Postthrombotic Syndrome After Hip or Knee Arthroplasty

A Cross-sectional Study

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Background: Although the incidence of the postthrombotic syndrome (PTS) has been addressed in patients with symptomatic deep vein thrombosis (DVT), less information is available on the incidence in patients who develop asymptomatic DVT after major hip or knee arthroplasty.

Objectives: To determine whether symptomatic PTS occurs more frequently in patients who develop DVT after hip or knee arthroplasty than those who are free of DVT and to provide an estimate of the incidence of PTS in patients who had undergone major hip or knee arthroplasty and had proximal DVT, distal (calf) DVT, or no DVT.

Design and Setting: A cross-sectional study conducted at the Hamilton Health Sciences Corporation, Hamilton, Ontario, and the Academic Medical Centre, Amsterdam, the Netherlands.

Subjects and Methods: Two hundred fifty-five subjects who had undergone major hip or knee arthroplasty 2 to 7 years previously and had routine predischarge venography showing proximal DVT (n = 25), distal DVT (n = 66), or no DVT (n = 164) were enrolled from March 1993 through December 1998. The presence of symptomatic PTS confirmed by the presence of objectively confirmed venous valvular incompetence was ascertained.

Results: The rates of PTS were low and not significantly different among the 3 subgroups: 1 (4.0%, 95% confidence interval [CI] = 0.1%-20.4%) of 25 patients with proximal DVT, 4 (6.1%, 95% CI = 1.7%-14.8%) of 66 patients with distal DVT, and 7 (4.3%, 95% CI = 1.7%-8.6%) of 164 patients with no DVT.

Conclusions: Symptomatic PTS is an uncommon complaint after major hip or knee arthroplasty. Patients who develop postoperative proximal or distal DVT and who receive 6 to 12 weeks of anticoagulant therapy are not predisposed to PTS.

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DEEP VEIN thrombosis (DVT) is common after major hip or knee arthroplasty and can be complicated by pulmonary embolism and the postthrombotic syndrome (PTS).[1] In patients who are not given prophylaxis, 40% to 70% will develop DVT detected by routine predischarge venography (20%-30% proximal and the remainder isolated to the calf).[1] Several effective prophylactic regimens have been evaluated that reduce the DVT rate to 15% to 30%.[1] Recent studies have shown that despite high residual DVT rates demonstrated by routine predischarge venography, when a postoperative 7- to 10-day course of warfarin sodium or low-molecular-weight heparin sodium is given, the incidence of symptomatic DVT or pulmonary embolism is less than 4% within 3 months of surgery.[2,3] In addition, the incidence of symptomatic DVT or pulmonary embolism seems to be similar with warfarin or low-molecular-weight heparin, an observation that is surprising since low-molecular-weight heparin has been shown to be superior to warfarin in reducing the incidence of venographic DVT.[2,3] The explanation for the small proportion of venographic DVTs that are destined to cause symptoms is unclear but is probably partly due to the fact that asymptomatic thrombi are less likely to grow and cause symptoms and that a short course of anticoagulant therapy abrogates clot growth.

Postthrombotic syndrome consists of pain, swelling, and, sometimes, ulceration of the leg that can occur immediately after DVT or can have a delayed onset.[4] Postthrombotic syndrome can cause major morbidity and socioeconomic loss, and treatment, which consists primarily of

SUBJECTS AND METHODS

The study was approved by the institutional review board of the participating hospitals. All participants gave informed written consent. Participating hospitals included the McMaster University-based hospitals, Hamilton, Ontario, and the Academic Medical Centre, Amsterdam, the Netherlands.

STUDY POPULATION

Patients who had major hip or knee arthroplasty within the previous 2 to 7 years of study (from March 1993 through December 1998) and who had bilaterally adequate routine venography before discharge from the hospital were potentially eligible; this was irrespective of whether they had received prophylaxis and of what prophylaxis. The patients were designated to 1 of 3 groups: (1) patients with proximal DVT, further defined as thrombosis involving the popliteal and/or more proximal veins with or without concomitant calf vein thrombosis; (2) patients with distal DVT, further defined as thrombosis confined to the calf without proximal DVT; and (3) patients with no DVT. All patients with DVT received 6 to 12 weeks of warfarin therapy. A total of 255 subjects participated in the study, 25 with proximal DVT, 66 with distal DVT, and 164 with no DVT.

