**N=110**	**N=62**	**N=69**	**N=105**	
Day 3	231,35 (481.47)	57,84 (200.48)	204,23 (592.90)	312,54 (382.20)	378,33 (609.06)	<0.001¥e*

ADL, activities of daily life; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; rSO2, regional cerebral oxygen saturation; SSD, subsyndromal delirium

Note. Data is presented as means (standard deviations) for continuous variables or as frequencies (percentages) for continuous variables. For categorical variables, Chi-Squared test was performed unless the cell count was less than n=5. In that case Fisher's exact test was performed. For continuous variables, analysis of variance (ANOVA) was performed unless otherwise indicated using the following symbols:

¥ Welsh test when Levene's test was significant and so when equality of variances could not be assumed

* Games-Howell test

a. Only C differs from the other trajectories.

b. All trajectories differ.

c. Only A differs from the other trajectories.

d. Only D differs from the other trajectories.

e. A and B differ from C and D.

f. A and B differ from one another and they also differ from C and D.

Table 3. Patient outcome per trajectories.

Outcomes	**All cohort**	**Trajectories** **A** *Absence of SSD and of delirium*	**B** *SSD only*	**C** *SSD and delirium*	**D** *Delirium only*	**P value**
	N=346	**N=110**	**N=62**	**N=69**	**N=105**	
Delirium, *yes*						
Day 1	39 (11,3)	0	0	10 (14.5)	29 (27.6)	<0.001
Day 2	104 (30,1)	0	0	35 (50.7)	69 (65.7)	<0.001
Day 3	142 (41,0)	0	0	50 (72.5)	92 (87.6)	<0.001
Day 4	108 (31,2)	0	0	30 (43.5)	78 (74.3)	<0.001
Time to first extubating, *hh:mm*	6:59 (4:53)	5:32 (3:38)	5:22 (3:58)	8:46 (5:03)	8:16 (5:39)	<0.001¥e*
Time to first mobilization, *hh:mm*	12:41 (7:03)	11:51 (6:39)	11:44 (7:08)	14:20 (6:30)	13:01 (7:35)	.112
Return to the OR, *yes*	13 (3.8)	1 (0.9)	3 (4.8)	4 (5.8)	5 (4.8)	0.28
Length of hospital stay, *days*	12.15 (9.6)	8.52 (4.85)	11.36 (6.71)	14.63 (14.43)	14.89 (9.88)	<0.001¥f*
Discharge location						0.004
Home	191 (55.2)	77 (70)	36 (58.1)	26 (37.7)	52 (49.5)	
Other hospital	117 (33.8)	23 (21)	19 (30.6)	31 (44.9)	44 (41.9)	
Readaptation or long-term care	28 (8.1)	8 (7.3)	3 (4.8)	9 (13)	8 (7.6)	
Death within 12 months post-surgery, *yes*	33 (9.5)	1 (0.9)	4 (6.5)	16 (23.2)	12 (11.4)	<0.001

OR, operating room; SSD, subsyndromal delirium

Note. Data is presented as means (standard deviations) for continuous variables or as frequencies (percentages) for continuous variables. For categorical variables, Chi-Squared test was performed unless the cell count was less than n=5. In that case Fisher's exact test was performed. For continuous variables, analysis of variance (ANOVA) was performed unless otherwise indicated using the following symbols:

¥ Welsh test

* Games-Howell test

a. Only C differs from the other trajectories.

b. All trajectories differ.

c. Only A differs from the other trajectories.

d. Only D differs from the other trajectories.

e. A and B differ from C and D.
f. A and B differ from one another and they also differ from C and D.