

## Risk factors for Delirium after major surgery

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### Abstract

**Aim:** The high prevalence of delirium in surgical clinics and risk factors need to be determined for evidence-based practices to prevent the adverse effects it causes in the early period. This study aimed to determine the development of delirium and associated risk factors in patients over 65 years of age after major surgical intervention.

**Material and Method:** This study was conducted as a descriptive and relation-seeker type study and it was held between September 2018-April 2019. Age-appropriate criteria for a total of 100 patients aged  $\geq 65$  who created the climb sample were used. The study used the Delirium Screening Scale (Nu-DESC) as data collection tools, Surgeon Before-During-Post-intervention Risk Factors Evaluation Form and a Mini-Mental Test. The SPSS 25.0 statistics package program was used to evaluate the data.

**Results:** Delirium was more common in men aged 75 years and over who were using multiple drugs, long anesthesia duration, high serum cytokine levels, low hemoglobin and albumin levels, and the results were statistically significant ( $p < 0.05$ ).

**Discussion:** Evidence-based effective treatment protocols for delirium after major surgery and risk factors for preventive interventions should be determined. When designing future delirium prevention strategies or in future etiological studies, they should focus on delirium-prone patients based on these risk factors.

### Keywords

Delirium; Major surgery; Old population; Postoperative Delirium

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## Introduction

Postoperative delirium (POD); Delirium, which can be seen after surgical intervention, occurs with sudden consciousness and disorientation due to physical or physiopathological reasons. It is defined as an acute neuropsychiatric syndrome characterized by temporary and reversible dysfunction of the brain. In addition to these assumptions in its physiopathology, delirium, in the classification made by taking psychomotor behavior changes into account, is divided into 3 (three) categories as hypoactive, hyperactive and mixed type.

These are [1] in the hyperactive delirium table, the psychomotor activity of the patient has increased; extremely sensitive to stimuli (i), the patient's psychomotor activity and sensitivity to stimuli are reduced in the hypoactive delirium table (ii), the mix delirium is a type of delirium in which the patient has a hyperactive and hypoactive picture during the day (iii). Postoperative delirium-related risk factors are evaluated as preoperative, intraoperative and postoperative risk factors [2]. Preoperative risk factors for delirium are age 80 and over [3], male gender [4], presence of urinary catheter [5], low serum albumin levels and lower body mass index [6], use of risky drugs and multiple drugs [7], low hemoglobin level, respiratory system diseases, fever, hypocalcemia, azotemia, liver function test disorders, glucose disorders, hyperamylasemia, hyperbilirubinemia, serum sodium-potassium disorders, metabolic acidosis, cognitive-auditory and visual disorders, inactivity, sleep disturbance [8]. Risk factors during surgery; the duration of surgical intervention and anesthesia, the type of anesthesia used, the depth of sedation, the amount of blood lost, hypotension, blood transfusion due to blood loss [9] are the duration of the surgical procedure. Delirium risk factors in the post-surgical period are fluid after surgery, electrolyte imbalances, infections, and postoperative hypoxia [3].

There is a need to determine the risk factors for evidence-based practices to prevent delirium at a high rate in surgical clinics and to prevent the negative effects it causes in the early period. These preventive practices will provide early diagnosis of delirium, reduce morbidity and mortality rates, and will positively affect diagnosis-treatment costs. In addition, with this study, which requires a multidisciplinary team approach, it will be able to raise awareness of health professionals about predicting-prevention in the care and management of delirium patients. This study was conducted to determine the development of delirium and associated risk factors in patients over 65 years of age after major surgical intervention.

## Material and Methods

The research was conducted as a descriptive and relation-seeker type study. It was held in the Orthopedics and Cardiovascular Surgery clinics of a training research hospital between September 2018 and May 2019.

### Study Design

In this study, patients were evaluated in terms of delirium one day before surgery and an average of 3 days after surgery. The population of the study consisted of patients aged 65 years and over who were hospitalized in the orthopedic clinic for cardiac surgery at the hip prosthesis surgery and cardiovascular surgery clinic, who accepted voluntary participation in the study, and

gave verbal and written consent. The study was conducted with 100 patients who met the inclusion criteria without selecting the sample. Those under 65 years of age, those with the Standard Mini Mental State Assessment Test (MMSE) score less than 24, patients with a history of delirium prior to surgery, patients with a history of neurological or mental illness, those using sedatives or antidepressants, infection or chronic inflammatory conditions, patients taking glucocorticoids from time to time, using anti-inflammatory drugs at least 3 days prior to surgery, having communication disabilities, alcohol or drug addiction were not included. This study was conducted to determine the development of delirium and associated risk factors in patients over 65 years of age after major surgical intervention.

