The Incidence of Deep Vein Thrombosis and Pulmonary Embolism after Total Knee Arthroplasty: The Screening Study by Radionuclide Venography

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Deep vein thrombosis (DVT) and pulmonary embolism (PE) are considered uncommon in Asian populations and thrombo-prophylaxis is rarely indicated. The objective of this study was to investigate the incidence of DVT and PE after total knee replacement in an Asian population.

Material and Method : *There were 100 patients who underwent total knee replacement enrolled in this study. No thrombo-prophylaxis was given to these patients. The possible risk factors such as age, sex, body mass index (BMI), operative time and the post-operative blood loss were recorded.*

Results : *The duplex ultrasonography (controlled) showed no evidence of DVT in all cases. There were 67 patients who completed radionuclide venography in this study. The incidence of DVT from positive radionuclide venography was 24% (16/67 patients) and PE was 12% (8/67 patients). All patients with positive imaging studies were asymptomatic. The risk factors were similar in both groups.*

Conclusion : *The incidence of DVT and PE in post-operative total knee replacement surgery, although lower than the incidence in Western populations, is higher than previously assumed. The radionuclide venography is less invasive and a useful diagnostic method for both DVT and PE. Because all patients with DVT and PE are asymptomatic, the use of thrombo-prophylaxis should be considered for risk and benefit.*

Keywords : *Deep vein thrombosis, Pulmonary embolism, Venoscintigraphy, Asian population*

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The incidence of deep-vein thrombosis (DVT) varies in different parts of the world, for reasons that are not yet completely understood[1]. In western countries, 34-63% prevalence of DVT in patients after total hip arthroplasty (THA) has been reported[2-7]; this increased to 41-88% after total knee arthroplasty (TKA)[8-11]. However, the data on the prevalence of DVT in Asian populations are still lacking. Local surgeons have the impression that clinically thromboembolic disease is uncommon and have not sought post-mortem autopsies; such actions have contributed to a low level of awareness of DVT. Recently, reports studied in Asia have shown a higher incidence of 10.0-64.3% in patients after THA and 22.6-76.5% after TKA[12-14]. The increased incidence in Asian populations may be related to the increasing number of TKA procedures in this region and the influence of Western dietary habits. Another reason for the increased incidence is the diagnostic criteria. From recent articles, the authors used venography as the gold standard, unlike the former reports, which used clinical signs. Clinical signs have been shown to be insensitive and not specific enough in estimating the true incidence of DVT[15,16].

Pulmonary embolism (PE) is another cause of death after lower extremity surgery and Lensing et al[16] found that 70-90% of PE came from DVT of lower extremities. Accurate diagnosis of DVT is important because untreated DVT can cause death or permanent

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impairment. Although duplex ultrasonography with venous compression is a good initial test for the majority of outpatients who present with symptoms and signs suggestive of acute DVT[17], this may have some limitation as a screening test[18]. Contrast venography is decreasingly used because it is sometimes painful, relatively expensive, time consuming and may cause side effects[19]. An alternative technique to detect both DVT and PE is radionuclide venography, which has long been accepted as useful investigation for the diagnosis of both DVT and PE[20-22].

There is only one report in Thailand[23], which found 4% incidence of DVT after hip surgery. There has been no study about the incidence of DVT after TKA in Thailand. The authors speculated that the incidence of DVT after TKA is higher than is commonly assumed among Thai clinicians. The purpose of this study was to investigate the incidence of deep vein thrombosis and pulmonary embolism after total knee arthroplasty using radionuclide venography.

Material and Method

This study was a prospective study in detecting DVT and PE after TKA by using radionuclide venography. The Institutional Ethics Committee approved this study and all of the patients gave their consent before participation.

Patients

The 100 consecutive patients who underwent TKA from June 2001 to June 2002 were enrolled in the study. The inclusion criteria were 1) the diagnosis of knee osteoarthritis, 2) age over 40, 3) the capability to communicate with doctors or nurses and 4) the obtainable consent. The exclusion criteria were patients who 1) were allergic to radionuclide agent, 2) were receiving unfractionated heparin, low molecular weight heparin, Heparinoid oral anticoagulant, Hirudin, antiplatelet agent (Aspirin but not NSAIDs) or Dextran before surgery, 3) had a history of significant hepatic, renal or cardiac disease, 4) were pregnant or lactating.

