BMJ Open

A Retrospective cohort study on the risk factors of deep vein thrombosis (DVT) for patients with traumatic fracture at Honghui Hospital

Wenjuan Zhang,[1,2,3] Ying Huai,[1,2,3] Wei Wang, Kaiyue Xue,[1,2,3] Lei Chen,[1,2,3] Chu Chen,[4] Airong Qian[1,2,3]

To cite: Zhang W, Huai Y, Wang W, *et al*. A Retrospective cohort study on the risk factors of deep vein thrombosis (DVT) for patients with traumatic fracture at Honghui Hospital. *BMJ Open* 2019;**9**:e024247. doi:10.1136/bmjopen-2018-024247

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2018-024247).

WZ and YH contributed equally.

Received 23 May 2018
Revised 9 November 2018
Accepted 14 November 2018

Check for updates

For numbered affiliations see end of article.

Correspondence to
Dr Chu Chen; chuchen09cqmu@163.com and Dr Airong Qian; qianair@nwpu.edu.cn

ABSTRACT

Objective To explore the risk factors of perioperative deep vein thrombosis (DVT) in patients with traumatic fracture after orthopaedic surgery and their potential diagnostic values in clinical.

Design Retrospective cohort study.

Setting Clinical Laboratory of Honghui Hospital, Xi'an JiaoTong University College of Medicine, Xi'an, Shaanxi, China.

Materials and methods A retrospective cohort study was conducted with surgically treated fracture patients in Honghui Hospital from 1 May 2016 to 31 February 2017. χ^2 test, independent sample t test and regression analysis were applied to examine the correlation between perioperative DVT and the factors of preoperative time, fracture sites, D-dimer value and chronic diseases (hypertension, diabetes and coronary disease).

Results 462 patients were enrolled for analysis. The preoperative time of patients with DVT was significantly longer than that of non-DVT patients (7.14±5.51 vs 5.45±3.75) (P<0.01). χ^2 test showed the significant differences in the rate of DVT among patients with different fracture sites (P<0.01). By the receiver-operating characteristic curve analysis, the cut-off value of preoperative D-dimer and postoperative D-dimer in diagnosing perioperative DVT was 4.01 µg/mL and 5.03 µg/mL, respectively. Area under the curve was 0.593 (95% CI 0.533 to 0.652) and 0.728 (95% CI 0.672 to 0.780), respectively. The sensitivity and specificity of preoperative D-dimer for DVT diagnosis were 71.30% and 44.83%, and as for postoperative D-dimer were 63.90% and 70.51%.

Conclusions Fracture site was correlated to the incidence of DVT; prolonged preoperative time and increased D-dimer value were independent risk factors for DVT in patients with lower extremity traumatic fractures.

Strengths and limitations of this study

- A retrospective cohort study was conducted in patients with lower extremity traumatic fracture to explore the potential risk factors for perioperative deep vein thrombosis (DVT).
- Our study indicated that preoperative time might be included in DVT risk assessment scale and advanced prophylaxis could be applied to patients with DVT during the preoperative time.
- Efficient prophylactic strategies for perioperative DVT are currently under evaluation.
- The main limitation of the study is the use of relatively small group of traumatic fracture population.

INTRODUCTION

Deep vein thrombosis (DVT) is a serious complication of the major orthopaedic surgery, especially to lower extremities, which could potentially result in significant morbidity and possible mortality for the patients with traumatic fracture.[1 2] The incidence of perioperative DVT could reach 50%–60%, and seriously it may cause pulmonary embolism (PE) after trauma.[1 3] The optimal mode of prophylaxis has yet to be determined. Rivaroxaban or low molecular heparin (LMH) represent pharmacological treatment modality for prophylaxis against DVT.[4] However, rivaroxaban and LMH have not been shown to be particularly effective in preventing DVT in patients with trauma; the DVT incidence still remains high to 20%–30%.[5–8]

The incidence of DVT correlates with multifactorial risks and complex pathogenesis,[9 10] such as age, sex, fracture sites and waiting period before fracture fixation.[11] For example, elderly female patients undergoing major orthopaedic surgery in postoperative period are more prone to DVT.[12 13] In the postoperative period, the incidence of DVT is caused by pre-existing factors such as surgical orthopaedic procedures, the condition of infection and the level of mobility.[12 14–16] Major surgery and especially undergoing major orthopaedic surgery (such as total hip arthroplasty, total knee arthroplasty, hip fracture surgery) confer the greatest risk for DVT.[17 18]

Additional factors increasing the incidence of DVT has also been identified, such as hypertension, obesity, myocardial infarction, congestive heart failure and immobility.[15 19 20] Moreover, the prolonged operation (≥2 hours), prolonged immobility and larger build/body mass index (BMI) are found to be significantly responsible for the development of DVT.[21] Therefore, an in-depth analysis of risk factors in perioperative DVT patients may help to diagnose and prevent the disease from progressing any further. Although various risk factors have been existed in DVT risk assessment scales, some factors such as preoperative time and different site of trauma may not be included.

