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Original Article

NLR value and IL-18 level and their clinical significance in patients with deep vein thrombosis after receiving the surgery for spinal degeneration

Yukun Zhang[1], Mingyu Cao[2], Jun Ren[1]

Departments of [1]Spine Surgery, [2]Joint Surgery, The Sixth Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang Uygur Autonomous Region, China

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Abstract: Objective: To investigate the value of the neutrophil-to-lymphocyte ratio (NLR) and Interleukin 18 (IL-18) level in patients with deep vein thrombosis after receiving surgery for spinal degeneration; and we explore their significance in clinical practice. Methods: This study was conducted in 296 patients who were treated in our hospital for spinal degeneration. After surgery, these patients were followed up for 1 month. After performing the color Doppler ultrasound examination, patients were divided into the thrombus group (n = 72) and the non-thrombus group (n = 224) based on the occurrence of deep vein thrombosis. Baseline data, NLR values and IL-18 levels before surgery, and at 1, 3, 5, and 7 days after surgery were compared between the two groups. Logistic regression analysis was implemented to analyze the risk factors for postoperative deep vein thrombosis. Patients in the thrombosis group were allocated to the mild, moderate, and severe group on the basis of the degree of thrombosis. NLR values and IL-18 levels at 3 days after surgery were compared among the three groups. The correlations between both NLR value and IL-18 level and the severity of deep vein thrombosis were analyzed with Pearson correlation. Receiver operating characteristic curve was used to assess the clinical value of NLR value and IL-18 level at 3 days after surgery in predicting postoperative deep vein thrombosis. Results: There were significant differences concerning age, the history of diabetes, and obesity between the two groups (all $P<0.05$). NLR values and IL-18 levels in both groups after surgery were increased when compared with before surgery (all $P<0.01$). In addition, NLR values and IL-18 levels reached a peak at 3 days after surgery. Compared with the non-thrombus group, NLR values and IL-18 levels in the thrombus group at 1, 3, 5, and 7 days after surgery were increased (all $P<0.01$). NLR value and IL-18 level in the thrombosis group at 3 days after surgery were increased with a worsened degree of thrombosis. In other words, both NLR value and IL-18 level were positively correlated with the degree of deep vein thrombosis. The results of logistic regression analysis displayed that age ≥60 years old, body mass index ≥23 kg/m^2, NLR value >4.34%, and IL-18 level >115.71 ng/mL were independent risk factors for postoperative deep vein thrombosis. The results of the ROC curve showed that the area under curves, which represent the formation of postoperative deep vein thrombosis, were above 0.7 when using NLR value and IL-18 level at 3 days after surgery (both $P<0.001$). Conclusion: Compared with the non-thrombus group, NLR value and IL-18 level in the thrombosis group after receiving surgery for spinal degeneration are significantly increased. In addition, the more severe the thrombosis is, the higher the NLR value and IL-18 level at 3 days after surgery. Therefore, NLR value and IL-18 level at 3 days after surgery have certain clinical value in predicting postoperative deep vein thrombosis and prognosis.

Keywords: Spinal degeneration, deep vein thrombosis, neutrophil-to-lymphocyte ratio, interleukin-18

Introduction

Spinal degeneration is a disease whose essential manifestation is the chronic hyperplasia and degeneration of bone and soft tissue structure and function [1, 2]. Studies have shown that surgical treatment is required for most patients with spinal degeneration. However, some patients are prone to deep vein thrombosis after surgery, seriously affecting the therapeutic effect and prognosis [3-5]. At present, color Doppler ultrasound is regarded as the gold standard for clinical diagnosis of deep vein thrombosis. Nevertheless, it is accompanied with disadvantages like complicated operations and high testing cost, making it unlikely to be accepted by patients [6, 7]. Therefore, it is extremely important and clinically significant to

