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Original Article

The efficacy and safety of low-molecular-weight heparin calcium combined with Xueshuantong injections in the treatment of elderly acute deep venous thrombosis patients

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Abstract: Objective: To explore the therapeutic effect of low-molecular-weight heparin calcium (LMWH-Ca) combined with Xueshuantong injections in treating elderly acute deep venous thrombosis (ADVT) patients, and to analyze the effect of this combination on the coagulation function, hemorheology, and safety. Methods: A total of 122 elderly patients with ADVT who were treated in our hospital were recruited as the study cohort. The patients were randomly divided into a control group (n=61) and an observation group (n=61). The patients in the control group were given abdominal subcutaneous injections of low-molecular-weight heparin calcium (LMWH-Ca). The patients in the observation group were given intravenous drips of LMWH-Ca (low-molecular-weight heparin calcium) and Xueshuantong injections. After the treatment, comparisons of the detumescence times of the affected limb, the differences in the circumferences of the lower limbs, the coagulation parameters, the overall response rates, the incidences of complications, and the hemorheological parameters were conducted between both groups. Results: After the treatment, the detumescence times and the average differences in the circumferences of the lower limbs were significantly reduced ($P<0.001$; all $P<0.001$), the prothrombin times (PT) and the activated partial thromboplastin times (APTT) were significantly extended (all $P<0.01$), the overall response rate was higher (all $P<0.05$), and the three hemorheological parameters (high shear viscosity, low shear viscosity, and plasma viscosity) were lower in the observation group than they were in the control group (all $P<0.001$), there were no statistical differences in the fibrinogen (FIB) levels, the incidences of complications, or the incidences of adverse drug reactions between the two groups ($P>0.05$; $P=0.343$; $P=0.298$). Conclusion: To sum up, low-molecular-weight heparin combined with Xueshuantong injections can effectively treat elderly ADVT patients, reduce the differences in the circumferences of the lower limbs, regulate the coagulation function, and improve the blood viscosity, so it is worthy of clinical promotion.

Keywords: Low-molecular-weight heparin calcium, Xueshuantong injections, acute deep venous thrombosis, elderly patients

Introduction

Acute deep venous thrombosis (ADVT) is a disease that causes edema, varicose veins, dyskinesias of the lower extremities, and even serious complications such as pulmonary embolism due to the stagnation of venous blood and hypercoagulation [1-3]. Studies have reported that if the proper treatment is not performed promptly, ADVT may result in an average death rate of 20-30% when patients have complications such as massive pulmonary embolism [4]. The treatment of deep venous thrombosis (DVT) includes anticoagulation, thrombolytic therapy, mechanical thrombectomy, indwelling of the inferior vena cava (IVC) filters, and combined therapies with traditional Chinese medicine, acupressure, and psychological intervention. Individualized treatment plans should be developed according to the patient's age, cause of the disease, disease course, and the classification of thrombus in clinical practice [5]. For ADVT, anticoagulants are better at dissolving blood clots. Low-molecular-weight heparin

Table 1. Comparison of the general baseline data between the two groups (n, $\bar{x} \pm sd$)

Characteristics	Observation group (n=61)	Control group (n=61)	χ^2/t	P
Age (years)	68.4±7.1	67.6±6.8	0.619	0.537
Gender (n)			0.521	0.472
Male	29	33		
Female	32	28		
Location of thrombosis (n)			2.101	0.152
Left lower limb	26	34		
Right lower limb	35	27		
Causes of thrombosis (n)			0.804	0.671
Prolonged bed rest	18	16		
Surgery	32	30		
Trauma	11	15		
Types of thrombosis (n)			0.641	0.730
Central type	30	28		
Peripheral type	21	25		
Mixed type	10	8		
Risk factors associated with DVT (n)				
Malignancy	10	12	0.222	0.638
Oral contraceptive	9	7	0.288	0.592
Fracture	34	37	0.303	0.582
Obesity	15	13	0.185	0.669