The study intended to evaluate the risk factors that were correlated to DVT in patients with traumatic fracture who underwent orthopaedic surgery in Honghui Hospital. More specifically, we would explore the factors such as preoperative time, fracture sites, chronic diseases and D-dimer levels to assess their potential diagnosis value for DVT in patients with lower extremity traumatic fracture by a retrospective cohort study.

MATERIAL AND METHODS

Design, sample and criteria for participation

The retrospective cohort was conducted in the clinical laboratory of Honghui Hospital, the Medical School of Xi'an JiaoTong University in Xi'an between May 2016 and February 2017. The study sample consisted of 462 patients who met the inclusion criteria. The following inclusion and exclusion criteria were applied. Patients (aged ≥50 years) who were hospitalised for orthopaedic surgery were the initial included subjects. All the patients who received the same prophylactic procedures during the postoperative period (LMH via hypodermic injection), graduated physical prophylaxis and early ambulation 24-48 hours postoperatively, were admitted to the study. The following patients were excluded: patients whose medical records were lost or incomplete; patients who had suffered haemorrhagic stroke, aortic dissection, cerebrovascular disease or otherwise local vascular anomalies; patients with previous vascular surgery history; patients who were taking LMH or rivaroxaban anticoagulant agent for other diseases at admission; malignant neoplasms patients and patients with uncontrolled hypertension; patients with underlying coagulopathy and severe cardiopulmonary dysfunction; patients whose ultrasound images were not judged by a senior physician. The selection process is illustrated in figure 1.

Patient and public involvement

In our retrospective cohort study, only medical records and case information were analysed, no patients were directly involved in setting the research questions or the outcome measures, nor were they involved in the recruitment to or implementation of the study.

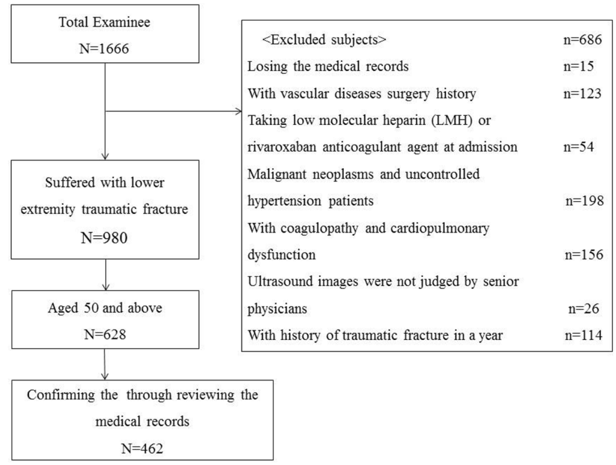

Figure 1 Process of selecting the study subjects.

DVT diagnosis

According to the guidelines for the prevention of venous thromboembolism in Chinese orthopaedic surgery, Colour Doppler ultrasound examination has gradually superseded venography as the primary diagnostic procedure, which is a preferred method for the diagnosis of DVT with high sensitivity and accuracy. All the patients had received Colour Doppler ultrasound (GE's Vivid 07) detection to diagnose DVT perioperatively from May 2016 to February 2017 in Honghui Hospital, the Medical School of Xi'an JiaoTong University (Youyi East Road No. 555, Beilin District, Xi'an, Shaanxi province). The DVT was diagnosed by 2D-heart views and colour Doppler flow image and the diagnostic criteria for DVT includes: (1) low, weak or medial echoes; (2) in injured part, incompressibility of the vein with probe pressure; (3) absence of flow signal in the venous thrombosed segments; (4) increased width and blood flow of the vessels of the affected limbs. All the subjects were divided into DVT group (337 patients) and non-DVT group (125 patients). In DVT group, all the patients suffered from acute deep vein thrombosis within 2 weeks after surgery. According to the guidelines for the prevention of venous thromboembolism in Chinese orthopaedic surgery, prophylaxis with LMH was administered in these patients postoperatively. In fact, no serious postoperative venous thromboembolic complication or post-thrombotic syndrome (PTS) such as PE was observed in DVT cases. Other associated symptoms, such as swelling and pain of the leg, enlarged thigh or calf girth and a positive Homans' sign or Neuhof's sign were variably present in 10 patients.[22]

D-dimer test

Vein blood samples were collected in vacuum tubes containing sodium citrate anticoagulant, which were centrifuged to separate plasma for testing. All the vein blood samples were tested within 6 hours by the Colour Doppler ultrasound. Then, D-dimer value detection was completed within 2 hours by immune scatter turbidimetry with Sysmex 5100 and related reagents.

