Lower Extremities' Postthrombotic Syndrome after Total Knee Arthroplasty

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Background: *Deep venous thrombosis (DVT) is a disease associated with high morbidity in 40-60% patients who underwent Total Knee Arthroplasty (TKA). Postthrombotic syndrome (PTS) is a common long-term complication that may develop within 6 months or more than 2 years after episode of DVT.*
Objective: *To examine the prevalence of PTS in patients who had history of previous DVT and non-previous DVT at least 2-year follow-up period after TKA.*
Material and Method: *Retrospective chart review was done. All patients who underwent TKA during October 2002-2005 were included. They were postoperatively assessed for PTS with Villalta score and duplex ultrasonography at $\geq$ 2 years. The confirmed diagnosis of DVT was done by contrast venography.*
Results: *22 of 76 patients (56 previous DVT, 20 non-previous DVT) had PTS based on the clinical assessment. The previous-DVT group had significantly higher risk to PTS (OR= 1.59; 95% CI: 1.294-1.949; p-value = 0.001). When diagnosed with duplex ultrasonography, 36 in 56 patients of previous-DVT group and 8 in 20 of non-previous-DVT group were found positive venous reflux. Most of venous reflux occurred at popliteal vein (77%) and posterior tibial vein (59%).*
Conclusion: *After TKA, the patients who developed DVT had higher risk to PTS (OR = 1.588). Treatment of DVT may not decrease this risk. Prevention of DVT becomes an important approach to prevent PTS.*

Keywords: *Postthrombotic syndrome, Deep venous thrombosis, Total knee arthroplasty*

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Deep vein thrombosis (DVT) is a common complication following to the major hip or knee surgery. One theory about the etiology of DVT is Virchow triad which involved the hypercoagulability, endothelial injury, and venous stasis)[1]. Incidence of DVT after Total Knee Arthroplasty (TKA) is relatively high, 40-70% in patients who are not given prophylaxis and 15-30% in prophylactic cases[2-5]. Low-molecular weight heparin (LMWH) prophylactic regimen could reduce DVT rate more than 40-50%[6-11]. In Thailand, Phramongkutklao hospital reported 61% DVT after TKA, 12% proximal DVT and 11% bilaterally[12]. Five critical risk factors were found associated with DVT: underlying cardiovascular disease, hematological disease, rheumatoid arthritis, oral herbal medicine more than one year before operation, and revision TKA[13]. DVT in postoperative hip fracture patients were also reported 47.9% (56% proximal DVT)[14].

Postthrombotic syndrome (PTS) is a general chronic complication of DVT. Both symptomatic and the asymptomatic DVT can be much complicated in patients with pulmonary embolism (PE) and PTS[2,6,15-21]. Some patients developed venous portal hypertension after DVT due to venous valvular incompetence which led to the occurrence of PTS in an operated leg or even in the opposite side. Clinical presentation of PTS consists of pain and swelling, including superficial vein thrombosis, varicose vein, deep vein insufficiency, static dermatitis, static ulcer, cellulitis, deep vein thrombosis and pulmonary_embolism[22,23]. PTS was clinically diagnosed with the typical pain and swelling which might be "chronic" (occurred daily for at least 1 month), or persistently, or occurred 6 months or

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longer after DVT[4]. This pain is worse after standing or vertical activity and can be relieved by rest or horizontal position.

There are 3 stages of DVT including the early stage which patients were suffered from pain and swelling with or without superficial vein thrombosis or superficial phlebitis, mostly unilateral, the intermediate stage which patients can be observed their hyperpigmentation at ankle or leg with deep vein insufficiency (or varicose vein, static dermatitis, static ulcer and cellulitis), and the late stage which the static hyperpigmentation with harden skin (with or without DVT & PE) were shown[13].

Incidence of PTS after TKA was reported 24-60%[4,16,17,19,22]. There were 60% of cases developed within 2 years after surgery and no increasing incidence rate was found at 5- and 8-year follow-up[13,21]. Patients who have never been diagnosed as DVT could develop PTS[16]. Incidence of PTS was found 58% in patients with a prior episode of DVT and 9.2% in patients without a prior episode of DVT[16,17].

