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Original Article

Relationship between neutrophil/lymphocyte ratio and postoperative delirium in elderly patients with proximal femoral nail anti-rotation for intertrochanteric fractures

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Abstract: Objective: Delirium is a common postoperative complication in elderly patients with intertrochanteric femur fracture. This study aimed at analyzing risk factors for postoperative delirium (POD) in patients after proximal femoral nail anti-rotation (PFNA). Methods: From February 2017 to February 2021, we included elderly patients with intertrochanteric fractures who underwent PFNA. The predictive ability and cut-off value of neutrophil/lymphocyte ratio (NLR) for POD were evaluated using receiver operating characteristic (ROC) curve. Univariate and multivariate analyses were used to investigate the association between NLR and POD. Results: We enrolled 315 patients. The ROC curve suggested that NLR ≥ 4.85 was the optimal cut-off value for POD. The POD and non-POD groups differed significantly in age, diabetes, time from injury to operation, preoperative albumin level, neutrophil count, and NLR ($P < 0.05$). Logistic regression indicated that NLR ≥ 4.85 (odds ratio [OR] = 3.491; 95% confidence interval [CI]: 1.731-5.982; $P < 0.001$), old age (OR = 1.921; 95% CI: 1.267-4.125; $P < 0.001$), time from injury to operation ≥ 48 h (OR = 1.733; 95% CI: 1.212-3.542; $P = 0.007$), and preoperative albumin level ≤ 35 g/L (OR = 2.274; 95% CI: 1.662-4.846; $P = 0.001$) increased the risk of POD. Conclusion: Old age, time from injury to operation ≥ 48 h, preoperative albumin level ≤ 35 g/L, and NLR ≥ 4.85 were independent risk factors for POD. Thus, NLR may predict POD in elderly patients with intertrochanteric femur fractures after PFNA.

Keywords: Postoperative delirium, PFNA, intertrochanteric fracture, neutrophil/lymphocyte ratio, risk factor

Introduction

Currently, most countries are experiencing population aging. Due to muscle atrophy, decreased motor coordination ability, and sometimes osteoporosis, the elderly people are prone to hip fractures after falls, particularly intertrochanteric femur fractures [1]. Proximal femoral nail anti-rotation (PFNA) is the most widely used internal fixation method to treat intertrochanteric fracture. It has the advantages of mild trauma, early fracture healing, and rapid functional recovery [2]. However, due to the influence of many factors, the incidence of complications after hip surgery, particularly postoperative delirium (POD), is high [3]. The morbidity of POD in patients with hip fracture is 12%-51% [4].

Delirium is an acute reversible change in mental state. Its clinical manifestations include concentration disorder, cognitive impairment, memory loss, and consciousness disorders [5, 6]. POD can also increase the incidence of other serious diseases postoperatively [7], delay treatment, increase the financial burden, and even cause secondary damage. Severe cases can lead to dementia, which reduces patients' self-care ability and increases mortality [9].

Although the pathophysiologic mechanisms of delirium are currently unknown, some previous studies have suggested a possible association with inflammation and oxidative stress [10]. In recent years, the neutrophil/lymphocyte ratio (NLR), an inflammatory marker, has attracted

attention owing to its simple clinical accessibility and low economic burden [11]. NLR shows good inflammation-related predictive ability in diseases such as coronary heart disease and diabetes [12]. It can predict POD in abdominal, cardiac, total hip arthroplasty (THA), and other surgeries [13-17] but has not been applied in elderly patients with intertrochanteric fractures who have a high prevalence of POD after internal fixation. Therefore, the aim of this study was to analyze the risk factors, including NLR, for POD in the elderly patients with intertrochanteric fracture after PFNA.

Materials and methods

Patients

We performed a retrospective analysis of the clinical data of the elderly patients with intertrochanteric fractures admitted to the Department of Traumatology and Orthopaedics of the Xi'an Honghui Hospital from February 2017 to February 2021. The study protocol was approved by the ethics committee of the hospital (202211018). All procedures were performed in accordance with relevant guidelines and regulations.

Inclusion criteria: (1) age ≥ 60 years; (2) clinically and radiographically confirmed intertrochanteric fractures; (3) time from injury to operation ≤ 1 week; (4) PFNA internal fixation.