Table 1 Risk factors associated with the development of deep vein thrombosis (DVT)

Variable	Patients with DVT	Non-DVT patients	*P* value
Number of patients (%)	337	125	/
Male gender (%)	139 (41.1%)	46 (38.1%)	0.088
Age (mean years±SD)	70.49±11.38	71.66±12.53	0.362
Preoperative time	7.14±5.15	5.45±3.75	<0.01**
Preoperative D-dimer	9.86±11.05	9.35±12.53	0.684
Preoperative diagnosis time	2.75±1.83	2.62±1.41	0.564
Postoperative D-dimer	8.21±6.98	4.73±4.20	<0.01**
Postoperative diagnosis time	2.74±1.78	2.35±1.44	0.087

Chronic diseases included hypertension, diabetes and coronary disease.
DVT versus non-DVT; **P*<0.05, ***P*<0.01; /: no corresponding data.
Preoperative time: the period from injury to the diagnosis of traumatic fractures.
Preoperative diagnostic time: the period from diagnosis to surgery.
Postoperative time: the period following a surgical operation to discharge.

Data collection and statistical analysis

Demographic information (age and gender), type of surgery and other medical records and characteristics such as chronic diseases, perioperative time and D-dimer level of patients were collected. Categorical variables were presented as numbers or percentages and analysed by the χ^2 tests for statistical comparisons between the two groups. Independent sample *t* tests were used to analyse the discontinuous variables and described as mean±SD Receiver-operating characteristic (ROC) curve analysis was conducted to evaluate the diagnostic value of D-dimer for DVT. Data were analysed using the Statistic Package for Social Science for Windows V.23.0 and Med-Calc 15.2.2 online software.[23] In this study, *P*<0.05 was considered as significant differences.

RESULTS

Patient information

Patient characteristics were provided in table 1. In total, 462 patients with traumatic fracture fell into two groups: DVT group (337) and non-DVT group (125), aged 50–102 years. The mean age was 70.49±11.38 years for DVT and 71.66±12.53 years for non-DVT patients. Concerning the age and gender, independent sample *t* tests indicated that no statistically significant correlations were observed between the two groups (*P*>0.05). In addition, preoperative time was longer in DVT group than that in non-DVT group (7.14±5.15 vs 5.45±3.75 days), and there was statistically significant difference between DVT group and non-DVT group (*P*<0.01).

Table 2 Correlation between fracture sites and deep vein thrombosis (DVT)

Fracture sites	DVT patients (n=337)	Non-DVT patients (n=125)	*P* value <0.01**
Hip (n, %)	240 (71.2%)	111 (88.8%)	/
Tibiofibula or plateau (n, %)	40 (11.9%)	10 (8.0%)	/
Femoral shaft (n, %)	35 (10.4%)	2 (1.6%)	/
Patella (n, %)	19 (5.6%)	3 (2.4%)	/
Pelvis (n, %)	2 (0.6%)	1 (0.8%)	/

***P*<0.01; /: no corresponding data.
n, the number of patients.

The distribution of fracture sites of patients in DVT and non-DVT groups is shown in table 2. In this study, fractures of the lower extremities were classified according to the site of trauma, either in the hip area, femoral shaft, knee joint, tibiofibula or plateau, patella and pelvis. In the 462 patients, 351 were hip fracture, 37 were femoral shaft fracture, 50 were tibiofibula or tibial plateau fracture, 22 were patella fracture and the rest were pelvis fracture. In addition, up to 71.2% of patients with DVT suffer a hip fracture, 11.9% patients were tibiofibula fracture and 10.4% DVT cases have femoral shaft fracture, showing that hip fracture group presented with the highest rate of DVT (figure 2). The χ^2 test analysis results indicated that there were significant differences in the rate of DVT among patients with different fracture sites (*P*<0.01).

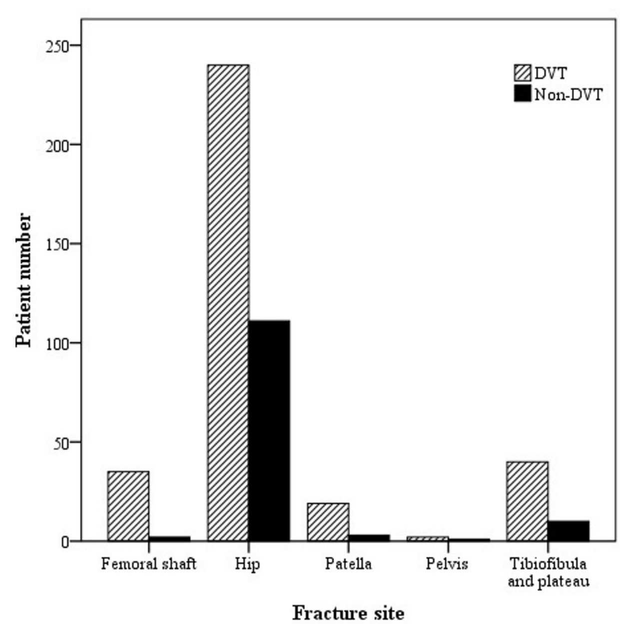

Figure 2 The distribution of deep vein thrombosis (DVT) in different fracture sites.