The purpose of this study is to assess PTS in patients who underwent TKA including those with previous DVT and no DVT. The diagnosis of PTA is based on the clinical presentations and duplex ultrasonography at more than 2-year follow-up period.

Material and Method

From October 2002 to October 2005, the prospective study was done at orthopaedics department, Phramongkutklao hospital, Thailand. Patients who underwent TKA since October 2002 to September 2003 were examined for DVT by "Gold standard" contrast venography before discharge from the hospital. We found total 91 TKA in 87 patients. There were 56 patients diagnosed DVT and the venography shown bilateral DVT in 11 cases. At 2-year follow-up, the patients were reexamined for PTS by Villalta score and duplex ultrasonography. The rationale for having 2 year as the minimum follow-up period is that there are studies reporting that 60% of PTS affected cases could be detected at this period.

Inclusion criteria

- Patients underwent TKA in Phramongkutklao hospital since October 2002 to September 2003 in which the recorded contrast venography were available
- Patients with no symptom or sign that could mimic the criteria for diagnosis of PTS
- Have $\geq$ 2 year follow-up data available
- Patients who had been diagnosed as DVT (symptomatic or asymptomatic) and were treated with full-course LMWH: Distal DVT: 1 mg/kg/dose for 4-6 weeks and Proximal DVT: 1 mg/kg/dose for 4 weeks + oral Warfarin to control INR 2-2.5 until 3 months

Exclusion criteria

- Patients who denied duplex ultrasonography examination
- Patient who lost follow-up

Since there is no "Gold standard" criteria for clinical diagnosis of PTS, we used "Villalta score" that has been widely used by many authors[23,24]. Villalta score consists of 5 symptoms: pain, cramps, heaviness, pruritus, and paresthesia , 6 signs: pretibial edema, induration of skin, hyperpigmentation, new venous ectasia, redness, and pain during calf compression.

For each item, the investigators assigned a score of 0 (not present or minimal) ranging to 3 (severe). The presence of a venous ulcer of the lower limb was recorded. In patients with bilateral thrombosis, the higher score was used. A total score of 15 or more or the presence of a venous ulcer indicated severe postthrombotic syndrome, and a total score of 5 to 14 indicated the mild postthrombotic syndrome. This score has been shown having good reproducibility and it also well correlates with the patient's perception of the interference of leg symptoms in daily life[21,23,24]

With duplex ultrasonography, we examined the venous incompetence or venous insufficiency or venous reflux in a common femoral vein, superficial femoral vein, popliteal vein, and/or posterior tibial vein. Previous studies reported the 43-98% sensitivity and 97-98% specificity of this method[3,5,7,9,25]. Clinical presentations of PTS were recorded in Villalta score by orthopaedics resident in two patient groups: previous DVT and non-previous DVT, who visited the orthopaedics OPD for the follow-up. Then the patients were referred to department of radiology for duplex ultrasonography examination. The comparison of number of PTS in both groups was done by Odds ratio analysis.

Results

After 2-year follow-up, 76 patients: 20 males (26.3%) and 56 females (73.7%)), were included in the study. Average postoperative duration was 28.84 months (24-36). 56 patients were found having previous DVT group and 20 patients with no previous DVT. Demographic data was shown in Table 1.

Table 1. Demographic and clinical data

	Patients with DVT	Patients with no DVT
Gender (%)		
Male	20 (26.3)	
Female	56 (73.7)	
Age (year)	72.13 ± 7.066	
Follow-up period (months)	28.84 ± 4.164	
DVT diagnosis		
Positive venogram	56 (73.7)	
Negative venogram	20 (26.3)	
Villalta Score	3.36 ± 2.393	
PTS diagnosed by Villalta score		
Yes	22 (28.9)	
No	54 (71.1)	
Venous reflux (%)		
Yes	44 (57.9)	
Grade 1	34 (77.3)	
Grade 2	10 (22.7)	
No	32 (42.1)	