Hypotheses tested in research;

i. H1; There is a difference between preoperative risk factors in patients with and without delirium.

ii. H2; There is a difference between the inoperative risk factors of patients with and without delirium.

iii. H3; There is a difference between postoperative risk factors in patients with and without delirium.

### Data Collection and Tools

All study data before, during, after, and during the implementation phase were collected by the researcher.

### Introductory Features Form

This form included twelve questions to determine the age, gender, marital status, educational status, medical diagnosis, comorbid chronic diseases, smoking, alcohol use status, continuous drug use status.

### Pre-During-Post- Surgery Risk Assessment Form

This form, which was developed using the literature, include three-stage follow-up forms that include delirium-related risk factors before surgery, during and after surgical intervention [10].

### Nursing Delirium Screening Scale (Nu-DESC)

This scale was used to screen delirium before and after surgery. It consists of five items: disorientation, inappropriate behavior, inappropriate communication, illusions/hallucinations, and psychomotor slowing [11]. The items are evaluated using 0, 1 and 2 points. In this study, the Turkish validity and reliability study of the scale was carried out first. Analyses were performed for the specificity, sensitivity, and diagnostic accuracy (ROC) of Nu-DESC. Cut off value was  $> 1$  as a result of ROC analysis. The sensitivity at the breakpoint was 92.27 and specificity was determined as 92.72.

### Standardized Mini-Mental State Evaluation

This test was developed in 1975. Its validity and reliability in Turkish were tested in 2002. It is the most commonly used test for dementia screening [12]. It consists of 11 questions and is rated on a 30-point scale. Normal level is indicated by 24–30, 18–23 points indicate mild dementia, and 6–17 points correspond to severe dementia. In this study, the first evaluations of all patients were made within 24 hours of their admission to the hospital. Patients with a score of  $< 23$  at the first evaluation were excluded from the study.

### Ethical Aspect of the Research

Approval was obtained from the Ethics Committee of XXX University Clinical Research (Decision number: KIA2018 / 195) and the chief physician of the hospital where the study was

conducted, in terms of the applicability of the study. Before completing the data collection forms, patients were informed about the study and their written and verbal consent was obtained.

**Evaluation of Data**

The IBM SPSS 25.0 (SPSS Inc., Chicago, IL, USA) package program was used to evaluate the data. The Kolmogorov-Smirnov, Shapiro Wilk-W test was performed and it was found that the data did not show a normal distribution. the Mann-Whitney U test, the Kruskal-Wallis test, and the Chi-square test were used. The results were evaluated at a 95% confidence interval and p <0.05 significance level.

**Table 1.** Comparison of delirium development status with preoperative risk factors

Risk Factors for Delirium Before Surgery	(n = 100)		P	X <sup>2</sup> / KS / U / t
	Delirium (n = 23)	No Delirium (n = 77)		
	≥2 n %	<2 n %		
Age	75.80 ± 5.7	71.57 ± 5.9	0.016	2.496
Gender				
Female	3 (13)	30 (39)	0.022	0.850
Male	20 (87)	47 (61)		
Chronic Disease;				
There is	23 (100)	45 (59)	0.048	2.684
None	0 (0)	32 (41)		
Chronic Illness				
Diabetes	5 (22)	28 (36)		
Hypertension	0 (0)	22 (29)		
Diabetes and Hypertension	18 (78)	12 (16)	0.628	0.267
Chronic obstructive lung disease	0	9 (12)		
Other (Urinary system, GIS, Musculoskeletal system)	0	6 (8)		
Medication Duration (Years)	10.09 ± 4.9	8.57 ± 6.2	0.032	-3.795
Number of Medications;				
No drugs,	0 (0)	15 (19)		
1-3 pieces,	0 (0)	42 (55)	0.042	2.250
4-6 pieces,	18 (78)	13 (17)		
7 and over	5 (22)	7 (9)		
Defect of vision				
No problem	8 (35)	56 (72)		
Yes Wears Glasses	15 (65)	21 (28)	0.047	3.726
Yes Not Wearing Glasses				
Untreatable Pain				
There is	16 (70)	0 (0)	0.048	3.884
No	7 (30)	77 (100)		
PO2	86.6 ± 4.8	85.9 ± 5	0.644	-0.465
Lab Findings				
Na	138 ± 2.8	139.3 ± 3.3	0.636	0.477
K	4.3 ± 0.5	4 ± 0.6	0.154	-1.449
Mg	1.9 ± 0.2	1.8 ± 0.3	0.694	-0.396
BUN / Creatinine	17.2 ± 8.9	14.3 ± 4.2	0.131	-1.535
Glucose	119 ± 42.12	112.9 ± 29.41	0.489	-0.698
Albumin	3.2 ± 0.6	3.6 ± 1.2	0.039	-3.154
Hb	14.2 ± 5.8	13 ± 1.9	0.291	-1.067