Exclusion criteria: (1) open fracture or fracture with pathologic factors; (2) a history of brain surgery; (3) previous hip injury; (4) severe nerve or vascular injury; (5) current taking of sedatives or antidepressants; (6) preoperative delirium or in-hospital death.

Data collection

Data collected were: (1) general information, including age, gender, body mass index (BMI), smoking status, hypertension, coronary heart disease, stroke, visual analog scale (VAS) score, American Society of Anesthesiologists (ASA) grade, and postoperative analgesic pump use; (2) surgery-related indicators, including durations of operation and anesthesia, mode of anesthesia, and intraoperative blood loss volume; (3) laboratory data, including preoperative albumin level, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), neutrophil count, lymphocyte count, and neutrophilto/lymphocyte ratio (NLR).

Delirium diagnosis

Delirium was assessed according to the Diagnostic and Statistical Manual of Mental Disorders [18] and the Confusion Assessment Method (CAM) [19]. CAM includes four contents: 1) acute change in the fluctuation of mental state; 2) lack of concentration; 3) confused thinking; and 4) changes in the level of consciousness. A nurse assessed all patients using CAM daily in a 20-min interview with the patient and by obtaining relevant information from the family and hospital records, starting from postoperative day 1 until hospital discharge.

Statistical analysis

Clinical information was statistically analyzed using SPSS 22.0 software. Measured data are expressed as mean ± SD. The independent-samples t-test or Mann-Whitney U test was used for measurement data. Counted data are expressed as number (%). The chi-square test was used for counted data. The receiver operating characteristic (ROC) curve was utilized for defining the best NLR for POD. After univariate analysis of all variables, potential risk factors with $P < 0.10$ among them subjected to a multivariate logistic regression analysis. A p-value < 0.05 was set to indicate statistical significance.

Results

Baseline data of the study subjects

Based on the inclusion and exclusion criteria, a total of 315 elderly patients with intertrochanteric fracture treated with PFNA were enrolled. The participants included 173 (54.92%) men and 242 (45.08%) women, with a mean age 74.31±6.75 (60-97) years. The average operation time was 82.92 min. POD occurred in 62 (19.68%) participants. We compared baseline data of the patients with and without delirium. The age, diabetes, time from injury to operation, preoperative albumin level, neutrophil count, and NLR value differed significantly between the POD and non-POD groups (all $P < 0.05$). The gender, BMI, smoking status, hypertension, coronary heart disease, stroke, preop-

Table 1. Comparison of baseline data between patients with POD and non-POD groups (χ ± s) [n (%)]

Variable	POD group (n = 62)	No POD group (n = 253)	*OR* (95% CI)	*p* value
Age (year)	76.51±7.22	72.34±6.28	1.982 (1.171-4.532)	**< 0.001**
Gender (male)	38 (61.29)	135 (53.36)	0.943 (0.372-2.216)	0.261
BMI ≥ 24	33 (53.23)	112 (44.27)	1.433 (0.821-2.501)	0.278
Smoking	21 (33.87)	92 (36.36)	0.652 (0.143-1.161)	0.149
Hypertension	45 (72.58)	172 (67.98)	0.802 (0.433-1.487)	0.542
Diabetes	35 (56.45)	104 (41.11)	1.657 (1.060-3.255)	**0.029**
Coronary heart disease	16 (25.81)	46 (18.18)	1.412 (0.739-2.699)	0.301
Stroke	17 (27.42)	59 (23.32)	1.242 (0.662-2.331)	0.510
Time from injury to operation ≥ 48 h	33 (53.23)	79 (31.23)	1.706 (1.224-4.411)	**0.002**
Preoperative VAS score	7.82±2.05	7.23±1.67	1.102 (0.202-2.146)	0.293
Duration of operation (min)	85.12±17.62	80.43±16.76	1.502 (0.231-2.284)	0.068
ASA physical status (ASA ≥ 3)	26 (41.94)	76 (30.04)	1.682 (0.959-2.979)	0.073
Duration of anesthesia (min)	107.32±18.53	103.51±17.24	1.136 (0.725-3.721)	0.126
Mode of anesthesia			1.614 (0.431-3.455)	0.094
Intraspinal anesthesia	14	87	-	-
General anesthesia	48	166	-	-
Intraoperative blood loss (ml)	79.23±17.65	75.62±16.32	0.536 (0.124-2.103)	0.126
Postoperative analgesic pump	37 (59.68)	174 (68.78)	0.687 (0.241-1.675)	0.178
Preoperative albumin level ≤ 35 g/L	36 (58.06)	86 (33.99)	2.112 (1.524-5.213)	**< 0.001**
CRP (mg/L)	8.72±3.46	8.13±2.92	0.882 (0.451-2.736)	0.171
ESR (mm/h)	15.4±9.3	14.5±8.7	0.575 (0.271-1.985)	0.565
Neutrophil count ($\times 10^9$/L)	6.41±3.24	5.34±2.98	1.646 (0.622-2.861)	**0.013**
Lymphocyte count ($\times 10^9$/L)	1.21±0.29	1.24±0.31	0.691 (0.297-1.753)	0.512
NLR value	5.41±1.62	4.22±1.13	2.542 (1.663-4.241)	**< 0.001**
NLR ≥ 4.85	43 (69.35)	106 (41.9)	3.139 (1.785-5.364)	**< 0.001**

