

## ORIGINAL ARTICLE

# DEVELOPMENT OF DEMENTIA IN ELDERLY PATIENTS WITH POSTOPERATIVE DELIRIUM FOLLOWING HIP FRACTURE SURGERY

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### Abstract

**Introduction:** Postoperative delirium (POD) is a prevalent and undesirable neurocognitive consequence that arises following surgery and anesthesia in geriatric adults. Patients experiencing postoperative delirium may be at increased risk of developing long-term postoperative cognitive dysfunction and dementia. However, it is still unclear how much postoperative delirium (POD) affects the likelihood of developing dementia in this patient population.

**Objective:** The aim of this study was to examine the association between the occurrence of postoperative delirium and the development of new-onset dementia in elderly patients within one year following hip fracture surgery.

**Materials and Methods:** The study included patients aged 65 and older who underwent surgical treatment for proximal femur fractures at the University Clinic for Traumatology and Orthopedics. Patients with pre-existing dementia or cognitive impairment were excluded. Preoperative cognitive status was evaluated using the Abbreviated Mental Test (AMT-10) and the Informant Questionnaire on Cognitive Decline in the Elderly – Short Form (IQCODE-SF). Postoperative delirium was assessed during hospitalization using the Confusion Assessment Method (CAM). Patients were followed for one year after surgery to identify newly diagnosed dementia through medical record reviews. Statistical analysis was performed with SPSS version 25.0.

**Results:** This pilot study involved 91 patients. Postoperative delirium occurred in 30 (32.97%) of them. At twelve-month follow-up, new-onset dementia was significantly more common in patients with postoperative delirium compared to those without POD (46.67% vs. 8.2%,  $p=0.000022$ ). Multivariate logistic regression analysis showed that postoperative delirium was an independent predictor of dementia (OR = 9.765, 95% CI 2.939–22.452,  $p < 0.0001$ ).

**Conclusion:** Postoperative delirium is a risk factor for subsequent dementia following hip fracture surgery. Elderly hip fracture patients who exhibit POD should be closely monitored for the development of dementia.

**Keywords:** *Delirium; dementia; elderly patients; hip fractures.*

## **Introduction**

As life expectancy rises and the population ages, the incidence of elderly individuals requiring emergency and elective procedures is increasing (1). Postoperative delirium (POD) is common in this group, with incidence rates ranging from 20% to 55% after high-risk procedures such as vascular, orthopedic, and cardiac surgeries (2-5). Hip fractures are frequent in older adults and often require emergency surgery. A meta-analysis of 26 studies on postoperative delirium showed incidence rates ranging from 4.0% to 53.3% in patients with hip fractures and from 3.6% to 28.3% in elective patients (6). Delirium involves a sudden change in consciousness levels and quickly occurring attention disturbances. These fluctuations often vary throughout the day and can be linked to other cognitive issues, such as memory loss or disorientation (7,8). Postoperative delirium is associated with adverse outcomes, including increased morbidity and mortality, cognitive and functional decline leading to loss of independence and lower quality of life, longer hospital stays, institutionalization, and higher healthcare costs. Patients with postoperative delirium may also develop long-term postoperative cognitive dysfunction and dementia (9,10). Delirium has been identified as a risk factor for dementia (11). Dementia is a syndrome caused by various diseases that gradually destroy nerve cells and damage the brain, usually leading to a decline in cognitive functions—such as thinking—that goes beyond normal aging. While consciousness remains intact, the decline in thought processes is often accompanied by, or even precedes, changes in mood, lack of emotional control, behavior, or motivation. In 2021, 57 million people worldwide had dementia, and over 60% of them live in low- and middle-income countries. Nearly 10 million new cases are diagnosed each year (1). The role of postoperative delirium (POD) in developing dementia among patients with hip fractures remains uncertain. The aim of this study was to examine the association between the occurrence of postoperative delirium and the development of new-onset dementia in elderly patients within one year following hip fracture surgery.

## **Material and Methods**

This pilot study included 91 patients aged  $\geq 65$  years without pre-existing cognitive impairment, classified as ASA I, II, or III, who were admitted to the University Clinic for Traumatology, Orthopedics, Anesthesia, Reanimation, Intensive Care, and Emergency department – Skopje for surgical treatment of proximal femur fractures during a two-year period. Written informed consent was obtained from all patients prior to their inclusion in the study. Patients with cognitive impairment, dementia or other neurodegenerative diseases, stroke with residual deficits, use of medications affecting cognitive functions, alcohol and drug abuse, blindness, deafness, contraindications to spinal anesthesia, and admission to the intensive care unit were excluded from the study. We assessed pre-existing cognitive impairment using two validated

