Original Article

Correlation analysis between the risk factors and lethal thrombus formation after lower limb fractures

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Abstract: Introduction: This research was to investigate the correlation between lethal thrombus formation and three risk factors including gender, fracture position and thrombus source. Methods: The study reviewed 144 cases of deep venous thrombosis after lower limb fracture who transplanted temporary inferior vena cava filter or retrievable filter. They were classified as lethal or nonlethal group based on the size of thrombus by the digital subtraction angiography (DSA). The thrombus above 10 mm in diameter and the diffuse multiple-thrombi were considered as lethal. The thrombus below 10 mm in diameter and invisible thrombus were considered as non-lethal. All patients were classified into different groups according to the gender, fracture position and the site of thrombus formation. The statistical analysis was performed to determine the correlation between the three risk factors and lethal thrombus. Results: There was no statistical difference between the male group and the female group ($\chi^2=0.0209$, $P>0.05$). As for fracture position, there was no statistical difference among the groups ($\chi^2=2.018$, $P>0.05$). The single fracture in different positions of lower limb and multiple fractures had similar potential to induce lethal thrombus. In terms of the thrombus source, the result showed statistical difference among the groups ($\chi^2=14.526$, $P<0.05$). The logistic linear regression suggested that the incidence rate of lethal thrombus in the group of above the popliteal vein (APV) was lower than the other three groups with statistical difference ($P<0.05$). Conclusion: Thrombus formed in popliteal vein and below the popliteal vein and multiple thrombi seems easier to induce lethal thrombus when compared to thrombus formed above the popliteal vein. It should be paid more attention in clinical practice.

Keywords: Deep vein thrombosis, lethal thrombus, lower limb fractures, digital subtraction angiography

Introduction

Lower limb fractures are often complicated by deep vein thrombosis (DVT) which can further induce pulmonary embolism (PE) [1, 2]. The incidence rate of the DVT after fracture ranges from 40% to 60% and 50%-60% DVT can trigger PE (10%-30% lethal PE) [3, 4]. In a systematic review, the incidence of first DVT in the general population was 0.5 per 1000 person-years [5]. DVT and PE conjointly affect approximately 900,000 people in the US each year and lead to about 300,000 deaths [6]. Thrombosis can occur in any position of the venous system, but most frequently in the deep veins of legs. The substantial post-thrombotic syndrome is the most common reason for fatality [7]. The high risk factors of the thrombogenesis have attracted widespread attention. Many factors including age, genetic factor, obesity, smoking history, diabetes, lower limb varicosity, hyperhomocysteinemia, chronic venous inflammation, etc. have been studied [8-11].

However, the correlation between potential risk factors and lethal thrombus formation is rarely reported, especially in the patients with lower limb fractures. This study reviewed 144 patients with DVT after lower limb fractures. Thrombus was evaluated and measured using the digital subtraction angiography (DSA). Three potential risk factors, including sex, fracture position and thrombosis source, were analyzed in order to find out the correlation between these risk factors and lethal thrombus formation.

Materials and methods

Patients

The study was approved by the ethic committee of the hospital and the written informed con-
Lethal thrombus formation & lower limb fractures

sents of all patients were obtained. The patients with lower-extremity trauma and DVT diagnosed by the color doppler ultrasound (CDUS) in the hospital from March 2014 to October 2014 were reviewed in the study. Inclusion criteria: all subjects suffered lower limb fractures, including 27 cases of femoral neck fractures, 20 cases of femoral intertrochanteric fractures, 23 cases of femoral shaft fractures, 12 cases of femoral ankle fracture, 14 cases of ridge fractures between tibiacondylar, 8 cases of patellar fractures, 16 cases of tibiofibular fractures, 2 cases of ankle joint fractures and 22 cases of multiple fractures in low extremities (more than 2 positions). Besides, D-Dimer value was above the normal reference value (500 ng/ml). Exclusion criteria: the patients with malignant tumor, autoimmune disease, varicose vein of lower limb and other vascular diseases. The patients with implanted permanen filter or the retrievable filters failed to be pullout were also excluded.

