Incidence of Postthrombotic Syndrome in Patients Undergoing Primary Total Knee Arthroplasty for Osteoarthritis

Christopher M. McAndrew MD, Steven J. Fitzgerald MD,
Matthew J. Kraay MD, Victor M. Goldberg MD

Received: 31 October 2008 / Accepted: 28 May 2009 / Published online: 19 June 2009
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Abstract Postthrombotic syndrome (PTS) is characterized by edema, venous ectasia, hyperpigmentation, varicose veins, venous ulceration, and pain with calf compression after deep venous thrombosis (DVT). We determined the incidence of PTS after DVT diagnosed on screening ultrasound in patients undergoing primary total knee arthroplasty (TKA) for osteoarthritis (OA). We retrospectively reviewed the records of 1406 patients who underwent primary TKA for osteoarthritis and compared the incidence of PTS in patients without and with DVT. All patients had postoperative screening ultrasound. From these 1406 patients we identified 66 (4.7%) who had DVT, 50 of whom had a minimum of 1 year followup (mean, 4.97 years; range, 1.00–7.53 years). PTS was diagnosed if any two of six signs were documented in the medical record. Three of 50 patients with DVT (6%) had signs consistent with PTS; two of these three had a DVT proximal to the soleal arch. Seven (8%) of 88 patients randomly chosen for primary TKA because of OA with similar mean age and gender, but without DVT, had signs of PTS. PTS does not seem to be a major sequela of DVT in patients undergoing primary TKA for OA.

Level of Evidence: Level III, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

PTS is a chronic condition in the lower extremity that develops after DVT. The reported incidence of PTS in the medical literature varies from 20% to 70% [2, 8–10], making it the most common complication after lower extremity DVT. By definition, PTS is a syndrome generally consisting of, but not limited to, edema, skin induration, hyperpigmentation, venous ectasia, redness, pain with calf compression, and venous ulceration. Three clinical scales [10] have been reported using various combinations of these clinical signs and imaging studies to diagnose and grade the severity of PTS. None of these instruments have been validated for use in routine clinical monitoring. PTS is believed to be a major problem after DVT, with an estimated annual US cost of \$200 million [14].

With currently accepted prophylaxis [7], the incidence of DVT after TKA is reportedly between 22% and 49% [5]. Although much effort has been devoted to preventing DVT and pulmonary embolus, there is little published regarding the morbidity caused by PTS after DVT in patients undergoing TKA. It is unclear if this is because of a low index of suspicion for PTS, insufficient clinical monitoring for PTS, or if PTS is not a major morbidity after DVT in patients undergoing TKA.

We identified only three studies specifically examining the incidence of PTS in patients with DVT after TKA. Schindler and Dalziel [15] reported a rate of asymptomatic DVT of 37.6% in patients undergoing TKA. Although this is within the range of accepted published rates for DVT

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C. M. McAndrew (✉), S. J. Fitzgerald, M. J. Kraay,
V. M. Goldberg
Case Western Reserve University, University Hospitals Case
Medical Center, 11100 Euclid Avenue, Hanna House, 6th Floor,
Cleveland, OH 44106, USA
e-mail: cmcandrew@mac.com

after TKA, they limited evaluation for PTS to patients who had affirmatively answered a subjective questionnaire detailing symptoms of PTS, which could lead to major selection bias. Deehan et al. [4] reported an incidence of PTS of 13% after TKA. However, this study used a patient population that was not treated with a standardized prophylaxis protocol, which could lead to overestimation of the incidence of DVT and subsequent PTS. Lonner et al. [13] reported an 8% overall incidence of PTS after DVT diagnosed by screening venography in a mixed population of patients who had arthroplasties. This rate was similar to the rate for PTS in patients without DVT on the same screening venograms after arthroplasty.

Assuming PTS arises from DVT, we sought to confirm whether the incidence of PTS is greater in patients with DVT than in patients without DVT in a consecutive series of patients who had TKAs for a diagnosis of OA alone.