Table 2. Clinical diagnosis of PTS with Villalta score in two patients groups: DVT and no DVT

		DVT		Total	p-value
		Yes	No		
PTS	Yes	22	0	22	0.001
	No	34	20	54	
Total		56	20	76	

Table 3. PTS diagnosed by duplex ultrasound in previous DVT and non-previous DVT patients

		DVT		Total	p-value
		Yes	No		
Reflux	Yes	36	8	44	0.059
	No	20	12	32	
Total		56	20	76	

Results of Villalta score and duplex ultrasonography in both groups are shown in Table 2 and 3 respectively.

With clinical evaluation, we found significantly that patients in previous DVT group had 1.588 times above non-previous DVT group to develop clinical presentations of PTS (95% CI: 1.29-1.95).

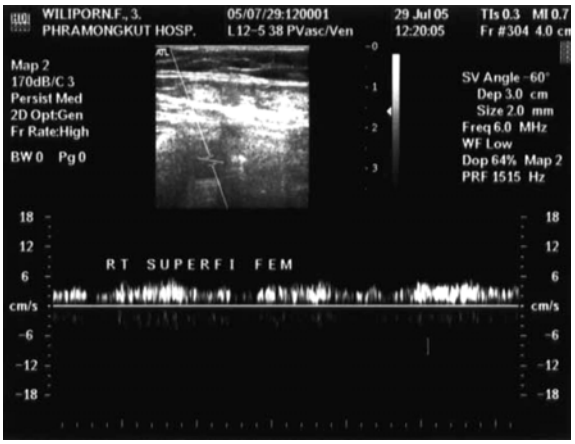

Fig. 1 Signal of normal vein without pressured or augmented

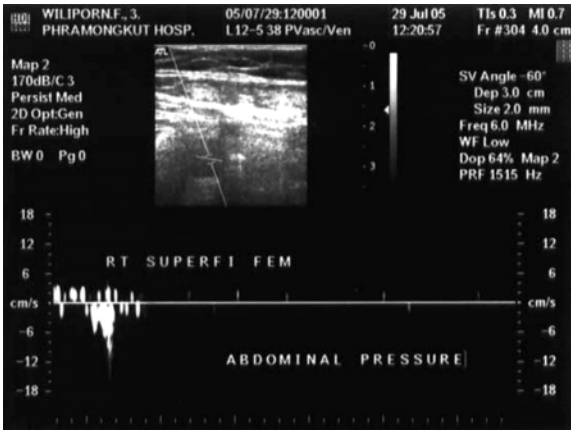

Fig. 2 Signal of normal vein with pressured indicating no reflux

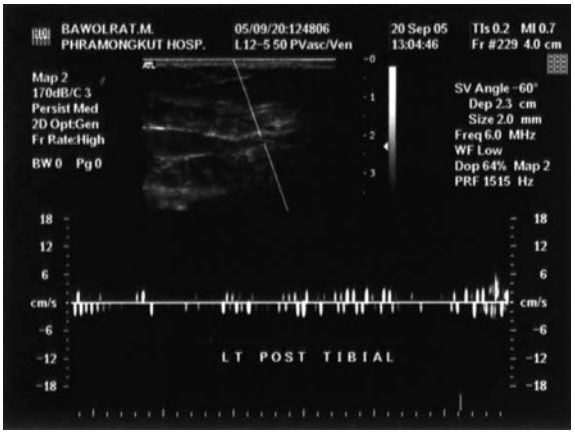

Fig. 3 Signal of Lt. posterior tibial v.augmented by compression indicating reflux grade I