Pearson X<sup>2</sup> test for categorical variables, Kolmogorov Smirnov test for X<sup>2</sup> tables with a categorical variable but not showing normal distribution and less than 5 cells of the observed variable, Mann-Whitney U test for two variables that are not categorically and normally distributed, Student t-test was used for two variables. Significance was evaluated at the p <0.05 level. Kolmogorov Smirnov test: KS, Mann-Whitney U: U, t: student t-test, COPD: Chronic Obstructive Pulmonary Disease, GIS: Gastro-Intestinal System, BUN: Blood Urea Nitrogen, Hb: Hemoglobin.

**Results**

Delirium developed in 23% of the patients (n = 23). This difference was statistically significant (p <0.05). It was determined that delirium developed more on the 1st day after surgery, and no new delirium was observed after the 3rd day, and the difference was statistically significant (p <0.05). Hypoactive delirium was in 18 patients, hyperactive delirium in 2 patients and myxdelirium in 3 patients. It was found that in 1 patient, hypoactive delirium turned into musky delirium (Table 1).

Preoperative risk factors of the patients were evaluated (Table 1). It was determined that there was a significant difference (p <0.05) between patients with and without delirium in age, gender, duration of drug use, and variables. It was determined that patients with delirium were mostly males (p <0.05). While the presence of chronic disease was detected in all patients (p > 0.05), there was a significant difference between patients who developed delirium and those who did not. The duration of drug use was found to be significantly different in patients with and without delirium (p <0.05). It was found statistically significant (p = 0.042 <0.05) according to the number of drugs. It was determined that the difference was caused by the use of 4-6 drugs. The values of the presence of visual impairment and the use of glasses were statistically significant (p <0.05). The values for the presence of incurable pain before surgery were statistically significant (p <0.05). There was no significant difference in laboratory findings, except for albumin value (p > 0.05). It was found that the albumin value, which may be associated with delirium after surgery, was low in patients who developed delirium (Table 1).

The difference between mean surgical duration scores during the surgical intervention, mean duration of the anesthesia applied, and mean scores of the pO2 level during the surgical

**Table 2.** Comparison of risk factors during surgery in patients with and without delirium

Variable Risk Factors for Delirium During Surgery	(n = 100)		P	X <sup>2</sup> / KS / U / t
	Delirium ≥2, n = 23 n %	No Delirium <2, n = 77 n %		
Surgical Operation Type: CVS, Orthopedics (%)	14, 9 (61, 39)	47, 30 (61, 39)	0.341	0.905
Surgery Operation Time (min.)	179.75 ± 58.73	147.57 ± 49.73	0.042	-2.085
Anesthesia Type: General, Spinal, Epidural (%)	16, 6, 1 (70, 26, 4)	57, 20, 0 (74, 26, 0)	0.875	0.173
Anesthesia Time (min.)	198.70 ± 64.56	166.33 ± 51.23	0.051	-1.952
Loss of Blood; <500, 500-1000, >1000 (%)	17, 6, 0 (74, 26, 0)	70, 7, 0 (91, 9)	0.815	0.635
Blood Transfusion, Done (%)	6 (26) 17 (74)	4 (5) 73 (95)	0.852	0.167
Transfusion Requirement 1 Unit (%)	6 (26)	4 (5)	0.737	0.644
Blood pressure: 130/85 mm / Hg, > 130/85, <130/85 (%)	11, 4, 8 (48, 17, 35)	33, 31, 13 (43, 40, 17)	0.452	0.404
Body temperature 36-37, > 37, <36	18, 5, 0 (78, 22, 0)	45, 32, 0 (59, 41, 0)	0.640	-0.877
PO2:	93.40 ± 5.26	98.06 ± 2.21	0.043	-2.946