explore specific biological indicators. Deep vein thrombosis is a network response caused by the body's inflammatory response, coagulation function and other factors [3]. Neutrophil-to-lymphocyte ratio (NLR) is a biomarker produced by stress stimulators, and has been widely applied as a biological indicator in the diagnosis and treatment of inflammatory diseases for characteristics like having a stable ratio, simple operation, and low cost [8]. It was previously confirmed that the increase of NLR value was closely correlated with the high mortality of venous thrombosis [9]. Interleukin 18 (IL-18), a member of the interleukin family, plays an important role in the inflammatory response and immune regulation [10]. However, there are few previous reports on NLR value and IL-18 level in patients with deep vein thrombosis after receiving surgery for spinal degeneration; there is still no unified conclusion about their value [11, 12]. In this study, we investigate NLR value and IL-18 level in patients with deep vein thrombosis after receiving surgery for column degeneration and explored their clinical significance, hoping to provide relevant evidence for the clinical auxiliary prediction and diagnosis of deep vein thrombosis in patients undergoing the surgery for spinal degeneration.

Materials and methods

General information

This prospective study was conducted in 296 patients who were treated in our hospital for spinal degeneration between January 2017 and January 2020. According to whether postoperative deep vein thrombosis was observed or not, these patients were assigned to the thrombosis group (n = 72) and the non-thrombosis group (n = 224). Totally, there were 160 males and 136 females, with an average age of 58.7±12.9 years. Among all patients, 134 had cervical spondylosis; 74 had lumbar spondylosis; and 91 had thoracic spondylosis. This study was approved by the Ethics Committee of our hospital. Patients and their family members were aware of the research content and signed the informed consent.

Inclusion and exclusion criteria

Inclusion criteria: (1) patients had complete clinical data; (2) patients were diagnosed with spinal degeneration by examination such as X-ray, computed tomography (CT), and magnetic resonance imaging (MRI); (3) patients took no drugs influencing the fibrinolytic and coagulation systems for six months prior; (4) patients had not received surgical treatment related to spinal degeneration one year previously; (5) and patients had no other serious diseases.

Exclusion criteria: (1) patients had heart, liver, lung or other dysfunction; (2) patients suffered from abnormal blood coagulation or autoimmune disorders; (3) patients had malignant tumors; (4) patients had poor compliance; (5) patients simultaneously participated in other research; (6) female patients were pregnant or breastfeeding.

Methods

A 10 mL volume of fasting venous blood (5 mL in each tube) were collected from all patients before operation, and at 1, 3, 5, and 7 days after operation, respectively. The blood in one tube was employed to detect the NLR value employing an automatic hematology analyzer (DxH800, Beckman Coulter Inc., USA). The blood in the other tube was centrifuged at 3000 r/min for 5 min to separate the serum. Thereafter, the level of IL-18 was determined by enzyme linked immunosorbent assay (ELISA) using multifunctional microplate reader (Microlab STAR, Hamilton Company, Switzerland).

After surgery, patients were followed up for 1 month. After receiving the color Doppler ultrasound examination, patients were allocated to the thrombus group (n = 72) and the non-thrombus group (n = 224) according to the occurrence of deep vein thrombosis. Relevant criteria established by the Vascular Surgery Group of the Chinese Medical Association Surgery Branch in 2012 were standards for the formation of postoperative deep vein thrombosis [13]. The severity of deep vein thrombosis was assessed as below. Zero points: fully compressed vascular cavity; full blood flow in the vascular cavity; normal spectrum morphology. One point: partially compressed vascular cavity; partially filled blood flow in the vascular cavity; partly normal spectrum morphology. Two points: completely uncompressed vascular cavity; completely miss-

Table 1. The values of variables in logistic regression analysis

Variable	The value of variable
Age	<60 years = 0, ≥60 years = 1
The history of diabetes	Absent = 0, present = 1
BMI (kg/m^2)	<23 = 0, ≥23 = 1
NLR value	≤4.34% = 0, >4.34% = 1
IL-18 level	<115.71 ng/mL = 0, >115.71 ng/mL = 1

Note: BMI: body mass index; NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18.

ing blood flow in the vascular cavity; obviously abnormal spectrum morphology. The scoring was graded mild, moderate, and severe when the total score was 1-2 points, 3-4 points, and over 4 points, respectively [13].

