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Diagnostic value of ultrasound combined with serum CCL3 and P-selectin for postoperative lower extremity deep vein thrombosis in patients with hip fracture

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Abstract: **Objective** To investigate the value of color Doppler ultrasound combined with serum chemokine C-C motif ligand 3(CCL3) and P-selectin levels for the diagnosis of postoperative lower extremity deep vein thrombosis (LEDVT) in patients with hip fractures. **Methods** Eighty patients with hip fractures complicated with LEDVT admitted to Xi'an Gaoxin Hospital from September 2022 to September 2024 were regarded as the LEDVT group, 80 patients with hip fractures without LEDVT admitted to Xi'an Gaoxin Hospital from September 2022 to September 2024 were considered as the LEDVT group. Eighty patients with hip fractures complicated with LEDVT admitted to Xi'an Gaoxin Hospital from September 2022 to September 2024 were regarded as the LEDVT group, 80 patients with hip fractures without LEDVT were regarded as the non-LEDVT group, and 80 healthy individuals who experienced physical check ups were regarded as the control group. The levels of serum CCL3 and P-selectin in three groups were compared. Color Doppler flow imaging (CDFI) was applied to measure the inner diameters of the common femoral vein (CFV) and deep femoral vein (PFV), and the subcutaneous tissue thickening was calculated. Multivariate logistic regression was applied to analyze the influencing factors of LEDVT in patients with hip fractures. ROC curve was applied to analyze the diagnostic value of ultrasound combined with serum CCL3 and P-selectin levels for LEDVT in patients with hip fractures. **Results** Compared with the control group, both serum CCL3 and P-selectin levels were significantly higher in the LEDVT group (P<0.05). Compared to the non-LEDVT group, the levels of serum CCL3, P-selectin, CFV, PFV, and subcutaneous tissue thickening were prominently higher in the LEDVT group (P<0.05). CFV, PFV, subcutaneous tissue thickening, CCL3, and P-selectin were influencing factors for LEDVT in patients with hip fractures (P<0.05).The combined area under the curve (AUC) (0.956) was significantly higher than that of any single indicator, with a sensitivity of 81.25% and specificity of 96.25%. **Conclusion** The levels of serum CCL3 and P-selectin are obviously upregulated in patients with hip fracture complicated with LEDVT, both of which are influencing factors for the occurrence of LEDVT in patients with hip fracture. Ultrasound combined with serum CCL3 and P-selectin levels has high diagnostic value for LEDVT in patients with hip fractures .

Keywords: Hip fracture; Chemokine C-C motif ligand 3; P-selectin; Lower extremity deep vein thrombosis

Hip fracture is one of the more serious types of osteoporotic fracture, which mostly occurs in the elderly population, and has a high incidence, disability, and fatality rate, which seriously affects the daily life and physical health of patients [1]. Currently, patients with hip fracture are mostly treated with surgery, such as internal fixation or arthroplasty, but the inability of rapid recovery after surgery and the need for long-term bed rest lead to an elevated risk of postoperative complications, among which, lower extremity deep vein thrombosis (LEDVT) is a common postoperative complication [2-3]. LEDVT has a high incidence and lethality rate, and if preventive and curative measures are not taken in a timely manner, it will seriously affect the recovery of patients [4]. Therefore, early diagnosis of LEDVT and timely adoption of effective treatment are of great significance in alleviating the progression of the disease and improving the postoperative condition of patients. Color ultrasound diagnosis of LEDVT is more widely used in the clinic and can be used to determine the status of thrombus, which has certain application value [5]. Chemokine C-C motif ligand 3 (CCL3), as a pro-inflammatory chemokine, is involved in the inflammatory response of multiple organisms, which can induce inflammatory cells and aggravate the inflammatory response [6]. It has been found that pro-inflammatory factors have a certain

regulatory role in the formation of venous thrombosis, and CCL3 plays an important role in the formation of deep vein thrombosis [7]. P-selectin belongs to the adhesion molecule selectin, which can increase vascular permeability and participate in the body's inflammatory response. Previous studies have shown that P-selectin is closely related to the thrombosis-related disease development [8-9]. However, the diagnostic value of serum CCL3 and P-selectin levels on the occurrence of LEDVT in patients with hip fracture is not yet known, therefore, this study further analyzed the diagnostic value of color ultrasound combined with serum CCL3 and P-selectin levels on the occurrence of LEDVT in patients with hip fracture by detecting the levels of serum CCL3 and P-selectin levels, to provide new ideas for clinical diagnosis.

1 Objects and Methods

1.1 Study subjects

Eighty patients with hip fracture complicating LEDVT admitted to Xi'an High-Tech Hospital from September 2022 to September 2024 were selected as the LEDVT group, of which 42 were male and 38 were female, aged 60-76 (67.38±6.87) years old; and another 80 patients with hip fracture without LEDVT were selected as the non-LEDVT group, of which 40 were male and 40 were female, aged 60-77 (67.51±6.93) years old.

Inclusion criteria: (1) all were diagnosed with hip fracture after CT examination and X-ray; (2) met the relevant diagnostic criteria of LEDVT [10]; (3) admitted to the hospital for treatment within 72 h after the fracture; (4) all met the indications for surgery and underwent internal fixation surgery; (5) they had complete medical records; and (6) all signed the informed consent.