Pearson's X<sup>2</sup> test for categorical variables, Kolmogorov Smirnov test for X<sup>2</sup> tables with a categorical variable but not showing normal distribution and less than 5 cells of the observed variable, Mann-Whitney U for two non-categorical and non-normally distributed variables, Student t-test was used for the variable. Significance was evaluated at the p <0.05 level. Kolmogorov Smirnov test: KS, Mann-Whitney U: U, t: student t-test. CVS: Cardiovascular Surgery

**Table 3.** Comparison of postoperative risk factors in patients with and without delirium

Day	Risk factors	n = 100		P	X <sup>2</sup> / KS / U / t
		Delirium (≥2) n = 23	No Delirium (<2) n = 77		
1 day	Number of Drugs; None, 1-3, 4-6, 7 and over (%)	0,0,23,0 (0,0,100,0)	15,42,13,7 (19,55,17,9)	0.047	2.693
2 days	//	0, 1, 2 2, 0 (0,33 67,0)	15, 42, 13, 7 (19, 55, 17, 9)	0.034	1.693
3 days	//	0,1, 2 2, 0 (0, 4 96, 0)	15, 42, 13, 7 (19, 55, 17, 9)	0.041	2.289
1 day	Pharmaceutical Groups; There are Medicines that Create Risk None (%)	2 3 (100) 0 (0)	9 (12) 68 (88)	0.029	3.989
2 days	//	2 3 (100) 0 (0)	9 (12) 68 (88)	0.029	3.989
3 days	//	2 3 (100)	9 (12) 68 (88)	0.120	0.729
1 day	Urinary Catheter; There is (%)	2 3 (100)	6 (8)	0.016	3.751
2 days	//	2 3 (100)	7 (9)	0.023	3.404
3 days	//	1 (4)	4 (5)	0.577	0.893
1 day	Untreatable pain; There is (%)	2 3 (100)	4 (5)	0.027	2.675
2 days	//	2 3 (100)	3 (4)	0.023	2.120
3 days	//	2 1 (91)	0	0.983	0.462
	SpO <sub>2</sub> :	90.33 ± 5.13	93.47 ± 5.74	0.047	3.465
Lab Findings					
	Na:	139.33 ± 2.08	139.21 ± 3.69	0.476	-0.719
	K:	4.10 ± 0.36	3.98 ± 0.55	0.476	-0.719
	Mg:	1.93 ± 0.28	1.83 ± 0.25	0.789	-0.270
	BUN / Creatinine:	20.41 ± 5.57	16.68 ± 4.48	0.042	-3.184
	Glucose:	128 ± 3.60	131.47 ± 39.98	0.484	-0.705
	Albumin:	3.30 ± 0.46	3.36 ± 0.39	0.042	3.872
	Hb:	11.56 ± 1.74	11.14 ± 1.15	0.966	0.043

Pearson's X<sup>2</sup> test for categorical variables, Kolmogorov Smirnov test for X<sup>2</sup> tables with less than 5 cells of the observed variable and not showing normal distribution, Mann-Whitney U for two non-categorical and non-normally distributed variables, Student's t-test was used for the variable. Significance was evaluated at the p <0.05 level. Kolmogorov Smirnov test: KS, Mann-Whitney U: U, t: student t-test.IV: Intra Venous , BUN : Blood Urea Nitrogen , Hb : Hemoglobin

intervention were found to be statistically significant (P <0.05), (Table 2).

While there was a significant difference between the patients who developed delirium and those who did not develop delirium after surgery, the number of drugs used, the presence of visual impairment, the presence of risky drugs, the presence of urinary catheters, untreatable pain, pO<sub>2</sub> and albumin values in laboratory findings (p <0.05), there was no significant difference between other risk factors (p > 0.05), (Table 3).

**Discussion**

In this study, the relationship between risk factors in surgical processes and delirium was evaluated. “H1: There was a difference between preoperative risk factors in patients with and without delirium. H2: There was a difference between risk factors for surgical sequence in patients with and without delirium. H3: The difference between postoperative risk factors in patients with and without delirium were confirmed.

