

## **Prevalence and potential risk factor of deep vein thrombosis in Chinese patients undergoing knee arthroscopy surgery without thromboprophylaxis in routine clinical practice: A retrospective study.**

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### **Abstract**

**Objective:** To assess the prevalence of Deep Vein Thrombosis (DVT) in Chinese patients undergoing knee arthroscopy surgery without thromboprophylaxis in routine clinical practice, and to identify the associated risk factors.

**Materials and methods:** Medical records of 864 successive Chinese patients ( $\geq 18$  year) who underwent different arthroscopic knee replacement surgery without thromboprophylaxis at Zhoushan Hospital, China between January 2012 to December 2014 were reviewed. Venogram of each patient was reviewed. To identify possible risk factor, age, operative time of surgical intervention, time spent in tourniquet, body mass index, gender, surgeon and type of surgical procedure was also reviewed. Univariate analysis was performed to assess the relationship between potential risk factor and DVT.

**Result:** Of total patients, 564 (65.27%) patients had DVT as confirmed using venography. Among patients with DVT, 23% of patients had proximal DVT, whereas 42 % of patients had distal DVT. Of 65% of cases of DVT, 25% of patients experienced signs and symptoms of deep vein thrombosis, whereas no signs of deep vein thrombosis were observed in 45% of patients. Increasing age and complex surgical procedures of arthroscopy surgery are strongly linked DVT ( $p < 0.01$ ). Incidence of DVT was significantly higher among patients who underwent complex procedure of arthroscopy surgery compared to simple surgical procedure ( $p < 0.01$ ).

**Conclusion:** Our study results suggested that high prevalence of DVT was found among Chinese patients undergoing knee arthroscopy surgery without thromboprophylaxis in routine clinical practice. We recommended close monitoring of patients undergoing advanced knee arthroscopy surgery for occurrence of DVT to prevent post-operative complications.

**Keywords:** Deep vein thrombosis, Thromboprophylaxis, Knee arthroscopy surgery.

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### **Introduction**

Deep Vein Thrombosis (DVT) is most common causes of morbidity, mortality, and increase economic burden to patients and their family [1,2]. It is commonly observed among Caucasians [3,4], and less common in Asian population including Chinese [5,6]. Non-invasive techniques are commonly used to identify the occurrence of venous thromboembolism, using duplex Doppler ultrasonography [7]. It has been reported that the routine thromboprophylaxis help to reduce the risk of venous thromboembolism by 15% to 30% [8]. Apart from the surgical intervention, there are other many factors which are responsible in causing thromboembolism such as patient with malignancy, renal disease, and haematological disorder; previous incidence of thromboembolism in individuals or patients with family history

of thromboembolism, and patients taking hormonal replacement therapy and oral contraceptive [8].

Routine thromboprophylaxis has been recommended to patients who had major surgery such as orthopaedics surgery; however, the routine thromboprophylaxis is often overlooked in Asian countries [9-11]. It has been reported that the prevalence of thromboembolism among Asian population undergoing major surgery such as orthopaedic surgery without thromboprophylaxis was significantly higher, especially among individuals (incidence rate 50%) who had fracture surgery [12]. Moreover, the incidence of thromboembolism was ranged from 10 to 64% among patients who had hip replacement surgery [13]; this range was increased to 11% to 77% in patients with total knee replacement [14,15]. The incidence rate of thromboembolism observed in Asian countries was found comparable with the data of western countries [1,2]. The

incidence of Pulmonary Embolism (PE) among Asian patients who underwent total hip replacement surgery was 1% [15], this was significantly lesser compared to prevalence of thromboembolism. However, the frequencies of serious PE have been increased over the time.

Incidences of venous thromboembolism following knee arthroscopy irrespective of use of thromboprophylaxis were 1.5% to 41% [16]. Due to different prevalence of venous thromboembolism in different studies evaluated incidence rate among patient following of knee arthroscopy, making right clinical decision seems difficult. A historical cohort study suggested that no need of prophylaxis as incidence rate was less than 0.4% after 1 month of surgery [17]. Studies also reported that the incidence rate of thromboembolism was in between 0.05 to 0.3% in large medical chart review study [16]. In studies with very low incidence of thromboembolism, patients with sign and symptoms of thromboembolism (symptomatic patients) who require treatment were studied. It has been observed that the patients with no symptoms and sign and symptoms of thromboembolism (asymptomatic patients) were ignored and even not subjected to any of non-invasive techniques (duplex Doppler ultrasonography and ventilation-perfusion scan technique). An asymptomatic case of thromboembolism leads to occurrence of post thrombotic syndrome [18].