Exclusion criteria: (1) the presence of a history of deep vein thrombosis; (2) suffering from malignant tumors; (3) suffering from dysfunction of the heart, liver and other vital organs; (4) the presence of diseases related to the blood and immune system; (5) pathological fracture; (6) communication disorders. Another 80 cases of healthy people with physical examination in the same period were selected as the control group, of which 39 cases were male and 41 cases were female, aged 60-75 (67.21±6.33) years. The difference of general information among the three groups was not statistically significant (P>0.05) and was comparable. The study was approved by the Ethics Committee of the hospital (Approval number: GX2022-016).

1.2 Reagents and instruments

Centrifuge (No.: MPC2000, Dinghao Yuan Pharmaceutical); enzyme-labeled instrument (No.: LabYeah, Shanghai BioScience); CCL3 ELISA kit (No. JC-A7201, Shanghai Kijun Industrial Co., Ltd.); P-selectin ELISA kit (No. JC-A5881, Shanghai Gelatins); Color Doppler Ultrasound Diagnostic Instrument (No.: K2, Shanghai Qi Sheng Biologics).

1.3 Methods

A total of 4 mL of fasting venous blood was collected from all patients and healthy individuals in the morning on the day of the physical examination. The blood samples were centrifuged at 3,000 r/min for 10 minutes with a centrifugation radius of 14 cm. The serum was separated, aliquoted into sterile EP tubes, and stored at -80 °C. The serum CCL3 and P-selectin levels were detected by ELISA. Briefly, 50 μL of serum samples were added to a 96-well plate and incubated at 37 °C for 1 hour, followed by washing. Then, 50 μL of enzyme-labeled antibody was added, and the samples were incubated at 37 °C for 1 hour, followed by another wash. Color development was initiated by adding the substrate solution for 20 minutes, after which the reaction was stopped by adding the termination solution. Finally, the absorbance was measured using an enzyme-linked immunosorbent assay reader.

1.4 Color ultrasound examination

One physician with extensive experience in ultrasound was selected to perform the procedure. A color Doppler ultrasound diagnostic instrument was used to examine all patients, with a probe frequency of 5.0-7.5 MHz. The patients were placed in a lying position, and the examination was conducted by sweeping from the groin area. The common femoral vein (CFV), the deep femoral vein (PFV), the posterior tibial vein, and the great saphenous vein were examined sequentially. The diameter of the vessels, the location of the thrombus, and its extent were observed. Blood flow changes were assessed using color Doppler flow imaging (CDFI). The inner diameters of the CFV and PFV were measured, and subcutaneous tissue thickening was calculated.

1.5 Statistical methods

SPSS 25.0 software was used. Measurement data all conformed to normal distribution, expressed by $\bar{x} \pm s$, and the two groups were compared by group t-test; 3 groups were compared by one-way ANOVA, and further two-by-two comparison was performed by SNK-q test; count data were expressed by cases (%), and χ^2 test was performed; multivariate logistic regression was performed to analyze the influencing factors on the occurrence of LEDVT in patients with hip fracture; and the ROC curves were performed to analyze the diagnostic value of color ultrasound combined with serum CCL3, P-selectin level on the diagnostic value of LEDVT in hip fracture patients. P<0.05 was considered statistically significant difference.

2 Results

2.1 General information

The differences in general characteristics among the three groups were not statistically significant (P>0.05). Additionally, the comparison of fracture types between the LEDVT group and the non-LEDVT group showed no statistically significant difference (P>0.05). **[Table 1]**

Tab.1 Comparison of general data among the three groups (*n*=80)

Item	LEDVT group	Non-LEDVT group	Control group	F/χ^2 value	*P* value
Age (years) [a]	67.38±6.87	67.51±6.93	67.21±6.33	0.040	0.961
Gender [b]					
Male	42 (52.50)	40 (50.00)	39 (48.75)	0.233	0.890
Female	38 (47.50)	40 (50.00)	41 (51.25)		
BMI (kg/m²)[a]	22.53±3.05	22.19±2.85	22.34±2.87	0.272	0.762
Type of fracture [b]					
Femoral neck fracture	33 (41.25)	36 (45.00)		0.229	0.632
Intertrochanteric Femur Fracture	47 (58.75)	44 (55.00)			
History of smoking [b]					
+	28 (35.00)	31 (38.75)	27 (33.75)	0.471	0.790
-	52 (65.00)	49 (61.25)	53 (66.25)		
History of alcohol consumption [b]				1.561	0.458
+	25 (31.25)	22 (27.50)	18 (22.50)		
-	55 (68.75)	58 (72.50)	62 (77.50)		
Hypertension [b]					
+	24 (30.00)	26 (32.50)	19 (23.75)	1.587	0.452
-	56 (70.00)	54 (67.50)	61 (76.25)		
Diabetes [b]					
+	26 (32.50)	22 (27.50)	15 (18.75)	4.003	0.135
-	54 (67.50)	58 (72.50)	65 (81.25)		

Note: [a] indicates that the data are expressed in $\bar{x} \pm s$; [b] indicates that the data are expressed in cases (%).