Materials and Methods

We retrospectively reviewed the records of all 1406 patients who underwent primary TKA for OA from 2001 through 2004. None of the patients included in this study had been diagnosed with PTS before their TKA. All patients were treated with a combination of mechanical (pressure stockings and sequential compression devices) and pharmacologic (warfarin at a weight and effect-adjusted dose with a goal international normalized ratio of 2.0) thromboprophylaxis. All patients underwent bilateral screening lower extremity ultrasound on postoperative Day 3 according to our protocol. If no DVT was diagnosed on postoperative Day 3, 4 weeks of warfarin was prescribed. If DVT was diagnosed on postoperative Day 3, 12 weeks of warfarin was prescribed [11]. Each patient, regardless of presence or absence of DVT, was followed up as an outpatient in the orthopaedic surgeon's office at 6 weeks, 3 months, 6 months, 1 year, 3 years, and every 2 years thereafter according to our protocol. Other interim followups were done at patients' requests for subjective concerns or if a complication necessitated more frequent followup. Neither DVT nor PTS were, specifically, considered complications requiring more frequent followup in this population. Demographic, diagnostic, surgical, and complication information for these patients was entered in our prospective Institutional Review Board-approved joint replacement registry database.

We identified 66 patients who had a DVT after primary TKA for OA diagnosed on screening ultrasound on postoperative Day 3. Fifty-one patients' records included specific anatomic data regarding location of the DVT. Of these patients, 50 were identified who had at least 1 year of postoperative followup and complete medical records

available for review. This followup time was chosen to exclude patients who presented with leg swelling during the immediate postoperative period. From the list of patients with negative DVT studies, we selected 100 in temporal order according to the day of their screening ultrasound, choosing groups of four to five sequential patients from among every listed group of 50 to 60 patients. Of these 100 patients, 88 had at least 1 year of postoperative followup. The two groups were similar in age at surgery (mean, 70.3 years in positive DVT group; mean, 68.3 years in negative DVT group) and gender (70% female in positive DVT group; 71.5% female in negative DVT group). The DVT group had a shorter ($p = 0.003$) followup compared with the no DVT group (3.1 versus 4.3 years).

We reviewed the outpatient medical records of these patients, including orthopaedic followup notes and the notes of medical and surgical specialists for documentation of six established signs of PTS: edema, venous ectasia, hyperpigmentation, varicose veins, venous ulceration, and pain with calf compression. The less specific diagnostic requirement (any two of six signs) was chosen to increase the sensitivity and decrease the false-negative rate of this review. The same clinical signs were searched for in the medical records of the control cohort.

The incidences of PTS in both groups were calculated and tested using logistic regression. Based on the group sizes of 60 and 102, we had 91.3% power to detect a medium effect (defined by estimated rates of 10% and 29% [5]) of a one-tailed test with alpha 0.05. To account for the nonindependence of patients providing two observations, we used the Huber correction [6] to produce robust estimates of variance. The relative risk of having these signs develop with a DVT was calculated. Confidence intervals for the relative risk were calculated [1]. As a result of patients' varying followups, we also estimated rates of PTS using Kaplan-Meier failure functions.

Results

The overall rate of DVT was 4.7% (66 of 1406). The DVT was located in the operative limb in 48 patients who had unilateral TKA and was contralateral in nine; in nine patients who had bilateral TKA, eight had a DVT in one extremity, and one had DVTs in both extremities (Table 1). Forty (79%) of 51 DVTs with specific anatomic data available were distal to the soleal arch and 11 (21%) were proximal to the soleal arch (Table 2).

Of the 50 patients with at least 1 year of followup, three (6%) had at least two signs of PTS. The most common sign was edema (three) with skin induration, venous ectasia, erythema, and pain with calf compression present in one

Table 1. Occurrence of ipsilateral and contralateral DVT

Unilateral		Bilateral	
Ipsilateral	48	Right	5
Contralateral	9	Left	3
		Bilateral	1
Total	57	Total	9

Table 2. Occurrence of DVT by anatomic relationship to the soleal arch

Location	Number
Distal	40
Proximal	11
Unknown	15

Table 3. Patients with and without DVT with signs of PTS

Signs	DVT	No DVT
Edema	4	7
Induration	1	1
Hyperpigmentation	0	3
Venous ectasia	1	3
Erythema	1	1
Pain with calf compression	1	1

patient each (Table 3). The average duration from presentation of these signs to resolution or last followup was 48 months (range, 17–66 months). Two of the three patients with PTS had a DVT located proximal to the soleal arch. The DVTs in these three patients were in the operative lower extremity. All of these patients had signs of PTS in the same operative extremity.

