

Role of Dyslipidemia in Postoperative Delirium

Postoperatif Deliryumda Dislipideminin Rolü

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Abstract

Introduction: Postoperative delirium (POD) is a condition characterized by an acute decline in cognitive function and attention, often seen in older adults.

Objective: This study aims to investigate the relationship between preoperative lipid levels and the development of postoperative delirium.

Method: This retrospective study included 41 patients who developed delirium after knee and hip operations in our hospital. Delirium was diagnosed by psychiatrists using the 'Confusion Rating Scale' questionnaire. Demographic characteristics, comorbidities, blood biochemistry and lipid levels were investigated.

Results: The mean age of patients who developed POD was 68.63±7.59 years and 61% were female. Total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), non-high density lipoprotein (HDL) levels and TG/HDL, LDL/HDL ratios were significantly higher in patients who developed postoperative delirium than in the control group (p<0.05). C-Reactive Protein (CRP) and ferritin levels were significantly higher in the group with postoperative delirium than in the control group (p<0.001, p= 0.003).

Conclusion: In conclusion, we found that preoperative TC, TG, LDL and non-HDL levels and new lipid-related biomarkers TG/HDL and LDL/HDL ratios were significantly higher in patients with POD compared to the control group. Lipid levels should be taken into consideration in the evaluation of the risk of postoperative delirium in patients and necessary precautions should be taken to improve the prognosis.

Keywords: Postoperative Delirium, Triglycerides, Low-Density Lipoprotein.

Özet

Giriş: Postoperatif deliryum (POD), sıklıkla yaşlı yetişkinlerde görülen, bilişsel işlevlerde ve dikkatte akut bir düşüşle karakterize bir durumdur.

Amaç: Bu çalışmanın amacı preoperatif lipid düzeyleri ile postoperatif deliryum gelişimi arasındaki ilişkiyi araştırmaktır.

Yöntem: Bu retrospektif çalışmaya, hastanemizde diz ve kalça operasyonları sonrası deliryum gelişen 41 hasta dahil edildi. Deliryum tanısı psikiyatristler tarafından 'Konfüzyon Değerlendirme Ölçeği' anketi kullanılarak konuldu. Hastaların demografik özellikleri, komorbiditeleri, kan biyokimya ve lipid düzeyleri araştırıldı.

Bulgular: POD gelişen hastaların yaş ortalaması 68,63±7,59 ve %61' i kadındı. Postoperatif deliryum gelişen hastaların total kolesterol (TK), trigliserid (TG), düşük yoğunluklu lipoprotein (LDL), non-yüksek yoğunluklu lipoprotein (HDL) düzeyleri ve TG/HDL, LDL/HDL oranları kontrol grubundan anlamlı derecede yüksek saptandı (p<0,05). C-Reaktif Protein (CRP) ve ferritin düzeyleri postoperatif deliryum gelişen grupta kontrol grubundan istatistiksel olarak anlamlı derecede daha fazla bulundu (p<0,001, p= 0,003).

Sonuç: Sonuçta POD gelişen hastalarda preoperatif TK, TG, LDL ve non-HDL seviyelerini ve lipitle ilgili yeni biyobelirteçler olan TG/HDL, LDL/HDL oranlarını kontrol grubundan anlamlı derecede yüksek bulduk. Hastalarda postoperatif deliryum riski değerlendirilmesinde lipid düzeyleri göz önünde bulundurulmalı, gerekli önlemler alınarak prognozun iyileştirilmesi sağlanmalıdır.

Anahtar Kelimeler: Postoperatif Deliryum, Trigliserid, Düşük Yoğunluklu Lipoprotein.

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INTRODUCTION

Delirium is a poorly recognized condition characterized by an acute decline in cognitive function and attention, which is highly prevalent in the elderly (1). Patients generally have impaired orientation and attention, disrupted sleep-wake cycles, perceptual disturbances, delusions, psychomotor symptoms (hypo- or hyper-activity) and a fluctuating course of symptoms (2). Delirium is frequently seen in hospitalized older adults and reaches an incidence of 50%, especially after high-risk operations such as cardiac surgery and hip fracture (3).

Studies have reported an association with prolonged hospitalization and increased mortality risk in patients who developed postoperative delirium (4,5). Jong et al. showed that the development of delirium after hip fracture surgery was an important predictor of nursing home admission and 1-year mortality (6). In another study, Pandharipande et al. found persistent impairment in cognitive and executive functions after discharge in patients who developed delirium in intensive care units (7). Therefore, identifying and managing etiologic factors for the development of postoperative delirium (POD) is of great importance for the prognosis of patients.