2.2 Serum CCL3 and P-selectin levels

Serum CCL3 and P-selectin levels were significantly higher in the LEDVT group compared with the control group and the non-LEDVT group (*P*<0.05). **[Table 2]**

2.3 Comparison of ultrasound findings between the LEDVT group and the non-LEDVT group

Compared with the non-LEDVT group, diameters of CFV and PFV, and subcutaneous tissue thickening of patients in the LEDVT group were significantly higher (*P*<0.05). **[Table 3]**

2.4 Multivariate logistic regression analysis of the influencing factors on the occurrence of LEDVT in patients with hip fracture

Multivariate logistic regression analysis was performed with whether LEDVT occurred in patients with hip fracture (yes=1, no=0) as the dependent variable; diameters of CFV and PFV, subcutaneous tissue augmentation thickness, CCL3, and P-selectin (input of unadjusted values) as the independent variables. The results showed that CFV, DFV, subcutaneous tissue thickening, CCL3, and P-selectin were independent influencing factors on the occurrence of LEDVT in hip fracture patients (P<0.05). **[Table 4]**

2.5 Diagnostic value of color ultrasound combined with serum CCL3 and P-selectin levels for the occurrence of LEDVT in hip fracture patients

The area under the curve (AUC) values for diagnosing LEDVT in hip fracture patients were 0.862, 0.850, 0.853, 0.862, and 0.859 for color ultrasound parameters (CFV, DFV, and subcutaneous tissue thickening, serum CCL3 and P-selectin levels, respectively). The AUC for the combined diagnosis using all five parameters reached 0.956, demonstrating significantly higher diagnostic accuracy compared to single-parameter assessments. The combined diagnostic approach showed a sensitivity of 81.25% and specificity of 96.25%. **[Table 5 & Figure 1]**

Tab.2 Comparison of serum CCL3 and P-selectin levels among the three groups (*n*=80, $\bar{x}$±s)

Groups	CCL3 (pg/mL)	P-selectin (ng/mL)
LEDVT group	19.52±4.29 [ab]	55.49±6.82 [ab]
Non-LEDVT group	13.36±3.54 [a]	46.38±5.67 [a]
Control group	12.19±3.38	44.59±4.83
***F* value**	87.859	80.402
***P* value**	<0.001	<0.001

Note: Compared with the control group, [a]*P*<0.05; compared with the non-LEDVT group, [b]*P*<0.05 .

Tab. 3 Comparison of color doppler ultrasound results between LEDVT group and non-LEDVT group (*n*=80, mm,$\bar{x}$±s)

Groups	CFV diameter	PFV diameter	Subcutaneous tissue thickening
LEDVT group	11.89±2.96	7.49±2.36	0.10±0.03
Non-LEDVT group	8.27±2.21	5.04±1.56	0.06±0.02
***t* value**	8.765	7.746	9.923
***P* value**	<0.001	<0.001	<0.001

Tab.4 Multivariate logistic regression analysis of factors influencing LEDVT in Hip fracture patients

Variables	*β*	*SE*	*Wald*	*P* value	*OR* value	95% *CI*
CFV diameter	0.839	0.312	7.238	0.007	2.315	1.256-4.267
DFV diameter	0.602	0.302	3.968	0.046	1.825	1.010-3.299
Subcutaneous tissue thickening	0.553	0.257	4.626	0.031	1.738	1.050-2.876
CCL3	0.801	0.341	5.519	0.019	2.228	1.142-4.347
P-selectin	0.738	0.328	5.064	0.024	2.092	1.100-3.979

Tab. 5 Diagnostic value of ultrasound combined with serum CCL3 and P-selectin levels for LEDVT in patients with hip fractures

Variables	AUC	Cut-off value	95% *CI*	Sensitivity (%)	Specificity (%)	Youden Index
CFV diameter	0.862	9.64 mm	0.799-0.912	81.25	77.50	0.588
DFV diameter	0.850	7.28 mm	0.785-0.902	85.00	78.75	0.638
Subcutaneous tissue thickening	0.853	0.09 mm	0.788-0.904	83.75	82.50	0.663
CCL3	0.862	17.35 pg/mL	0.798-0.911	81.25	86.25	0.675
P-selectin	0.859	51.77 ng/mL	0.795-0.909	81.25	87.50	0.688
Combination of the five	0.956		0.912-0.982	81.25	96.25	0.775

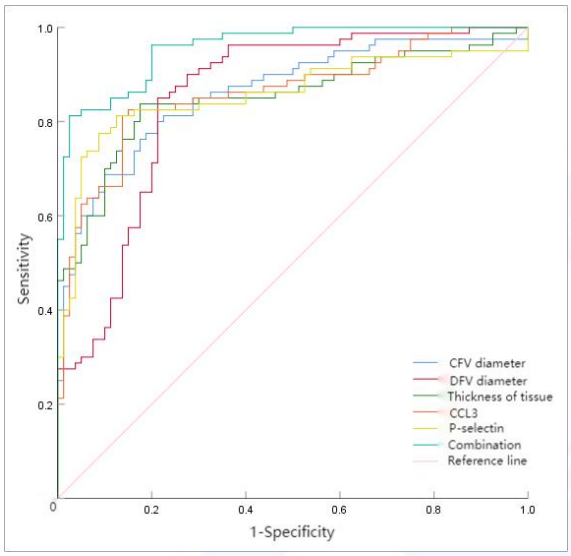

Fig. 1 ROC curve of LEDVT diagnosis in patients with hip fracture using ultrasound combined with serum CCL3 and P-selectin levels