Limited clinical data on prevalence of thromboembolism among Chinese patients undergoing knee arthroscopy surgery is available. We, therefore, designed this retrospective study with aim to assess the prevalence of thromboembolism occurred after different type of arthroscopic surgical procedure in Chinese patients who were not received any thromboprophylaxis, and to identify the associated risk of developing venous thromboembolism.

## Materials and Methods

We reviewed the medical records of 864 successive Chinese patients ( $\geq 18$  year old) who were underwent different arthroscopic knee replacement surgery without any kind of thromboprophylaxis intervention at Zhoushan Hospital of traditional Chinese Medicine, China between January 2012 to December 2014. We used computerized database of Zhoushan hospital to collect required data to fulfil the objective of our study. All the patients whose medical records were reviewed were received general anaesthesia including lumbar anaesthesia, and surgical procedure was carried out by two surgeons. During the surgical procedure, none received any kind of anti-coagulant or anti-platelet agents as thromboprophylaxis. All the patients were underwent four type of surgical procedure: Simple (minor surgical diagnostic procedure, removals of cyst, meniscal restoration); Anterior Cruciate Ligament Reconstruction (ACLR); Posterior Cruciate Ligament Reconstruction (PCLR); Combination of ACLR and PCLR surgical procedure. None of patients were prescribed Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) during first two week after surgical intervention. Most of the patients were

discharged on 4<sup>th</sup> day after arthroscopic knee replacement surgery.

We have excluded the medical records of patients who received anti-coagulant or anti-platelet agents as thromboprophylaxis before, during and after surgery. We have omitted the data of individuals with age of less than 18 year. Patients who were pregnant and already taking anti-coagulant with the history of thromboembolism or pulmonary embolism or had cancer were excluded. Institutional ethics committee approval was obtained. Since, this was a retrospective, observational study, and patients whose medical records reviewed were not contacted, or are named in the study, thus the requirement for obtaining formal informed consent was waived by ethics committee.

As per the protocol of our hospital, all the patients who underwent arthroscopic knee replacement surgery were subjected in radiography of a vein (venography) on 3<sup>rd</sup> day after surgery. We have collected and reviewed the venogram of all the patients who were underwent different arthroscopic knee replacement surgery without any kind of thromboprophylaxis intervention, and each venogram was studied by physician and radiologist, and final diagnosis were recorded. We have also recorded the clinical symptoms of thromboembolism were recorded, and the most common signs of thromboprophylaxis/deep vein thrombosis were swelling in leg, high skin temperature, and/or redness around affected area. In individuals with Pulmonary Embolism (PE), the most common abnormalities observed in chest which were increase size of heart due to excess volume, excess fluid between the layers of the pleura outside the lungs (pleural effusion), and fluid accumulation in the lungs (pulmonary oedema). Identification of PE among patients who underwent knee replacement surgery was mostly based on respiratory signs. By reviewing medical records, we identified number of patients with venous thromboembolism (cases of pulmonary embolism, distal and proximal) was calculated. Thromboembolism was categorized as proximal when thrombosis present in iliac or back of the knee (in popliteal veins) with or without leg vein thrombosis. Thromboembolism was categorized as distal when thrombosis was isolated to the leg veins.

We analysed incidences of venous thromboembolism by age, operative time of surgical intervention, time spent in tourniquet, body mass index, gender, different type of surgical intervention, to identify possible risk factor in developing venous thromboembolism among individuals with no thromboprophylaxis. Characteristic of patients who underwent different type of arthroscopy knee surgery was analysed using descriptive statistics. Quantitative variable was presented as mean  $\pm$  standard deviation, and data were compared using parametric/non-parametric statistical test based number of comparison group and distribution of data, using 2 sided statistical tests. Normality test (Kolmogorov-Smirnov test or Shapiro-Wilks test) will be used to check the distribution of data of quantitative data. Categorical variables was presented as absolute number and/or percentage of subjects in each category, and were compared using Chi-square or fisher exact

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test based on size of data, using 2 sided statistical tests. In all cases, a  $P < 0.05$  was considered to be statistically significant among comparison groups. Univariate analysis was performed to assess the relationship between potential risk factor and DVT. Data from each patient was coded and analysed using Graph Pad Prism statistical analysis software (version 6.0).