instruments: the Abbreviated Mental State Test (AMT 10) (12,13) and the Cognitive Decline Information Questionnaire - Short Form (IQCODE - SF) (14). Screening for POD began immediately after surgery and was monitored throughout the hospital stay with the Confusion Assessment Method (CAM) (15). Postoperatively, patients were divided into two groups: those with postoperative delirium and those without. They were monitored for the development of dementia through medical record review for one year after surgery. The diagnosis of dementia was confirmed by neurologists and psychiatrists in patients who had previously undergone psychological testing by psychologists. The Ethics Committee of the Faculty of Medicine in Skopje approved the study. Statistical analysis of the data was performed using SPSS (ver. 25.0; IBM, SPSS, USA). The Shapiro-Wilk test was used to assess the normality of the data distribution. Categorical (attributive) variables are presented with absolute and relative numbers. Numerical (quantitative) variables are presented with mean, standard deviation, minimum, and maximum values. The Fisher's exact test and the chi-square test were used to compare categorical variables, and the Student t-test was used to compare quantitative variables. Logistic regression analysis was used to determine the predictive role of postoperative delirium in predicting dementia. Statistical significance was defined as  $p < 0.05$ .

## Results

This study presents the results of the analysis of samples and data from 91 patients admitted to the University Clinic for Traumatology, Orthopedics, Anesthesia, Reanimation, Intensive Care, and Emergency department – Skopje for surgical treatment of proximal femur fractures. The patients' age and gender distribution are shown in Table 1. Postoperative delirium occurred in 30 (32.97%) patients, and dementia within one year postoperatively was observed in 19 (20.88%). (Table 1)

**Table 1. Patients' characteristics**

Variable	
<b>Gender</b> n(%)	
female	77 (84.62)
male	14 (15.38)
<b>Age</b> (years)	
(mean $\pm$ SD) (min – max)	(79.9 $\pm$ 6.4) (66 – 95)
<b>POD</b> n(%)	30 (32.97)
<b>Dementia</b> n(%)	19 (20.88)

Patient gender was not significantly associated with the occurrence of postoperative delirium and dementia ( $p=0.812$  and  $p=1.0$ , respectively). (Table 2) The prevalence of postoperative delirium and dementia was similar in female and male patients (32.47% vs 35.71% and 20.78% vs 21.43%, respectively). (Table 2)

**Table 2. Gender distribution - patients with/without POD and with/without dementia**

variable		gender			p-level
		n	female n (%)	male n (%)	
<b>POD</b>	yes	30	25 (32.47)	5 (35.71)	X <sup>2</sup> =0.056 p=0.812
	no	61	52 (67.53)	9 (64.29)	
<b>Dementia</b>	yes	19	16 (20.78)	3 (21.43)	two-tailed p=1.0
	no	72	61 (79.22)	11 (78.57)	
total		91	77	14	

The age of patients with and without postoperative delirium did not differ significantly ( $81.1 \pm 5.1$  vs  $79.2 \pm 6.9$  years,  $p=0.19$ ). (Table 3) Patients with dementia were significantly older than those without dementia ( $82.6 \pm 5.3$  vs  $79.2 \pm 6.4$  years,  $p=0.035$ ). (Table 3, Figure 1)

**Table 3. Age of patients with/without POD and with/without dementia**

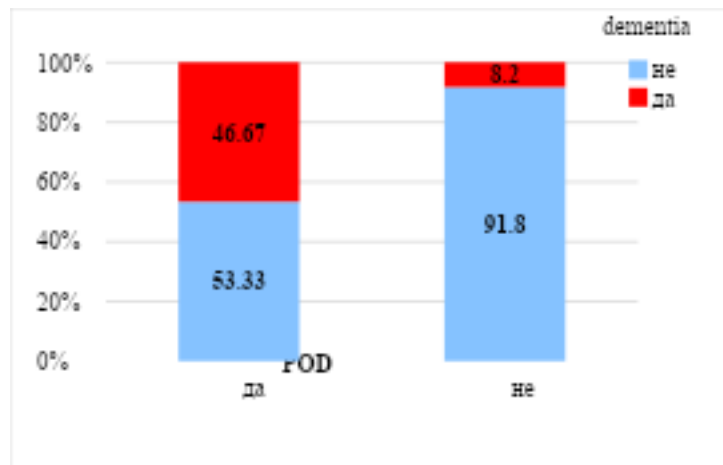
variable		statistical parameters - age			p-level
		n	mean $\pm$ SD	min – max	
<b>POD</b>	positive	30	$81.1 \pm 5.1$	73 – 94	t=1.3 p=0.19
	negative	61	$79.2 \pm 6.9$	66 – 95	
<b>Dementia</b>	yes	19	$82.6 \pm 5.4$	73 – 94	t=2.14 p=0.0353
	no	72	$79.1 \pm 6.4$	66 – 95	

**Figure 1. Average age – patients with/without dementia**

Dementia was significantly more common in patients with postoperative delirium compared to patients who did not have postoperative delirium (46.67% vs 8.2%,  $p=0.000022$ ). (Table 4, Figure 2)

**Table 4. POD – patients with/without dementia**

variable		dementia			p-level
		n	да n (%)	не n (%)	
<b>POD</b>	yes	30	14 (46.67)	16 (53.33)	X <sup>2</sup> =18.02 ***p=0.00022
	no	61	5 (8.20)	56 (91.80)	
total		91	19	72	



**Figure 2. POD – individuals with or without dementia**

Table 5 presents the results of univariate and multivariate logistic regression analysis evaluating the role of POD as an independent predictor of dementia. In the univariate analysis, both age and postoperative delirium were found to be factors significantly associated with dementia ( $p=0.04$  and  $p<0.0001$ ). The multivariate analysis confirmed only postoperative delirium as an independent significant predictor of dementia ( $p<0.0001$ ). Patients with POD have a 9.765 times greater chance of developing dementia compared to patients without POD (OR = 9.765 (95% CI 2.939-22.452)).