3 Discussion

Hip fracture is a prevalent traumatic condition in orthopedic practice, particularly among the elderly population who are susceptible to osteoporosis due to osteopenia and reduced bone metabolism, making them vulnerable to hip fractures even from minor impacts, with the incidence increasing alongside the progression of population aging [11]. LEDVT constitutes a frequent postoperative complication in hip fracture patients, resulting from abnormal blood coagulation within deep veins that initiates thrombus formation, subsequently obstructing venous return, leading to limb swelling and functional impairment, while simultaneously elevating the risk of complications including varicose veins and other potentially life-threatening conditions [12]. Nevertheless, the absence of specific manifestations during the early disease stages complicates timely diagnosis, prompting the predominant clinical utilization of imaging modalities, among which color Doppler ultrasound offers distinct advantages of reproducibility, non-invasiveness, and operational simplicity [13]. The findings of this investigation demonstrated significantly elevated CFV and DFV diameters, and subcutaneous tissue thickness in patients with concurrent LEDVT compared to their non-LEDVT counterparts, indicating a potential association between alterations in these parameters and LEDVT development. Previous investigations have established that vascular ultrasound assessments of CFV and DFV diameters, and subcutaneous tissue thickness possess substantial clinical significance in LEDVT diagnosis and maintain a strong correlation with venous thrombosis grading [14].

CCL3, a member of the CC class chemokine subfamily, is predominantly expressed in macrophages and neutrophils, exhibiting chemotactic properties that modulate leukocyte migration; furthermore, CCL3 potentially participates in various physiological and pathological processes, including cell proliferation, hematopoiesis, and neovascularization within the tumor microenvironment [15]. In this study, serum CCL3 concentrations were markedly elevated in patients presenting with concurrent LEDVT compared to those without LEDVT, indicating that alterations in serum CCL3 levels may contribute to the pathogenesis of LEDVT. Previous research has demonstrated that CCL3 levels are significantly increased in postoperative inflammatory states, stimulating the secretion of inflammatory mediators and cytokines while inducing tissue factor expression in macrophages, thereby influencing the coagulation cascade [16]. These findings have been corroborated by studies confirming elevated CCL3 levels in LEDVT patients [17], aligning with the results of the present study which suggest that CCL3 expression changes are implicated in LEDVT pathogenesis and possess diagnostic efficacy as a potential clinical biomarker.

P-selectin is widely distributed on the surface of platelet alpha-granules and vascular endothelial cells, and plays an adhesive role between cells and matrix, which can promote thrombus formation [18]. It has been found that after trauma to the organism, platelet activation is stimulated to promote P-selectin secretion, which in turn mediates the role of platelets, neutrophils, and other factors that promote monocyte tissue factor secretion and induce thrombus formation [19]. The results of the present study showed that serum P-selectin levels were significantly elevated in patients with concurrent LEDVT compared with those without LEDVT, suggesting a link between changes in P-selectin levels and LEDVT generation. Previous studies have pointed out that P-selectin is an important indicator that affects the interaction of vascular endothelial cells and platelets, and is closely related to the formation of thrombus, which further confirms that if the P-selectin gene is knocked down, it can inhibit the formation of thrombus, and can

be used as a biomarker of venous thrombosis [20-21]. In conjunction with the present study, it is clear that P-selectin plays an important role in the development of LEDVT and can be used in clinical diagnosis.

The results of multivariate logistic regression analysis showed that CFV and DFV diameters, subcutaneous tissue thickening thickness, CCL3, and P-selectin were the influencing factors for the occurrence of LEDVT in patients with hip fracture, and the clinical practice should pay close attention to the above indexes, and take timely and effective measures to alleviate the disease progression in case of any abnormality, which can improve the patients' postoperative conditions. Further ROC curve analysis showed that the AUC of CFV and DFV diameters, subcutaneous tissue thickening combined with serum CCL3 and P-selectin levels for diagnosis of LEDVT in patients with hip fracture were 0.862, 0.850, 0.853, 0.862, 0.859, respectively, and the AUC of the combination of the five was 0.956, which is significantly higher than the single indicator diagnosis, indicating that color ultrasound is an important factor in the diagnosis of LEDVT. higher than that of single index diagnosis, indicating that color ultrasound examination combined with serum indexes can effectively improve the diagnostic accuracy, which can be used for clinical auxiliary diagnosis and provide a reference for the guidance of the follow-up treatment plan.

In conclusion, this study demonstrated significant upregulation of serum CCL3 and P-selectin levels in patients with hip fracture complicated by LEDVT, identifying both biomarkers as influential factors in LEDVT development among this patient population. The combined diagnostic approach utilizing color ultrasound alongside serum CCL3 and P-selectin levels exhibited substantial diagnostic value for LEDVT detection in hip fracture patients. However, several limitations should be acknowledged in this study: the serum biomarker measurements represent single time-point evaluations, lacking dynamic monitoring of their temporal patterns. Furthermore, the relatively limited sample size constrained the ability to perform comprehensive analyses regarding the precise roles of these serum biomarkers in LEDVT pathogenesis among patients with hip fracture. Future investigations will address these limitations through expanded sample sizes and more in-depth analyses.

