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Risk assessment of lower-limb deep vein thrombosis in patients with lumbar spondylolisthesis: A retrospective study.

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Abstract

Objective: This retrospective study was designed to make risk assessment of lower-limb DVT in patients with lumbar spondylolisthesis.
Methods: Medical records of lumbar spondylolisthesis were retrospectively collected between 01/2014 and 01/2017. Univariate analyses were performed to determine risk factors for DVT.
Results: A total of 140 patients were admitted into this study, including 33 males and 107 females, aged from 16 to 80 y old (median 57, IQR 14). Incidence of DVT detected by ultrasonography was only 9.3% (13 cases out of 140 cases) in patients with lumbar spondylolisthesis, which were all asymptomatic. All comparisons of surgical data including surgical duration, blood loss, blood transfusion and incision length, showed no statistical difference. Notably, D-dimer was found 0.24 (IQR 0.18) mg/L in DVT group and 0.14 (IQR 0.13) mg/L in non-DVT group. And this was statistically different (Z=-2.369, p=0.017).
Conclusions: In summary, this study has further confirmed the risk of high-level D-dimer for lower-limb DVT, which may contribute to the better understanding of risk assessment for lower-limb DVT.

Keywords: Deep vein thrombosis, Spine surgery, Risk assessment, Lumbar spondylolisthesis, VTE.

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Introduction

To our knowledge, Venous Thromboembolism (VTE) is clinically common and potentially lethal to the patients, including both Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) [1]. There exist potential harms resulting from VTE. One is severe morbidity with poor quality of life; the other is even sudden death due to PE. It has been reported that more than one hundred thousand deaths occur in the U.S. alone every year caused by VTE [2]. In fact, VTE and following complications lay a heavy burden on the U.S. medical service system [2]. Thus, VTE has been receiving much attention and has been well studied in recent years. It has been known from the previous studies that VTE may be related to these factors, smoking, obesity, advanced age, high blood pressure, blood transfusion, hospitalization, immobilization, major surgery, neurological deficit, trauma, malignancy, inherited hypercoagulable state, oral contraceptive use, as well as D-dimer [3-6].

It has been stated in some previous studies that about half of all untreated patients with DVT are concurrently accompanied by PE, and on the contrary, 50% to 80% of all untreated patients with PE are related to DVT [7]. In the field of spinal surgery, the factors for venous stasis may be lack of muscle tone, long time horizontal ventral decubitus, venous compression by retractors and postoperative bed rest [8]. It has been estimated that DVT incidence of patients without clinical symptoms surpasses 15%, and DVT incidence with clinical symptoms is only about 0.5% to 2.5% in the patients with spine diseases [9].

The purpose of this study is to investigate the current prevalence of lower-limb DVT in patients with lumbar spondylolisthesis who need fusion surgery. The second goal is to explore the risk factors associated with lower-limb DVT.

Patients and Methods

Ethics statement

As a retrospective study, it has been approved by Ethics Committee of The Third Hospital of Hebei Medical University.

Patients

This study included patients who were diagnosed as lumbar spondylolisthesis and admitted into Department of Spinal Surgery in our hospital, between 01/2014 and 01/2017. The inclusion criteria were complete medical records including patient number, age, sex, body height, body weight, regional distribution, hospital stay, occupation, hypertension, diabetes, heart disease, spinal epidural hematoma, level and number of vertebrae fusion, operation duration, blood loss, blood transfusion, incision length, Prothrombin Time Activity (PTA), Fibrinogen (FIB), Thrombin Time (TT), D-dimer, HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein), Total Cholesterol (TC), Total Bilirubin (T-BIL), and Direct Bilirubin (D-BIL) and Indirect Bilirubin (I-BIL). All of the above biochemical factors were detected before surgery. All of the included patients were routinely examined by lower extremity ultrasonography pre- and postoperatively. After spine surgery, subfascial drainage was routinely used. In addition, all patients routinely received prophylactic treatment with Low-Molecular-Weight Heparin (LMWH) at 4100 IU once per day. Simultaneously, the patients were encouraged to do lower-limb exercise on bed to accelerate blood circulation. The exclusion criteria were that the patients did not undergo lumbar interbody fusion, or suffered pre-operation DVT, or ever took anticoagulant such as warfarin, aspirin and clopidogrel during one week before surgery.

Methods

The methods were performed in accordance with the approved guidelines. Two authors (SL and SDY) identified and anonymously collected all the medical records according to inclusion criteria and exclusion criteria. Then two authors (DLY and WYD) were responsible for data input using Microsoft Office Excel. In addition, two authors (SL and SDY) were responsible for data analyses. Disagreements were resolved by discussion among the authors.

Statistical analyses were performed using SPSS for Windows, version 18.0 (SPSS Inc., USA). All measurement data were presented as mean ± SD (Standard Deviation) or median (IQR, interquartile range) where applicable. Statistical analysis was performed using Student's t test or Mann-Whitney U test where applicable. All count data were presented as a frequency number, and Chi-square test or Fisher's exact test was used for data analysis where applicable. P<0.05 was regarded as significant.