It was determined that delirium developed more on the 1st day after surgery, and no new delirium was observed after the 3rd day, and the difference was statistically significant (p <0.05).

Hypoactive delirium was in 18 patients, hyperactive delirium in 2 patients, and myxdelirium in 3 patients. It was found that in 1 patient, the hypoactive delirium turned into musky delirium. With these results, it was determined that the delirium incidence was very low and the type of delirium that developed was hypoactive. In a study by Lin et al. (2015), the most common type of delirium was mixed type with 47.05 percent, followed by hypoactive delirium with 38.24 percent [13]. According to a systematic review, the most common delirium type in 2011 is mixed (55%) and hypoactive (46%) delirium [14]. It was determined that the results obtained in our study are supported by the literature.

In the study, mean age was found to be higher in patients with delirium than in those without delirium (p <0.05). In one study, it was stated that increasing age was related to the cause of delirium, and this confirms our result [15]. In the literature, it has been reported that the incidence of delirium is higher in male patients and that male gender is a risk factor in this respect [4]. Advanced age, decreased cognitive function, and multiple drug use are known risk factors for delirium [16]. The results obtained in the study are supported by the literature.

Diabetes and hypertension were found to be high in patients who developed delirium as a chronic disease (p <0.05). It is thought that these results are due to the fact that the sample of the study consists of patients aged 65 and over, and there are comorbid problems in this age group. In a study, it was reported that there is a significant relationship between increasing comorbid diseases and delirium[17]. Our results are supported by the literature. The duration of drug use was found to be significantly different in patients with and without delirium (p <0.05). In addition, the number of risky drugs used in these delirium patients and the presence of untreatable pain were found to be higher than patients without delirium, while the albumin value was found to be low.

It was determined that the mean duration of surgery, duration of anesthesia and pO<sub>2</sub> points of patients with delirium were higher than the mean scores of patients without delirium, and there was a significant difference. The literature reports about prolonged surgery and anesthesia duration, hypoxia, and delirium development after surgery [18]. The results obtained are supported by the literature.

In this study, the development of delirium was found to be higher in patients who underwent general anesthesia. Although different results were reported on the effect of the type of anesthesia on the development of delirium after surgery, there are studies indicating that general anesthesia is a risk factor for delirium after surgery. Monk et al. (2011) found that spinal anesthesia decreased the delirium incidence in patients with hip fracture [19]. In a published meta-analysis, it was reported that the type of anesthesia was not effective in terms of delirium development, but that postoperative cognitive function was significantly impaired in patients receiving general anesthesia [20]. The urinary catheter is an important risk factor for delirium as it leads to physical limitation and disrupts physiological functions [5].

There are studies reporting that low serum albumin levels and body mass index below normal as an indicator of malnutrition are associated with delirium [6]. It is reported that some drugs

and multiple drug use cause delirium [7]. Low hemoglobin level, respiratory system diseases, fever, hypocalcemia, azotemia, impaired liver function tests, glucose disorders, hyperamylasemia, hyperbilirubinemia, serum sodium-potassium disorders, metabolic acidosis, cognitive-auditory and visual disturbances, inactivity, sleep disturbance are important risk factors [8]. In the literature, it has been emphasized that high rates of BUN (Blood Urea Nitrogen) -creatinine are associated with delirium [21]. Björkelund et al. (2010) also found a significant relationship between delirium and high serum potassium, creatinine levels and low hemoglobin concentrations [17]. In this study, it was found that BUN and creatinine values were higher in patients with delirium, and hemoglobin and albumin values were low. It was determined that the obtained results were supported by the literature.

### Conclusion

It was found that the presence of risk factors for delirium in patients with delirium before, during and after surgery was higher than in other patients who did not develop delirium. It is necessary to identify and prevent the risk factors effective in delirium development before, during and after surgery to prevent and reduce delirium that may occur after surgery. Based on these results:

- i. Determination of risk factors in predicting, recognizing and monitoring delirium development guides preventive interventions. Therefore, when designing future strategies for the prevention of delirium or in future etiological studies, it is recommended to focus on delirium-prone patients based on these risk factors.
- ii. It is recommended to carry out an interdisciplinary study involving a wider patient group and their nurses to support this study and obtain evidence-based results.
- iii. It is recommended to develop scales for the diagnosis of delirium, to train health professionals on this issue, and to add these screening methods to daily routine follow-up.

### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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### Conflict of interest

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