Note: DVT: deep venous thrombosis.

calcium (LMWH-Ca) can reduce the activity of the coagulation factors and the blood viscosity and can significantly alleviate hypercoagulation [6, 7]. Xueshuantong injections can prolong the clotting time, inhibit thrombosis, and improve microcirculation in the lower extremities in patients with ADVT [8]. Elderly patients are mostly in a hypercoagulable state due to underlying diseases, and they are usually bedridden for a long time or have vascular damage caused by the surgery, so they are a high-risk population for ADVT [9]. Although there are some studies on treating ADVT with low-molecular-weight heparin calcium (LMWH-Ca) combined with Xueshuantong injections conducted at home and abroad, there is still a lack of therapeutic studies regarding elderly patients [10]. Therefore, our study mainly investigated the effect of low-molecular-weight heparin calcium combined with Xueshuantong injections in treating elderly patients with ADVT and analyzed the effect of such treatment on the differences in the circumferences of the lower limbs, the coagulation parameters, the complications, and the patients' hemorheological parameters, in order to provide guidance for clinical interventions.

Materials and methods

General data

A total of 122 elderly ADVT patients admitted to the Department of General Surgery in Zhuji People's Hospital of Zhejiang Province from February 15, 2017 to July 6, 2019 were recruited as the study cohort and divided into the observation group and the control group, with 61 cases in each group. See **Table 1** for the general data of the patients in the two groups. This study was conducted with the approval of the Medical Ethics Committee of Zhuji People's Hospital of Zhejiang Province.

Inclusion criteria: (1) patients who met the criteria for an ADVT diagnosis as published in "Guidelines for diagnosis and treatment of deep venous thrombosis", patients who were in the acute phase of ADVT, and patients who were diagnosed with ADVT through venography of the lower limbs, color Doppler ultrasound, and D-dimer results [11, 12], (2) patients who had no allergies to the drugs used in this study, (3) patients ≥60 years old, and (4) patients who were informed of the purpose of this study and who signed an informed consent form.

Exclusion criteria: (1) patients with bleeding disorders, (2) patients with severe liver or kidney dysfunction, (3) patients who had received relevant antithrombotic therapy within 1 week before their admission, (4) patients with severe mental illness, (5) patients with cognitive dysfunction.

Methods

The patients in both groups received routine treatment and care. The patients were instructed to rest in bed with a 30-degree elevation of the affected limbs. Low-fat, high-vitamin, high-protein diets were suggested to ensure smooth bowel movements and to prevent thrombosis embolism shedding. If the patient had traumatic injuries, anti-infection, detumescence, and other drug treatments were provided. Also, in addition to the routine treatment and care, the patients in the control group were treated with abdominal subcutaneous injections of low-molecular-weight heparin calcium (Hainan Unipul Pharmaceutical Co., Ltd., China), 5,000 IU each time, twice a day for a 14-day course of treatment. The patients in the observation group also received low-molecular-weight heparin calcium (abdominal subcutaneous injection, 5,000 IU each time, twice a day) and Xueshuantong injections (Livzon Pharmaceutical Group Co., Ltd., China), with 500 mL of 5% glucose solution (Guangdong Sake Biotechnology Co., Ltd., China) added to the 20 mL Xueshuantong injection for an intravenous drip, once a day for a 14-day course of treatment.

Outcome measures

Primary outcome measures: (1) The patients' detumescence times were observed and recorded in both groups; (2) After 14 days of treatment, the average differences in the circumferences of the lower limbs were compared between the two groups: the circumferences 15 cm above and 10 cm below the kneecap of the patients' affected limbs were measured, and the average circumference difference of the lower limbs was calculated (circumference of the affected limbs-circumference of the healthy limbs). (3) After 14 days of treatment, the two groups were compared in terms of the therapeutic effects: ineffective: vascular ultrasonography revealed a recanalization rate of <40% for the popliteal and femoral veins, an absence of collateral circulation, and no alleviation of the swelling and pain symptoms in the affected limbs; markedly effective: vascular ultrasonography revealed a recanalization rate of 40%-75% for the popliteal and femoral veins, inadequate collateral circulation, and a partial alleviation of the swelling and pain symptoms in the affected limbs; cured: vascular ultrasonography revealed a recanalization rate of 76%-90% for the popliteal and femoral veins, an adequate collateral circulation, and a significant alleviation of the swelling and pain symptoms in the affected limbs [13].