**Results**

Medical records of total 864 individuals (530 male, 294 female) with average age of 50.05 (6.4) had knee surgery during January 2012 to December 2014 without undergoing thromboprophylaxis were reviewed and analysed. Majority of OA of knee patients were male, underwent simple type of operative procedure. The average (SD) age of patients with DVT after surgery was 59.3 (1.8), it was 51.6 (1.3) in patients with no evidence of DVT. The operative time (in minutes) was

higher among patients with DVT (84.7) as compared to patients without DVT (69.3). Operative time in PCLR was higher as compared to other surgical interventions. Mean (SD) duration of the tourniquet time was greater in patients with DVT than individuals without DVT (66.4 (8.46) Vs. 59.7 (5.42) minutes). Gender distribution among both the subgroups was also found similar, with the higher proportion of patients were male in both the sub-groups of patients. In patients with DVT, the tourniquet time was higher when compared with the patients with no DVT. Incidence of DVT was higher among individuals who underwent complex procedure (ACLR and PCLR) when compared to simple surgical procedure (minor surgical diagnostic procedure, removals of cyst, meniscal restoration). Demography, surgical and baseline characteristic of patients who underwent arthroscopy knee surgery are indicated in Table 1.

**Table 1.** Characteristic of patients who underwent different type of arthroscopy knee surgery.

Patient's characteristic	Type of Surgical intervention				All
	Simple	Anterior Cruciate Ligament Reconstruction (ACLR)	Posterior Cruciate Ligament Reconstruction (PCLR)	ACLR+PCLR	
Number of patients in each category n (%)	340 (39.35%)	370 (42.82)	90 (10.42)	64 (7.41)	864
Age (year), Mean (SD)	42.4 (4.6)	49.8 (7.6)	52.3 (5.6)	55.7 (7.8)	50.05 (6.4)
Body Mass Index (kg/m <sup>2</sup> ), Mean (SD)	24.7 (2.23)	25.8 (1.42)	23.9 (1.56)	25.4 (1.86)	24.95 (1.76)
Male/Female, n	210/130	230/100	60/30	30/34	530/294
Operation time (in minutes), Mean (SD)	68.4 (6.13)	86.3 (4.2)	98.3 (7.34)	189.23 (8.34)	110.55 (6.50)
Tourniquet time (in minutes), Mean (SD)	48.6 (2.34)	72.4 (3.46)	78.7 (4.82)	87.35 (5.34)	71.76 (3.99)
Number of patients with proximal deep vein thrombosis, n (%)	19 (5.58%)	29 (7.83%)	14 (15.5%)	12 (18.75%)	200 (23.1%)
Number of patients with distal deep vein thrombosis, n (%)	45 (13.23%)	99 (26.75%)	26 (28.88%)	21 (32.81%)	364 (42.12%)
Total cases of deep vein thrombosis, n (%)	64 (18.82%)	128 (34.59%)	40 (44.44%)	33 (51.56%)	564 (65.27%)

Values are expressed as absolute number or percentage for categorical variables. Mean (Standard Deviation (SD)) for continuous variables. n=number of patient in each treatment group.

A total of 564 (65.27%) patients had DVT as confirmed using venography. Individuals with DVT, 23% of patients had proximal DVT, whereas 42 % of patients had distal DVT. Of 65% of cases of DVT, 25% of patients experienced signs and symptoms of deep vein thrombosis, whereas no signs of deep vein thrombosis were observed in 45% of patients. The patients with no symptoms of deep vein thrombosis would have been missed if venography was not performed. None of patients with DVT were died or presented with clinically significant

pulmonary embolism. We found there was no statistical significant difference in the occurrence of DVT when compared between different surgeons who performed all the knee related surgical intervention. Gender, BMI, surgical time and tourniquet application were also not significantly associated with the development of DVT. However, age of patient ( $p < 0.01$ ) and type of surgical intervention were found to have significant relationship ( $p < 0.01$ ) in occurrence of DVT, and looked to be noteworthy risk factor in development of

DVT. We also observed that the incidence of DVT was significantly greater with complex surgical inventions such as ACLR and PCLR than other surgical procedures which are indicated in Table 2.

**Table 2.** Relationship between risk factor and DVT.

Parameters	Patient without DVT (N=263) n (%)	Patient with DVT (N=601) n (%)	P value
Age (in year), Mean (SD)	51.6 (1.3)	59.3 (1.8)	0.005
Male/Female, (%)	64/36	66/34	0.1
Body Mass Index (kg/m <sup>2</sup> ), Mean (SD)	24.7 (2.23)	25.8 (1.42)	0.34
Operation time (in minutes), Mean (SD)	69.3 (5.21)	84.7 (6.5)	0.52
Tourniquet time (in minutes), Mean (SD)	59.7 (5.42)	66.4 (8.46)	0.54
<b>Type of surgical intervention</b>			
Simple	64 (18.82%)	276 (81.17%)	<.0001
Anterior Cruciate Ligament Reconstruction (ACLR)	128 (34.59%)	242 (65.40%)	0.0002
Posterior Cruciate Ligament Reconstruction (PCLR)	40 (44.44%)	50 (55.55%)	0.0001
ACLR+PCLR	31 (48.43%)	33 (51.56%)	0.00032

Values are expressed as absolute number or percentage for categorical variables. Mean (Standard Deviation (SD)) for continuous variables. n=number of patient in each treatment group. P value calculated using univariate analysis for categorical variables. Qualitative/categorical data were analysed using fisher exact test. Unpaired t-test for continuous/quantitative data variables.

