Common risk factors of deep vein thrombosis after arthroscopic posterior cruciate ligament reconstruction: a 5-year retrospective study

Dai Xiaoyu
Changzhou First People's Hospital
Ding Wenge
Changzhou First People's Hospital
Li Huan
Changzhou First People's Hospital
Peng Xu
Changzhou First People's Hospital
Wang Kejie
Changzhou First People's Hospital
Zhao Yiwen
Changzhou First People's Hospital
Zhang Naidong
Changzhou First People's Hospital
Zhihui Huang (jing20170427@163.com)
Changzhou First People's Hospital

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Abstract

Background To analyse the common risk factors of deep venous thrombosis (DVT) after knee arthroscopic posterior cruciate ligament (PCL) reconstruction in patients with PCL injury. Methods From August 2014 to December 2019, a total of 86 patients who had accepted knee arthroscopic PCL reconstruction underwent the color Doppler ultrasound of bilateral lower-extremities deep veins on 3 days postoperatively. Based on the inspection results, patients were divided into DVT group (9 males and 4 females, mean age 43.62 years) and non-DVT group (54 males and 19 females, mean age 33.96 years). The potential associations of DVT risk and age, gender, body mass index (BMI), diabetes, hypertension, smoking and other factors were analysed. Results High BMI and post-surgery D-dimer values were significantly associated with DVT risk. Conclusions Increased BMI and postoperative D-dimer levels are risk factors of DVT following knee arthroscopic PCL reconstruction in patients with PCL injury.

Background

As a common complication of major orthopedic surgery such as total knee and hip arthroplasty, venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE), which has gradually attracted people's attention in recent years due to its life-threatening potential[1, 2]. It has been confirmed that DVT of the lower extremities is the main manifestation of VTE[3] and the death of patients due to PE also occurred after knee arthroscopic surgery[4, 5] with a relatively low incidence[6, 7]. At the present time, the use of anticoagulation in patients undergoing knee arthroscopic surgery remains controversial[6, 7]. Previously, the American College of Chest Physicians (8th Edition) has pointed out that conventional anticoagulation is not required after arthroscopic surgery unless there exist other risk factors that may cause DVT[8]. However, recent studies have shown that the incidence of DVT after knee arthroscopy was 1.50% – 41.20% without anticoagulation during the perioperative period[6]. Noteworthily, the incidence of DVT after arthroscopic anterior cruciate ligament reconstruction can reach 8.00% – 41.20%[9]. Considering the objective factors such as the high-energy mechanism of posterior cruciate ligament (PCL) injury, relatively long operation time, and special anatomical structures of PCL, Dong et al. stated that postoperative DVT incidence in patients undergoing arthroscopic PCL reconstruction without thromboprophylaxis was 17.40%[1]. This potentially suggested the necessity of effective anticoagulant intervention for these patients.

Some epidemiological studies have shown that common risk factors such as age, gender, and body mass index (BMI) can partly affect the occurrence of DVT[10]. To our best knowledge, reearches on whether perioperative prophylaxis should be used in patients undergoing knee arthroscopic PCL surgery and how to do a targeted anticoagulant therapy in these patients have yielded conflicting results[1, 9]. Still, DVT prophylaxis may potentially lead to the risks of deep inflammation, bleeding events, and prolonged wound drainage[11]. We herein aims to provide a comprehensive and systematic analysis on common risk factors of DVT after arthroscopic PCL reconstruction in patients with PCL injury for a better guiding on the prevention and treatment of DVT in clinic.

Materials And Methods

Patients and blood sampling

From August 2014 to December 2019, a total of 86 patients who received knee arthroscopic PCL reconstruction due to PCL injury or rupture were consecutively enrolled in our department. All patients were diagnosed by clinical symptoms (such as limited knee mobility, etc.), physical examination, and MRI imaging. The color Doppler Ultrasound of both lower limbs was performed within 24 hours after admission and on the 3rd day after surgery. Exclusion criteria of the patients were: (1) congenital or secondary coagulation abnormalities; (2) severe liver and kidney function intolerance to surgery; (3) a history of VTE and VTE events within half a year; (4) anticoagulant, lipid-lowering, or steroid drugs therapy with half a year; (5) a history of lower limb vein surgery; (6) the injury of PCL combined with other ligaments; (7) DVT before arthroscopic surgery.