Table 3 Multivariate logistic regression analysis

Risk factors	OR (95% CI)	*P* value
Preoperative time	3.056 (1.032 to 1.188)	<0.01**
Preoperative D-dimer	1.992 (0.533 to 0.652)	<0.01**
Postoperative D-dimer	4.265 (1.104 to 1.341)	<0.01**

**P<0.01.

Multivariate analysis of risk factors

Multivariate logistic regression analysis was used to further illustrate the correlation of perioperative DVT with preoperative time, preoperative and postoperative plasma D-dimer. As shown in table 3, the ORs of preoperative time, preoperative and postoperative plasma D-dimer were 3.059, 1.992 and 4.265, respectively, indicating that they were independent high-risk factors for DVT in patients with lower extremity fractures ($P<0.01$).

ROC curve analysis for D-dimer value

ROC curve analysis was introduced to determine the diagnostic value of D-dimer in patients with perioperative DVT (figure 3). The detailed results were listed in table 4, which showed that preoperative D-dimer value greater than 4.01 µg/mL was considered as significant predictor for perioperative DVT in patients with traumatic fracture ($P<0.05$). The area under the curve (AUC) of preoperative D-dimer value was 0.593 (95% CI 0.533 to 0.652), with the sensitivity at 71.30% and the specificity at 44.83%. As for the postoperative D-dimer, the cut-off value was 5.03 µg/mL, and the AUC was 0.728 (95% CI 0.672 to 0.780). Besides, the sensitivity and specificity of postoperative D-dimer were 63.90% and 70.51%, respectively.

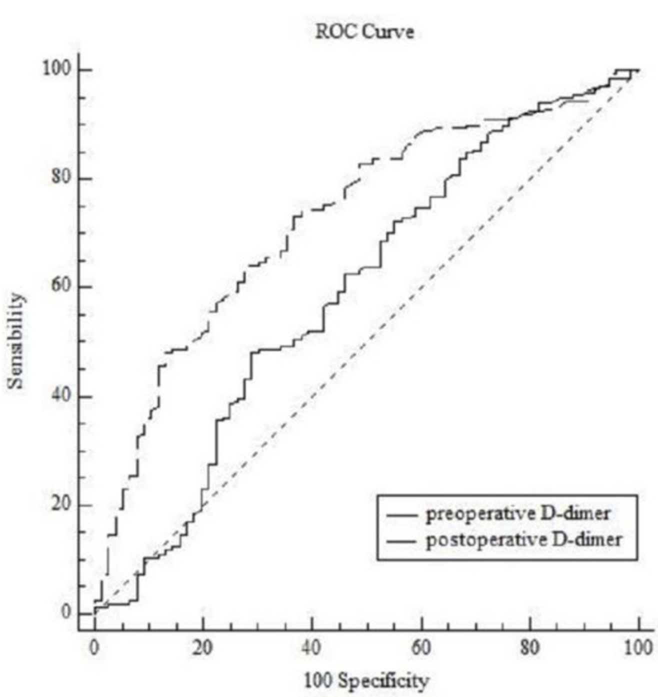

Figure 3 The receiver-operating characteristic (ROC) curves of the preoperative time and D-dimer value.

Table 4 Receiver-operating characteristic curve analysis of D-dimer

Risk factors	Preoperative D-dimer	Postoperative D-dimer
Area under the curve (AUC)	0.593	0.728
95% CI	0.533 to 0.652	0.672 to 0.780
P value	0.01886*	<0.01**
Cut-off value	4.01	5.03
Sensitivity (%)	71.30	63.90
Specificity (%)	44.83	70.51

*P<0.05.
**P<0.01.

Moreover, both perioperative and postoperative D-dimer levels were significantly different between DVT and non-DVT group ($P<0.05$), suggesting that D-dimer value was an important indicator of DVT in patients with traumatic fracture.

Perioperative DVT and chronic diseases

In patients with traumatic fracture, 216 of 337 patients with DVT suffered from chronic diseases, whereas there was 88 in the 125 non-DVT patients (table 5). Furthermore, to identify the effect of chronic diseases on DVT, all the patients were classified into three categories: patients with one chronic disease, two chronic diseases and three chronic diseases. χ^2 tests analysis manifested that (shown in table 5) there was no significant association between chronic diseases and DVT ($P>0.05$). These results indicated that the medical correlation between chronic diseases and perioperative DVT was not observed in this study.