Of the 88 without DVT and at least 1 year of followup, seven (8%) had at least two signs of PTS. The most common sign was edema (seven) with hyperpigmentation of the skin and venous ectasia present in three patients each. Skin induration, erythema, and pain with calf compression were present in one patient each (Table 3). The average duration of these signs was 28 months (range, 2–71 months).

Controlling for differing followups, the relative risk of patients having signs of PTS develop after diagnosis of DVT by routine ultrasound after primary TKA for OA when compared with age-matched control subjects without DVT is 1.01 (95% confidence interval, 0.31–3.27). The incidence of PTS in patients with and without DVT by screening ultrasound after TKA for OA was similar (5% versus 7%; odds ratio, 1.48; 95% confidence interval, 0.35–6.30). Kaplan-Meier failure functions estimated that the incidence of PTS was 24% in the no DVT group at 7.5 years followup and 37% in the DVT group at 6.5 years followup (Fig. 1).

Fig. 1 The risk for postthrombotic syndrome is shown in this chart.

Discussion

PTS is a recognized complication of DVT. In the medical literature, the reported incidence of PTS developing in patients with symptomatic DVT ranges from 20% to 70% [2, 8–10]. Commonly referenced historical literature suggests DVT develops in 22% to 49% [3] of patients undergoing an arthroplasty procedure, the total number of which was 604,600 in 2003 [12]. If PTS develops at the same rate of incidence in patients with asymptomatic DVT diagnosed on screening studies (ie, after total joint arthroplasty), the clinical and financial burdens would be staggering. We undertook this study to determine the incidence of PTS in a well-defined population of patients undergoing TKA to better delineate the magnitude of this syndrome.

This study is limited by its retrospective nature. Specific inquiry regarding symptoms and observation of signs of a newly reported syndrome is likely to be limited in routine followup. Furthermore, inherent bias is introduced when reviewing surgeons' followup evaluation notes in a retrospective manner. We attempted to reduce this bias by including notes from primary care physicians, other medical specialists, and other surgical specialists. Also, the number and availability of unbiased observer notes varies widely among our population. Finally, a 12% rate of loss to followup at 1 year decreased the total numbers of the control cohort, although this seems to have had little statistical effect. However, we had a relatively large population followed closely with prospective data. With large numbers, we were able to focus this study on a well-defined subset of patients undergoing arthroplasty to minimize potential confounding factors that may affect the rate of PTS, such as previous surgery or systemic inflammatory disease. Our protocol includes routine screening for DVT with ultrasound of the bilateral lower extremities in all patients undergoing TKA. This study includes a control

cohort with similar age and gender demographics to compare with the study group and better define the effect the presence of DVT has on development of PTS.

If PTS is a complication of DVT in asymptomatic patients screened by ultrasound after TKA, then the incidence of PTS should be greater in patients diagnosed with DVT than in patients without DVT in this population. Our data showed no difference in the incidence of PTS in patients with and without DVT after TKA. In comparison to the work of Schindler and Dalziel [15], our reported rate of DVT after TKA was much decreased (5% compared with 37.6%). Furthermore, patients in their study were symptomatic, by virtue of their questionnaire. Their rate of PTS (12.5%) is slightly greater than our rate of 6%, but these likely do not reflect real differences given the population sizes in each study. Schindler and Dalziel made no comparisons to patients without DVT. Deehan et al. [4] reported an incidence of PTS of 13% after TKA in all patients with or without a diagnosis of DVT. Without radiographic or ultrasound evidence of DVT, they simply performed clinical examinations on all patients after TKA. They surmised that PTS may occur as a result of some other underlying disorder, and PTS “may not depend entirely on the extent of the initial thrombosis and may occur in the absence of thrombosis” [4]. Although our approach to the study of PTS differs from theirs, our overall incidence is nearly the same for all patients undergoing TKA with and without DVT. Lonner et al. [13] reported an incidence of each of the signs of PTS between 12% and 18% after DVT diagnosed by screening venography. This was similar to the rates of the signs of PTS without DVT in the same population. Although their radiographic modality differed, their study most closely resembled ours. However, their mixed population of patients undergoing arthroplasty by procedure and by preoperative diagnosis may contribute to their slightly greater rates of the signs of PTS.