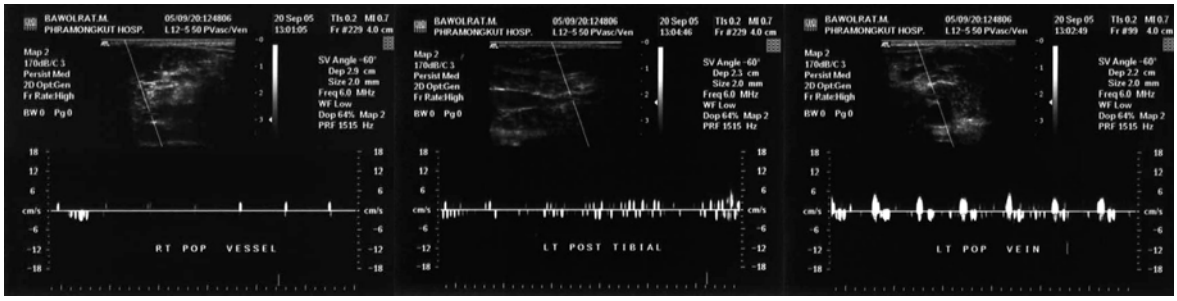

Fig. 4 (left) Rt. popliteal v. indicating normal signal (no reflux), (middle) Lt. posterior tibial & Lt. popliteal v. indicating venous reflux grade I, (right) Lt. posterior tibial & Lt. popliteal v. indicating venous reflux grade II

Based on the duplex ultrasonography, we found the risk of venous reflux developed in previous DVT group was 1.309 times [unadjusted odds ratios] higher than non-previous DVT group, but the result was not significant (95% CI: 0.968-1.771).

There were 44 patients had venous reflux. Comparable number of patients were found having single or multiple lesions. Details of reflux found in PTS patients were shown in Table 4.

Discussion

We found 44 of 76 patients developed venous reflux resulting in a prevalence rate = 57.9%. There were 22 cases had symptoms of PTS (28.9%) and all of them were in previous DVT group. Comparing to non-previous DVT group, all cases in DVT group had no clinical presentations of PTS even in those who had positive venous reflux confirmed by duplex ultrasonography.

Table 4. Venous reflux detected by duplex ultrasonography in PTS patients

Variable	Number
Site of venous reflux (total sites = 52)	
Single lesion	22
Multiple lesions	22
Bilateral lesions	8
Locations of venous reflux (total locations = 68)	
Common femoral v.	2
Superficial femoral v.	6
Popliteal v.	34
Posterior tibial v.	26
Reflux grade (total patients = 44)	
Grade 1	34
Grade 2	10
Grade 3	0

From our findings, it can be concluded that that patients with history of prior DVT have significant higher risk of developing PTS symptoms. Based on the duplex ultrasonography, there were 36 in 56 patients of previous DVT group and 8 in 20 of non-previous DVT group having positive venous reflux. The insignificant different was possibly due to two reasons. Firstly, the number of patients in both group was considerably different (56 vs. 31). Secondly, the natural history of PTS itself may accelerate the development of symptoms to be detected than the venous reflux. With duplex ultrasonography, there was no different number in single-lesion and multiple-lesion venous reflux. It also occurred in bilateral lesions. Most of them were mild (grade I) and found at the popliteal & posterior tibial vein.

Limitation of this study is related to a small number of included patients. There were 91 TKA in 87 patients, 56 DVT & 31 non-DVT. However, after 2-year follow-up period, all of DVT cases (56/56) were included in the study but there were only 20 of 31 non-DVT patients visited the hospital for their follow-up. This might be because patients with non-previous DVT patients may not develop any symptoms disturbing their quality of life then follow-up visits were not considered necessarily for them.

Conclusion

According to relatively high incidence of DVT after TKA reported in previous studies, the value of prophylactic regimens has been greatly discussed. PTS is a common long-term clinical outcome that may develop up to ten years after episode of DVT and significantly decrease patients' quality of life. When PTS symptoms occur, only conservative treatment can be done.

This study shows higher risk of developing

PTS symptoms in previous-DVT patients. Treatment of DVT may be too late and not be able to reduce the risk of PTS. Instead of treatment, the prevention of DVT such as thromboprophylaxis becomes an important alternative to further prevent PTS following to DVT.