P values were calculated by Chi-square test, Fisher exact test, Mann Whitney U-test or t-test. POD, Postoperative Delirium; BMI, Body Mass Index; VAS, Visual Analogue Scale; ASA, American Society of Anesthesiologists; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; NLR, Neutrophilto/Lymphocyte Ratio. Bold indicates *P*-values less than 0.05.

erative VAS score, duration of operation, ASA physical status, duration and mode of anes thesia, intraoperative blood loss volume, use of postoperative analgesic pump, CRP, ESR, and lymphocyte count did not differ significantly between the two groups (all $P > 0.05$; **Table 1**).

Predictive power of NLR

ROC curve analysis showed that NLR had a satisfactory predictive power for POD with an area under the curve (AUC) of 0.827 (95% confidence interval [CI]: 0.736-0.917, $P < 0.001$). The optimal cut-off value of NLR was calculated using the Jorden index method as 4.85. The corresponding sensitivity was 81.12%, and the specificity was 78.21%. The proportion of patients with delirium with NLR ≥ 4.85 was significantly higher than that of patients without delirium (43 [69.35%] vs. 106 [41.9%], $P < 0.001$; **Figure 1**).

Univariate and multivariate logistic regression analyses of risk factors for POD

Univariate logistic regression indicated that older age, diabetes, time from injury to operation ≥ 48 h, preoperative albumin level ≤ 35 g/L, neutrophil count, and NLR value were predictors of POD ($P < 0.05$). Subsequently, ten potential risk factors ($P < 0.1$) according to univariate analysis were entered into the multivariate logistic regression model, and two of the variables, NLR and NLR ≥ 4.85, were included in models 1 and model 2, respectively. Model 1 (adjusted for NLR value, age, diabetes, time from injury to operation, duration of operation, ASA, mode of anesthesia, preoperative albu-

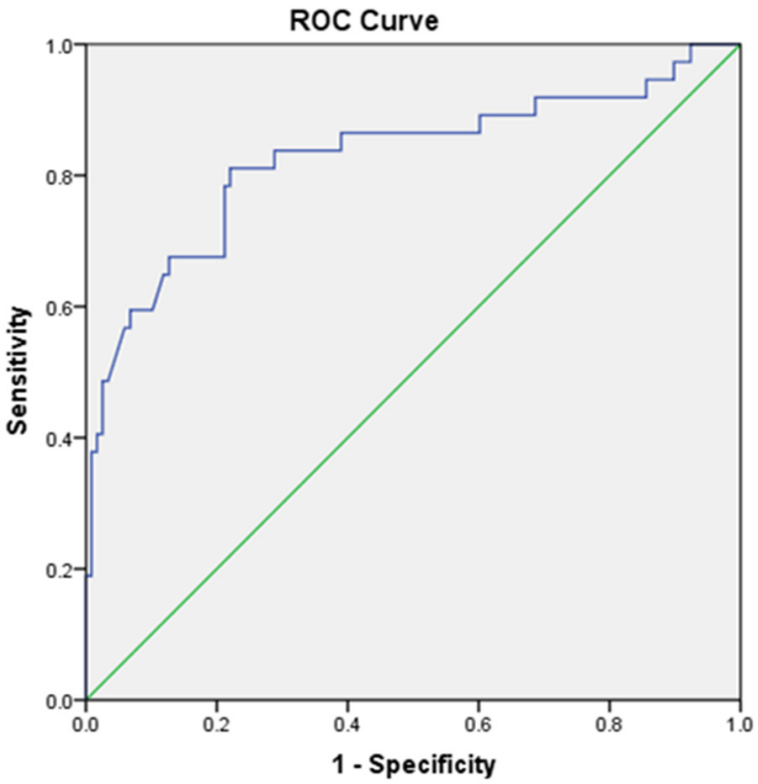

Figure 1. Receiver operating characteristic (ROC) curve analysis for the predictive power of NLR for POD.