Outcome measures

Main outcome measures: NLR values and IL-18 levels were detected before operation, and at 1, 3, 5, and 7 days after operation. The receiver operating characteristic (ROC) curve was used to analyze the clinical value of NLR value and IL-18 level at 3 days after operation in predicting postoperative deep vein thrombosis.

Secondary outcome measures: Baseline data, such as age, gender, operation method, operation time, intraoperative blood loss, postoperative in-bed time, the history of drinking, the history of hypertension, the history of diabetes, and body mass index (BMI) were compared between the two groups. Risk factors for postoperative deep vein thrombosis, which were displayed in **Table 1**, were analyzed with a logistic regression method. Patients were assigned to the mild, moderate, and severe group based on the degree of thrombosis. NLR value and IL-18 level at 3 days after surgery were compared among the three groups. Pearson correlation analysis was employed to analyze the correlation between both NLR value and IL-18 level and the severity of deep vein thrombosis.

Statistical methods

All data were analyzed using SPSS statistical software version 22.0. The enumeration data were calculated as number/percentage (n/%); comparison was conducted with chi-square test. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm sd$); t test was used for the comparison. Multivariate logistic regression analysis was further performed in indicators with statistical differences in univariate analysis results. Pearson correlation analysis was used to analyze the correlation between both NLR value and IL-18 level and the severity of deep vein thrombosis. ROC curve was implemented to analyze the clinical value of NLR value and IL-18 level at 3 days after operation in predicting postoperative deep vein thrombosis. The difference was statistically significant when the *P* value was less than 0.05.

Results

Baseline data

There were significant differences concerning age, the history of diabetes, and obesity between the two groups (all P<0.05, **Table 2**).

NLR value and IL-18 level

As shown in **Table 3**, there were no significant differences concerning preoperative NLR value and IL-18 level between the two groups (both P>0.05). Compared with before surgery, NLR values and IL-18 levels in the two groups after surgery were increased (both P<0.01). NLR values and IL-18 levels in both groups reached a peak at 3 days after surgery, while decreased at 5 and 7 days after surgery. NLR values and IL-18 levels in the thrombosis group at 1, 3, 5, and 7 days after surgery were higher than those in the non-thrombosis group (all P<0.01).

The results of logistic regression analysis

As displayed in **Table 4**, age ≥60 years old, BMI ≥23 kg/m^2, NLR value >4.34% and IL-18 level >115.71 ng/mL were independent risk factors for postoperative deep vein thrombosis.

NLR value and IL-18 level at 3 days after surgery

As displayed in **Table 5**, NLR values and IL-18 levels in both the moderate group and the severe group at 3 days after surgery were high-

Table 2. Baseline data ($\bar{x}$ ± sd)

Group	Thrombosis group (n = 72)	Non-thrombosis group (n = 224)	χ^2/t	P
Age (n)			10.084	0.002
≥60 years	31	53		
<60 years	41	171		
Gender (n)			0.001	0.982
Male	39	121		
Female	33	103		
Operation method (n)			0.163	0.997
Anterior cervical spine	13	42		
Posterior cervical spine	15	48		
Combination of the anterior and posterior cervical spine	11	35		
Posterior lumbar spine	21	66		
Posterior thoracic spine	12	33		
Operation time (min)	122.45±21.37	123.57±22.06	0.378	0.706
Intraoperative blood loss (mL)	154.33±34.51	152.58±30.22	0.413	0.680
Postoperative in-bed time (d)	7.2±1.3	7.0±1.1	1.282	0.201
The history of drinking (n)			0.152	0.697
Present	18	51		
Absent	54	173		
The history of hypertension (n)			0.081	0.777
Present	16	45		
Absent	58	179		
The history of diabetes (n)			5.610	0.018
Present	37	80		
Absent	35	144		
BMI (kg/m^2)			15.321	<0.001
≥23	29	40		
<23	43	184		

Note: BMI: body mass index.