Lists of potentially eligible patients were obtained from the database that was generated as a part of several different orthopedic studies that have been performed at McMaster University and the Academic Medical Centre in the last 10 years. These studies enrolled patients who received therapy with a variety of low-molecular-weight heparins, warfarin, aspirin, or placebo as part of DVT prophylaxis. Patients were allocated according to the presence or absence of DVT and the location of DVT not according to the prophylaxis received. Consequently, all 3 groups (proximal DVT, distal DVT, and no DVT) had patients who received different prophylactic regimens.

STUDY INCLUSION CRITERIA

Potentially eligible patients were those who had undergone major knee or hip surgery 2 to 7 years prior to the study and had successful bilateral routine predischarge venography. Exclusion criteria among the patients meeting the inclusion criteria included the following: (1) geographic inaccessibility and (2) inability or refusal to give informed consent.

DIAGNOSIS OF PTS

There is no universal agreement on a definition of PTS. In its classic form, the afflicted patient will have swelling that is invariably progressive and usually is best in the morning (or after sleep) and worst at bedtime (after a full day of activity).

For this study, we used a definition that incorporates clinical relevance with objective evidence of venous valvular incompetence. Therefore, PTS was diagnosed when the patient had (1) typical pain and swelling—worse after standing and vertical activity and relieved by rest and the horizontal position—that was chronic (occurring daily for at least 1 month), persistent, occurred 6 months or longer after DVT, and (2) evidence of venous valvular incompetence by photoplethysmography and/or venous Doppler and/or air plethysmography (see the 3 subsections of the "Intervention" section).

INTERVENTION

Consenting eligible patients were first evaluated with the following tests for venous valvular incompetence.

Photoplethysmography

Photoplethysmography is a noninvasive test of venous valvular function in which a shortened venous refilling time is used to diagnose venous valvular incompetence.[5] Photoplethysmography was performed according to standard techniques.[5] Published reports, including our own, suggest that a venous refilling time of 20 seconds or longer is normal and suggests the absence of venous reflux, whereas a venous refilling time of less than 20 seconds strongly suggests the presence of venous reflux.

Venous Doppler

The detection of reflux in the common femoral, superficial femoral, popliteal, and/or posterior tibial veins is a reliable indication of valvular incompetence and was assessed.[5] For this study, we used duplex Doppler, which is the combination of venous Doppler and B-mode imaging.

Air Plethysmography

Air plethysmography is a noninvasive test that accurately measures venous valvular incompetence qualitatively and quantitatively, the latter providing advantages over photoplethysmography and venous Doppler. Therefore, not only can the presence or absence of venous reflux be ascertained but also the amount of reflux in milliliters per second can be estimated. The performance of the test has been standardized and preliminary evidence has suggested that reflux of 2 mL/sec indicates venous valvular incompetence (J.S.G., unpublished information, 1998), which was used as the cutoff point for this study.

MAIN OUTCOME MEASURES

The primary outcome measure for the study was the diagnosis of PTS. To make a diagnosis of PTS, patients had to have both of the following: (1) typical pain and swelling as described in the "Diagnosis of PTS" subsection of the "Subjects and Methods" section, and (2) evidence of venous valvular incompetence as assessed by abnormal photoplethysmography and/or venous Doppler and/or air plethysmographies. Patients who had symptoms but no reflux or reflux but no symptoms were considered to not have PTS.

STATISTICAL ANALYSIS

The primary analysis was a comparison of the proportions of patients who had PTS among the groups with proximal DVT, distal DVT, and no DVT. Proportions were reported as point estimates and their corresponding 95% confidence intervals (95% CIs) and compared using the Fisher exact test.

graduated compression stockings, often provides incomplete relief. The true incidence of PTS after major hip or knee arthroplasty is unknown because of a lack of well-designed studies; determining the incidence is further hampered by a lack of uniform definition of PTS. An accurate estimate of the incidence of PTS after major hip or knee arthroplasty is important because, if a significant proportion of asymptomatic thrombi are destined to cause morbidity from PTS, this would provide further impetus to develop agents that are superior to warfarin and low-molecular-weight heparin in reducing the incidence of postoperative DVT and/or to extend prophylaxis beyond discharge from the hospital to prevent new thrombi from developing. It would also suggest that although most asymptomatic DVT are not destined to enlarge and cause acute pulmonary embolism, they are clinically important.

To provide estimates of the incidence of PTS after major hip or knee arthroplasty, we conducted a cross-sectional study. The study population consisted of patients who had undergone major hip or knee arthroplasty 2 to 7 years previously (from March 1993 through December 1998) and had routine predischarge venography. Based on the results of the venogram, patients were categorized as having proximal DVT, distal (calf) DVT only, or no DVT. Patients completed a questionnaire (designed to determine if they had symptoms of PTS) and objective tests of venous valvular incompetence, all performed by personnel who were unaware of the DVT status of the patient.