Table 2. Multivariate analysis of risk factors for postoperative delirium (POD) in 315 patients

	OR	95% CI	*p* value*
Model 1 (NLR value)			
Age (high vs. low)	1.874	1.171-4.134	**< 0.001**
Time from injury to operation ≥ 48 h	1.692	1.152-3.416	**0.009**
Preoperative albumin ≤ 35 g/L	2.213	1.524-4.183	**0.001**
NLR value (high vs. low)	2.675	1.677-5.042	**< 0.001**
Model 2 (NLR ≥ 4.85)			
Age (high vs. low)	1.921	1.267-4.125	**< 0.001**
Time from injury to operation ≥ 48 h	1.733	1.212-3.542	**0.007**
Preoperative albumin level ≤ 35 g/L	2.274	1.662-4.846	**0.001**
NLR ≥ 4.85	3.491	1.731-5.982	**< 0.001**

POD, Postoperative Delirium; ASA, American Society of Anesthesiologists; NLR, neutrophilto/Lymphocyte Ratio; OR, Odds Ratio; CI, Confidence Interval; Bold indicates *P*-values less than 0.05. *Multivariable adjusted for age, diabetes, time from injury to operation ≥ 48 h, preoperative albumin ≤ 35 g/L, neutrophil count, NLR value (NLR ≥ 4.85).

min level, neutrophil count) showed that NLR value (adjusted odds ratio [aOR] = 2.675; 95% CI: 1.677-5.042; $P < 0.001$), advanced age (aOR = 1.874; 95% CI: 1.171-4.532; $P < 0.001$), time from injury to operation ≥ 48 h (aOR = 1.692; 95% CI: 1.152-3.416; $P = 0.009$), preoperative albumin level ≤ 35 g/L (aOR = 2.213; 95% CI: 1.524-4.183; $P = 0.001$) were correlated with an increased risk of POD; model 2 (adjusted for NLR ≥ 4.85, age, diabetes, time from injury to operation, duration of operation, ASA, mode of anesthesia, preoperative albumin level, neutrophil count) showed that NLR ≥ 4.85 (aOR = 3.491; 95% CI: 1.731-5.982; $P < 0.001$), advanced age (aOR = 1.921; 95% CI: 1.267-4.125; $P < 0.001$), time from injury to operation ≥ 48 h (aOR = 1.733; 95% CI: 1.212-3.542; $P = 0.007$), and preoperative albumin level ≤ 35 g/L (aOR = 2.274; 95% CI: 1.662-4.846; $P = 0.001$) were correlated with an increased risk of POD (**Table 2**).

Discussion

In this study, 62 of 315 (19.68%) elderly patients with intertrochanteric fractures developed delirium postoperatively, similar to previous studies [20-22]. The ROC curve indicated an AUC of the preoperative NLR of 0.827, with the optimal cut-off value being 4.85. The logistic regression analysis of clinical indicators of the select study participants showed that a higher NLR, advanced age, time from injury to operation ≥ 48 h, and preoperative albumin level ≤ 35 g/L were independent risk factors for POD in patients with intertrochanteric fractures. In addition, patients with NLR ≥ 4.85 had a 3.5-fold increased risk of POD, further indicating the predictive power of NLR. POD in the elderly patients with intertrochanteric fractures after PFNA can lead to prolonged bed rest and hospitalization, postoperative feeding difficulties, sleep disorders, and

delayed postoperative rehabilitation, which in turn increases the risk of complications, such as decubitus ulcers, deep vein thrombosis, and pulmonary infections, Moreover, delayed postoperative rehabilitation also affects the long-term outcome of patients after hospital discharge [23]. Therefore, prevention of delirium-related risk factors may help to reduce the incidence of postoperative complications and improve outcome in patients with intertrochanteric fractures.