Secondary outcome measures: (1) Comparison of the coagulation parameters in the two groups: Before the treatment and after 14 days of treatment, 3 mL of venous blood was collected from all the fasting patients in the morning and centrifuged at 3000 r/min for 10 min. Serum, plasma, and whole blood samples were separated and stored for future use. Then plasma samples were analyzed to determine their fibrinogen (FIB), prothrombin time (PT), and activated partial thromboplastin time (APTT) levels with the use of an SK9000 automatic coagulation analyzer (Shenzhen Shengxinkang Technology Co., Ltd., China). (2) The incidence of complications such as thrombocytopenia, hematuria, and dyspnea during the treatment was compared between the two groups. If one patient had multiple complications, the total incidence was calculated including these complications. Total incidence = cases of complications/total number of cases * 100%. (3) The two groups' hemorheological parameters were compared: before and after 14 days of treatment, whole blood samples were analyzed to determine their high shear viscosity, low shear viscosity, and plasma viscosity using an N7500A automatic hemorheometer (Shanghai Hanfei Medical Instrument Co., Ltd., China). (4) During the treatment, the occurrence of adverse drug reactions (rash, dizziness, nausea and vomiting, abdominal pain and diarrhea) was compared between both groups.

Statistical analysis

SPSS 20.0 software was employed to analyze all the data. The enumeration data were expressed as n/%, and were examined using χ^2 tests. The measurement data conforming to a normal distribution and homogeneity of vari-

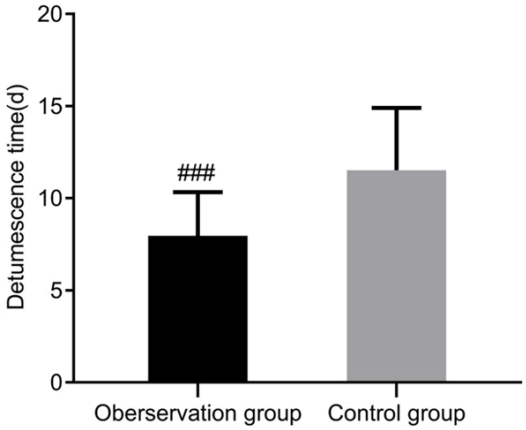

Figure 1. Comparison of detumescence times between the two groups. ###P<0.001 as compared with the control group.

ances were expressed as the means ± standard deviation ($\bar{x}$ ± sd), with the comparisons between groups performed using independent-samples t-tests, and the comparisons before and after the treatment within the same group using paired t-tests. The measurement data violating a normal distribution and homogeneous variances were displayed as the median and interquartile range; the comparisons between groups were performed using rank sum tests, and the comparisons within the same group were conducted using Wilcoxon sign rank tests before and after the treatment. A *P* value of less than 0.05 was deemed statistically significant.

Results

Comparison of the general baseline data between the two groups

No significant differences were observed regarding age, gender, location of the thrombosis, causes of the thrombosis, type of thrombosis, or the risk factors associated with DVT between the two groups (P>0.05), so they were comparable. See **Table 1**.

Comparison of the detumescence times between the two groups

After the treatment, the detumescence times in the observation group were significantly shorter than they were in the control group (P<0.001). See **Figure 1**.