Conflict of interest None

Reference

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·论　著·

彩超联合血清趋化因子配体 3 及 P 选择素对髋部骨折患者术后下肢深静脉血栓的诊断价值

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摘要：目的　探讨彩超技术与血清中趋化因子配体 3(CCL3)及 P 选择素(P-selectin)水平相结合的方法，对于诊断髋部骨折患者术后下肢深静脉血栓(LEDVT)的价值。**方法**　选取 2022 年 9 月至 2024 年 9 月西安高新医院收治的 80 例髋部骨折并发 LEDVT 患者为 LEDVT 组，80 例髋部骨折无 LEDVT 患者为无 LEDVT 组，另选同期 80 例体检健康者为对照组。比较 3 组血清中 CCL3、P-selectin 的水平；通过彩色多普勒血流显像(CDFI)测量股总静脉(CFV)、股深静脉(DFV)内径，并计算皮下组织增厚度。多因素 logistic 回归分析髋部骨折患者发生 LEDVT 的影响因素；ROC 曲线分析彩超联合血清 CCL3、P-selectin 水平对髋部骨折患者发生 LEDVT 的诊断价值。**结果**　与对照组相比，LEDVT 组血清 CCL3、P-selectin 水平均明显升高($P<0.05$)。与无 LEDVT 组相比，LEDVT 组血清 CCL3、P-selectin 水平以及 CFV、PFV、皮下组织增厚度均明显升高($P<0.05$)。Logistic 回归分析显示，CFV、PFV、皮下组织增厚度、CCL3、P-selectin 为髋部骨折患者发生 LEDVT 的独立影响因素($P<0.05$)。五者联合诊断的曲线下面积(AUC)(0.956)明显高于单一指标诊断，五者联合诊断的敏感度为 81.25%，特异度为 96.25%。**结论**　髋部骨折并发 LEDVT 患者血清 CCL3、P-selectin 水平均明显上调，且均为髋部骨折患者发生 LEDVT 的独立影响因素，彩超联合血清 CCL3、P-selectin 水平对髋部骨折患者发生 LEDVT 具有较高的诊断价值。

关键词：髋部骨折；趋化因子配体 3；P 选择素；下肢深静脉血栓

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Abstract: Objective　To investigate the value of color Doppler ultrasound combined with serum chemokine C-C motif ligand 3(CCL3) and P-selectin levels for the diagnosis of postoperative lower extremity deep vein thrombosis(LEDVT) in patients with hip fractures. **Methods**　Eighty patients with hip fractures complicated with LEDVT admitted to Xi'an Gaoxin Hospital from September 2022 to September 2024 were regarded as the LEDVT group, 80 patients with hip fractures without LEDVT were regarded as the non-LEDVT group, and 80 healthy individuals who experienced physical examination were regarded as the control group. The levels of serum CCL3 and P-selectin in three groups were compared. Color Doppler flow imaging (CDFI) was applied to measure the inner diameters of the common femoral vein (CFV) and deep femoral vein (DFV), and the subcutaneous tissue thickening was calculated. Multivariate logistic regression was applied to analyze the influencing factors of LEDVT in patients with hip fractures. ROC curve was applied to analyze the diagnostic value of ultrasound combined with serum CCL3 and P-selectin levels for LEDVT in patients with hip fractures. **Results**　Compared to the control group, both serum CCL3 and P-selectin levels were significantly higher in the LEDVT group ($P<0.05$). Compared to the non-LEDVT group, the levels of serum CCL3, P-selectin, CFV, DFV, and

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subcutaneous tissue thickening were prominently higher in the LEDVT group ($P<0.05$). CFV, PFV, subcutaneous tissue thickening, CCL3, and P-selectin were influencing factors for LEDVT in patients with hip fractures ($P<0.05$). The combined diagnostic AUC (0.956) was significantly higher than that of any single indicator, with a sensitivity of 81.25% and specificity of 96.25%. **Conclusion** The levels of serum CCL3 and P-selectin are obviously upregulated in patients with hip fracture complicated with LEDVT, both of which are influencing factors for the occurrence of LEDVT in patients with hip fracture. Ultrasound combined with serum CCL3 and P-selectin levels has high diagnostic value for LEDVT in patients with hip fractures.

Keywords: Hip fracture; Chemokine C-C motif ligand 3; P-selectin; Lower extremity deep vein thrombosis

髋部骨折是骨质疏松性骨折中较为严重的一种，多发于老年人群，具有较高的发病率、致残率以及致死率，严重影响患者的日常生活及身体健康[1]。目前，髋部骨折患者多采用手术治疗，如内固定术或关节置换术，但是由于术后无法快速康复，需要长期卧床，导致患者发生术后并发症的风险升高，其中，下肢深静脉血栓（lower extremity deep vein thrombosis，LEDVT）是术后常见的一种并发症[2-3]。LEDVT 具有较高的发生率、致死率，若不及时采取防治措施，会严重影响患者的恢复[4]。因此，尽早诊断 LEDVT，及时采取有效治疗措施，对缓解病情发展、改善患者预后有重要意义。彩超诊断 LEDVT 在临床中应用较为广泛，可用于判断血栓状态，具有一定的应用价值[5]。趋化因子配体 3（chemokine C-C motif ligand 3，CCL3）作为一种促炎趋化因子，参与机体炎症反应，可诱导炎性细胞，加重炎症反应[6]。研究发现，促炎因子对于静脉血栓的形成具有一定的调控作用，CCL3 在深静脉血栓的形成过程中发挥重要作用[7]。P 选择素（P-selectin）可增加血管通透性，参与机体炎症反应。既往研究表明，P-selectin 与血栓相关疾病的发生发展密切相关[8-9]。但是血清 CCL3、P-selectin水平对髋部骨折患者发生 LEDVT 的诊断价值尚未可知。因此，本研究通过检测血清 CCL3、P-selectin水平，进一步分析彩超联合血清 CCL3、P-selectin 水平对髋部骨折患者发生 LEDVT 的诊断价值，为临床诊断提供新的思路。

