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# Incidence of Deep Vein Thrombosis and Its Natural History Following Unilateral Primary Total Knee Replacement in Local Chinese Patients—A Prospective Study 本地中國籍患病者接受單側全膝關節置換後出現深部靜脈栓塞的發病率 和自然史 — 一個前瞻性研究

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## ABSTRACT

*Purpose:* This prospective study was to investigate the incidence and the fate of deep vein thrombosis (DVT) among Chinese patients following unilateral primary total knee replacement (TKR). The influence of tourniquet time and the mode of anaesthesia on DVT were evaluated.

*Method*: 390 patients who underwent unilateral cemented primary TKR were investigated. Patients whose body-mass- index (BMI) exceeded 30kg/m<sup>2</sup> were given chemoprophylaxis with low molecular heparin postoperatively. DVT was diagnosed using duplex ultrasonography on 4<sup>th</sup> to 7<sup>th</sup> days after operation. DVT was classified into two groups, distal and proximal. Patients who had DVT on the first scan were assigned two follow-up scans.

*Result:* The incidence of DVT was 25.7%. 97 patients (24.9%) had distal DVT, whereas 3 had proximal DVT (0.8%). Among patients with DVT, 18 (18%) of them resolved at first follow up scan, 82 persisted, and there were no proximal progression. At the 6<sup>th</sup> week scanning, 57 patients (57%) were free from DVT, while 42 patients (42%) had persistent DVT. There was one (1%) case which the distal DVT had proximal migration, but there was no pulmonary embolism. Tourniquet time and mode of anaesthesia did not reveal any statistical significance on the incidence of DVT.

*Conclusion:* This prospective study showed that the incidence of DVT after unilateral primary TKR in Hong Kong Chinese patient was high. However, most of them are distal to popliteal vein with low risk of proximal migration. More than half of them resolved at about two months after the operation.

# 中文摘要

目的:本前瞻性研究是調查本地中國籍患者接受單側全膝關節置換 (total knee replacement,TKR) 後出現深部 靜脈栓塞 (deep vein thrombosis,DVT) 的發病率和結果。止血帶使用時間和麻醉模式對 DVT 的影響也進行了 評估。

方法:我們調查了 390 個接受 TKR 的患者。如果患者的身體質量指數 (body mass index, BMI) 超過 30 公斤/ 平方米,我們便給予低分子肝素藥物作為術後預防。我們採用術後 4 日至 7 天的多普勒超聲波來診斷 DVT。深 部靜脈栓塞被劃分成兩組:遠端和近端。患者在第一次掃描為診斷有 DVT 後,會再接受兩次後續掃描。

結果: DVT 的發生率為 25.7%。 97 例 (24.9%) 有DVT 遠端,而 3 例有近端 DVT (0.8%)。在 DVT 患者中, 18 (18%) 在第一次後續掃描時發現已經消失, 82 例依然存在,卻並沒有向近端進展。在術後第 6 週的掃描中, 57 例 (57%) DVT 已經消失, 而 42 例 (42%) 有持續性的深部靜脈栓塞。有一例 (1%) 遠端 DVT 出現向近端進展的 情况,但沒有出現肺栓塞。止血帶時間和麻醉模式對 DVT 發病率並沒有統計學上有意義的影響。

結論:這項前瞻性研究表明,在香港中國患病者接受單側全膝關節置換後出現深部靜脈栓塞的發病率是很高的。然而,他們大多是遠端 DVT, 近端進展的風險低。其中一半以上的 DVT 在手術後約兩個月內消失。

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## Introduction

Venous thromboembolism (VTE) is one of the most common complications following total knee replacement (TKR). It may present as asymptomatic deep vein thrombosis (DVT), symptomatic DVT with calf pain and swelling, and fatal pulmonary embolism. The reported incidence of DVT in Europe and North America ranged from 17% to 51% with an accepted form of prophylaxis.<sup>1–3</sup> Without prophylaxis, the incidence was quoted between 58% and  $84\%.^{2-4}$ 

The incidence of DVT in the Asian population was believed to be low compared with the Caucasian population. However, recent studies showed that the incidence was comparable with that in Western countries, ranging from 36% to 65%.<sup>5–7</sup>

There are scanty local data about the incidence of DVT after TKR and no data on its natural history. The objective of this prospective study was to estimate the incidence of DVT in local Hong Kong Chinese patients after unilateral primary TKR. The natural history of DVT was evaluated by serial ultrasound. The influence of tourniquet time and the mode of anaesthesia on DVT were also evaluated.

# Methods

Three hundred and ninety local Chinese patients who were admitted to our department for elective unilateral cemented primary TKR from April 2012 to March 2013 were evaluated in this study. Patient demographics are summarized in Table 1. Patients who had a previous history of venous thromboembolic event (VTE) or a body mass index (BMI) of > 30 were given chemoprophylaxis. Low-molecular-weight heparin (enoxaparin) was used in the study, which was started on the 2<sup>nd</sup> postoperative day and continued for 7 days. All patients received foot pumps to both lower limbs as a mechanical prophylaxis for 5 days after the operation.