Table 3. NLR value and IL-18 level ($\bar{x}$ ± sd)

Time	Before surgery	1 d after surgery	3 d after surgery	5 d after surgery	7 d after surgery
NLR value (%)					
Thrombosis group (n = 72)	3.91±1.01	5.68±2.34	9.06±3.51	7.65±3.02	5.33±2.87
Non-Thrombosis group (n = 224)	3.87±0.94	4.54±1.26	5.17±2.74	4.67±1.33	4.34±1.18
T	0.308	3.954	9.721	8.124	2.851
P	0.758	<0.001	<0.001	<0.001	0.006
IL-18 level (ng/ml)					
Thrombosis group (n = 72)	98.47±17.45	146.71±33.29	187.42±59.02	171.34±31.75	153.22±29.91
Non-thrombosis group (n = 224)	97.34±19.22	104.98±23.46	115.71±49.66	109.57±24.43	103.31±21.04
T	0.443	9.877	10.165	15.131	13.152
p	0.658	<0.001	<0.001	<0.001	<0.001

Note: NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18.

er than those in the mild group (all P<0.05). Compared with the moderate group, NLR value and IL-18 level in the severe group at 3 days after surgery were increased (both P<0.05).

Table 4. The results of logistic regression analysis

Variable	β	SE	Wald	P	OR	95% CI
Age (≥60 years)	0.08	0.04	18.443	<0.001	2.44	1.32-3.37
BMI (≥23 kg/m^2)	0.19	0.16	16.734	<0.001	3.11	1.65-5.48
NLR value (>4.34%)	0.22	0.09	19.621	<0.001	34.21	9.97-58.54
IL-18 level (>115.71 ng/mL)	0.16	0.11	22.358	<0.001	29.86	10.45-44.38

Note: BMI: body mass index; NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18.

Table 5. NLR value and IL-18 level at 3 days after surgery ($\bar{x} \pm sd$)

Group	NLR value (%)	IL-18 level (ng/ml)
Mild group (n = 24)	6.03±1.29	155.44±38.21
Moderate group (n = 31)	9.11±3.24[a]	187.28±57.42[a]
Severe group (n = 17)	12.45±2.02[a,b]	224.57±23.58[a,b]
F	34.067	11.648
P	<0.001	<0.001

Note: NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18. Compared with mild group, [a]P<0.05; Compared with moderate group, [b]P<0.05.

Table 6. The results of correlation analysis

Variables	NLR value (%)	IL-18 level (ng/mL)
r	0.446	0.512
P	<0.001	<0.001

Note: NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18.

The results of correlation analysis

Both NLR value and IL-18 level in the thrombosis group at 3 days after surgery were positively correlated with the degree of thrombosis (both P<0.001, **Table 6**).

The results of ROC curve

As shown in **Table 7** and **Figure 1**, AUCs, which represent the formation of postoperative deep vein thrombosis, were 0.803 and 0.827 when the cut-off value of NLR and IL-18 were 6.274% and 128.250 ng/mL, respectively (both P<0.001).

Discussion

The pathogenesis of postoperative deep vein thrombosis still needs to be clarified. Studies have shown that it might be related to factors like genetic factors, inflammatory reactions, and long-term in-bed rest [3, 4]. It is of important clinical significance to explore the risk factors for postoperative deep vein thrombosis to improve the prognosis and prevent adverse complications.

The body's muscle pump function tends to decline with aging, while the activity of coagulation factors increases. After lying in bed for a long time, it is easy for blood to accumulate in the veins, increasing the risk of thrombosis [14]. Elderly patients' blood vessel elasticity is weakened. Meanwhile, their endothelial cell function is decreased. As a result, the function of the venous valves is reduced. If they were accompanied with cardiovascular diseases, the risk of thrombosis would be further increased [15]. High BMI may be correlated with hyperlipidemia and atherosclerosis. What's more, patients with high BMI may have less exercise and activity. Accordingly, the pressure on the venous valves is raised. In this way, an abnormal rate of hemodynamics and the risk of venous thrombosis are increased [16]. In our study, the results of logistic regression analysis showed that both age ≥60 years and BMI ≥23 kg/m^2 were risk factors for postoperative deep vein thrombosis.