Ultrasonography

The ultrasound examinations were performed with a 7 and 12 MHz linear-array color duplex scanner (Advance Technology Laboratories, USA). The common femoral, superficial femoral, and popliteal veins were examined first, and then the upper half of the peroneal and posterior tibial veins. The deep veins were considered patent if the veins were completely compressible and the doppler signals were normal. Thrombus was characterized by an inability to completely compress the imaged vein or by abnormal or absent Doppler flow signals. Ultrasonography was performed between the 5^{th} - 7^{th} postoperative day before ambulation and immediately before radio-nuclide venography: and were recorded as normal, abnormal, or inadequate for interpretation.

Radionuclide Venography

Bilateral ascending radionuclide venography was done in the supine position with the injection of 4 mCi of Technetium 99m macroaggregated albumin (Tc-99m MAA) into each dorsal foot vein with an application of a tourniquet above the ankle. The study was acquired using continuous whole body acquisition with the speed of the collimator at 60 cm/min. The radiotracers were injected to both legs simultaneously followed by saline flushing. The images of whole body covering from the ankle to the lung were taken. The radionuclide venography was recorded as normal, abnormal, or inadequate for interpretation. The criteria for the diagnosis of DVT in radionuclide venography included nonfilling or nonvisualization of the deep vein, interruption of the flow, asymmetric filling of a deep vein and presence of abnormal collateral vessels[24]. The proximal venous system was defined as the deep veins in the pelvis, the thigh, and the popliteal region cephalad to the trifurcation of the calf veins.

Perfusion lung scan was performed after the radionuclide venography with the patient in the supine position to avoid the perfusion gradient between the apex and base of the lung. Eight views of images were obtained in anterior, posterior, both lateral, both anterior and posterior oblique projections. To avoid unnecessary ventilation study, aerosol for the ventilation study (Tc-99m DTPA) was performed after the perfusion study in selected patients. The diagnostic criteria for PE were categorized into four probabilities according to revised PIOPED criteria[25] (Table 1).

Statistical analysis

The authors used patients instead of legs for the unit of analysis. The incidence of DVT, PE, sensitivity, specificity, and positive predictive value of the imaging studies were calculated.

Table 1. Criteria for categorizing probability of pulmonary embolism (Revised PIOPED)

Probability	Descriptions of Abnormality
NORMAL	No Q defects
LOW	Non segmental Q defect
	Any Q defect << CXR abnormality
	V/Q matches provided that the CXR is normal and perfusion in some areas of the lungs is normal[a]
	Any number of small[b] Q defects with a normal CXR
INTERMEDIATE	1 moderate to 2 large V/Q mismatches or the arithmetic equivalent in moderate or large and moderate defects[c]
	Single V/Q match and normal CXR
	Difficult to categorize as low or high, or not described as low or high
HIGH	$\geq$ 2 large V/Q mismatches or the arithmetic equivalent in moderate or large and moderate defects[b]

PIOPED criteria:

a. Very extensive defects can be categorized as low probability. Single V/Q matches are borderline for low probability and thus should be categorized as intermediate in most circumstances by most readers, although individual readers may correctly interpret individual scans with this pattern as showing low probability

b. small, <25% of a segment; moderate, 25-75% of a segment; large, >75% of a segment

c. Two large V/Q mismatches are borderline for high probability. Individual readers may correctly interpret individual scans with this pattern as showing high probability for pulmonary embolism. In general, it is recommended that more than this degree of mismatched be present for inclusion in the high-probability category

Results

Patients

There were sixty-seven patients (67 patients) in whom both ultrasonography and bilateral radionuclide venography was performed. Six patients (from 100) were excluded because ultrasonography or radionuclide venography could not be done in one or both legs. Sixteen patients were excluded because of Aspirin use before surgery. Three patients were excluded because of Methotrexate use before surgery. Also, eight patients were excluded because of unobtainable consent. The age range of the 67 patients was 50-83 years (mean 66 years). There were 57 females and 10 males. The mean body mass index (BMI) was 27.26 (Table 2). All patients were Asian (Mongoloid).