Although psychosocial stress and neurotransmitter theories are thought to be at the forefront in the pathogenesis of postoperative delirium, no evidence has yet been presented to fully explain it (8). Multiple causes such as metabolic disorders, inflammation, electrolyte disturbances, chronic renal, cardiac, pulmonary, hepatic and central nervous system diseases, including aging and brain function, are thought to contribute to the pathophysiology (9). Alzheimer's disease is a neurodegenerative disease and its etiologies are thought to be similar to delirium (10). It has been previously shown that plasma cholesterol plays a role in the neurodegenerative process by damaging the integrity of the blood brain barrier, accumulating in the vascular endothelium, causing atherosclerosis and increasing β -amyloid production, which is involved in the development of Alzheimer's disease (11,12). In this study, we aimed to investigate the role of demographic characteristics, comorbidities, blood biochemistry and lipid levels in the etiology of patients with POD.

METHOD

The retrospective study was approved by City Hospital Ethics Committee (E2-23-4071). All procedures were applied in accordance with the principles of the Declaration of Helsinki. The study included 41 patients who developed delirium after knee and hip operations in the orthopedic service of our hospital and 51 volunteers who did not develop postoperative delirium. Patients with liver and thyroid disorders, acute or chronic inflammatory diseases, and diseases affecting cognition such as Alzheimer's, Parkinson's and cerebrovascular diseases were not included in the patient and control groups. Patients with psychoactive drug use such as antipsychotics, anticholinergics, antidepressants, chronic alcohol use, inconsistent information and patients who refused to participate in the study were excluded from the patient and control groups.

The chronic diseases of the groups were classified as diabetes mellitus (DM), hypertension (HT), cardiac disease (CD) and chronic obstructive pulmonary disease (COPD). Hemogram, biochemistry, C-reactive protein (CRP) and lipid panel values were recorded. Blood samples of the study population were collected after 12 hours of fasting. In the study, data were collected from the medical records of the patients evaluated by psychiatrists. Delirium diagnosis was determined by using "Confusion Assessment Method" (CAM) survey (13).

Statistical Analysis

The analyses in the study were conducted using the IBM SPSS Statistics 26 package program. While evaluating the study data, descriptive statistics (mean, standard deviation) were given for numerical variables and frequencies (number, percentage) were given for categorical variables. The Kolmogorov Smirnov normality test was used for the normality assumptions of the numerical variables and it was determined that some variables were normally distributed and some variables were not normally distributed. Therefore, both parametric and nonparametric statistical methods were utilized in the study. Whether there is a difference between two independent groups according to their mean scores was analyzed by Independent Sample T Test for those with normal distribution and Mann Whitney U analysis for those without normal distribution. The relationships between two independent categorical variables were analyzed with Chi-Square analysis. Statistical significance was checked at the 0.05 level.

RESULTS

The mean age of patients with postoperative delirium was 68.63 ± 7.59 years and 61% were female. In the group that developed delirium, 51.2% had HT, 41.5% had DM, 19.5% had CD, and 9.8% had COPD. There was no statistically significant difference between the patients with POD and the control group in terms of comorbidity ($p > 0.05$) (Table 1).

Table 1. Demographic Characteristics of the Groups

		Delirium(+) (n=41)	Delirium(-) (n=51)	t	p
		Mean±SD	Mean±SD		
Age		68.63±7.59	67.37±7.76	0.783	0.436
		n(%)	n(%)	Chi-square	p
Gender	Female	25(61.0)	31(60.8)	0.000	0.985
	Male	16(39.0)	20(39.2)		
DM	Yes	17(41.5)	16(31.4)	1.006	0.316
	No	24(58.5)	35(68.6)		
HT	Yes	21(51.2)	19(37.3)	1.804	0.179
	No	20(48.8)	32(62.7)		
CD	Yes	8(19.5)	7(13.7)	0.558	0.455
	No	33(80.5)	44(86.3)		
COPD	Yes	4(9.8)	3(5.9)	0.485	0.486
	No	37(90.2)	48(94.1)		

t: Independent Sample T-Test, DM: Diabetes Mellitus, HT: Hypertension CD: Cardiac Disease, COPD: Chronic Obstructive Pulmonary Disease.