All the subjects were imbedded with temporary or retrievable vena cava filters under DSA radiography. The D-Dimer value was measured in the laboratory.

Implantation of the filters and determination of thrombus by DSA radiography

After the right internal jugular venous puncture with Seldinger technology and the location of renal veins with DSA, the temporary inferior vena cava filter was imbedded. As for the implantation of the convertible inferior vena cava filters, it was performed following the femoral vein puncture and the location of renal veins with DSA.

The inferior vena cava venography was performed under DSA monitor two weeks after the filter implantation. The thrombus captured by the filter was measured. The filters were removed 2-4 weeks after the implantation. The implementation of the inferior vena cava filters

Figure 1. The lethal thrombus and non-lethal thrombus under DSA monitor. A. The ischemic filling defect occurred in the inferior vena cava which indicates the multiple thrombosis formation. B. The image shows no contrast medium and blood flow interrupting which imply the lethal thrombus formation. C. The lethal thrombus under DSA radiography. D. The image shows the diameter of the thrombus captured by the filter is less than 10 mm. E. The blood gets across the inferior vena cava filters wimmingly under the DSA monitor, indicating that there is no lethal thrombus formation.
Lethal thrombus formation & lower limb fractures

Classification method

The thrombus diameter larger than 10 mm, as well as the multiple diffusive blood clots in the inferior vena cava of the lower limbs (Figure 1A-C), were considered as lethal thrombus. The thrombus diameter less than 10 mm and unobvious thrombus (Figure 1D, 1E) were taken as non-lethal.

The patients were divided into male group and female group according to the gender. In terms of the fracture position, the subjects were divided into four groups including the group of above knee (AK), the knee joint (KJ) group, the group of below knee (BK) and the group of multiple fractures (MFL). The AK group contained femoral neck fracture, femoral intertrochanteric fracture and femoral shaft fracture. The KJ group consisted of femoral ankle fracture, patellar fractures and ridge fractures between tibia condyle. The BK group included tibiofibular fractures and ankle joint fractures. The subjects were also divided into four groups according to the thrombus formulating position diagnosed by the CDUS: the group of above the popliteal vein (APV), popliteal vein group (PV), the group of below the popliteal vein (BPV) and multiple thrombus group (MT). The above potential risk factors for lethal thrombus were evaluated.

Statistical analysis

All measurement data were analyzed by SPSS 19.0. The comparison of measurement data was analyzed by t-test. The enumeration data were analyzed by $\chi^2$-test and logistic linear regression analysis. P<0.05 was considered as statistical difference.

Results

One hundred and forty-four patients (98 males, 46 females; average age: 55) satisfied the criteria and were enrolled in the study. The average D-Dimer value was 2169±1165 ng/ml and all were higher than the normal reference value (P<0.05).

The results indicated there was no statistical difference between the male group and the female group ($\chi^2=0.0209$, P>0.05; Table 1). As for fracture position, there was no statistical difference among the AK, KJ, BK and MFL groups ($\chi^2=2.018$, P>0.05; Table 2). The results suggested that both single fracture in different positions of lower limb and multiple fractures as described above had similar potential to induce lethal thrombus.

In terms of the thrombus source, the result showed statistical difference among the APV, PV, BPV and MT groups ($\chi^2=14.526$, P<0.05; Table 3). The logistic linear regression suggested that the incidence rate of lethal thrombus in APV group was lower than the other three groups with statistical difference (P<0.05). It suggested that thrombus formulated in popliteal vein and below the popliteal vein and multiple thrombi is significantly easier to induce lethal thrombus when compared to thrombus formulated above the popliteal vein.