The venous thrombosis

None of the 100 consecutive patients had symptoms of DVT or PE during the hospital stay (average 7 days). The result of ultrasonography in 100 patients included in this study were negative. Among 16/67 patients (24%) who had abnormal findings on radionuclide venography, 6 patients had evidence of distal DVT and 10 had proximal DVT (Table 3). There were no complications from radionuclide venography.

Table 2. Comparison of demographic and operative characteristics of the patients

Variables Total (N = 67)	Positive Radionuclide Venogram (N = 16)	Negative Radionuclide Venogram (N = 51)	P Value of difference	Mean
Age (years) $\pm$ SD	66.4 $\pm$ 7.9	66.3 $\pm$ 7.3	0.746	66 (50-83)
Sex (female/male) Total = 57/10	12/4	45/6		
Body mass index $\pm$ SD	28.1 $\pm$ 3.8	26.9 $\pm$ 3.6	0.22	27.3 (19.8-37.6)
Side of operation (Rt/Lt) Total = 32/35	8/8	24/27	1.00*	
Operative time (minutes) $\pm$ SD	140 $\pm$ 16.5	137.8 $\pm$ 26.6	0.53	138 (85-205)
Post-operative bleeding(ml) Mean $\pm$ SD	718.1 $\pm$ 330	753.5 $\pm$ 259	0.43	745 (280-1620)

* Fisher exact test

Table 3. Results of Radionuclide venography

		Ipsi-lateral	Contra-lateral	Both sides	Total
Proximal	Iliac vein	2	3	0	10
	Femoral vein	2	1	0	
	Popliteal vein	1	1	0	
Proximal and Distal	Popliteal and Calf vein	2	0	0	6
Distal	Calf vein	2	1	1	

The pulmonary embolism

There were 16 patients who had abnormal lung perfusion scan. After categorization by revised PIOPED criteria, the authors classified the patients into high, intermediate and low probability of PE (Table 4).

Statistical analysis

The incidence of DVT detected from radionuclide venography was 24% (16/67 patients) while 0% from ultrasonography. The incidence of PE was 12% (8/67 patients) in high probability, 4.5% (3/67 patients) in intermediate probability and 7.5% (5/67 patients) in low probability. When the authors considered the incidence of PE, which occurred with proximal DVT, the incidence was 7.5% (5 patients). Sensitivity and specificity of the radionuclide study could not be analysed because all patients with positive studies did not have symptoms of DVT or PE. In addition, all the results of ultrasonography were negative.

Table 4. Demonstration of 16 patients who had abnormal lung perfusion scan

	Probability of Pulmonary embolism by revised PIOPED criteria		
	HIGH	INTERMEDIATE	LOW
V/Q mismatched	8	3	5
Associated with abnormal radio-nuclide venography	5/0	2/1	
Proximal/distal			
Associated with normal radionuclide venogram	3	0	5

Discussion

Venous thromboembolic disease (VTE) is a major cause of morbidity and mortality in orthopaedic surgery. In Western countries, the incidence of DVT was reported to be 34-63% in patients after THA[2-7] and 41-88% after TKA[8-11]. Also, PE has been reported as another cause of death. The thrombo-prophylaxis is routinely used due to the high incidence of the disease and its harmful consequences. In contrast, thrombo-prophylaxis has rarely been used in major orthopaedic surgery, especially total knee replacement in Asian patients. The incidence of DVT has traditionally been considered low in Asian countries presumably because of ethnic and environmental factors. There is a paucity of studies in Asia about deep venous thrombosis after orthopedic surgery. In 1979, Mok[26] reported the incidence of 53.3% in Hong Kong. In 1988-89, a few reports showed a very low incidence of DVT in Asian countries (10% in Korea, 9.7% in Singapore and 4% in Thailand)[14,23,27]. Some recent Asian clinical trials have shown a high incidence (14%-70%)of DVT,[12,13,28-33] which correspond to our result (24% prevalence). The increasing incidence in Asian populations may be due to an increased aging population, increased number of TKA performed in this region and better diagnostic criteria[34]. From the present study and recent articles in Asia, it was found that the clinical signs are not as reliable as they are in Western studies. There was no correlation between the clinical signs and venographic findings[27] and the clinical signs can present in the absence of positive venography[12,14].