**Table 5. Binary logistic regression analysis evaluating the role of POD in the occurrence of dementia**

Discussion	variable	Univariate				Multivariate			
		p	Exp (B)	95% CI for Exp (B)		p	Exp (B)	95% CI for Exp (B)	
				Lower	Upper			Lower	Upper
Our findings support the hypothesis that postoperative	age	0.04	1.092	1.004	1.188	0.069	1.101	0.993	1.22
	POD	0.000	9.8	3.065	21.339	0.000	9.765	2.939	22.4

delirium is a risk factor for subsequent dementia following hip fracture surgery. Dementia was significantly more common in patients with postoperative delirium compared to patients who did not have postoperative delirium (46.67% vs 8.2%,  $p=0.000022$ ). Patients with POD were 9.8 times more likely to develop dementia than patients without POD (OR = 9.765 (95% CI 2.939-22.452)). Recent systematic reviews also find that delirium in older hospitalized patients is strongly associated with long-term cognitive decline and new-onset dementia, particularly following hip fracture surgery. A 2020 JAMA Neurology meta-analysis (24 studies,  $\approx 10,500$  patients) found that delirium was associated with worse cognitive outcomes at  $\geq 3$  months (Hedges'  $g \approx 0.45$ ,  $OR \approx 2.3$ ) (16). A 2020 meta-analysis in Archives of Gerontology (6 cohort studies, 844 patients) found that postoperative delirium (POD) following hip surgery increased the risk of dementia approximately 9-fold ( $OR \approx 8.96$ , 95%CI 5.34–15.03) (17). A 2021 international meta-analysis in J. Geriatric Psychiatry (6 studies, older hospitalized patients) reported an almost 12-fold increased odds of new dementia ( $OR \approx 11.9$ , 95% CI 7.3–19.6) if delirium occurs (18). The largest and most recent review (Ageing 2025) included 253 studies (about 137,000 patients) and found that delirium increases the odds of dementia incidence by about 5.4 times ( $OR \approx 5.37$ ) and is associated with higher rates of objective cognitive decline ( $OR \approx 1.58$ ) (19).

It has been hypothesized that delirium can lead to uncovering or identifying pre-existing cognitive impairment that was unrecognized or undiagnosed. However, recent studies indicate that the relationship between delirium and cognitive impairment may be bidirectional, suggesting that dementia is a strong predictor of delirium, and delirium may also have an independent effect on the progression of cognitive decline (20).

Understanding whether delirium merely exposes pre-existing cognitive vulnerability or actively contributes to neurodegeneration remains a critical clinical and research question. Understanding this relationship is crucial as the world population ages and more individuals undergo surgery. If delirium increases the risk of dementia, then preventing and managing delirium becomes more than an immediate postoperative goal, as it may have long-term implications for patients' quality of life.

The role of anesthetic management in postoperative cognitive outcomes has also been explored. Comparative studies of inhalational anesthetics such as desflurane and sevoflurane have demonstrated differences in recovery characteristics and early cognitive function after general anesthesia, suggesting that perioperative factors may contribute to the development of postoperative neurocognitive disorders. In contrast to studies evaluating the effects of general anesthesia on postoperative cognitive function, the patients in our cohort were managed under spinal anesthesia. This may have minimized the potential impact of anesthetic agents on early postoperative neurocognitive changes and allowed a clearer assessment of the relationship between postoperative delirium and subsequent dementia (21).

This study has several limitations, including the relatively small sample size and the single-center design, which may limit the generalizability of the findings. In addition, dementia diagnosis during follow-up relied partly on medical record review, which may have underestimated the true incidence. Finally, the one-year follow-up period may not fully reflect long-term cognitive outcomes in elderly patients following hip fracture surgery.

## **Conclusion**

Postoperative delirium following hip fracture surgery significantly increases the risk of dementia incidence within one year. Elderly hip fracture patients who present with delirium should be closely monitored for the development of dementia. More studies are needed to examine the long-term cognitive consequences of delirium.

**Ethics Approval:** The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee for Research Involving Humans, Faculty of Medicine, “Ss. Cyril and Methodius” University in Skopje. Approval protocol number: 0905-1270/120

**Consent for publication:** Written informed consent was obtained from all patients prior to their inclusion in the study.

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