The prevalence of venous thromboembolism after hip and knee replacement surgery

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ABSTRACT

Objective: To determine the prevalence of venous thromboembolism (VTE) after total hip replacement (THR), total knee replacement (TKR) or bilateral TKR in a large sample of patients in a major hospital orthopaedic unit.

Design, setting and patients: The Mater Misericordiae Hospital, North Sydney, NSW, a 195-bed private hospital. All patients who had THR, TKR or bilateral TKR at the hospital between 1 April 1995 and 31 December 2001 had physical prophylaxis (graduated compression elastic stockings or intermittent pneumatic compression, or both) and chemical prophylaxis (anticoagulant) against VTE. All underwent ultrasonography of both legs before discharge, with a small, symptomatic group also undergoing a ventilation/perfusion lung scan (V/Q scan) and computed tomographic pulmonary angiography.

Main outcome measures: Prevalence of deep-vein thrombosis (DVT) and symptomatic pulmonary embolism (PE) before discharge.

Results: Among a total of 5999 patients, the pre-discharge prevalence of DVT after THR, TKR or bilateral TKR was 8.9%, 25.6% and 36.9%, respectively. The prevalence of symptomatic non-fatal in-hospital PE was 1.9%, while the prevalence of fatal in-hospital PE was 0.05%.

Conclusions: Despite short-term chemical and physical thromboprophylaxis, the prevalence of DVT after lower-limb joint replacement, measured by pre-discharge ultrasonography, was high. The rate of symptomatic non-fatal in-hospital PE was moderate, but fatal in-hospital PE was rare.

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Total hip replacement (THR) surgery, as we know it, began in 1960.[1] Total knee replacement (TKR), as currently performed, was first described in 1971.[2] While these operations are very successful, deep-vein thrombosis (DVT) and pulmonary embolism (PE) have been significant complications. The reported prevalence of DVT in patients not receiving prophylaxis in clinical trials using mandatory venography has been 45%–57% after THR[3-6] and 40%–84% after TKR.[7-10] The reported prevalence of PE in other trials has been 0.7%–30% after THR[11-15] (prevalence of fatal PE, 0.1%–0.4%), and 1.8%–7% after TKR (prevalence of fatal PE, 0.2%–0.7%).[16,17]

Lower-limb and respiratory symptoms and signs can be difficult to assess in the first few days after THR and TKR, making the clinical diagnosis of DVT and PE unsatisfactory.

Ultrasonography has improved greatly in recent years and is now capable of detecting even calf DVT satisfactorily. We believe it is suitable for pre-discharge screening of large numbers of patients after lower-limb joint replacement. Ventilation/perfusion nuclear scanning (V/Q scanning) is well established in the diagnosis of PE, with computed tomographic pulmonary angiography performed on selected patients in whom diagnostic doubt exists after a V/Q scan. In 1995, these investigations were readily available in our hospital.

The aim of our study was to determine the prevalence of venous thromboembolism (VTE) after THR, TKR or bilateral TKR in a large patient sample in a single institution over an extended period. The surgical procedures were accompanied by short-term chemical and physical prophylaxis. The diagnostic techniques used were ultrasonography, V/Q scanning and computed tomographic pulmonary angiography. To our knowledge, such a study had not been done before in Australia, with most reports in the literature describing multicentre studies involving relatively small numbers of patients at each institution.

METHODS

Setting and patients

Our study was conducted in the orthopaedic unit of the Mater Misericordiae Hospital ("the Mater Hospital"), North Sydney, NSW. This is a 195-bed private hospital affiliated with the University of Sydney.

All hospital patients who had THR, TKR or bilateral TKR during the period 1 April 1995 to 31 December 2001 were included in the study. Twenty-two orthopaedic surgeons were involved with performing these procedures during the study period.

In the majority of cases, the same physician who saw the patient before admission treated the patient for any postoperative medical complications.

Prophylaxis

All patients were given chemical and physical prophylaxis.

Chemical prophylaxis. Patients were given either low-molecular-weight heparin (LMWH) or warfarin, according to the surgeon's preference. Administration of LMWH (once-daily subcutaneous enoxaparin 40 mg or dalteparin 5000 IU) or warfarin orally, to achieve an INR of 2.0–3.0 in 48 hours) was begun on the night of the operation and continued throughout the hospital stay of 6–7 days.

No aspirin, anti-inflammatory drugs or preoperative anticoagulants were used.

Physical prophylaxis. Full-leg graduated compression elastic stockings were worn postoperatively. From June 1996 (15 months after the beginning of the study), all patients were given intermittent pneumatic calf compression from the time of admission and wore the apparatus at all times they were in bed until they were fully ambulant