In considering the main risk factors of DVT such as age, major surgery, prolonged immobility, malignancy, prior VTE and oral contraception, Asian people have a similar risk, to Westerners[8,13,28]. In the present study, no relationship was found between the main risk factors and the DVT. No difference was found in the mean of age, sex, BMI, operative time and postoperative bleeding between the groups.

In the present study, all subjects were asymptomatic. There are many reasons for the cause of asymptomatic patients. First, two thirds of DVT are confined to the calf veins in asymptomatic patients. Second, when proximal DVT is present, it is often less extensive in asymptomatic patients than in symptomatic patients. Third, the asymptomatic thrombi may be of more recent onset and may have undergone less organization[35]. The rate of asymptomatic DVT after TKA was reported to be as high as 24% (2.5%-24%)[36,37]. Although this group of

patients were asymptomatic, subsequent PE from DVT have been the most serious complications in TKA. From recent studies[12,13,30-33] the prevalence of non-fatal PE was between 1.0%-8.3%. The incidence of Fatal-PE is very difficult to ascertain because of the low rate of autopsy. In the present study, the authors found 16 patients with abnormal lung perfusion scan on radionuclide venogram. By using revised PIOPED criteria, the incidence of high probability PE was 12% (8/67 patients), and that of PE associated with DVT was 7.5% (5/67 patients). All these patients were asymptomatic.

There are two methods of preventing postoperative venous thrombosis. First, primary prevention is deterrence of disease process before it begins. A course of thrombo-prophylaxis was given to all patients who underwent high risk operations. On the other hand, these patients will be exposed to the risk of anticoagulant therapy[38,39]. Major bleeding occurs in 2%-7% of patients[40,41], and intravenous administration of heparin leads to thrombocytopenia in 1% of patients[42]. Therefore, accurate diagnosis of acute DVT is needed to avoid inappropriate anticoagulation. Second, the secondary prevention is the detection and treatment of an asymptomatic disease before it becomes symptomatic.

The gold standard for detecting DVT has been contrast venography, whereas the diagnostic imaging method used most frequently in the United States is ultrasonography. Contrast venography is decreasingly used because it is frequently painful to the patient, relatively expensive, time consuming and may cause side effects. The test may be technically inadequate or the finding is very difficult to interpret in 10%-30% of patients[40,43].

Duplex ultrasonography is increasingly used in combination with color Doppler flow imaging, and is accepted to be highly sensitive and specific for venous evaluation between the pelvis and the knees in patients with localizing signs and symptoms[44-47]. Ultrasonography is highly dependent on operator's skill and experience (technically difficult in patients who are obese or have swollen limbs and is not useful in patients fitted with orthopedic casts)[48]. As shown in the present study, all studied patients had negative findings on ultrasonography. Although the patients were asymptomatic, 16 patients were found with DVT on radionuclide venography. Ultrasonography was considered to be the most accurate noninvasive test for the diagnosis of a first symptomatic proximal DVT, but not so accurate in asymptomatic postoperative patients and unreliable as a routine surveillance after total joint replacement[18,39,49].

Radionuclide venography is considered to be less invasive compared to contrast venography in the diagnosis of acute DVT. This technique has long been accepted as a useful diagnostic method for both DVT and PE[50-52]. Radionuclide venography is performed by Tc^{99m} macro aggregated albumin (MAA) injection via the dorsal foot vein using a small needle and low volume of isotope(1ml each leg). The patient receives low-dose radiation and it is not painful during injection. The extremity with DVT will show filling defects and collateral flow of the venous drainage. Meanwhile, the MAA particles will accumulate in the lungs (perfusion lung scan) rendering the diagnosis of pulmonary embolism being possible. Then two-purpose investigations can be done in one study. Thus, radionuclide venography in this study will offer the best benefit for the patients who undergo TKA by the ability of diagnosis of concomitant PE after DVT.

Conclusion

The incidence of DVT in the present study was 24% and that of PE was 7.5%, which correspond to those described in the West but all of the presented patients were asymptomatic.

Radionuclide venography is considered to be less invasive and a useful diagnostic method for both DVT and PE.

Ultrasonography, due to its operator-dependence, showed variable reliability in this situation.