1　对象与方法

1.1　*研究对象*　选取 2022 年 9 月至 2024 年 9 月西安高新医院收治的 80 例髋部骨折并发 LEDVT 患者为 LEDVT 组，其中男 42 例，女 38 例，年龄 60～76（67.38±6.87）岁；另选 80 例髋部骨折无 LEDVT 患者为无 LEDVT 组，其中男 40 例，女 40 例，年龄 60～77（67.51±6.93）岁。纳入标准：（1）均经过 CT 检查及 X 线片确诊为髋部骨折；（2）LEDVT 符合相关诊断标准[10]；（3）骨折后 72 h 内入院治疗；（4）均符合手术指征，并进行内固定手术；（5）病历资料完整；（6）均签署知情同意书。排除标准：（1）存在深静脉血栓病史；（2）患恶性肿瘤；（3）患心、肝等重要器官功能障碍；（4）存在血液、免疫系统相关疾病；（5）病理性骨折；（6）沟通障碍。另选同期 80 例体检健康者为对照组，其中男 39 例，女 41 例，年龄 60～75（67.21±6.33）岁。3 组一般资料比较差异无统计学意义（$P>0.05$），具有可比性。本研究取得医院伦理委员会批准（批号：GX2022-016）。

1.2　*试剂与仪器*　离心机（型号：MPC2000，鼎昊源生物公司）；酶标仪（型号：LabYeah，上海百赛生物技术公司）；CCL3 ELISA 试剂盒（货号：JC-A7201，上海机纯实业有限公司）；P-selectin ELISA 试剂盒（货号：JC-A5881，上海机纯实业有限公司）；彩色多普勒超声诊断仪（型号：K2，企晟医疗器械有限公司）。

1.3　*方法*　所有患者及健康体检者取早晨空腹静脉血 4 mL，3 000 r/min 离心 10 min，离心半径 14 cm，分离血清，分装于无菌 EP 管中，在−80 ℃冰箱中保存。采用 ELISA 对血清 CCL3、P-selectin 水平进行检测，吸取 50 μL 血清样品加入 96 孔板中，37 ℃孵育 1 h 后洗涤，加入酶标抗体 50 μL，37 ℃孵育 1 h 后洗涤，加入显色液显色 20 min，加入终止液终止反应，最后用酶标仪测定。

1.4　*彩超检查*　选用 1 位超声工作经验丰富的医师进行操作，采用彩色多普勒超声诊断仪对所有患者进行检查，探头频率为 5.0～7.5 MHz，取患者平卧位，自腹股沟进行扫查，依次检查股总静脉（CFV）、股深静脉（DFV）、胫后静脉、大隐静脉，并观察管径、栓子部位、范围等。通过彩色多普勒血流显像（CDFI）观察血流变化，测量 CFV、DFV 内径，并计算皮下组织增厚度。

1.5　*统计学方法*　采用 SPSS 25.0 软件处理数据。计量资料均符合正态分布，以 $\bar{x}\pm s$ 表示，两组比较采用成组 t 检验；3 组比较采用单因素方差分析，进一步两两比较用 SNK-q 检验；计数资料以例（%）表

示，行 χ^2 检验；多因素 logistic 回归分析髋部骨折患者发生 LEDVT 的影响因素；ROC 曲线分析彩超联合血清 CCL3、P-selectin 水平对髋部骨折患者发生 LEDVT 的诊断价值。$P<0.05$ 为差异有统计学意义。

2 结　果

2.1　一般资料　3 组一般资料比较差异无统计学意义（$P>0.05$）；LEDVT 组患者的骨折类型与无 LEDVT 组相比差异无统计学意义（$P>0.05$）。见表 1。

2.2　血清 CCL3、P-selectin 水平　与对照组、无 LEDVT 组相比，LEDVT 组血清 CCL3、P-selectin 水平均明显升高（$P<0.05$）。见表 2。

2.3　LEDVT 组和无 LEDVT 组彩超检查结果比较　与无 LEDVT 组相比，LEDVT 组患者的 CFV 内径、DFV 内径、皮下组织增厚度均明显升高（$P<0.05$）。见表 3。

2.4　多因素 logistic 回归分析髋部骨折患者发生 LEDVT 的影响因素　以髋部骨折患者是否发生 LEDVT（是 = 1，否 = 0）为因变量，以 CFV 内径、DFV 内径、皮下组织增厚度、CCL3、P-selectin（原值代入）为自变量，进行多因素 logistic 回归分析显示，CFV、DFV、皮下组织增厚度、CCL3、P-selectin 为髋部骨折患者发生 LEDVT 的独立影响因素（$P<0.05$）。见表 4。