Comparison of the average differences in the circumferences of the lower limbs after the treatment in the two groups

After the treatment, the average differences in the circumferences 15 cm above and 10 cm below the knees of the patients in both groups were significantly lower than they were before the treatment (P<0.001), and the differences were significantly smaller in the observation group (2.19±0.38 cm; 1.17±0.22 cm) than they were in the control group (3.20±0.44 cm; 2.02±0.23 cm; P<0.001). See **Figures 2** and **3**.

Comparison of the coagulation parameters in the two groups

After the treatment, no statistical difference was noted in the FIB (fibrinogen) levels between the two groups; the PT (prothrombin time) and APTT (activated partial thromboplastin time) levels were significantly higher in the observation group than in the control group (14.24±2.15 s vs 11.34±2.06 s; 46.08±3.26 s vs 44.21±3.37 s; all P<0.01). See **Table 2**.

Comparison of the overall response rates between the two groups

The overall response rate was significantly higher in the observation group than in the control group (P<0.05). See **Table 3**.

The incidences of complications in the two groups

The incidences of complications in the two groups were not statistically significant (P> 0.05). See **Table 4**.

Comparison of the hemorheological parameters after the treatment in the two groups

After the treatment, the hemorheological parameters in both groups were lower than they were before the treatment (P<0.001); the hemorheological parameters were significantly lower in the observation group than in the control group (P<0.001). See **Table 5**.

Comparison of the incidences of adverse drug reactions between the two groups

In the observation group, there were 18 cases (29.51%) of adverse reactions, including 5 cases of rash, 4 cases of dizziness, 5 cases of

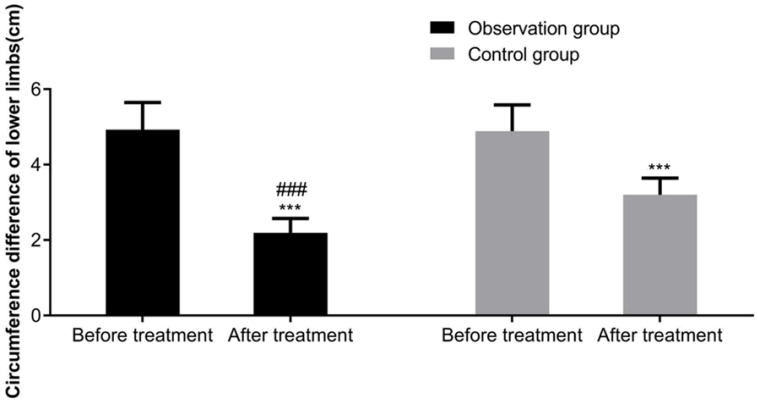

Figure 2. Comparison of average differences in the circumferences at 15 cm above the knees in the two groups. ###P<0.001 as compared with the control group; ***P<0.001 as compared with that before treatment.

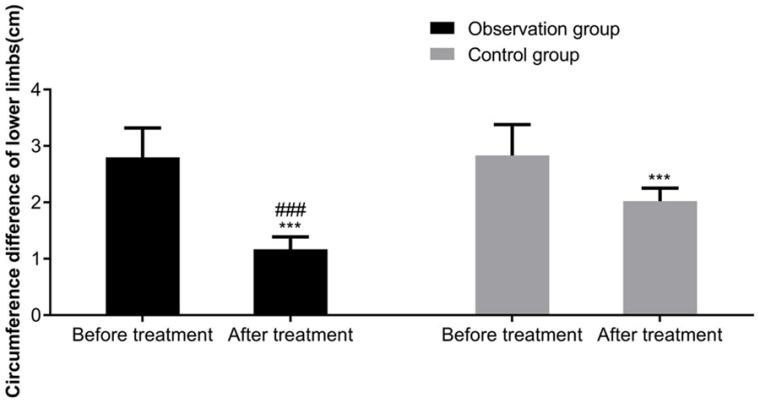

Figure 3. Comparison of average differences in the circumferences at 10 cm below the knees in the two groups. ###P<0.001 as compared with the control group; ***P<0.001 as compared with before the treatment.

nausea and vomiting, and 4 cases of abdominal pain and diarrhea. In the control group, there were 13 cases (21.31%) of adverse reactions, including 3 cases of rash, 4 cases of dizziness, 2 cases of nausea and vomiting, and 4 cases of abdominal pain and diarrhea. The cases of adverse drug reactions showed no statistical difference between the two groups (P>0.05). See **Table 6**.