## Discussion

To the best of our knowledge, this was the first investigation to evaluate prevalence of venous thromboembolism in Chinese patients undergoing knee arthroscopy surgery. In present study, a total of 65% of patients who underwent knee arthroscopy surgery without thromboprophylaxis had DVT, of this 25% of cases experienced symptoms of DVT, while 45% of cases reported no symptoms of DVT. Our finding of prevalence of symptomatic DVT was consistent with finding of Sun et al. [16] and Mulder et al. [19]. Higher incidence of asymptomatic DVT was observed in our study.

The prevalence of symptomatic DVT was comparatively low, when compared to other published studies. Symptomatic DVT can be identified in clinical practice without any kind of diagnosis method. The incident of asymptomatic DVT was

45%, which is significantly higher than occurrence of symptomatic DVT. High incidence of asymptomatic DVT shown that approximately 80% of DVT in patients underwent knee related surgery would have been unnoticeable after surgery if not diagnosed using venography. Asymptomatic DVT often ignored in clinical practice, and preference is given to symptomatic DVT, this may be risky since asymptomatic DVT is remain undiagnosed for longer time, then management of asymptomatic DVT with anti-coagulant/thrombolysis/anti-platelet drugs seems to be difficult.

We observed that there was no relation between occurrences of DVT with gender, tourniquet application, BMI and surgical procedure time since there was no significant association with the development of DVT in patient underwent knee surgery. Age and type of surgical intervention (simple and complex) was found to be significantly associated with incidence of DVT after knee arthroscopic surgery. Age is well known and acceptable risk factor in development of DVT which can be due to diminished physical activity, increased rigidity and stimulation of blood coagulation pathway with increased age. The prevalence of DVT was meaningfully higher among patients who underwent complex type of procedure of arthroscopy surgery (ACLR and PCLR) than patients who had simple surgical procedure. Our results suggested that increasing age and complex surgical interventions of arthroscopy surgery (ACLR and PCLR) are strongly linked with DVT. Based on our findings, close monitoring of elderly patients undergoing advanced and complex type of knee arthroscopy surgery for occurrence of DVT irrespective of symptoms of DVT is recommended, to prevent post-operative complications among patients who undergoing knee arthroscopy surgery without thromboprophylaxis.

In our study, occurrence of DVT was significantly higher in patients who had ACLR and PCLR. Since, rupture of anterior and posterior cruciate ligament requires complex arthroscopic intervention such as ACLR and PCLR. Anterior and posterior cruciate ligament reconstruction procedure is a more invasive procedure, which leads to greater operating trauma which could be most likely cause of developing DVT as compared to routine arthroscopic surgical procedure. Operative and tourniquet application time was significantly longer during reconstruction of cruciate ligament using ACLR and PCLR than simple surgical procedure (minor surgical diagnostic procedure, removals of cyst, meniscal restoration etc.). It has been reported that the longer tourniquet application time could results in development of DVT, since tourniquet encourages immobility, with vascular injury in patients undergoing surgical intervention may lead to thrombosis. We observed that the individuals undergoing complex surgical procedure (reconstruction of anterior or posterior cruciate or both the ligaments) are at higher risk of development of DVT. There are greater chances of complications after surgical procedure if patients had pre-operative DVT which was unnoticed before surgical intervention.

## Conclusion

In our study, total 65% of patients undergoing arthroscopy surgery without thromboprophylaxis had DVT, of this 25% of cases experienced symptoms of DVT, while 35% of cases reported no symptoms of DVT. There was no relation between occurrences of DVT with surgeons, gender, body mass index, and operation time and tourniquet application. Increasing age and complex surgical interventions of arthroscopy surgery (ACLR and PCLR) are strongly linked DVT. Based on our findings, close monitoring of elderly patients undergoing advanced and complex type of knee arthroscopy surgery for occurrence of DVT irrespective of symptoms of DVT is recommended, to prevent post-operative complications among patients who undergoing knee arthroscopy surgery without thromboprophylaxis.

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