表 1　3 组一般资料比较　（$n=80$）

Tab. 1　Comparison of general data among the three groups　（$n=80$）

项目	LEDVT 组	无 LEDVT 组	对照组	F/χ^2 值	P 值
年龄（岁）[a]	67.38±6.87	67.51±6.93	67.21±6.33	0.040	0.961
性别[b]					
男	42(52.50)	40(50.00)	39(48.75)	0.233	0.890
女	38(47.50)	40(50.00)	41(51.25)		
BMI（kg/m^2）[a]	22.53±3.05	22.19±2.85	22.34±2.87	0.272	0.762
骨折类型[b]					
股骨颈骨折	33(41.25)	36(45.00)		0.229	0.632
股骨转子间骨折	47(58.75)	44(55.00)			
吸烟史[b]					
有	28(35.00)	31(38.75)	27(33.75)	0.471	0.790
无	52(65.00)	49(61.25)	53(66.25)		
饮酒史[b]					
有	25(31.25)	22(27.50)	18(22.50)	1.561	0.458
无	55(68.75)	58(72.50)	62(77.50)		
高血压[b]					
有	24(30.00)	26(32.50)	19(23.75)	1.587	0.452
无	56(70.00)	54(67.50)	61(76.25)		
糖尿病[b]					
有	26(32.50)	22(27.50)	15(18.75)	4.003	0.135
无	54(67.50)	58(72.50)	65(81.25)		

注：[a] 表示数据以 $\bar{x}\pm s$ 表示；[b] 表示数据以例（%）表示。

2.5　彩超联合血清 CCL3、P-selectin 水平对髋部骨折患者发生 LEDVT 的诊断价值　彩超参数 CFV、DFV、皮下组织增厚度联合血清 CCL3、P-selectin 水平诊断髋部骨折患者发生 LEDVT 的曲线下面积（AUC）分别为 0.862、0.850、0.853、0.862、0.859，五者联合诊断的 AUC 为 0.956，五者联合诊断的 AUC 明显高于单一指标诊断，五者联合诊断的敏感度为 81.25%，特异度为 96.25%。见表 5 和图 1。

表 2　3 组患者血清 CCL3、P-selectin 水平比较　（$n=80$，$\bar{x}\pm s$）

Tab. 2　Comparison of serum CCL3 and P-selectin levels among the three groups　（$n=80$，$\bar{x}\pm s$）

组别	CCL3（pg/mL）	P-selectin（ng/mL）
LEDVT 组	19.52±4.29[ab]	55.49±6.82[ab]
无 LEDVT 组	13.36±3.54[a]	46.38±5.67[a]
对照组	12.19±3.38	44.59±4.83
F 值	87.859	80.402
P 值	<0.001	<0.001

注：与对照组相比，[a] $P<0.05$；与无 LEDVT 组相比，[b] $P<0.05$。

表 3　LEDVT 组和无 LEDVT 组彩超检查结果　（$n=80$，mm，$\bar{x}\pm s$）

Tab. 3　Color doppler ultrasound results between LEDVT group and non-LEDVT group　（$n=80$，mm，$\bar{x}\pm s$）

组别	CFV 内径	DFV 内径	皮下组织增厚度
LEDVT 组	11.89±2.96	7.49±2.36	0.10±0.03
无 LEDVT 组	8.27±2.21	5.04±1.56	0.06±0.02
t 值	8.765	7.746	9.923
P 值	<0.001	<0.001	<0.001

表 4　多因素 logistic 回归分析髋部骨折患者发生 LEDVT 的影响因素

Tab. 4　Multivariate logistic regression analysis of factors influencing LEDVT in hip fracture patients

指标	β	SE	$Wald$	P 值	OR 值	95%CI
CFV 内径	0.839	0.312	7.238	0.007	2.315	1.256~4.267
DFV 内径	0.602	0.302	3.968	0.046	1.825	1.010~3.299
皮下组织增厚度	0.553	0.257	4.626	0.031	1.738	1.050~2.876
CCL3	0.801	0.341	5.519	0.019	2.228	1.142~4.347
P-selectin	0.738	0.328	5.064	0.024	2.092	1.100~3.979

表 5　彩超联合血清 CCL3、P-selectin 水平对髋部骨折患者发生 LEDVT 的诊断价值

Tab. 5　Diagnostic value of ultrasound combined with serum CCL3 and P-selectin levels for LEDVT in patients with hip fractures

变量	AUC	截断值	95%CI	敏感度（%）	特异度（%）	约登指数
CFV 内径	0.862	9.64 mm	0.799~0.912	81.25	77.50	0.588
DFV 内径	0.850	7.28 mm	0.785~0.902	85.00	78.75	0.638
皮下组织增厚度	0.853	0.09 mm	0.788~0.904	83.75	82.50	0.663
CCL3	0.862	17.35 pg/mL	0.798~0.911	81.25	86.25	0.675
P-selectin	0.859	51.77 ng/mL	0.795~0.909	81.25	87.50	0.688
五者联合	0.956		0.912~0.982	81.25	96.25	0.775