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การศึกษาอุบัติการณ์ ภาวะหลอดเลือดดำลึกของขาอุดตัน ภายหลังการผ่าตัดเปลี่ยนข้อเข่าเทียม โดยการใช้ duplex ultrasonography และ Radionuclide venography

ชาติชาย ภูกาญจนมรกต, รจนา ศิริศรีโร, ชรินทร์ เอื้อวิไลจิตร, สุภนีวรรณ เชาว์วิศิษฐ, อิสระ โกยสมบัติโอฬาร

ภาวะหลอดเลือดดำลึกของขาอุดตัน และภาวะลิ่มเลือดอุดตันในปอด เชื่อว่าเป็นโรคที่มีอุบัติการณ์น้อยในประเทศไทย ทำให้ศัลยแพทย์ไม่ค่อยนึกถึงและป้องกันการเกิด โดยการให้ยาสลายลิ่มเลือดภายหลังการผ่าตัดใหญ่ที่มีอัตราเสี่ยงสูง จุดประสงค์ในการศึกษาครั้งนี้ เพื่อทำการหาอุบัติการณ์ของการเกิดภาวะหลอดเลือดดำลึกส่วนขาอุดตัน และ ภาวะลิ่มเลือดอุดตันในปอด ภายหลังการผ่าตัดเปลี่ยนข้อเข่าเทียม

***วิธีการ** : ได้ทำการศึกษาไปข้างหน้าโดยทำการขอตรวจผู้ป่วย 100 รายที่ได้รับการผ่าตัดเปลี่ยนข้อเข่าเทียม โดยวิธีการ radionuclide venography (RNV) และ การทำ duplex ultrasonography โดยที่ผู้ป่วยเหล่านี้ไม่ได้รับหรือวางแผนว่าจะได้รับการป้องกันการเกิดภาวะหลอดเลือดดำลึกส่วนขาอุดตัน ทำการบันทึกปัจจัยเสี่ยงต่อการเกิดโรค เช่น อายุ, เพศ, ดัชนีมวลกาย (BMI), ระยะเวลาในการผ่าตัด และ การเสียเลือดภายหลังการผ่าตัด*

***ผลการศึกษา** : มีผู้ป่วยที่เข้าร่วมโครงการจนสมบูรณ์จำนวน 67 ราย ไม่พบภาวะหลอดเลือดดำลึกส่วนขาอุดตันในผู้ป่วยทั้งหมด โดยการตรวจ duplex ultrasonography พบอุบัติการณ์ของการเกิด ภาวะหลอดเลือดดำลึกของขาอุดตัน โดยการตรวจ radionuclide venography 24% (16/67 ราย) และอุบัติการณ์ภาวะลิ่มเลือดอุดตันในปอดพบ 12% (8/67 ราย) แต่ผู้ป่วยทุกรายที่ให้ผลบวกจากการตรวจไม่มีอาการแสดงของโรค ปัจจัยเสี่ยงในการเกิดโรคเท่ากันทั้งสองกลุ่ม*

***สรุป** : ภาวะหลอดเลือดดำลึกของขาอุดตัน และภาวะลิ่มเลือดอุดตันในปอด ภายหลังการผ่าตัดเปลี่ยนข้อเข่าเทียม ถึงแม้ว่าจะมีอุบัติการณ์ต่ำกว่าที่มีรายงานในประเทศตะวันตก แต่ก็พบว่ามีอุบัติการณ์สูงกว่าที่เคยคิดกันไว้ การตรวจหาโรคโดยวิธีการ radionuclide venography ดีกว่าการตรวจโดยวิธี duplex ultrasonography และทำได้ง่าย เกิดผลข้างเคียงต่ำ สามารถตรวจหา ภาวะลิ่มเลือดอุดตันในปอดได้ในขบวนการเดียวกัน แต่อย่างไรก็ตามเนื่องจากผู้ป่วยที่ตรวจพบทั้งหมดไม่มีอาการแสดง ดังนั้นการพิจารณาใช้ยาเพื่อป้องกันการ เกิดหลอดเลือดดำลึกส่วนขาอุดตันภายหลังการผ่าตัดเปลี่ยนข้อเข่า ควรพิจารณาเป็นราย ๆ ไป*