IL-18 can induce endothelial cell damage which is usually closely related to the formation of deep vein thrombosis by indirectly promoting the adhesion between blood vessels and cells [17-20]. It was also reported that IL-18 level in patients with deep vein thrombosis of the lower extremities was significantly increased [20]. In our study, the increase of IL-18 level in the thrombosis group after surgery was more than that in the non-thrombosis group. Additionally, it reached a peak at 3 days after surgery and then decreased slightly, which was consistent with other results that have been reported previously [17-20]. These results indicate that there might be a certain correlation between IL-18 and deep vein thrombosis. Moreover, we detected the level of IL-18 at 3 days after sur-

Table 7. The results of ROC curve

Variable	Cut-off value	AUC	95% CI	Sensitivity	Specificity	*P* value
NLR value (%)	6.274	0.803	0.745, 0.862	0.778	0.741	<0.001
IL-18 level (ng/mL)	128.250	0.827	0.773, 0.881	0.861	0.701	<0.001

Note: ROC: receiver operating characteristic; NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18. AUC: area under curve; CI: confidence interval.

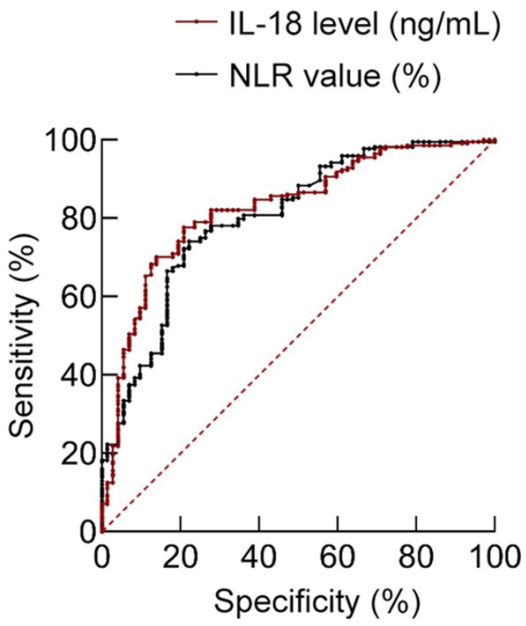

Figure 1. ROC curve. ROC: receiver operating characteristic; NLR: neutrophil-to-lymphocyte ratio; IL-18: interleukin 18.

gery. Our results showed that the level of IL-18 in patients with deep vein thrombosis was closely correlated with the severity of thrombosis. The results of logistic regression analysis displayed that the risk of postoperative deep vein thrombosis in patients with IL-18 level >115.71 ng/mL was 34.21 times that in patients with IL-18 level ≤115.71 ng/mL, suggesting that attention needs to be paid to patients' postoperative change of IL-18 level. In addition, we analyzed the clinical value of IL-18 level at 3 days after surgery in predicting postoperative deep vein thrombosis by drawing a ROC curve. Our results showed that AUC, which represents the formation of postoperative deep vein thrombosis, was 0.827 when the cut-off value of IL-18 was 128.250 ng/mL. This denotes that it is of certain clinical value to predict the formation of deep vein thrombosis by detecting IL-18 level at 3 days after surgery.

Studies have displayed that the increased number of neutrophils is closely related to macrophages. Cells like macrophages can promote the secretion of chemokines, which in turn contributes to the increased number of neutrophils. Increased number of neutrophils further promotes the release of vascular endothelial growth factors, leading to the formation of new blood vessels [21]. Lymphocytes mainly mediate immune responses. The decrease in the number of lymphocytes in the body corresponds to weakened immune function regulation ability [22, 23]. Farah et al, found that increased NLR value might promote inflammatory reactions and raise the risk for thrombosis [24]. Grimnes et al, also reported that NLR value was closely related to the mortality of patients with venous thrombosis [9]. In our study, results displayed that NLR values in the two groups after surgery were increased when compared with before surgery; the increase in the thrombosis group was more than that in the non-thrombosis group; NLR values in the two groups reached a peak at 3 days after surgery and then decreased slightly; three days after surgery, NLR value in patients with deep vein thrombosis was closely related to the severity of thrombosis. These results indicate that NLR value may be involved in the formation of postoperative deep vein thrombosis. The results of logistic regression analysis denote that high NLR value may increase the risk of postoperative deep vein thrombosis. Moreover, ROC curve also displayed that NLR value at 3 days after surgery has a certain clinical value in predicting postoperative deep vein thrombosis (AUC = 0.803). In a word, NLR value at 3 days after surgery can be used as one of the auxiliary indicators to predict the occurrence of postoperative deep vein thrombosis.