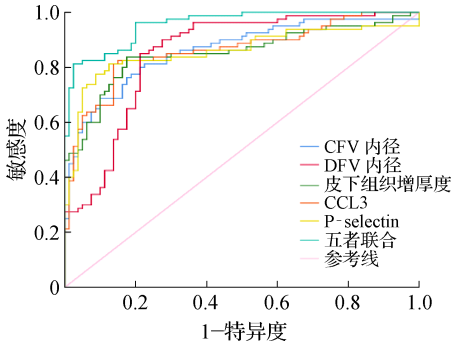

图 1　彩超联合血清 CCL3、P-selectin 水平诊断髋部骨折患者发生 LEDVT 的 ROC 曲线

Fig. 1　ROC curve of LEDVT diagnosis in hip fracture patients using ultrasound combined with serum CCL3 and P-selectin levels

3　讨　论

髋部骨折是骨科常见的外伤性疾病，老年人群由于骨质流失，骨代谢下降，易发生骨质疏松，轻微碰撞即可造成髋部骨折，随着社会老龄化进展，髋部骨折发生率呈上升趋势[11]。LEDVT 是髋部骨折患者术后常见的并发症，是因深静脉血液异常凝结，引发血栓生成，进而使血液回流受阻，进而导致肢体发生肿胀、功能障碍，增加患者发生静脉曲张等并发症的风险，危及生命[12]。但是由于该疾病早期缺乏特异性表征，早期诊断难度大，目前，临床多采用影像学检查，彩超具有可重复、无创且操作简单等特点[13]。本研究结果显示，并发 LEDVT 患者 CFV 内径、DFV 内径以及皮下组织增厚度与无 LEDVT 患者相比明显升高，提示 CFV 内径、DFV 内径以及皮下组织增厚度变化与 LEDVT 的发生存在一定联系。既往研究表明，血管超声检查结果中，CFV 内径、DFV 内径以及皮下组织增厚度等指标在 LEDVT 诊断中具有一定的临床价值，并且与静脉血栓分级密切相关[14]。

CCL3 属于 CC 类趋化因子亚家族，多表达在巨噬细胞、中性粒细胞中，具有趋化作用，可调控白细胞的迁移，另外，CCL3 可参与细胞增殖、造血以及肿瘤微环境新生血管的形成等生理病理活动[15]。本研究中，并发 LEDVT 患者血清 CCL3 水平与无 LEDVT 患者相比明显升高，提示血清 CCL3 水平变化可能参与 LEDVT 的发生过程。既往研究发现，在术后炎症状态，CCL3 水平明显升高，促进炎性递质和细胞因子的分泌，诱导巨噬细胞表达组织因子，进而对机体凝血系统产生影响[16]。经证实，CCL3 水平在 LEDVT 患者中显著升高[17]，与本研究结果一致，CCL3 水平变化与 LEDVT 的发生相关，具有一定的诊断价值，可作为生物标志物用于临床诊断。

P-selectin 广泛分布在血小板 α 颗粒及血管内皮细胞表面，对细胞及基质间起到黏附作用，可促进血栓的形成[18]。研究发现，在机体受到创伤后，刺激血小板活化，促进 P-selectin 分泌，进而介导血小板、中性粒细胞等作用，促进单核细胞组织因子分泌，诱导血栓形成[19]。本研究结果显示，并发 LEDVT 患者血清 P-selectin 水平与无 LEDVT 患者相比明显升高，说明 P-selectin 水平变化与 LEDVT 生成存在一定联系。既往研究指出，P-selectin 是影响血管内皮细胞、血小板相互作用的重要指标，与血栓的形成密切相关，进一步证实，若敲除 P-selectin 基因，可抑制血栓的形成，可作为静脉血栓生成的生物标志物[20-21]。结合本研究可知，P-selectin 在 LEDVT 的发生发展过程发挥重要作用，可用于临床诊断中。

多因素 logistic 回归分析结果显示，CFV 内径、DFV 内径、皮下组织增厚度、CCL3、P-selectin 为髋部骨折患者发生 LEDVT 的影响因素。临床应密切关注上述指标，若出现异常，及时采取有效措施，缓解病情发展，可改善患者术后情况。进一步 ROC 曲线分析可知，CFV 内径、DFV 内径、皮下组织增厚度联合血清 CCL3、P-selectin 水平诊断髋部骨折患者发生 LEDVT 的 AUC 分别为0.862、0.850、0.853、0.862、0.859，五者联合诊断的 AUC 为0.956。五者联合诊断的 AUC 明显高于单一指标诊断，说明彩超检查联合血清指标能有效提高诊断准确性，可用于临床辅助诊断，并为后续治疗方案的指导提供一定参考。

综上所述，髋部骨折并发 LEDVT 患者血清 CCL3、P-selectin 水平均明显上调，且均为髋部骨折患者发生 LEDVT 的影响因素，彩超联合血清 CCL3、P-selectin水平对髋部骨折患者发生 LEDVT 具有较高的诊断价值。本研究存在一些不足之处，血清指标检测结果仅为某一时间点的表达水平，缺乏动态监测。另外，由于样本量不足，缺少对血清指标在髋部骨折患者发生 LEDVT 中作用机制的深入分析，后续将增加样本量，进一步深入研究。

利益冲突　无

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