The height and weight of all patients were measured by the same nurse after admission and the corresponding BMI values were then calculated and recorded. A range of normal BMI is from 20 to 25 kg/m^2, overweight is considered as a BMI of 25.1 to 29.9 kg/m^2, and obesity is defined as a BMI of 30 kg/m^2 or higher[12]. Accordingly, BMI values were divided into 2 categories: < 25 kg/m^2 and ≥ 25 kg/m^2 in this study. Clinical data of each patient was collected according to their self-report, which mainly includes age, hypertension, diabetes, and smoking status. In addition, blood pressure (BP) was measured for 3 times with a random-zero sphygmomanometer at least and the mean of the last 2 of 3 measurements were adopted. We suggested systolic arterial pressure ≥ 140 mmHg or diastolic arterial pressure ≥ 90 mmHg, or a history of anti-hypertension treatment for definition of hypertension. Diabetes mellitus was defined as fasting glucose values ≥ 7.0 mmol/L (126 mg/dL) or higher, non-fasting glucose values ≥ 11.1 mmol/L (126 mg/dL) or higher, or the history of glucose-lowering therapy.

Two tubes of 5 ml venous blood were obtained from every untreated patient by standard veinpuncture at 7.00 a.m. after over-night fasting (12–14 hours) on the first day after admission, of which one tube of blood was centrifuged at 4 °C and the serum sample was immediately sent to the clinical laboratory of our hospital. Serum levels of triglycerides (TG) and total cholesterol (TC) were then detected. Meanwhile, another tube of blood was used to detect the platelet count. Subsequently, on the 3rd day after surgery, 5 ml of blood of each post-surgery patient was also collected in the morning to measure the prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), and the levels of fibrinogen (FIB) and D-dimer. The rising temperature and redness of the skin around the knee and calf, pain in the calf on dorsiflexion (Homan test), calf tenderness (Neuhof test) were conventionally examined and recorded by the same doctor following the surgery. This study was approved by the ethical committee of the First People's Hospital of Changzhou and all patients signed the informed consents.

Surgery and DVT prophylaxis

All the operations were performed under general anesthesia in the supine position by three senior surgeons. A thigh tourniquet inflated to 270 mmHg was used on the operated leg, which was deflated if

the procedure lasted more than 90 minutes and was reinflated 10 minutes later if necessary. The use time of tourniquet in all patients was less than 90 minutes in this study. For patients undergoing arthroscopic PCL reconstruction, a single tunnel combined with autologous hamstring tendon reconstruction was used by the same surgeon. All patients were not given anticoagulant therapy before and after surgery, and only mechanical and physical prevention for DVT was performed. For every patient, the operated leg was bandaged with the moderate pressure and pneumatic compression was applied for 30 minutes twice per day postoperatively. Isotonic, progressively restrictive exercises for the quadriceps and ankle pump were begun 24 h after operation. All patients were equipped with knee joint adjustable braces for weightless flexion and extension training.

DVT diagnosis and treatment

Considering that the color Doppler ultrasound is a non-invasive test with low cost and high specificity for the diagnosis of acute DVT[1], all patients underwent ultrasound examination of bilateral lower extremity veins on postoperative day 3 by one experienced radiologist. The DVT diagnostic criteria are: (1) absence of venous flow; (2) complete noncompressibility of the vein; (3) the presence of an echogenic thrombus mass in the normally anechoic vein. According to the results of ultrasound, DVT involving in the iliac, femoral, or popliteal veins on either side of the limb was classified as a proximal DVT, and the rest of the DVTs present in the calf veins were defined as distal DVTs. Patients with DVT on either side of the leg were assigned to the DVT group. Simultaneously, DVT pateints were all treated with low molecular weight heparin (LMWH) for anticoagulation and ultrasound reexamination of both lower limbs were done every 3 days to observe the change and outcome of thrombosis. Proximal DVT patients were restricted from getting out of bed and all DVT patients were discharged from the hospital when the thrombosis disappeared.