Tourniquet was used during the operation, which was set at a value two times the systolic blood pressure of the patient during the operation. Walking exercise commenced on the 2<sup>nd</sup> post-operative day. Patients were closely monitored for the signs and symptoms of VTE, including fever, thigh or calf pain, calf circumference, prominence of superficial vein, and shortness of breath.

Routine duplex ultrasonography of both lower limbs was performed between the 4<sup>th</sup> day and 7<sup>th</sup> day after the operation. Ultrasonography was performed by the duty radiologist from the radiology department of the centre using the GE Healthcare LOGIQ

Table 1	1
Patient	demographics

Number	
<i>N</i> = 390	
115	
275	
1:2.3	
68.6	
43-88	
27.3	
16.5-44.3	
190	
200	
1:1.1	
119	
271	
1:2.3	
93.3	
50-140	

BMI = body mass index.

E9 ultrasound machine (General Electric Company, United States). Thrombosis was diagnosed if a vein was not fully compressible, there was any hyperechoic signal, or the venous flow was absent or diminished. DVT was classified into proximal and distal groups. Proximal DVT was defined as thrombosis in the superficial femoral vein, common femoral vein, or more proximal veins. Distal DVT included thrombosis occurring in popliteal or calf veins. Patients who had DVT were assigned two further duplex ultrasound scans, which were scheduled at 1 week and 6 weeks after the initial scan. The status of the thrombus was evaluated in the second and third scans, which was classified as resolution, static, or progression.

Patients who developed distal DVT were closely monitored for the signs and symptoms of proximal progression of the emboli clinically and by radiological studies. They were not given anticoagulants. However, patients who had proximal DVT or pulmonary embolism received warfarin as an anticoagulant for a period of 3 months.

The effects of tourniquet time, BMI, and anaesthesia on the incidence of DVT was analysed. Statistical analysis was performed using the Chi-square and one-way analysis of variance (ANOVA) tests using 95% confident interval.

# Results

The overall incidence of DVT was 25.7% (100 out of 390). Distal DVT accounted for 97% of all DVT cases. Three patients had proximal DVT. The 100 patients with positive DVT in the first scan were assigned two further follow-up scans. Upon the second scan, 18% (18 of 100) of the DVT resolved, while 82% of them persisted. There was nil proximal progression of thrombosis. At the third scan, 57% (57 of 100) of the thrombus resolved spontaneously. By contrast, 42% of them persisted. There was proximal progression of thrombosis from distal to proximal in one patient (1%). None of the patients had signs or symptoms of pulmonary embolism.

The effect of tourniquet time on the incidence of DVT was analysed statistically. The mean tourniquet time was 93.3 minutes. The patients were divided into two groups, with or without DVT. The mean tourniquet time of the two groups was compared using one-way ANOVA test (no DVT group = 93.6 minutes; DVT group = 92.5 minutes), which showed that there was no significant correlation between them (p = 0.624).

The mode of anaesthesia adopted for the arthroplasty was evaluated. There were 69 DVT cases (25.4% incidence) among patients who received spinal anaesthesia. However, the result was comparable when general anaesthesia was adopted (31 patients, 26.0% incidence). The influence on the incidence of DVT was analysed with the Chi-square test. It showed that there was no statistical influence on the incidence of DVT (p = 0.902).

#### Subgroup analysis

Since chemoprophylaxis was given in patients with BMI >30, a subgroup analysis was carried out to evaluate the influence of BMI on the incidence of DVT. In the analysis, the first group (Group A) was composed of patients with BMI > 30, all of whom received chemoprophylaxis. The second group (Group B) included patients with BMI  $\leq$  30, who received no chemoprophylaxis. Seven cases with BMI  $\leq$  30, who received chemoprophylaxis for a previous history of VTE, were excluded from this subgroup analysis. The incidence of DVT in Group A is given in Table 2. There were 13 DVT cases out of 86 patients, with an incidence of 15.2%. The influence of tourniquet time and the mode of anaesthesia adopted were statistically analysed in a similar manner. The mean tourniquet time was 101 minutes, with p = 0.398 on one-way ANOVA test. The result of anaesthesia and

Table 2	
Incidence of DVT (1st scan) in subgroup analys	is

	DVT incidence	%
Group A ( <i>n</i> = 86)	Distal	14
(BMI > 30, with chemoprophylaxis)	Proximal	1.2
	Total	15.2
Group B ( <i>n</i> = 297)	Distal	27.6
(BMI ≤30, without chemoprophylaxis)	Proximal	0.7
	Total	28.3

BMI = body mass index; DVT = deep vein thrombosis.

the incidence of DVT were analysed using Chi-square test, which showed p = 0.750. Both factors showed that there was no statistical effect on the DVT incidence.