DISCUSSIONS

DVT, a subclinical disease, is a blood clot that forms within a deep vein in the body, typically in the lower extremities.[2 24 25] The occurrence of DVT generally relates to Virchow's triad, which states three prime reasons: stasis, hypercoagulability and endothelial changes.[26 27]

Table 5 Results of χ^2 test for chronic diseases

Variable	DVT group	Non-DVT group	Total	*P* value
All the patients	337	125	462	/
Patients with one chronic disease	118	43	161	0.521
Patients with two chronic diseases	77	38	115	0.079
Patients with three chronic diseases	21	7	28	0.814

DVT, deep vein thrombosis.

For patients with traumatic fractures, enormous external energy such as fall injury or traffic traumas may lead to vascular injuries. Besides, immobilisation combined with long-time bedridden would slow down the venous return and make the patients be susceptible to spontaneous intravascular coagulation.[28] The development of DVT might trigger symptomatic PE and PTS, which could result in paralysis of the lower limbs and even lead to death.[29 30] Despite LMH or rivaroxaban, as anticoagulants, has been extensively applied to patients with traumatic fracture,[4 31 32] the incidence of perioperative DVT is still high, posing a challenge for the disease prevention.[33] Nowadays, some factors in the DVT risk assessment scales were widely used for the thrombosis prophylaxis, while the factors such as preoperative time and fracture sites were rarely defined as risk factors in most of the assessment scales.[34] Therefore, we investigated some potential risk factors including preoperative time, different fracture sites, chronic diseases and their effect on the incidence of DVT in patients with traumatic fracture by a retrospectively research to provide more evidence for clinical prophylaxis on DVT.

Multiple documented DVT risk assessment scales such as Autar and Caprini risk assessments have been widely used for the evaluation of DVT in many trauma centres.[35] Factors such as age, BMI, orthopaedic surgery and history of DVT have been included in both Autar and Caprini scales on the risk assessment of DVT. In the present study, multivariate analysis showed that there were significant differences of preoperative time and plasma D-dimer between the DVT and non-DVT patients (P<0.05) (table 3), which is consistent with the previous studies,[36–38] while the assess scale ignored the preoperative time as a potential risk factor for DVT. In our study, we found that prolonged preoperative time combined with increased plasma D-dimer could be as a high-risk factor for DVT. While, sometimes the prolonged preoperative time is inevitable. For example, some patients in developing countries must be referred to higher authority medical institutions due to the poor medical resources in primary hospital, which greatly increases the incidences of perioperative DVT.[8] For patients undergoing transfer treatment or elective operation, it is beneficial to take antithrombotic drugs early after the risk assessment of bleeding for DVT prevention.

Moreover, in the cohort study, we performed a χ^2 test to determine the correlation between fracture sites and the incidence of perioperative DVT. The analysis results implied that the rate of DVT after a major orthopaedic surgery seems to range between 0.6% and 71.2% in various fracture sites, while hip fractures bear the highest risk of DVT, followed by tibiofibular fracture and femoral shaft fracture. Many authors also demonstrated that hip fracture was a considerable risk factor for DVT and had a significant correlation with the occurrence of DVT.[39] In general, patients who undergo a hip fracture exhibit all three risk factors associated with Virchow's triad, which contribute to the high occurrence of DVT.[40] Besides, we observed statistical differences in the incidence of DVT of different fracture sites (P<0.01), indicating a similar result as Awadalla Adam' research, which found that the incidence of DVT after orthopaedic trauma appears to be associated with the sites of fractures.[41] Of the multiple fracture sites, we found hip fracture presented with the highest rate of DVT, demonstrating that hip fracture may be a risk factor for DVT. This finding may help orthopaedic surgeons make reasonable treatment strategy based on the trauma sites and minimise prevent the occurrence of this disease effectively.[42]

According to the ROC curve analysis, the cut-off point of preoperative plasma D-dimer was 4.01 µg/mL, the sensitivity was 71.30% and the specificity was 44.83%. The postoperative plasma D-dimer was 5.03 µg/mL; the sensitivity and specificity were 63.90% and 70.51%, respectively. Usually, plasma D-dimer level increases when a thrombus or blood clot develops in the venous circulation, which could be an independent predictor of early DVT.[43–45] However, it is infeasible to rely solely on D-dimer values for the screening or diagnosis of perioperative DVT in patients with traumatic fracture, owing to that both trauma and open wound would greatly increase the D-dimer value due to its high sensitivity.[46] Therefore, making modest adjustments to cut-off threshold was necessary and valuable for clinical diagnosis of perioperative DVT, for example, age-adjusted D-dimer value has been widely applied to DVT diagnosis.[47] Dynamic monitoring of the plasma D-dimer could be used for the evaluation of the clinical effect of anticoagulant therapy and might act as an indicator for the prediction of acute thrombosis.