Statistical analysis

The comparison of categorical variables between two groups was performed using the $\chi 2$ test and the continuous variables were performed using the The Student's test. The multivariate analysis was performed by Logistic regression analysis. In all the tests, a 2-tailed probability value of less than 0.05 was considered to be statistically. All the data were analyzed by SPSS 19.0 (IBM SPSS, Chicago, IL).

Results

DVT incidence

There were 13 patients in the DVT group, including 9 males and 4 females, with an average age of 43.62 ± 13.56 years, and 73 patients in the non-DVT group, including 54 males and 19 females, with an average age of 33.96 ± 11.90 years. The incidence of DVT after knee arthroscopyic PCL reconstruction was 15.12% (13/86) (Table 1). Additionally, DVT incidence was 14.29% (9/63) and 17.39% (4/23) among male and female patients, respectively (Table 2). Of all the 13 DVT patients, proximal DVT was detected in the popliteal vein in 2 patients (2.33%) (Table 2). Among the distal cases, 5 involved ≥ 2 veins. Notably,

8 of the 13 patients were asymptomatic (61.54%) and no patients showed symptoms of PE. After thrombolytic therapy with LMWH, the 2 proximal DVTs disappeared and there were no compilications of anticoagulation in all DVT patients.

Table 1
The locations of DVT

Locations	no.
Proximal DVT	2
Iliac vein	0
Femoral vein	0
Popliteal vein	2
Distal DVT	11
Anterior tibial vein	0
Posterior tibial vein	1
Peroneal vein	1
Muscular veins	4
Muscular + peroneal veins	3
Muscular + peroneal + anterior tibial veins	1
Muscular + peroneal + posterior tibial veins	1
DVT deep vein thrombosis, no. number	

Table 2

Clinical characteristics of patients

Clinical Characteristics	DVT pateints	Non-DVT patients	P value
Patients, no.	13	73	-
Gender (male/female, no.)	9/4	54/19	P = 0.987[a]
Mean age, years (SD)	43.62 (13.56)	33.96 (11.90)	P = 0.010
Mean BMI, kg/m^2 (SD)	26.20 (3.00)	23.73 (3.97)	P = 0.035
(< 25 kg/m^2, no.)	3	50	-
(≥ 25 kg/m^2, no.)	10	23	P = 0.005[a]
Diabetes mellitus, (with/without, no.)	1/12	2/71	P = 0.422[b]
Hyoertension, (with/without, no.)	2/11	6/67	P = 0.763[a]
Smoking, (with/without, no.)	4/9	17/56	P = 0.820[a]
Homans test (+/-, no.)	5/8	6/67	P = 0.011[a]
Neuhof test (+/-, no.)	5/8	4/69	P = 0.002[a]
TG, mmol/L (SD)	1.34 (0.48)	1.52 (1.28)	P = 0.619
TC, mmol/L (SD)	4.49 (0.68)	4.09 (0.83)	P = 0.109
Platelet count, 10^{12}/L (SD)	219.92 (56.90)	208.70 (61.18)	P = 0.540
Duration of surgery, min (SD)	105.38 (21.06)	99.00 (21.55)	P = 0.326
Duration of tourniquet, min (SD)	73.38 (13.67)	69.11 (14.75)	P = 0.334
PT, s (SD)	11.76 (0.89)	11.56 (0.66)	P = 0.328
APTT, s (SD)	28.62 (3.75)	28.06 (4.21)	P = 0.655
TT, s (SD)	15.76 (1.44)	16.02 (1.66)	P = 0.600
FIB, g/L (SD)	4.17 (0.97)	4.39 (4.36)	P = 0.856

DVT deep venous thrombosis, no. number, SD standard deviation, BMI body mass index, TG triglycerides, TC total cholesterol, min minute, PT prothrombin time, APTT activated partial thromboplastin time, TT thrombin time, FIB fibrinogen

[a]: Continuous correction test

[b]: Likelihood ratio $\chi 2$ test

Clinical Characteristics	DVT pateints	Non-DVT patients	P value
D-dimer, mg/L (SD)	1.81 (1.99)	0.62 (0.52)	P = 0.000
DVT deep venous thrombosis, no. number, SD standard deviation, BMI body mass index, TG triglycerides, TC total cholesterol, min minute, PT prothrombin time, APTT activated partial thromboplastin time, TT thrombin time, FIB fibrinogen			
[a]: Continuous correction test			
[b]: Likelihood ratio $\chi 2$ test			