Based on our data and those from other published studies regarding PTS in the arthroplasty population [4, 13, 15], the incidence is far lower than that reported in the medical literature [2, 8–10]. Furthermore, our findings and those of Deehan et al. [4] and Lonner et al. [13] show the rates of PTS are similar in patients undergoing arthroplasty with and without DVT. Although PTS has been reported as the most common complication after DVT in the general medical literature [8], it does not contribute major morbidity in patients with DVT after TKA based on our clinical experience. Our study and the literature [4, 13, 15] suggest the incidence of PTS in patients with DVT after

primary TKA for OA is 6% to 12%, which is similar to the incidence of PTS in patients without DVT in the same population. Based on these data, we believe PTS is not a clinically important complication of DVT after TKA for OA, and prognosis for having these sequelae is no different for patients with or without DVT in this subset of patients undergoing arthroplasty.

Acknowledgments We thank Carter Petty and Patty Conroy, RN, BSN, for assistance with this project.

References

1. Armitage P, Berry G. *Statistical Methods in Medical Research*. Ed 3. London, England: Blackwell; 1994:131.
2. Bernardi EP, Prandoni P. The post-thrombotic syndrome. *Curr Opin Pulm Med*. 2000;6:335–342.
3. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Ed 2. Hillsdale, NJ: Erlbaum; 1988.
4. Deehan DSMW, Pinder IM, Lingard EM. Postphlebotic syndrome after total knee arthroplasty. *Acta Orthop Scand*. 2001;72:42–45.
5. Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA, Wheeler HB. Prevention of venous thromboembolism. *Chest*. 2001;119(suppl):132S–175S.
6. Huber PJ. The behavior of maximum likelihood estimates under non-standard conditions. *Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability*. 1967;1:221–233.
7. Johanson NA, Lachiewicz PF, Lieberman JR, Lotke PA, Parvizi J, Pellegrini V, Stringer TA, Tornetta P, Haralson RH, Watters WC. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. *J Am Acad Orthop Surg*. 2009;17:183–196.
8. Kahn S. Frequency and determinants of the postthrombotic syndrome after venous thromboembolism. *Curr Opin Pulm Med*. 2006;12:299–303.
9. Kahn SR, Ginsberg JS. The post-thrombotic syndrome: current knowledge, controversies, and directions for future research. *Blood Rev*. 2002;16:155–165.
10. Kahn SR, Ginsberg JS. Relationship between deep venous thrombosis and the postthrombotic syndrome. *Arch Intern Med*. 2004;164:17–26.
11. Kraay MJ, Goldberg VM, Herbener TE. Vascular ultrasonography for deep venous thrombosis after total knee arthroplasty. *Clin Orthop Relat Res*. 1993;286:18–26.
12. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am*. 2007;89:780–785.
13. Lonner JH, Frank J, McGuire K, Lotke PA. Postthrombotic syndrome after asymptomatic deep vein thrombosis following total knee and hip arthroplasty. *Am J Orthop*. 2006;35:469–472.
14. MacDougall DA, Feliu AL, Boccuzzi SJ, Lin J. Economic burden of deep-vein thrombosis, pulmonary embolism, and post-thrombotic syndrome. *Am J Health Syst Pharm*. 2006;63(suppl 6):S5–S15.
15. Schindler OS, Dalziel R. Post-thrombotic syndrome after total hip or knee arthroplasty: incidence in patients with asymptomatic deep venous thrombosis. *J Orthop Surg*. 2005;13:113–119.