However, there are two shortcomings in this study. Firstly, the limitation of indicators: the indicators are not further expanded to explore the clinical significance of other biological indicators in patients with deep vein thrombosis after receiving the surgery for spinal degeneration. Secondly, the clinical value of NLR value and IL-18 level in predicting long-term progno-

sis are not discussed here. Therefore, subsequent study still needs to be conducted to perfect our present research.

In summary, NLR value and IL-18 level in the thrombosis group after receiving surgery for spinal degeneration are significantly increased when compared with the non-thrombus group. What's more, the more severe the thrombosis, the higher the NLR value and IL-18 level at 3 days after surgery are. In other words, NLR value and IL-18 level at 3 days after surgery have certain clinical value in predicting postoperative deep vein thrombosis and prognosis.

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Disclosure of conflict of interest

None.

Address correspondence to: Yukun Zhang, Department of Spine Surgery, The Sixth Affiliated Hospital of Xinjiang Medical University, No. 39 Wuxing South Road, Tianshan District, Urumqi 830002, Xinjiang Uygur Autonomous Region, China. Tel: +86-13565927065; E-mail: zyk126130@163.com

References

[1] Moayer A, Mohebali N and Razmkon A. Incidence of deep vein thrombosis in patients undergoing degenerative spine surgery onprophylactic dalteparin; a single center report. Bull Emerg Trauma 2016; 4: 38-42.

[2] Hohl JB, Lee JY, Rayappa SP, Nabb CE, Devin CJ, Kang JD, Ward WT and Donaldson WF 3rd. Prevalence of venous thromboembolic events after elective major thoracolumbar degenerative spine surgery. J Spinal Disord Tech 2015; 28: E310-E315.

[3] Krekoukias G, Gelalis ID, Xenakis T, Gioftsos G, Dimitriadis Z and Sakellari V. Spinal mobilization vs conventional physiotherapy in the management of chronic low back pain due to spinal disk degeneration: a randomized controlled trial. J Man Manip Ther 2017; 25: 66-73.

[4] Turkmenoglu ON, Kanat A, Yolas C, Aydin MD, Ezirmik N and Gundogdu C. First report of important causal relationship between the Adamkiewicz artery vasospasm and dorsal root ganglion cell degeneration in spinal subarachnoid hemorrhage: an experimental study using a rabbit model. Asian J Neurosurg 2017; 12: 22-27.

[5] Olaf M and Cooney R. Deep venous thrombosis. Emerg Med Clin North Am 2017; 35: 743-770.

[6] van der Hulle T, Cheung WY, Kooij S, Beenen LFM, van Bemmel T, van Es J, Faber LM, Hazelaar GM, Heringhaus C, Hofstee H, Hovens MMC, Kaasjager KAH, van Klink RCJ, Kruip MJHA, Loeffen RF, Mairuhu ATA, Middeldorp S, Nijkeuter M, van der Pol LM, Schol-Gelok S, Ten Wolde M, Klok FA and Huisman MV; YEARS study group. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. Lancet 2017; 390: 289-297.

[7] Lee SY, Niikura T, Iwakura T, Sakai Y, Kuroda R and Kurosaka M. Thrombin-antithrombin III complex tests. J Orthop Surg (Hong Kong) 2017; 25: 170840616684501.

[8] Guo D, Han A, Jing W, Chen D, Jin F, Li M, Kong L and Yu J. Preoperative to postoperative change in neutrophil-to-lymphocyte ratio predict survival in colorectal cancer patients. Future Oncol 2018; 14: 1187-1196.

[9] Grimnes G, Horvei LD, Tichelaar V, Brækkan SK and Hansen JB. Neutrophil to lymphocyte ratio and future risk of venous thromboembolism and mortality: the Tromsø study. Haematologica 2016; 101: e401-e404.