General comparison

In Table 2, there was no statistical difference in the distribution of patients' gender (P = 0.987) between DVT and non-DVT patients. It is worth noting that DVT group has the significantly higher BMI (P = 0.035), age (P = 0.010), and postoperative D-dimer levels (P = 0.000) than non-DVT group. Also, there existed more overweight and obese patients (P = 0.005) and higher positive rates of Homan test (P = 0.011) and Neuhof test (P = 0.002) in DVT patients than those in controls. However, there were no significant differences in blood TG, TC, and FIB levels, platelet count, operation time, and tourniquet using time (P 0.05). A parallel distribution of diabetes, hypertension, and smoking was observed between two groups (P 0.05).

Multivariate analysis

In the multivariate analysis (Table 3), both a high BMI (OR = 1.490; 95% CI = 1.051–2.111; P = 0.025) and an increased post-surgery D-dimer (OR = 4.817; 95% CI = 1.349–17.206; P = 0.015) values are significantly associated with an elevated DVT risk after knee arthroscopic PCL reconstruction. In addition, we failed to find any significant association of DVT incidence and other risk factors in this study (P 0.05).

Table 3
Risk factors of postoperative DVT

Risk factors	OR	95% CI	P value
Gender	1.347	0.131–13.835	P = 0.802
Age	1.089	0.996–1.191	P = 0.062
BMI	1.490	1.051–2.111	P = 0.025
Diabetes mellitus	0.873	0.008–66.253	P = 0.954
Hypertension	0.914	0.013–1.241	P = 0.967
Smoking	0.825	0.052–13.020	P = 0.891
TG	0.075	0.005–1.106	P = 0.059
TC	2.255	0.443–11.480	P = 0.327
Platelet count	1.000	0.980–1.019	P = 0.961
Duration of surgery	0.991	0.928–1.059	P = 0.791
Duration of tourniquet	1.064	0.932–1.213	P = 0.358
PT	66.060	0.057-76216.820	P = 0.244
APTT	0.893	0.629–1.267	P = 0.527
TT	1.081	0.564–2.071	P = 0.815
FIB	0.664	0.227–1.939	P = 0.454
D-dimer	4.817	1.349–17.206	P = 0.015

BMI body mass index, TG triglycerides, TC total cholesterol, PT prothrombin time, APTT activated partial thromboplastin time, TT thrombin time, FIB fibrinogen

Discussion

In this study, we retrospectively investigated the common risk factors for DVT after knee arthroscopic PCL reconstruction in patients with PCL injury alone and excluded the potential impacts of multiple ligaments injury. By the multivariate analysis, an elevated BMI value (BMI ≥ 25 kg/m^2) was associated with a 0.49-fold increased risk of DVT postoperatively. Also, postoperative DVT risk in patients with an increased D-dimer level was also 3.82 times higher than that in controls. It further indicated that both high BMI and D-dimer values might have underlying effects on post-surgery DVT in these patients.

In recent years, obesity has been proven to be an independent risk factor for VTE[13], which is often accompanied by disturbances of lipid metabolism such as increased TG or reduced high-density lipoprotein (HDL) cholesterol levels[14]. Previously, Griffin et al.[15] and Mineo et al.[16] pointed out that