This study provided evidences to confirm that patients in early stage of PTS may develop symptoms without venous reflux detected by duplex ultrasonography. The clinical manifestations are important for physician to diagnose PTS earlier as it can lead to early appropriate treatment.

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กลุ่มอาการผิดปกติภายหลังภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของขา หลังการผ่าตัดเปลี่ยนข้อเข่าเทียมในโรงพยาบาลพระมงกุฎเกล้า

สารเดช เขื่องศิริกุล, สุดศรีลักษณ์ สัมปัชชลิต, ตระกูล ฟูเจริญยศ, ธไนนิธย์ โชตนภูติ

***ภูมิหลัง**: การศึกษาก่อนหน้านี้พบว่าภายหลังการผ่าตัดข้อเข่าเทียมจะสามารถเกิดภาวะ Deep vein thrombosis (DVT) ได้ 40-60% ซึ่งส่งผลให้มีกลุ่มอาการข้างเคียงในระยะยาวที่สำคัญคือ Postthrombotic Syndrome (PTS) โดยพบได้ตั้งแต่ระยะเวลา 6 เดือนถึง 2 ปีขึ้นไป การศึกษาอาการผิดปกติ PTS ในผู้ป่วยผ่าตัดข้อเข่าเทียม จึงมีความสำคัญเพื่อให้ได้ข้อมูลสำคัญในการป้องกันภาวะความผิดปกติดังกล่าว*

***วัตถุประสงค์**: เพื่อศึกษาความชุกการเกิดภาวะ PTS ในผู้ป่วยกลุ่มที่เคยตรวจพบว่ามี DVT และกลุ่มที่ตรวจไม่พบ DVT ภายหลังรับการผ่าตัดข้อเข่าเทียมจากรพ.พระมงกุฎเกล้า ซึ่งติดตามการรักษาที่ระยะเวลามากกว่า 2 ปี และศึกษาความเสี่ยงของ PTS ที่เกี่ยวข้องกับ DVT*

***วัสดุและวิธีการ**: ที่ระยะเวลา 2 ปีขึ้นไปหลังการผ่าตัด ติดตามผู้ที่เคยตรวจหาภาวะ DVT ด้วย contrast venogram มาแบ่งเป็น 2 กลุ่มคือ กลุ่มที่เคยตรวจพบ DVT และกลุ่มที่ตรวจไม่พบ DVT นำทั้งสองกลุ่มมาประเมินหาภาวะ PTS ด้วย Villalta score และ Duplex ultrasound เพื่อเปรียบเทียบความชุกของการเกิด PTS ในแต่ละกลุ่ม*

***ผลการศึกษา**: จากผู้ที่ติดตามมาได้ 76 ราย (56 รายเคยตรวจพบ DVT, 20 รายตรวจไม่พบ DVT) เมื่อใช้เกณฑ์การวินิจฉัยตามอาการพบว่าเกิด PTS 22 ใน 76 ราย ผู้ที่อยู่ในกลุ่ม DVT มีความเสี่ยงต่อการเกิด PTS เป็น 1.588 เท่าของกลุ่มที่ไม่พบ DVT (95% CI : 1.294-1.949) ทั้งนี้เมื่อตรวจด้วย Duplex ultrasound พบว่าเกิด venous reflux 36 ใน 56 รายของกลุ่มที่พบ DVT และ 8 ใน 20 รายของกลุ่มที่ไม่พบ DVT โดยส่วนมากจะพบ venous reflux บริเวณ Popliteal vein (77%) และ Posterior tibial vein (59%)*

***สรุป**: หลังการผ่าตัดข้อเข่าเทียมมีความเสี่ยงสูงที่จะเกิดภาวะ PTS ตามมา (OR = 1.588) โดยเฉพาะในผู้ที่เคยมีปัญหา DVT มาก่อนแม้ว่าจะได้รับการรักษามาแล้วก็ตาม ดังนั้นการป้องกันการเกิด DVT จึงมีประโยชน์ และได้ผลดีกว่าการรักษา complications ที่อาจเกิดตามมา*