Results

General data of patients included

These criteria were met in 140 cases, which were therefore incorporated into this study. The 140 patients included 33 males and 107 females, aged from 16 to 80 y old (median 57, IQR 14). Average hospital stay was 15 (IQR, 5 d). Of them, only 13 cases (9.3%) developed postoperative DVT, which were all asymptomatic. One DVT site was found with 6 DVT cases, and two DVT sites were found with the other 7 cases. With regard to DVT distribution, DVT with 12 cases were distributed in venous plexus of calf muscle, and only 1 DVT site was found in posterior tibial veins. Besides, no patients with PE or spinal epidural hematoma were identified in this study.

Age, gender, and regional distribution

Age of the DVT group was 56 (IQR 10 y old), and the non-DVT group was 57 (IQR 12 y old). Mann-Whitney U test showed no significant difference between the patients with DVT and those without DVT (Z=-1.602, p=0.103). Of the DVT cases (13 cases), 3 cases were males, 10 females. Of the non-DVT cases (127 cases), 30 cases were males, 97 females. Fisher's exact test indicated that there was no statistical difference regarding gender distribution between DVT group and non-DVT group (p=0.507).

Comparison of surgical data

The surgical data included surgical duration, blood loss, blood transfusion and incision length according to patients' operation records. As shown in Table 1, all comparisons of surgical data between the two groups showed no statistical difference (Mann-Whitney U test, all p>0.05).

Chronic disease history

Chronic disease history was compared between DVT group and non-DVT group, including High Blood Pressure (HBP), Diabetes Mellitus (DM) and Heart Disease (HD). As shown in Table 2, all comparisons between DVT group and non-DVT group were of no difference (Fisher exact test, all p>0.05).

Biochemical analyses

As shown in Table 3, biochemical analyses including PTA, HDL and LDL were compared between DVT group and non-DVT group. It was found that there was no significant difference between the two groups (Student's t test, all p>0.05). As shown in Table 4, biochemical analyses were compared between DVT group and non-DVT group, including FIB, TT, D-dimer, TC, T-BIL, D-BIL, and I-BIL. Notably, it was statistically different regarding D-dimer comparison (Z=-2.412, p=0.017). However, there were no difference found in other comparisons (all p>0.05).

Table 1. *Comparison of surgical data associated with postoperative DVT.*

Items	DVT group (13 cases)	Non-DVT group (127 cases)	Mann-Whitney U test	
	Median (IQR)	Median (IQR)	Z-value	p-value
Surgical duration	160 (100 min)	170 (71 min)	-0.242	0.758

Blood loss	620 (510 ml)	610 (520 ml)	-0.039	0.861
Blood transfusion	350 (400 ml)	350 (350 ml)	-0.178	0.824
Incision length	14 (11 cm)	15 (10 cm)	-0.841	0.415

DVT: Deep Vein Thrombosis; IQR: Interquartile Range.

Table 2. Comparison of chronic disease history associated with postoperative DVT.

Items	DVT patients (13 cases)	Non-DVT patients (127 cases)	Fisher exact test
	Yes/No	Yes/No	p-value
HBP	3/10	30/97	0.568
DM	1/10	12/115	0.942
HD	1/10	3/124	0.915

DVT: Deep Vein Thrombosis; HBP: High Blood Pressure; DM: Diabetes Mellitus; HD: Heart Disease.

Table 3. Biochemical analyses related to postoperative DVT by Student's t test.

Items	DVT group	Non-DVT group	Student's t test	
	Mean ± SD (13 cases)	Mean ± SD (127 cases)	t-value	p-value
PTA	110% ± 14%	111% ± 15%	-0.157	0.845
HDL	1.19 ± 0.21 mmol/L	1.13 ± 0.22 mmol/L	1.453	0.142
LDL	3.14 ± 0.79 mmol/L	3.15 ± 0.78 mmol/L	-0.458	0.704

DVT: Deep Vein Thrombosis; PTA: Prothrombin Time Activity; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; SD: Standard Deviation

Discussion

It is well known that the incidence of VTE is different among surgical sites or surgical procedures in the field of orthopedics. Lower-extremity fracture, hip or knee arthroplasty, and spinal cord injury may contribute to VTE with high risk [7], while upper limb surgery [10] and cervical spinal surgery [11] in particular have a low risk of VTE. Although there has been more and more studies on VTE after spinal surgery, the exact incidence or risk factors of DVT and PE after spinal surgery has not been well clarified, due to the same drawback that many kinds of surgical procedures and surgical levels were estimated together.

A prospective clinical study from Japanese scientists [11] reported that the prevalence of VTE after elective spinal surgery was different among these following groups, including cervical degenerative disease treated with posterior decompression (2.8%), cervical degenerative disease treated with instrumentation for spinal fusion (3.4%), thoracolumbar degenerative disease treated with instrumentation for spinal fusion (10.8%), lumbar spinal stenosis treated with posterior decompression (12.5%), and lumbar spondylolisthesis treated with one-level posterior lumbar interbody fusion (10.1%). Obviously, the biggest advance in the above study is that the prevalence of VTE was estimated according to different kinds of surgical procedures and surgical levels, which has overcome the drawback mentioned above.