Discussion

The early stage of DVT is clinically known as the acute phase of deep venous thrombosis [14]. Knowing when to treat and knowing what the effect of the anticoagulant thrombolytic therapy will be are closely related to the DVT prognosis, otherwise it will likely develop into post-thrombotic syndrome, threatening the patient's life [15]. The incidence of DVT is positively correlated with age. Older age is associated with a higher the risk of DVT. Especially in the elderly, the risk of DVT is up to 5.36‰. This is mainly because the elderly are mostly also suffering from vascular endothelial damage and underlying diseases, which slows down the blood flow [16]. Therefore, in this study, we observed the effect of drug treatment in elderly patients with ADVT.

Low-molecular-weight heparin calcium (LMWH-Ca) is characterized by a long half-life and a high bioavailability. It can reduce the activity of the coagulation factors, and it has a potent antithrombotic effect. Meanwhile, it can also activate plasminogen to dissolve the thrombus, which is the drug of choice for the prevention and treatment of DVT in clinical practice [17]. B. u et al. found that, compared with the circumferences before the treatment, the differences in the circumferences at 15 cm above the kneecap and 10 cm below the tuberosity of the tibia, the visual analogue scale (VAS) scores, and the coagulation and hemorheological parameters were significantly improved after the treatment in patients treated with low-molecular-weight heparin calcium (LMWH-Ca) [18]. In the study of Chen et al., 96 patients with malignant tumors with deep venous thrombosis complications were included [19]. The patients in the control group were administered low-molecular-weight heparin calcium, while the patients in the observation group received ligustrazine hydrochloride in addition to the treatment administered in the control group. After the treatment, the results showed that the swelling in the patients' lower limbs in both groups were subsided to different extents, but the combined use of drugs had a better effect at improving the deep venous thrombosis and had more therapeutic advantages.

Table 2. Comparison of the coagulation parameters between the two groups ($\bar{x}$ ± sd)

Group	FIB (g/L)		PT (s)		APTT (s)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group (n=61)	5.39±1.23	3.28±1.02	10.38±2.13	11.34±2.06	35.79±3.59	44.21±3.37
Observation group (n=61)	5.42±1.19	3.39±1.13	10.44±2.20	14.24±2.15	35.70±3.67	46.08±3.26
t	0.137	0.564	0.153	7.607	0.137	3.115
P	0.891	0.574	0.879	0.000	0.891	0.002

Note: FIB: fibrinogen; PT: prothrombin time; APTT: activated partial thromboplastin time.

Table 3. Comparison of the overall response rates between the two groups (n, %)

Group	Cured	Markedly effective	Ineffective	Overall response rate
Control group (n=61)	31 (50.82)	15 (24.59)	15 (24.59)	46 (75.41)
Observation group (n=61)	37 (60.66)	19 (31.15)	5 (8.2)	56 (91.80)
χ^2		6.001		5.980
P		0.049		0.014

Table 4. The incidences of complications in the two groups (n, %)

Group	Hematuria	Allergy	Thrombocytopenia	Dyspnea	Total
Control group (n=61)	2 (3.28)	2 (3.28)	2 (3.28)	1 (1.64)	7 (11.48)
Observation group (n=61)	2 (3.28)	1 (1.64)	1 (1.64)	0 (0.00)	4 (6.56)
χ^2	0.000	0.342	0.342	0.000	0.899
P	1.000	0.559	0.559	1.000	0.343

Table 5. Comparison of the hemorheological parameters after treatment between the two groups (mPa/s, $\bar{x}$ ± sd)