RESULTS

The study began in March 1993 and finished in December 1998. A total of 255 subjects participated in the study, 25 with proximal DVT, 66 with distal DVT, and 164 with no DVT.

The demographic data and main results are given in the **Table**. The 3 groups are comparable for key covariables. Overall, 1 (4.0%, 95% CI = 0.1%-20.4%) of 25 patients with proximal DVT, 4 (6.1%, 95% CI = 1.7%-14.8%) of 66 patients with distal DVT, and 7 (4.3%, 95% CI = 1.7%-8.6%) of 164 patients with no DVT had PTS; these proportions are not significantly different ($P = .83$).

Demographics and Results of Patients With Postthrombotic Syndrome (PTS)

Demographic Characteristic	Deep Vein Thrombosis Group		
	Proximal	Distal (Calf)	None
Mean age, y	73.4	73.1	71.5
No. (%) male	13 (52)	30 (45)	72 (44)
Mean weight (range), kg	79.5 (61.5-108.5)	79.1 (51.9-117.5)	77.3 (47.5-118.9)
Mean duration of follow-up, y*	5.0	4.7	5.5
Type of surgery			
Elective hip	16	40	118
Elective knee	7	22	38
Fractured hip	2	4	8
History of VTE†	3	3	15
Subsequent history of VTE, No. (%) of patients	1 (4.0)	4 (4.8)	11 (6.9)
PTS positive, No. (%) of patients	1 (4.0)	4 (6.1)	7 (4.3)

**Mean duration of follow-up refers to the number of years from the time of the qualifying surgery to the time of postthrombotic syndrome.*
†VTE indicates venous thromboembolism.

COMMENT

The results of our study show that symptomatic PTS is an uncommon complication of major hip or knee arthroplasty and that postoperative proximal or distal DVT does not predispose to PTS in patients who receive 6 to 12 weeks of anticoagulant therapy for their postoperative DVT. The likely explanation is that the current practice of widespread prophylaxis not only reduces the incidence of venous thromboembolism, but also probably reduces the size of the thrombi in those who do develop DVT; such small thrombi are much less likely than the generally larger thrombi seen in symptomatic patients to cause venous valvular damage and obstruction that is associated with PTS. Although we cannot prove this directly, evidence from other studies indicates that thrombi are generally larger and more proximal in symptomatic outpatients than in postoperative orthopedic patients.[6]

It is important to examine the validity and generalizability of our study. First, our definition of PTS is stringent and one that is likely to miss mild cases of PTS because it necessitated specific symptoms and at least 1 objective test showing venous valvular incompetence. Our experience suggests that although persistent, mild, unilateral leg swelling is common after symptomatic DVT, and that in our study we would categorize such patients as "PTS-negative," such patients have minor morbidity. We believed it was important to have a specific diagnosis of PTS since leg swelling is common in the elderly, particularly those who have had major hip or knee arthroplasty. Second, the number of subjects in our study (and, in particular, those with proximal DVT) is small and it is possible that we missed a true small increase, but this is unlikely to be of major clinical significance. Third, it could be argued that the short interval between surgery and the study (average 4-5 years) was insufficient to allow us to evaluate accurately the true prevalence of PTS since it has been reported to have a latent onset—as long as 10 to 15 years. However, in our experience, latent development of PTS is uncommon. Finally, although we made efforts to minimize bias, there are 2 potential sources of bias in the study: first, there may have been selection bias in choosing control subjects, and second, a large proportion of potentially eligible patients died, and therefore it is possible that our study sample is not representative of all patients with postoperative DVT. However, both possibilities are unlikely to bias our study in a major way.

Recent studies have shown that almost 20% of patients who undergo major hip or knee arthroplasty and have a normal predischarge venogram develop DVT

within 1 month of hospital discharge if venography is repeated.[7,8] This, combined with the fact that many of our patients developed recurrent DVT, means that our classification underestimated the proportion of patients with proximal and distal DVT. However, since the prevalence of PTS was low in all 3 groups, this does not change our conclusion that the prevalence of PTS (both overall and after DVT) is low.

Our results should not be seen as questioning the need for primary prophylaxis in patients who have major hip or knee arthroplasty since prophylaxis reduces the incidence of venous thromboembolism and also probably reduces thrombus size in those that do break through. In addition, the identification of DVT and treatment of affected patients with anticoagulants could reduce the incidence of DVT by preventing thrombus extension and recurrence, both of which might predispose to PTS. This practice might contribute to the low incidence of PTS. However, our study suggests that the incidence of PTS is low after orthopedic surgery.

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