HDL could inhibit platelet aggregation, reduce blood viscosity, enhance protein C anticoagulation mechanism, and reduce VTE formation by acting on vascular endothelium. Simultaneously, low-density lipoprotein could promote the expression of thrombin, tissue factor, factor VII and X, and accelerate the activation of platelets to induce the formation of VTE. Also, TG could increase the production of coagulation factors VII, VIII, IX, and plasminogen activation inhibitory factor-1, partially exerting a prothrombotic effect on thrombosis[15, 17]. All these findings further suggested that the high BMI may eventually play a partial role in the development of VTE by affecting lipid metabolism which could acted on the coagulation and fibrinolytic system. As a kind of commonly used lipid-lowering drugs, statins have been confirmed to reduce the risk of VTE potentially[18–20]. Importantly, Delluc et al. indicated that the anti-VTE effect of statins is likely due to its direct actions on the systemic coagulation mechanism[18]. Previously, it has been suggested that the increase in subcutaneous fat and visceral fat caused caused by obesity can promote the secretion of multiple pro-inflammatory factors and mediators such as C-reactive protein, tumor necrosis factor-α, interleukin-6, and interleukin-18[21]. Also, Rodriguez et al.[20] remarkably proposed that statins might reduce the occurrence of VTE by down-regulating the expression of inflammatory mediators. Summarily, these existing research results ulteriorly illustrated that the low-grade inflammatory state associated with obesity itself was very likely to be a major reason for the increased risk of VTE. Although the specific association of a high BMI and VTE is still not clear, for the obese patients with PCL injury, there is quite a necessity to take some measures exactly as strengthening physical prevention, taking lipid-lowering medication, and anticoagulant intervention for a decrease in DVT incidence after knee arthroscopic PCL reconstruction.

D-dimer is widely used in clinical practice as an indicator to monitor DVT with a high sensitivity and specificity[22]. Although the D-dimer level is affected by inflammation, bleeding and some other factors[9], effective anticoagulation is still necessary for patients with high D-dimer levels after knee arthroscopic PCL reconstruction. Considering the fact that the hypercoagulable status of patients after surgery usually lasts no more than 48 hours which is the peak period of the formation of acute DVT in the lower limbs[7], the blood D-dimer level was routinely measured on postoperative day 3 in this study and then the ultrasound of both legs was performed. This might largly ensure the reliability and accuracy of our findings. Follow-up studies will continue to be focused on the monitoring of D-dimer levels in such patients in order to better predict and assess the initiation, progress and outcome of postoperative DVT.

The incidence rates of symptomatic and asymptomatic DVT were 5.81% (5/86) and 9.30% (8/86) respectively, which were also close to the findings of Sun et al.[7]. Furthermore, it was worth noting that the positive rate of Homans and Neuhof tests in DVT group was significantly higher than that in non-DVT group, which largely implied that DVT after knee arthroscopic PCL reconstruction was usually associated with some corresponding symptoms and signs. Therefore, timely and targeted anticoagulation for patients with symptoms postoperatively may reduce the risk of DVT to a certain extent. Although the long-term risk of symptomatic or asymptomatic DVT after knee arthroscopy is still unknown and allow for the relatively high incidence of asymptomatic DVT (9.30%) in this study, it is still necessary to make a clear diagnosis of DVT by using ultrasound and further perform a effective intervention. Definitely, find

more specific and predictable risk factors associated with postoperative DVT is also an issue that needs to be solved.

In this study, the Doppler ultrasound of both lower limbs were used as the criteria for diagnosing DVT and the common risk factors of DVT after knee arthroscopic PCL reconstruction in patients with PCL injury were systematically analyzed. However, due to the limited sample size, we failed to do a in-depth analysis after stratified by gender. Still, there existed a lack of dynamic and continuous monitoring of postoperative DVT by ultrasound.

Conclusions

In conclusion, a high BMI and an elevated postoperative D-dimer level are risk factors for DVT after knee arthroscopic PCL reconstruction in patients with PCL injury. DVT prophylaxis and prevention in these patients is still of certain importance.

Abbreviations

DVT: deep venous thrombosis; PCL: posterior cruciate ligament; BMI: body mass index; PE: venous thromboembolism; PE: pulmonary embolism; TG: triglycerides; TC: total cholesterol; PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time; FIB: fibrinogen; LMWH: low molecular weight heparin; OR: odds ratio; CI: confidence interval; HDL: high-density lipoprotein

Declarations

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Authors' contributions

D XY and H ZH designed the study and wrote the article. W KJ, Z YW, and D WG collected the blood samples and provided the funding. D WG, L H, and X P did the operations. D XY and Z ND did the data analysis. Z ND made the postoperative DVT diagnosis. D XY, WGD, L H, X P, W KJ, and H ZH revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethical committee of The First People's Hospital of Changzhou. Informed consents were obtained fromall the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Orthopedics, The First People's Hospital of Changzhou Affiliated to Soochow University, Changzhou 213000, China.

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