Group	Control group (n=61)	Observation group (n=61)	t	P
High shear viscosity				
Before treatment	6.38±1.18	6.57±1.09	0.924	0.357
After treatment	5.36±0.87	4.55±0.79	5.383	0.000
t	5.434	11.720		
P	0.000	0.000		
Low shear viscosity				
Before treatment	12.98±1.21	12.73±1.68	0.943	0.348
After treatment	7.81±1.09	5.01±1.16	13.739	0.000
t	24.794	29.534		
P	0.000	0.000		
Plasma viscosity				
Before treatment	1.79±0.40	1.70±0.23	1.523	0.131
After treatment	1.41±0.09	0.98±0.10	24.963	0.000
t	7.239	22.422		
P	0.000	0.000		

Xueshuantong injections are a traditional Chinese medicine preparation made from *Salvia miltiorrhiza*, Scrophulariae Radix, Notoginseng Radix Et Rhizoma, and Astmgali Radix, also known as Tianqi injection. It has the effects of dredging the channels and collaterals, activating the blood to resolve stasis, dilating the blood vessels, dissolving thrombosis, preventing blood clots, removing oxidation, protecting endothelial cells, inhibiting apoptosis, scavenging free radicals, and improving hypoxia tolerance. Zhou et al. enrolled a total of 78 patients with deep venous thrombosis after hip arthroplasty and randomly divided them into an observation group (n=39) and a control group (n=39) [20]. The patients in the control group were given rivaroxaban oral tablets, and the patients in the observation group were given rivaroxaban tablets plus Xueshuantong injections. The results demonstrated that the clinical efficacy and improvement of the coagulation parameters were greater in the observation group than they were in the control

Table 6. Comparison of the incidences of adverse drug reactions in the two groups

Group	Rash	Dizziness	Nausea and vomiting	Abdominal pain and diarrhea	Total
Control group (n=61)	3 (4.92)	4 (6.56)	2 (3.28)	4 (6.56)	13 (21.31)
Observation group (n=61)	5 (8.20)	4 (6.56)	5 (8.20)	4 (6.56)	18 (29.51)
χ^2	0.541	0.000	1.363	0.000	1.082
P	0.464	1.000	0.243	1.000	0.298

group, indicating that the drug combination can significantly improve patients' coagulation statuses. In our study, the patients in the observation group were treated with LMWH-Ca (low-molecular-weight heparin calcium) plus Xueshuantong injections. Compared with the patients using LMWH-Ca alone, the results demonstrated that the clinical effective rate was significantly higher in the observation group than in the control group, and no difference was found in the incidences of complications between both groups, which indicated that LMWH-Ca combined with Xueshuantong injection has a better efficacy and a higher safety at improving ADVT in the elderly.

As indicators reflecting the levels and activities of the relevant coagulation factors in the intrinsic and extrinsic coagulation pathways of the human body, APTT and PT have been widely used in the determination of coagulation function [21]. PT mainly reflects the levels of the coagulation factors derived from body tissues, such as factors I, II, V, VII, and X, while APTT mainly reflects the levels of the coagulation factors from the blood including factors VIII, IX, XI, and XII. PLT can accumulate and adhere to the bleeding site to promote hemostasis, and activated PLT and its cleavage products have a good coagulation effect. FIB, the final substrate from the common pathway of endogenous and exogenous coagulation, is synthesized by the liver to regulate plasma viscosity. Lan et al. studied 182 patients with ADVT, and found that the three coagulation indicators (PT, APTT, and the PLT levels) of patients treated with LMWH-Ca plus Xueshuantong (observation group) were effectively improved compared with those in the control group [22]. In our study, the therapeutic effects of the patients treated with LMWH-Ca plus Xueshuantong injections were compared with those treated with LMWH-Ca alone, and the results showed that the improvement effects of the coagulation indicators (PT, APTT) were also greater in the observation group than in the control group, and the results were consistent with the results of similar studies. Furthermore, compared with the control group, the patients' differences in the circumferences 15 cm above and 10 cm below the knees were significantly smaller, and the detumescence times were shorter in the observation group, indicating that compared with using LMWH-Ca alone, LMWH-Ca plus Xueshuantong injections is more effective at improving the coagulation function and inhibiting thrombosis in patients [23-25]. In addition, no difference was noted in the adverse drug reactions between both groups in this study, indicating that the addition of Xueshuantong injections is safe and will not increase adverse effects of drugs in patients.