The analysis of Group B was evaluated similarly. The overall incidence of DVT was 28.3%; 84 out of 297 patients had DVT as shown in Table 2. The mean tourniquet time was 91 minutes, and the one-way ANOVA test showed that p = 0.630. It showed no statistical correlation between tourniquet time and DVT incidence. The mode of anaesthesia had no influence on the incidence of DVT, as shown in the Chi-square test (p = 0.990).

### Discussion

This study was one of the largest local studies evaluating the incidence of DVT after primary cemented TKR. A similar local study conducted by  $Ko^8$  in 2003 showed that the incidence was 31% in a sample of 58 cases using ultrasound for diagnosis.

In our study, the overall incidence was 25.7% (28.3% without chemoprophylaxis). Studies from other Asian countries revealed a higher DVT incidence: 41.4% in Korea,<sup>7</sup> 65.3% in Japan,<sup>6</sup> and 50% in the SMART Study.<sup>5</sup> However, all the above three studies were conducted using venography. Venography is considered the gold standard for the diagnosis of DVT, but it is an invasive procedure and may incur certain risk and complications.<sup>9</sup> With improvements in technology, ultrasound has become a favourable alternative. Ultrasound is a noninvasive procedure with almost no contraindication. However, ultrasound is operator dependent, and the accuracy of diagnosing distal DVT was reported to be less favourable. The sensitivity and specificity of ultrasound ranged from 87% to 94%, and from 63% to 100%, respectively.<sup>10,11</sup> Therefore, it might be arguable that our study underestimated the actual incidence of DVT.

Gandhi<sup>12</sup> found that patients with metabolic syndrome (defined BMI above 30, diabetes, hypertension, and hyperas cholesterolaemia) had 3.2 times risk of DVT following total knee arthroplasty. Obesity (BMI > 30) has shown to be a major risk factor for the development of DVT in patients having total hip arthroplasty, as reported by White and Henderson<sup>13</sup> and Lowe et al.<sup>14</sup> In our subgroup analysis, patients with BMI < 30 and without chemoprophylaxis showed a DVT incidence of 28.3%, while those with BMI > 30 who had all received chemoprophylaxis had an incidence of only 15.2%. We believed that if patients in our study with BMI > 30 were not given chemoprophylaxis, the actual incidence of DVT in this subgroup might be higher than 28.3%. Chemoprophylaxis with low-molecular-weight heparin is known to be effective against DVT after total knee arthroplasty.<sup>15</sup> In our study, it was not possible to evaluate the efficacy of low-molecularweight heparin directly due to BMI being a confounder. A separate study is required to confirm its efficacy. However, our study suggested that low-molecular-weight heparin might have a role as a DVT prophylaxis in local Chinese patients with TKR.

Regarding the location of the venous segment thrombosis, soleal sinuses were the most common sites for thrombi to occur early.<sup>16</sup>

Our study found that distal DVT had a far higher incidence than its proximal counterpart, which accounted for 97% of all DVT cases. Wang et al<sup>17</sup> reported a figure of 95.6% in 105 cases. However, Kim and Kim<sup>7</sup> showed a lower incidence of 65.2% in unilateral TKR and 78.4% in bilateral TKR.

The natural history of DVT is a result of a dynamic process, with both thrombolysis and thrombus extension occurring after an episode of DVT.<sup>18</sup> The fate of the thrombus would be lysis with recanalization or progression (propagation).

Markel et al<sup>19</sup> evaluated 110 patients with DVT using ultrasound for 5 consecutive years. Clinical and duplex evaluations were performed at intervals of 1 day, 7 days, 1 month, and 3 months for the 1<sup>st</sup> year, and yearly thereafter. It revealed that when only legs with initial complete occlusion were considered, the prevalence of occlusion progressively decreased to 33% after 6 months, 17% after 1 year, and 0% after 3 years. Our study showed a similar finding, with 57% of DVT resolved after 6 weeks.

Being one of the large-scale local studies regarding the DVT incidence after unilateral primary TKR, our study has a few limitations. The operator bias about duplex ultrasonography could have been reduced if the same radiologist screened all the cases. The DVT prophylaxis given in patients with a high BMI might have reduced the actual incidence of DVT. After all, our study provided valuable information on the natural history of DVT after primary TKR. However, a randomized control study would be useful to evaluate the DVT incidence and the effect of chemoprophylaxis.

#### Conclusion

This prospective study showed that the incidence of DVT after unilateral primary TKR in Hong Kong Chinese patients was comparable with that in Western countries. However, most of the DVT cases are distal to popliteal veins with a low risk of proximal migration. More than half of the cases were resolved within 2 months after the operation.

# **Conflict of interest**

The authors declared no conflict of interest in this study. The authors declared no financial support is received for this study.

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