The incidence of DVT is affected by multiple chronic diseases, such as rheumatoid arthritis, haematological diseases, chronic kidney diseases and so on.[48] Among of them, hypertension, cardiovascular disease and diabetes are the three typical diseases that influence the incidence of DVT, which have been well studied.[44 49 50] Other research showed patients with hypertension suffer a higher incidence rate of deep venous thrombosis after total knee arthroplasty compared with those with normal blood pressure.[51] Whereas, in this study, the χ^2 tests demonstrated that no statistically significant association between chronic disease and DVT incidence were observed in patients aged 50 and older (P>0.05). There are two biases that possibly influenced the study results: the first is the small sample size in the trial; the other is that all patients aged 50 and older in our study; thus, chronic diseases are more susceptible to develop. Further large-scale cohort studies would be performed on the correlation of perioperative DVT and chronic diseases to explore the instructional clinical value in the prevention of DVT.

We concluded that preoperative time, fracture sites and increased D-dimer are potential risk factors for DVT in patients with traumatic fracture; therefore, we suggest that physicians should pay more attention to the DVT detection in special fracture sites (such as hip and tibiofibula) properly and in time. In addition, for patients with selective operation due to the restricted conditions, the physicians must assess the bleeding risk of patients at first. And then combining with the D-dimer test, anticoagulant therapy should be implemented as soon as possible. In summary, orthopedists should take measures to reduce DVT risk as soon as possible by shortening the preoperative time, detecting the D-dimer levels and providing individualised anticoagulant measures for patients during the perioperative period.

Strengths and limitations of this study

The highlight of our study is that preoperative time might be included in DVT risk assessment scale and be applied to DVT prophylaxis. We suggest that physicians should pay more attention to the DVT detection in special fracture sites (such as hip and tibiofibula) properly and in time. In addition, for patients with selective operation due to the restricted conditions, the physicians must assess the bleeding risk and D-dimer of patients, and they should offer anticoagulant therapy as soon as possible. Nevertheless, some limitations still exist. First, bias in patient selection and the short follow-up period would influence the results of retrospective analysis. Second, due to the minor specimen, the further researches based on more large survey samples are needed to do. Third, it is difficult to eliminate the inherent defects of cohort studies, which might have effect on the statistical analysis results.

CONCLUSIONS

In conclusion, all the results indicated that preoperative time, fracture sites and increased D-dimer are potential risk factors and indicators for DVT in patients with traumatic fracture. In addition, the retrospective cohort study suggested that preoperative time might be included in DVT risk assessment scale. The increased plasma D-dimer value combined with the risk assessment scales is beneficial to the prediction and diagnosis of DVT in advance. Hence, we recommend that orthopedist evaluate the preoperative time, fracture sites and D-dimer levels of patients during the perioperative period, which is conducive to the development of reasonable individualised treatment plan.

Author affiliations
[1]Lab for Bone Metabolism, Key Lab for Space Biosciences and Biotechnology, School of Life Sciences, Northwestern Polytechnical University, Xi'an, China
[2]Research Center for Special Medicine and Health Systems Engineering, School of Life Sciences, Northwestern Polytechnical University, Xi'an, China
[3]NPU-UAB Joint Laboratory for Bone Metabolism, School of Life Sciences, Northwestern Polytechnical University, Xi'an, China
[4]Clinical Laboratory of Honghui Hospital, Xi'an JiaoTong University College of Medicine, Xi'an, China

Acknowledgements All the authors of the manuscript are immensely grateful to their respective universities and institutes for their technical assistance and valuable support in the completion of this research project.

Contributors AQ, WZ and CC conceived and designed the study, and helped to draft and revise the manuscript. YH developed the method, performed the data analysis and the results validation, and wrote the manuscript. WW helped to analyse the data and conduct the analysis software. LC and KX checked the format of the final manuscript.

Funding This work was supported by Fund of Aviation Research and Project of Scientific Research of Shaanxi (2017ZDXM-SF-009), China's Post-doctoral Science Fund (2017M623249) , the Fundamental Research Funds for the Central Universities (No. 3102017OQD050), the National Science Foundation of China (No.31570940) and the Key Research and Development Project of Shaanxi Province (No.2018SF-363).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study belongs to retrospective research and the study was approved by the Ethics committee of Honghui Hospital, Xi'an JiaoTong University College of Medicine.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available. All data from this study are available to all qualified researchers/research groups and to international researchers.