The results of this study suggest that age is an independent risk factor for POD, consistent with by Wang et al.'s study [24] involving 200 orthopedic patients over 65 years of age who developed POD. The risk of POD might be mediated by a progressively degenerating body and brain, such as diminished organ compensatory capacity, the weakening of physical fitness, decreased regulatory capacity, increased susceptibility to stressors, and abnormal excitatory conduction capacity, manifesting as different clinical symptoms and signs of delirium. Moreover, with aging, the brain volume decreases, resulting in a loss of synapses of nerve cells, elevated cortisol levels, reduced acetylcholine levels, sleep disturbances, and the gradual decline in memory and attention, which can all cause POD [25].

The elderly patients with intertrochanteric fractures with a short time from injury to operation have a relatively short surgery duration and a relatively small amount of intraoperative blood loss [26]. Early surgical treatment after injury positively reinforces the curative effect of intertrochanteric fractures in the elderly. The present multivariate analysis indicated that the time from injury to operation ≥ 48 h was an independent risk factor for POD ($P < 0.05$). Patients with intertrochanteric fractures lie in bed for prolonged durations preoperatively and the pain in the fracture area damages the digestive and respiratory systems, which in turn lead to brain ischemia, hypoxia, and delirium. After early internal fixation, patients are routinely able to sit up, lie on their side, get out of bed, and carry a tolerable weight-bearing on the affected limb with protection, reducing bed-rest-related complications.

Chang et al. [27] retrospectively analyzed the risk factors associated with POD in 288 patients who underwent open heart surgery. Their results indicated that preoperative hypoproteinemia was a significant independent predictor, consistent with a previous study [28]. Albumin performs functions of antioxidation, scavenging metabolites, protecting the microcirculation, and promoting drug binding and transport [29], supporting the results of this study. Elderly patients have reduced albumin levels, most frequently because of poor dietary intake. Further, oxygen free radicals are increased in production and cannot be cleared rapidly, thereby passing via the blood-brain barrier to cause damage to brain the cells. In addition, reduced albumin levels weaken the binding ability of drugs (such as central nervous system side effects drugs) and increase the concentration of free drugs in the body, which leads to delirium. Therefore, for patients with reduced albumin levels during elective surgery, etiology should be determined and removed and the state of hypoalbuminemia should be corrected to reduce the occurrence of POD.

The NLR is a composite inflammatory index integrating the information of neutrophil and lymphocyte counts. In recent years, the relationship between elevated NLR levels and neurocognitive changes has attracted more and more attention. The neutrophil count is significantly increased and the lymphocyte count is significantly decreased in patients with schizophrenia, and even an elevated NLR to some extent can indicate the activity of the disease [30]. In addition, a recent multicenter prospective study revealed NLR can be utilized as an indicator to predict POD after THA in the elderly patients [17]. However, THA is generally used to treat elderly patients with femoral neck fractures, which causes more trauma and blood loss. Most elderly patients with intertrochanteric fractures undergo relatively minimally invasive PFNA internal fixation, and the association between POD and NLR is unknown. This study indicated that a higher preoperative NLR value was an independent risk factor for POD in elderly patients with intertrochanteric fractures after PFNA, and the NLR was higher in the POD group ($P < 0.05$). The AUC, optimal cut-off value, sensitivity, and specificity of preoperative NLR for predicting POD were 0.827, 4.85, 81.12% and 78.21%, respectively. Furthermore, patients with NLR ≥ 4.85 had an approximately 3.5-fold increased risk of POD. These results suggest that NLR can also be a good biologic

index for predicting POD after PFNA in the elderly patients with intertrochanteric fracture. Inflammatory reaction and oxidative stress are linked to the occurrence and development of POD [10]. Under stress, the body can release peripheral inflammatory factors to damage the blood-brain barrier, enter the central nervous system to induce the activation of microglia, and release inflammatory mediators to cause the inflammatory cascade in the central nervous system, which affects the synaptic connection and transmission of neurons, impairs learning and memory function, and leads to the occurrence of POD [31]. It can simultaneously activate the non-specific immune system, resulting in elevated neutrophil levels and reduced lymphocyte levels [32]. After activation of neutrophils, reactive oxygen species and peroxidase can be released to destroy the blood-brain barrier, while lymphopenia can cause excessive activation of inflammatory reaction. Further, the synergistic effect of the two can further induce delirium [17].