There was a statistically significant difference between the patients who developed POD and the control group in terms of CRP and ferritin levels ($p < 0.05$). CRP and ferritin levels of the group who developed POD were statistically significantly higher than the control group ($p < 0.001$, $p = 0.003$) (Table 2).

Table 2. Biochemical Test Results and Differences by Groups

	Delirium(+) (n=41)	Delirium(-) (n=51)	Test Statistics	p
	Mean±SD	Mean±SD		
Glucose(mg/dl)	93.41±12.81	90.59±7.27	Z=-0.909	0.364
Urea(mg/dl)	15.22±3.69	13.78±3.67	Z=-1.612	0.107
Creatinine(mg/dl)	0.70±0.16	0.65±0.14	Z=-1.486	0.137
Na(mmol/l)	139.56±2.10	139.14±2.00	Z=-1.079	0.281
K(mmol/l)	4.27±0.32	4.17±0.61	Z=-0.718	0.473
CRP(mg/l)	0.32±0.20	0.18±0.09	Z=-4.587	<0.001*
Hb(gr/dl)	13.72±1.29	13.52±1.23	Z=-0.826	0.409
Iron(ug/dl)	77.29±32.91	86.47±30.69	t=-1.380	0.171
Ferritin(ng/ml)	99.64±94.75	49.80±42.71	Z=-2.989	0.003*

t: Independent Sample T-Test, Z: Mann Whitney U, *:p<0.05, Na: Sodium, K: Potassium, CRP:C-Reactive Protein, Hb: Haemoglobin.

There was a statistically significant difference between patients with POD and the control group in terms of TC, TG, LDL, TG/HDL, LDL/HDL and non HDL (p<0.05). TC, TG, LDL and non HDL levels of patients who developed POD were significantly higher than the control group (p<0.001). TG/HDL, LDL/HDL ratios of patients who developed postoperative delirium were significantly higher than the control group (p<0,001, p=0,001) (Fig. 1, Fig. 2) (Table 3).

Table 3. Biochemical Test Results and Differences by Groups

	Delirium(+) (n=41)	Delirium(-) (n=51)	Test Statistics	p
	Mean±SD	Mean±SD		
TC(mg/dl)	238.22±29.38	178.59±35.78	t=8.592	<0.001*
TG(mg/dl)	200.27±73.12	105.08±42.30	Z=-6.348	<0.001*
LDL(mg/dl)	142.17±27.11	105.82±32.22	t=5.766	<0.001*
HDL(mg/dl)	55.34±13.09	51.10±14.16	t=1.477	0.143
TG/HDL	4.05±2.40	2.21±1.06	Z=-4.454	<0.001*
LDL/HDL	2.67±0.62	2.19±0.76	Z=-3.331	0.001*
Non HDL(mg/dl)	182.88±26.38	127.49±33.19	t=8.699	<0.001*

t: Independent Sample T-Test, Z: Mann Whitney U, *:p<0.05,TC: Total Cholesterol, TG: Triglyceride, LDL: Low-Density Lipoprotein, HDL: High-Density Lipoprotein.