REFERENCES

1. Decker S, Weaver MJ. Deep venous thrombosis following different isolated lower extremity fractures: what is known about prevalences, locations, risk factors and prophylaxis? *Eur J Trauma Emerg Surg* 2013;39:591–8.
2. Cooray R, Lake C. Prevention of deep vein thrombosis and pulmonary embolism. *Anaesth Intens Care* 2015;16:457–61.
3. Lee SY, Ro duH, Chung CY, *et al*. Incidence of deep vein thrombosis after major lower limb orthopedic surgery: analysis of a nationwide claim registry. *Yonsei Med J* 2015;56:139.
4. Jian L I, Yun-Ji C, Xie JT, *et al*. Efficacy and safety of rivaroxaban in the prevention of deep vein thrombosis in patients with hip arthroplasty. *J Clin Pharmacol* 2014.
5. Calder JD, Freeman R, Domeij-Arverud E, *et al*. Meta-analysis and suggested guidelines for prevention of venous thromboembolism (VTE) in foot and ankle surgery. *Knee Surg Sport Tr A* 2016;24:1409–20.
6. Yamada SM, Tomita Y, Murakami H, *et al*. Deep vein thrombosis in the lower extremities in comatose elderly patients with acute neurological diseases. *Yonsei Med J* 2016;57:388–92.
7. Yin H-Z, Shan C-M. The effect of nursing intervention based on Autar scale results to reduce deep venous thrombosis incidence in orthopaedic surgery patients. *Int J Nurs Sci* 2015;2:178–83.
8. Song K, Yao Y, Rong Z, *et al*. The preoperative incidence of deep vein thrombosis (DVT) and its correlation with postoperative DVT in patients undergoing elective surgery for femoral neck fractures. *Arch Orthop Trauma Surg* 2016;136:1459–64.
9. Chang C-J, Chen Y-T, Liu C-S, *et al*. Atrial fibrillation increases the risk of peripheral arterial disease with relative complications and mortality. *Medicine* 2016;95:e3002.
10. Agarwal S, Rana A, Gupta G, *et al*. Total knee arthroplasty in a diagnosed case of deep vein thrombosis - our experience and review of literature. *J Orthop Case Rep* 2017;7:16–19.
11. Chen F, Xiong JX, Zhou WM, *et al*. Differences in limb, age and sex of Chinese deep vein thrombosis patients. *Phlebology* 2015;30:242–8.
12. Choi M, Hector M. Management of venous thromboembolism for older adults in long-term care facilities. *J Am Acad Nurse Pract* 2012;24:335–44.
13. Schiff RL, Kahn SR, Shrier I, *et al*. Identifying orthopedic patients at high risk for venous thromboembolism despite thromboprophylaxis. *Chest* 2005;128:3364–71.
14. Fowkes FJ, Price JF, Fowkes FG. Incidence of diagnosed deep vein thrombosis in the general population: systematic review. *Eur J Vasc Endovasc Surg* 2003;25:1–5.
15. Collins R, Maclellan L, Gibbs H, *et al*. Venous thromboembolism prophylaxis: The role of the nurse in changing practice and saving lives. *AJAN* 2010;27:83–9.