This study has some limitations. First, the study was a retrospective case-control retrospective study with limited inclusion of indicators and sample size, and further prospective studies are required to refine the results. Second, we did not follow-up the patients after hospital discharge, and the long-term risk of delirium remains unknown. Third, we assessed only preoperative NLR values and not dynamic changes in NLR, which may yield an incomplete results.

Conclusion

The results of this study showed that higher NLR value, older age, time from injury to operation ≥ 48 h, and preoperative albumin level ≤ 35 g/L were independent risk factors of POD. NLR can be utilized as a predictor of POD in elderly patients with intertrochanteric fractures who undergo PFNA.

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Disclosure of conflict of interest

None.

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References

[1] Su H, Liu H, Liu J and Wang X. Elderly patients with intertrochanteric fractures after intramedullary fixation: analysis of risk factors for calf muscular vein thrombosis. Orthopade 2018; 47: 341-346.

[2] Huang SG, Chen B, Zhang Y, Nie FF, Ju L, Li M and Zhang YH. Comparison of the clinical effectiveness of PFNA, PFLCP, and DHS in treatment of unstable intertrochanteric femoral fracture. Am J Ther 2017; 24: e659-e666.

[3] Kong D, Luo W, Zhu Z, Sun S and Zhu J. Factors associated with post-operative delirium in hip fracture patients: what should we care. Eur J Med Res 2022; 27: 40.

[4] Gottschalk A, Hubbs J, Vikani AR, Gottschalk LB and Sieber FE. The impact of incident postoperative delirium on survival of elderly patients after surgery for hip fracture repair. Anesth Analg 2015; 121: 1336-1343.

[5] Oberai T, Oosterhoff JHF, Woodman R, Doornberg JN, Kerkhoffs G and Jaarsma R. Development of a postoperative delirium risk scoring tool using data from the Australian and New Zealand hip fracture registry: an analysis of 6672 patients 2017-2018. Arch Gerontol Geriatr 2021; 94: 104368.

[6] Bai J, Liang Y, Zhang P, Liang X, He J, Wang J and Wang Y. Association between postoperative delirium and mortality in elderly patients undergoing hip fractures surgery: a meta-analysis. Osteoporos Int 2020; 31: 317-326.

[7] Lin HS, Watts JN, Peel NM and Hubbard RE. Frailty and post-operative outcomes in older surgical patients: a systematic review. BMC Geriatr 2016; 16: 157.

[8] Lee SJ, Jung SH, Lee SU, Lim JY, Yoon KS and Lee SY. Postoperative delirium after hip surgery is a potential risk factor for incident dementia: a systematic review and meta-analysis of prospective studies. Arch Gerontol Geriatr 2019; 87: 103977.

[9] Morandi A, Mazzone A, Bernardini B, Suardi T, Prina R, Pozzi C, Gentile S, Trabucchi M and Bellelli G. Association between delirium, adverse clinical events and functional outcomes in older patients admitted to rehabilitation settings after a hip fracture: a multicenter retrospective cohort study. Geriatr Gerontol Int 2019; 19: 404-408.