Hemorheological parameters are also important for evaluating the formation of DVT. In this study, we also explored the effects of the two treatment methods on the hemorheology of patients, and we found that the expression levels of the three hemorheological indicators were lower in the observation group than in the control group. Thus, we came to the conclusion that the combined use of drugs contributes to maintaining patients' hemorheological health. However, we did not follow up on the recurrence rate of the patients after their discharge, so long-term efficacy studies with large sample sizes in elderly patients should be conducted in the future to confirm the efficacy and safety of such drug combinations in elderly patients suffering from ADVT.

In conclusion, low-molecular-weight heparin combined with Xueshuantong injections can effectively treat elderly patients with ADVT, reduce the differences in the circumferences of their lower limbs, regulate their coagulation function, and improve their blood viscosity, so it is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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References

[1] Luo ZX, Chen W, Li YS, Wang XM, Zhang WL, Zhu YB and Zhang FQ. Preoperative incidence and locations of deep venous thrombosis (DVT) of lower extremity following ankle fractures. Sci Rep 2020; 10: 10266.

[2] Jeong MJ, Kwon H, Noh M, Ko GY, Gwon DI, Lee JS, Kim MJ, Choi JY, Han Y, Kwon TW and Cho YP. Relationship of lower-extremity deep venous thrombosis density at CT venography to acute pulmonary embolism and the risk of postthrombotic syndrome. Radiology 2019; 293: 687-694.

[3] He L, Zeng YF, Huang ZY and Shi L. Effect of operating room nursing interventions on infection, stress response, and deep venous thrombosis of the lower extremity in patients with fracture surgery. Int J Clin Exp Med 2019; 12: 5606-5613.

[4] Essien EO, Rali P and Mathai SC. Pulmonary embolism. Med Clin North Am 2019; 103: 549-564.

[5] Li PY and Shen DF. Research progress in the treatment of lower extremity deep venous thrombosis. Chin J Med Clin Sci 2019; 19: 1999-2000.

[6] Chang GMT, Atkinson HM, Berry LR and Chan AKC. Inhibition of plasmin generation in plasma by heparin, low molecular weight heparin, and a covalent antithrombin-heparin complex. Blood Coagul Fibrinolysis 2017; 28: 431-437.

[7] Zee AA, van Lieshout K, van der Heide M, Janssen L and Janzing HM. Low molecular weight heparin for prevention of venous thromboembolism in patients with lower-limb immobilization. Cochrane Database Syst Rev 2017; 8: Cd006681.

[8] Wang JX, Li RL, Deng ZY, Sun ZY, Chai LJ, Guo H, Wang H, Chen L, Hu LM and Wang SX. Xueshuantong for injection Ameliorates diabetic nephropathy in a rat model of streptozotocin-induced diabetes. Chin J Physiol 2018; 61: 349-359.

[9] Hu JY. Early recognition and nursing of venous thrombosis of lower extremity in elderly patients. Throm Hemo 2018; 24: 1047-1049.

[10] Chen K, Shi L, Pan H, Deng JX, Ai P, Chen C and Deng CY. Efficacy analysis of low molecular weight heparin combined with Xueshuantong in the treatment of lower extremity deep vein thrombosis. New Chin Med 2018; 531: 61-64.