16. Edmonds MJ, Crichton TJ, Runciman WB, *et al*. Evidence-based risk factors for postoperative deep vein thrombosis. *ANZ J Surg* 2004;74:1082–97.
17. Altintaş F, Gürbüz H, Erdemli B, *et al*. [Venous thromboembolism prophylaxis in major orthopaedic surgery: A multicenter, prospective, observational study]. *Acta Orthop Traumatol Turc* 2008;42:322–7.
18. Deitelzweig SB, McKean SC, Amin AN, *et al*. Prevention of venous thromboembolism in the orthopedic surgery patient. *Cleve Clin J Med* 2008;75 Suppl 3:S27–36.
19. Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon* 2005;51:70–8.
20. Rice KL, Walsh ME. Minimizing venous thromboembolic complications in the orthopaedic patient. *Orthop Nurs* 2001;20:21???27.
21. Bagaria V, Modi N, Panghate A, *et al*. Incidence and risk factors for development of venous thromboembolism in Indian patients undergoing major orthopaedic surgery: results of a prospective study. *Postgrad Med J* 2006;82:136–9.
22. Yang YH, Wang JC, Yun-Tao WU, *et al*. Effects of different operation on postoperative deep venous thrombosis in lower extremities of old patients with femoral neck fracture. *Journal of Jilin University* 2008;34:150–2.
23. Wink J, Wolterbeek R, Aarts LP, *et al*. Upper thoracic epidural anaesthesia: effects of age on neural blockade and cardiovascular parameters. *Acta Anaesth Scand* 2013;57:767–75.
24. Protty MB, Aithal S, Hickey B, *et al*. Mechanical prophylaxis after hip fracture: what is the risk of deep vein thrombosis? A retrospective observational study. *BMJ Open* 2015;5:e006956.
25. Paydar S, Sabetian G, Khalili H, *et al*. Management of deep vein thrombosis (dvt) prophylaxis in trauma patients. *Bull Emerg Trauma* 2016;4:1–7.
26. Rota E, Vallisa D, Morelli N, *et al*. Iatrogenic coagulopathy and the development of posterior reversible encephalopathy syndrome after l-asparaginase chemotherapy. *J Clin Imaging Sci* 2016;6:7.
27. Chang CJ, Chen YT, Liu CS, *et al*. Atrial fibrillation increases the risk of peripheral arterial disease with relative complications and mortality: a population-based cohort study. *Medicine* 2016;95:e3002.
28. Liu FY, Wang MQ, Fan QS, *et al*. Endovascular embolization of pulmonary arteriovenous malformations. *Chin Med J* 2010;123:23-8.
29. Goldfisher R. Lower-extremity venous ultrasound - past, present and future. *Pediatr Radiol* 2017;47:1209–13.
30. Kearon C, Akl EA, Ornelas J, *et al*. Antithrombotic therapy for vte disease: chest guideline and expert panel report. *Chest* 2016;149:315–52.
31. Zhou J, Liu ZD, Lin WL. Efficacy and safety of rivaroxaban on anti-deep venous thrombosis for patients undergoing hip arthroplasty. *J Clin Pharmacol* 2015.
32. Toker S, Hak DJ, Morgan SJ. Deep vein thrombosis prophylaxis in trauma patients. *Thrombosis* 2011;2011:505373–.
33. Matharu GS, Porter KM. Deep vein thrombosis following hip fracture surgery. *Trauma* 2010;12:203–10.
34. Caprini JA. Risk assessment as a guide to thrombosis prophylaxis. *Curr Opin Pulm Med* 2010;16:448.52.
35. Di Nisio M, Squizzato A, Rutjes AW, *et al*. Diagnostic accuracy of D-dimer test for exclusion of venous thromboembolism: a systematic review. *J Thromb Haemost* 2007;5:296.
36. de Moerloose P, Palareti G, Aguilar C, *et al*. A multicenter evaluation of a new quantitative highly sensitive D-dimer assay for exclusion of venous thromboembolism. *Thromb Haemost* 2008;100:505.
37. Xu Z, Shi D, Zhang C, *et al*. Postoperative plasma D-dimer value for predicting deep venous thrombosis following hip arthroplasty with nadroparin prophylaxis. *Hip Int* 2013;23:411–6.
38. Liu P, Fu Y, Wang P, *et al*. Application of risk assessment of RAPT scale in risk assessment for thromboembolism among elderly patients with hip fracture. *Modern Clinical Nursing* 2016.
39. Li Q, Chen X, Wang Y, *et al*. Analysis of the occurrence of deep venous thrombosis in lower extremity fractures: A clinical study. *Pak J Med Sci* 2018;34.
40. Cho YH, Byun YS, Jeong DG, *et al*. Preoperative incidence of deep vein thrombosis after hip fractures in Korean. *Clin Orthop Surg* 2015;7:298–302.
41. Adam A, Yousef M, Wahab BA, *et al*. Duplex ultrasound for evaluation of deep venous blood flow in fractured lower extremities. *Pol J Radiol* 2018;83:47–53.
42. Wang H, Kandemir U, Liu P, *et al*. Perioperative incidence and locations of deep vein thrombosis following specific isolated lower extremity fractures. *Injury* 2018:1353–7.
43. Carrier M, Le Gal G, Bates SM, *et al*. D-dimer testing is useful to exclude deep vein thrombosis in elderly outpatients. *J Thromb Haemost* 2008;6:1072–6.
44. Geersing GJ, Zuithoff NP, Kearon C, *et al*. Exclusion of deep vein thrombosis using the Wells rule in clinically important subgroups: individual patient data meta-analysis. *BMJ* 2014;348:g1340.
45. Luxembourg B, Schwonberg J, Hecking C, *et al*. Performance of five D-dimer assays for the exclusion of symptomatic distal leg vein thrombosis. *Thromb Haemost* 2012;107:369–78.
46. Bates SM. D-dimer assays in diagnosis and management of thrombotic and bleeding disorders. *Semin Thromb Hemost* 2012;38:673–82.
47. Broen K, Scholtes B, Vossen R. Predicting the need for further thrombosis diagnostics in suspected DVT is increased by using age adjusted D-dimer values. *Thromb Res* 2016;145:107–8.
48. Chotanaphuti T, Ongnamthip P, Songpatanasil T, *et al*. Risk factors of deep vein thrombosis (DVT) after total knee arthroplasty (TKA) at Phramongkutklao Hospital. *J Med Assoc Thai* 2007;90:485.
49. Zhu MH, Shi-Fei L I, Long AH, *et al*. A study on risk factors for deep venous thrombosis after knee arthroplast. *Chinese Journal of Bone & Joint* 2016.
50. Daneschvar H, Seddighzadeh A, Piazza G, *et al*. Deep vein thrombosis in patients with chronic kidney disease. *Thromb Haemost* 2008;99:1035–9.
51. Wang PC, Li C, Yang DS, *et al*. Correlation between hypertension and deep venous thrombosis after bilateral total knee arthroplasty. *CJTER* 2015.