[10] Oh S and Park JY. Postoperative delirium. Korean J Anesthesiol 2018; 72: 4-12.
[11] Maldonado JR. Neuropathogenesis of delirium: review of current etiologic theories and common pathways. Am J Geriatr Psychiatry 2013; 21: 1190-222.
[12] Bonaventura A, Liberale L, Carbone F, Vecchié A, Bonomi A, Scopinaro N, Camerini GB, Papadia FS, Maggi D, Cordera R, Dallegri F, Adami G and Montecucco F. Baseline neutrophil-to-lymphocyte ratio is associated with long-term T2D remission after metabolic surgery. Acta Diabetol 2019; 56: 741-748.
[13] Kinoshita H, Saito J, Takekawa D, Ohyama T, Kushikata T and Hirota K. Availability of preoperative neutrophil-lymphocyte ratio to predict postoperative delirium after head and neck free-flap reconstruction: a retrospective study. PLoS One 2021; 16: e0254654.
[14] Oyama T, Kinoshita H, Takekawa D, Saito J, Kushikata T and Hirota K. Higher neutrophil-to-lymphocyte ratio, mean platelet volume, and platelet distribution width are associated with postoperative delirium in patients undergoing esophagectomy: a retrospective observational study. J Anesth 2021; 36: 58-67.
[15] Ida M, Takeshita Y and Kawaguchi M. Preoperative serum biomarkers in the prediction of postoperative delirium following abdominal surgery. Geriatr Gerontol Int 2020; 20: 1208-1212.
[16] Kotfis K, Ślozowska J, Safranow K, Szylińska A and Listewnik M. The practical use of white cell inflammatory biomarkers in prediction of postoperative delirium after cardiac surgery. Brain Sci 2019; 9: 308.
[17] He R, Wang F, Shen H, Zeng Y and Zhang LJ. Association between increased neutrophil-to-lymphocyte ratio and postoperative delirium in elderly patients with total hip arthroplasty for hip fracture. BMC Psychiatry 2020; 20: 496.
[18] Sachdev PS, Mohan A, Taylor L and Jeste DV. Dsm-5 and mental disorders in older individuals: an overview. Harv Rev Psychiatry 2015; 23: 320-8.
[19] Inouye SK, Dyck CHV and Alessi CA, Balkin S, Siegal AP and Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. Ann Intern Med 1990; 113: 941-8.
[20] Eshmawey M, Arlt S, Ledschbor-Frahnert C, Guenther U and Popp J. Preoperative depression and plasma cortisol levels as predictors of delirium after cardiac surgery. Dement Geriatr Cogn Disord 2020; 48: 207-214.
[21] Sieber FE, Neufeld KJ, Gottschalk A, Bigelow GE, Oh ES, Rosenberg PB, Mears SC, Stewart KJ, Ouanes JP, Jaberi M, Hasenboehler EA, Li T and Wang NY. Effect of depth of sedation in older patients undergoing hip fracture repair on postoperative delirium: the stride randomized clinical trial. JAMA Surg 2018; 153: 987-995.
[22] Shin JE, Kyeong S, Lee JS, Park JY, Lee WS, Kim JJ and Yang KH. A personality trait contributes to the occurrence of postoperative delirium: a prospective study. BMC Psychiatry 2016; 16: 371.
[23] Mazzola P, Bellelli G, Broggini V, Anzuini A, Corsi M, Berruti D, De Filippi F, Zatti GJ and Annoni G. Postoperative delirium and pre-fracture disability predict 6-month mortality among the oldest old hip fracture patients. Aging Clin Exp Res 2014; 27: 53-60.
[24] Wang J, Li Z, Yu Y, Li B, Shao G and Wang Q. Risk factors contributing to postoperative delirium in geriatric patients postorthopedic surgery. Asia Pac Psychiatry 2015; 7: 375-82.
[25] Guo Y, Zhang Y, Jia P, Wang W, Zhou Q, Sun L, Zhao A, Zhang X, Wang X, Li Y, Zhang J and Jiang W. Preoperative serum metabolites are associated with postoperative delirium in elderly hip-fracture patients. J Gerontol a Biol Sci Med Sci 2017; 72: 1689-1696.
[26] Bellas N, Stohler S, Staff I, Majk K, Lewis C, Davis S and Kumar M. Impact of preoperative specialty consults on hospitalist comanagement of hip fracture patients. J Hosp Med 2019; 15: 16-21.
[27] Chang YL, Tsai YF, Lin PJ, Chen MC and Liu CY. Prevalence and risk factors for postoperative delirium in a cardiovascular intensive care unit. Am J Crit Care 2008; 17: 567-75.
[28] Scholz AF, Oldroyd C, McCarthy K, Quinn TJ and Hewitt J. Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery. Br J Surg 2015; 103: e21-8.
[29] Quinlan GJ, Martin GS and Evans TW. Albumin: biochemical properties and therapeutic potential. Hepatology 2005; 41: 1211-9.
[30] Kulaksizoglu B and Kulaksizoglu S. Relationship between neutrophil/lymphocyte ratio with oxidative stress and psychopathology in patients with schizophrenia. Neuropsychiatr Dis Treat 2016; 12: 1999-2005.
[31] Sun L, Jia P, Zhang J, Zhang X, Zhang Y, Jiang H, Jiang W and Guo Y. Production of inflammatory cytokines, cortisol, and Aβ1-40 in elderly oral cancer patients with postoperative delirium. Neuropsychiatr Dis Treat 2016; 12: 2789-2795.
[32] Dhabhar FS, Malarkey WB, Neri E and McEwen BS. Stress-induced redistribution of immune cells--from barracks to boulevards to battlefields: a tale of three hormones--curt richter award winner. Psychoneuroendocrinology 2012; 37: 1345-68.