Also, our previous study [6] has found that the prevalence of DVT is 17% (147/861 patients) after spine surgery, and the important risk factors for developing postoperative VTE are advanced age, D-dimer and hypertension. However, the patients included in our previous study were diagnosed as cervical spondylosis, lumbar stenosis, lumbar disc herniation, thoracolumbar scoliosis, and lumbar spondylolisthesis. In addition, different kinds of surgical procedures and surgical levels existed together. Thus, the biggest limitation in our previous study is that the prevalence of VTE and risk factors were estimated together, without consideration of various confounders. The incidence of VTE was reported up to 10.1% in patients with lumbar spondylolisthesis treated with one-level posterior lumbar interbody fusion [11]. Given that only one existing study was focused on VTE in patients with lumbar spondylolisthesis, the current study was designed to explore the prevalence of lower-limb DVT and make risk assessment in patients with lumbar spondylolisthesis after surgery. As a result, incidence of VTE detected by ultrasonography was 9.3% (13 cases out of 140 cases) in patients with lumbar spondylolisthesis, all being asymptomatic. It is consistent with the 10.1% prevalence of VTE reported previously [11].

Notably, D-dimer was found 0.24 (0.18) mg/L in DVT group and 0.14 (0.13) mg/L in non-DVT group. And only D-dimer in this study was found statistically different with significance ($Z=-2.412$, $p=0.017$). There was no difference regarding other items compared between DVT group and non-DVT group (all $p>0.05$). To our knowledge, it has been widely reported that postoperative D-dimer assay can effectively predict DVT occurrence [5,12,13]. Even though the diagnostic significance of the D-dimer test is well-known for predicting VTE symptoms, the role of high D-dimer levels in the postoperative state following spinal surgery has been controversial and its cut-off value for predicting the risk of developing VTE still remains debatable [13].

One previous study [5] reported that D-dimer level more than or equal to 0.5 mg/L was considered as a risk factor for DVT after spinal surgery. In addition, a prospective clinical study [13] reported that the optimum D-dimer cut-off value on d 3 following spine surgery in the VTE group was determined to be more than 2.1 mg/L with a sensitivity of 100% and a specificity of 80.7%. Moreover, a study examined D-dimer concentrations one week after spinal surgery. It was found that patients, who had D-dimer levels ≥ 10 mg/L, did not suffer from VTE complications; on the other hand, patients who developed asymptomatic VTE, had mean D-dimer levels below 5.7 mg/L [14]. Recently, Japanese scientists [15] further confirmed that the cut-off values for the diagnosis or prediction of DVT varied. They reported that the cut-off values for the prediction of postoperative DVT for orthopedic surgery patients were ≥ 1.7 μg/mL (D-dimer A-D) and ≥ 1.0 μg/mL (D-dimer E-H). Furthermore, evidence based on previous studies indicate that postoperative D-dimer tests may not be accurate in sensitivity and specificity [5,12-16], such as in a great variety of inflammatory conditions even there is no DVT. Therefore, choice of the cut-off value depends on the methods employed and populations studied.

Unavoidably, this study goes along with some limitations. First, this is a retrospective study which has a limitation in the study design. Second, the small sample size included in this study is another limitation. Third, only a small number of patients with VTE were identified and analysed in this study, which is also a limitation to the conclusion drawn from the results.

In summary, D-dimer in this study was identified as a risk factor for postoperative lower-limb DVT in patients with lumbar spondylolisthesis. Nevertheless, this study has further confirmed the risk of high-level D-dimer for lower-limb DVT, which may contribute to the better understanding of risk assessment for lower-limb DVT.

Table 4. *Biochemical analyses related to postoperative DVT by Mann-Whitney U test.*

Items	DVT group	Non-DVT group	Mann-Whitney U test	
	Median (IQR) (13 cases)	Median (IQR) (127 cases)	Z-value	p-value
FIB	3.04 (0.60 g/L)	2.89 (0.91 g/L)	-1.045	0.198
TT	14.89 (2.65 s)	14.6 (1.6 s)	-0.434	0.701
D-dimer	0.24 (0.18 mg/L)	0.14 (0.13 mg/L)	-2.369	0.017
TC	4.75 (1.36 mmol/L)	4.76 (1.10 mmol/L)	-0.141	0.902
T-BIL	12.23 (6.01 μmol/L)	12.10 (5.60 μmol/L)	-0.071	0.899
D-BIL	3.70 (1.30 μmol/L)	3.60 (1.80 μmol/L)	-0.041	0.958
I-BIL	8.70 (3.60 μmol/L)	8.40 (4.10 μmol/L)	-0.184	0.859

DVT: Deep Vein Thrombosis; IQR: Interquartile Range; FIB: Fibrinogen; TT: Thrombin Time; TC: Total Cholesterol; T-BIL: Total Bilirubin; D-BIL: Direct Bilirubin; I-BIL: Indirect Bilirubin.

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Declaration of Conflicting Interests

The Author(s) declare(s) that there is no conflict of interest.

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