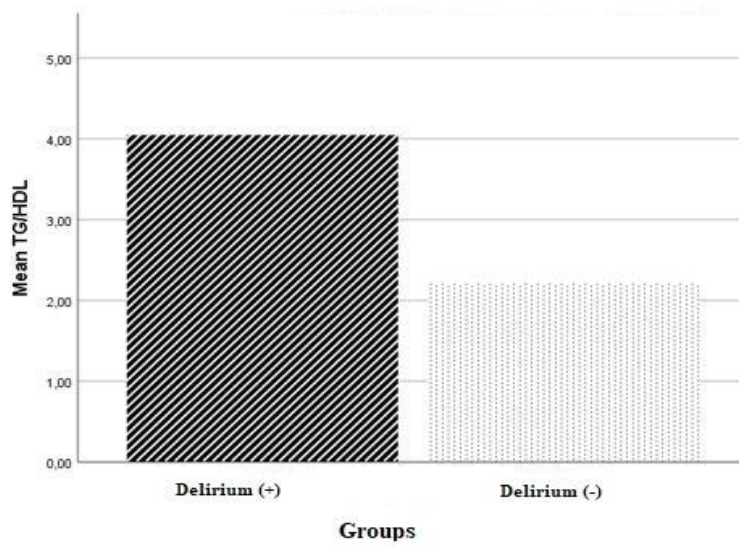


Figure 1. TG/HDL Ratio by Groups

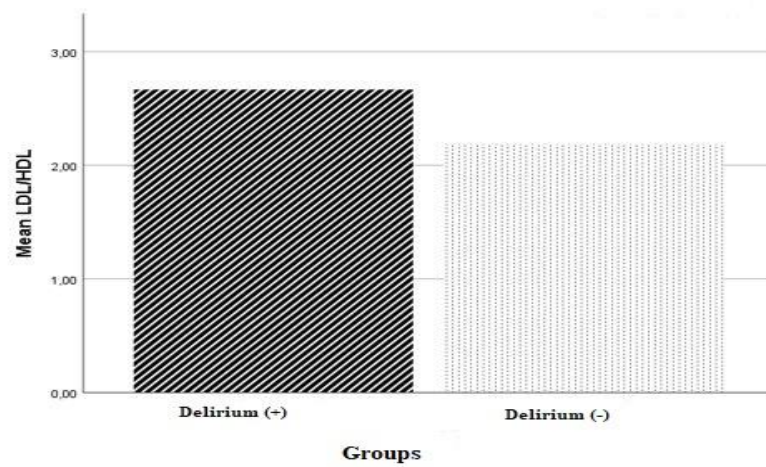


Figure 2. LDL/HDL Ratio by Groups

DISCUSSION

POD is a growing public health problem, causing poor prognosis in many vulnerable older adults and increased health costs in societies (14). The European Society of Anesthesiology has shown comorbidities such as advanced age, diabetes, heart disease and peripheral vascular diseases as risk factors for POD (15). In our study, we found that the mean age of patients who developed delirium after knee and hip operations was 68.63 years. HT (51.2%) and DM (41%) were the most common comorbidities in patients who developed delirium, but no significant difference was found with the control group.

In a meta-analysis of 758 patients who developed POD, Huang et al. found that serum inflammatory variables such as CRP and IL-6 were significantly higher in patients who did not develop delirium immediately after surgery (16). In another study, Zhang et al. showed that changes in CRP within 24 hours in the intensive care unit were risk indicators for delirium (17). In our study, we found that CRP and ferritin levels were significantly higher in patients who developed POD than in the control group in accordance with these results. In addition to indicating blood iron levels, serum ferritin levels are also used as an acute phase reactant in inflammatory diseases (18). Although there was no significant difference between hemoglobin and serum iron levels between the groups in our study, ferritin levels were significantly higher in the group that developed POD, suggesting an increase due to inflammation.

The brain is rich in cholesterol and increasing epidemiologic evidence supports the association of hypercholesterolemia with Alzheimer's disease (19). Previously, delirium has been associated with long-term risk of cognitive decline and dementia development (20). In a study of 562 patients, Lin et al. showed that serum TC, TG and LDL cholesterol were risk factors for the development of POD, while HDL concentration was a protective factor (21). Similarly, in our study, we found significantly higher levels of TC, TG, LDL, and non-HDL in patients with POD compared to the control group, but we did not find any difference between HDL levels. Recently, ratios such as TG/HDL and LDL/HDL are thought to better reflect the level of lipid metabolism in the body and to be valuable markers for metabolic and cardiovascular diseases (22,23). In their study, Pillai et al. associated high plasma TG/HDL ratio with mild cognitive impairment and poor cognitive outcome in patients with dementia (24). In another study, Zaciragic et al. found that TG/HDL, LDL/HDL ratios were lower in patients with Alzheimer's disease and vascular dementia (25). In our study, we found TG/HDL, LDL/HDL ratios significantly higher in patients with POD than in the control group. To our knowledge, this is the first time that these ratios have been examined in patients with postoperative delirium.

The study has some limitations. First, it was conducted with a relatively small number of patients. Secondly, the diagnosis of delirium in the patients included in the study was based on psychiatric records. We think that some patients who could have been diagnosed with hypoactive delirium may have been missed during clinical follow-up.

CONCLUSION

We found that inflammation indicators such as preoperative CRP and ferritin and lipid levels such as TC, TG, LDL and non-HDL were significantly higher in patients who developed POD compared to the control group. In addition, we showed that the new lipid-related biomarkers TG/HDL and LDL/HDL ratios were higher in patients who developed POD. Inflammation and lipid levels should be taken into consideration in the evaluation of the risk of

postoperative delirium in patients, and necessary measures should be taken to improve the prognosis.

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