[10] Ovsyannikova IG, Haralambieva IH, Kennedy RB, O'Byrne MM, Pankratz VS and Poland GA. Genetic variation in IL18R1 and IL18 genes and Inteferon γ ELISPOT response to smallpox vaccination: an unexpected relationship. J Infect Dis 2013; 208: 1422-1430.

[11] Vakili H, Shirazi M, Charkhkar M, Khaheshi I, Memaryan M and Naderian M. Correlation of platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio with thrombolysis in myocardial infarction frame count in ST-segment elevation myocardial infarction. Eur J Clin Invest 2017; 47: 322-327.

[12] Diem S, Schmid S, Krapf M, Flatz L, Born D, Jochum W, Templeton AJ and Früh M. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as prognostic markers in patients with non-small cell lung cancer (NSCLC) treated with nivolumab. Lung Cancer 2017; 111: 176-181.

[13] Vascular Surgery Group, Chinese Society of Surgery. Guidelines for the diagnosis and treatment of deep vein thrombosis (Second Edition). Chin J Gen Surg 2012; 7: 605-607.

[14] Nastasi AJ, Canner JK, Lau BD, Streiff MB, Aboagye JK, Kraus PS, Hobson DB, Van Arendonk KJ and Haut ER. Characterizing the relationship between age and venous thromboembolism in adult trauma patients: findings from the National Trauma Data Bank and the National Inpatient Sample. J Surg Res 2017; 216: 115-122.

[15] Xing F, Li L, Long Y and Xiang Z. Admission prevalence of deep vein thrombosis in elderly Chinese patients with hip fracture and a new predictor based on risk factors for thrombosis screening. BMC Musculoskelet Disord 2018; 19: 444.

[16] 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.

[17] Kurtipek E, Büyükterzi Z, Büyükterzi M, Alpaydın MS and Erdem SS. Endothelial dysfunction in patients with pulmonary thromboembolism: neutrophil to lymphocyte ratio and platelet to lymphocyte ratio. Clin Respir J 2017; 11: 78-82.

[18] Samnegård A, Hulthe J, Silveira A, Ericsson CG, Hamsten A and Eriksson P. Gender specific associations between matrix metalloproteinases and inflammatory markers in post myocardial infarction patients. Atherosclerosis 2009; 202: 550-556.

[19] Chandrasekar B, Vemula K, Surabhi RM, Li-Weber M, Owen-Schaub LB, Jensen LE and Mummidi S. Activation of intrinsic and extrinsic proapoptotic signaling pathways in interleukin-18-mediated human cardiac endothelial cell death. J Biol Chem 2004; 279: 20221-20233.

[20] Dziedziejko V, Kurzawski M, Paczkowska E, Machalinski B and Pawlik A. The impact of IL18 gene polymorphisms on mRNA levels and interleukin-18 release by peripheral blood mononuclear cells. Postepy Hig Med Dosw (Online) 2012; 66: 409-414.

[21] Huang C and Li S. Association of blood neutrophil lymphocyte ratio in the patients with postmenopausal osteoporosis. Pak J Med Sci 2016; 32: 762-765.

[22] Lin L, Yang F, Wang Y, Su S, Su Z, Jiang X, Zheng Y, Deng Y, Lv H, Zhao J, Lin R, Wang B and Sun C. Prognostic nomogram incorporating neutrophil-to-lymphocyte ratio for early mortality in decompensated liver cirrhosis. Int Immunopharmacol 2018; 56: 58-64.

[23] Ertaş G, Sönmez O, Turfan M, Kul S, Erdoğan E, Tasal A, Bacaksiz A, Vatankulu MA, Altıntaş O, Uyarel H and Göktekin O. Neutrophil/lymphocyte ratio is associated with thromboembolic stroke in patients with non-valvular atrial fibrillation. J Neurol Sci 2013; 324: 49-52.

[24] Farah R, Nseir W, Kagansky D and Khamisy-Farah R. The role of neutrophil-lymphocyte ratio, and mean platelet volume in detecting patients with acute venous thromboembolism. J Clin Lab Anal 2020; 34: e23010.