Discussion

DVT is a clinical challenge for doctors of all disciplines. It is highly prevalent and poses a bur-
Lethal thrombus formation & lower limb fractures

den on health economy. The disorder and its sequelae are also among the best examples of preventable diseases. Endothelial injury or dysfunction, the blood flow retardation or stagnation and hypercoagulability which are considered to contribute to thrombosis constitute the Virchow’s triad [12]. The destruction of the stress reaction and the integrity of the local vessel after the fracture can activate the coagulation system, which increases the agglutinant and turns into the hypercoagulable state. Besides, due to the fixation and pain after the fracture, the finite movement of the injured limbs causes the decreasing blood velocity in veins. The tissue injury, limb swelling and inflammatory infiltration also impede the venous return meanwhile benefit the platelets adhesion, aggregation and thrombus formation [5]. Therefore, it is meaningful to find out the risk factors for thrombus formation after lower limb fractures. The present study showed that thrombus formulated in popliteal vein and below the popliteal vein and multiple thrombi are significantly easier to induce lethal thrombus.

The clinical symptoms of the DVT mainly contain swelling, pain, pyrexia, superficial varicosis, high skin temperature of the wounded limb, pitting edema, femoral triangle tenderness, calf tenderness, etc. The patients with DVT symptoms can be easily diagnosed and immediately treated. However, the asymptomatic patients should be put a new premium on the accurate diagnosis and precaution. In the present study, CDUS, laboratory examination and DSA radiography were conjointly used. The CDUS of lower limb should be performed even for the asymptomatic DVT fracture patients to judge DVT formation [13]. The D-dimer plays a prominent role in ruling out acute deep vein thrombosis due to its high sensitivity and because the D-dimer measurement is rapid, simple and inexpensive test [14]. Hooman Bakhshi proposed that D-Dimer is an applicable test for detection of posttraumatic deep vein thrombosis in lower limb fracture [15]. Although CDUS is recognized as the first choice for the DVT examination [16], it only can estimate the position and quantity of the DVT in the lower limb indirectly rather than the size and property. DSA is the gold standard for the vascular disease examination and is the most sensitive and accurate test for diagnosis of DVT [17].

In previous studies, DVT were usually divided into central type, peripheral type and mixed type. The subjects were divided into health control, thrombus and non-thrombus group. The present study classified the thrombus as lethal and nonlethal according to the thrombus diameter detected by DSA examination. The lethal thrombus was defined as the thrombus diameter larger than 10 mm; the diffuse multiple-thrombus between postcava and peripheral vein was also considered as lethal.

The results of present study indicated there was no statistical difference between the male group and the female group (P>0.05). However, previous studies reported that risk for first deep vein thrombosis seems to be slightly higher in men than in women [18, 19]. In a population-based cohort study, the age-adjusted incidence of first venous thromboembolism was 1.3 per 1000 person-years in men and 1.1 per 1000 person-years in women [20]. It is probably attributed to the following reasons: firstly, the sample size was small; second, all the present patients suffered lower limb fractures; third, the different classification method, that is, we focused on lethal thrombus and nonlethal ones rather than healthy controls and thrombus.

As for fracture position, the subjects were divided into AK, KJ, BK and MFL groups. There was no statistical difference among the four groups (P>0.05), suggesting that both single fracture in different positions of lower limb and multiple fractures has similar potential to induce lethal thrombus. In terms of thrombus formation site, the incidence rate of lethal thrombus in APV group was lower than the PV, BPV and MT groups with statistical difference (P<0.05). It suggested probably that thrombus formulated in popliteal vein and below the popliteal vein and multiple thrombi is significantly easier to induce lethal thrombus when compared to thrombus formulated above the popliteal vein. The highest lethal thrombus rate was observed in PV group where the thrombus came from the popliteal vein.

There were some limitations in the present study. The sample size is small. This research only enrolled the patients with inferior vena caval temporal filters and retrievable filter. The subjects carrying the permanent filter were excluded because they didn’t perform DSA radiography. The old people are the high risk group
of DVT [21]. But age was not taken into consideration because permanent filter was used in most of elderly patients above 65 years old. In conclusion, thrombus formulated in popliteal vein and below the popliteal vein and multiple thrombi seems easier to induce lethal thrombus when compared to thrombus formulated above the popliteal vein. It deserves more attention in clinical practice.

Disclosure of conflict of interest

None.

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Lethal thrombus formation & lower limb fractures