[11] Vascular Surgery Group, Chinese Medical Association Surgery Branch, Li XQ and Wang SM. Guidelines for the diagnosis and treatment of deep vein thrombosis. Chin J Gener Surg 2013; 23: 235-238.

[12] Xie HJ, Zhang SJ, Xia Q, Hu JH, Chen YM, Huang JX and Song HX. Clinical study of color doppler ultrasound combined with D-dimer level detection in the early diagnosis of deep vein thrombosis of lower extremities. J Inner Mongol Med Colle 2018; 40: 255-258, 267.

[13] Huang XL, Ye YQ, Chang GQ, Li SQ and Wang SM. Application value of color doppler ultrasound in diagnosis and efficacy evaluation of deep vein thrombosis of the lower extremity-an analysis of 531 cases. Chin J Mod Med 2002; 12: 40-42.

[14] Wang F, Wang ZR, Liu FR and Gao XR. Clinical study of tirofiban in the treatment of elderly patients with acute lower extremity deep venous thrombosis. Chin J Cardiol 2016; 21: 59-63.

[15] Rabinovich A and Kahn SR. The postthrombotic syndrome: current evidence and future challenges. J Thromb Haemost 2017; 15: 230-241.

[16] Liu K, Wang XK, Chen J, Lin B, Shi L, Zhao DB and Shi JD. Comparison of the efficacy of catheter thrombolysis and systemic thrombolysis in the treatment of acute lower extremity deep venous thrombosis. Chin J Basi Clin Pract Gene Surg 2017; 24: 307-311.

[17] Felder S, Rasmussen MS, King R, Sklow B, Kwaan M, Madoff R and Jensen C. Prolonged thromboprophylaxis with low molecular weight heparin for abdominal or pelvic surgery. Cochrane Database Syst Rev 2018; 11: Cd004318.

[18] Bu Y. Clinical observation of Tongmai Huoxue decoction combined with low molecular weight heparin calcium in the treatment of lower extremity deep vein thrombosis after spinal surgery. Chin Trad Med Emerg 2016; 25: 1780-1782.

[19] Chen LW and Jia YJ. Clinical observation of ligustrazine hydrochloride combined with low-dose low-molecular-weight heparin calcium in the treatment of malignant tumor complicated with deep venous thrombosis. Shaanxi Trad Chin Med 2015; 176-177.

[20] Zhou YH, Wu Z, Song JH and Feng YY. Efficacy of Xueshuantong injection combined with rivaroxaban in the treatment of lower extremity deep venous thrombosis after hip replacement. Mod Med Clin 2015; 30: 1490-1493.

[21] Yuan WF, Jiang L and Zheng SJ. Effects of urokinase thrombolytic therapy on coagulation function, D-dimer and N-terminal pro brain natriuretic peptide in patients with lower extremity deep vein thrombosis complicated with

acute pulmonary embolism. Chin J Gener Med 2017; 15: 2068-2070.
[22] Lan JY, Xiang HM and Fan XM. Efficacy of low molecular weight heparin calcium combined with Xueshuantong in the treatment of acute lower extremity deep venous thrombosis. Chin J Trad Chin Med 2019; 37: 1193-1196.
[23] Zeng XB, Liu S, Huang JY, Xiao SX and Rao D. Effect of Xueshuantong combined with low molecular weight heparin calcium in the prevention of deep vein thrombosis of lower limbs after hip fracture surgery. Clin Med Engin 2018; 25: 1461-1462.
[24] Zhang YW, Dai Y and Zhang WL. Clinical effect of low molecular weight heparin calcium combined with Xueshuantong Injection on lower extremity deep venous thrombosis after hip replacement. Clin Res Trad Chin Med 2018; 10: 80-82.
[25] Sun HW, Yang WD, Zhang HQ, Wang CS, Zhong YM, Su Y, Gao B, Sun Y and Zou XW. Anti-thrombotic effect of combination of low molecular heparin and Xueshuantong after replantation of amputated finger. Trop J Phar Res 2019; 17: 2249-2254.