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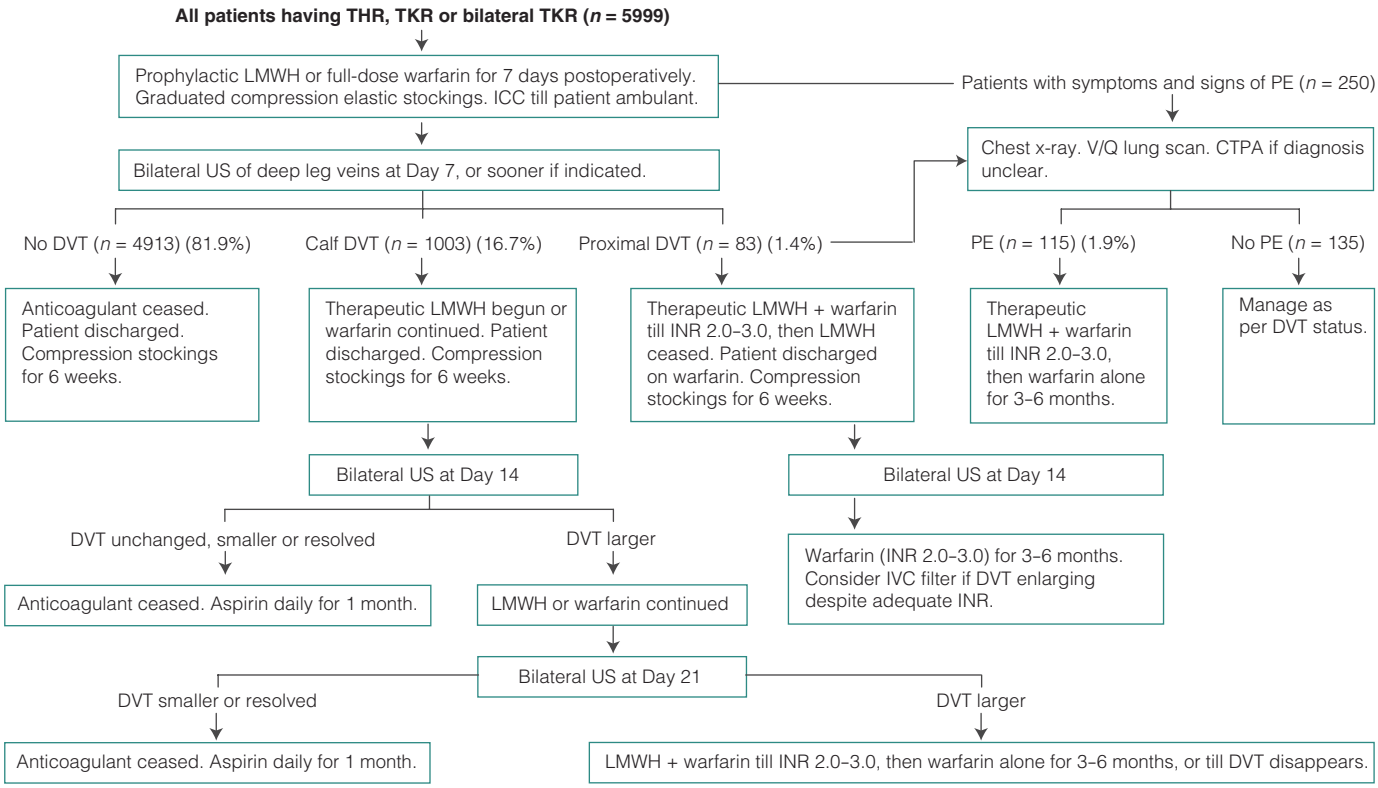
1 Management algorithm for patients having THR, TKR or bilateral TKR at the Mater Misericordiae Hospital, North Sydney, NSW, Apr 1995–Dec 2001



CTPA = computed tomographic pulmonary angiography. DVT = deep vein thrombosis. ICC = intermittent calf compression. INR = international normalised ratio. IVC = inferior vena cava. LMWH = low-molecular-weight heparin. PE = pulmonary embolism. THR = total hip replacement. TKR = total knee replacement. US = ultrasonography. V/Q lung scan = ventilation/perfusion lung scan.

3–4 days after surgery. This technique was not readily available before June 1996.

Scanning techniques

Ultrasonography

For all patients at the Mater Hospital who had THR, TKR or bilateral TKR during the study period, bilateral ultrasonography of the veins of both legs, from groin to lower calf, was performed on Day 7 postoperatively, or sooner if clinically indicated. There were no exclusions.

Both legs were examined. Deep veins imaged were the axial veins (common femoral, superficial femoral, popliteal, peroneal and posterior tibial veins) and extra-axial veins (gastrocnemius and soleus veins).

The common femoral veins were interrogated by doppler ultrasound to elicit phasic response (normal variation in waveform with breathing and talking), confirming patency of the common and external iliac vessels.

The patient was required to sit or, preferably, stand. The thigh vessels were examined with the patient supine, and the popliteal fossae and calves with legs dependent.

Early imaging was performed with a Diasonics 2D Gateway device (Aliso Viejo, Calif, USA) and, from February 2000, a GE Logiq 9 device (Milwaukee, Wis, USA) with a 5.0 MHz/60 matched-impedance convex-linear-array probe, using similar but updated technology.

All vessels were imaged in B mode (cross-sectional ultrasound), compressed by probe and interrogated by doppler imaging as appropriate.

Ventilation/perfusion nuclear scanning

Six-view planar aerosol ventilation scans and six-view Tc 99m MAA (macroaggregated albumin) perfusion lung scans were performed on patients showing any signs or symptoms of PE.

Management

Our management approach is summarised in the algorithm in Box 1. If no DVT was found within 7 days, the patient was discharged to home or a rehabilitation hospital with no chemoprophylaxis against VTE, although most surgeons advised patients to wear graduated compression elastic stockings for 6 weeks.

Distal (calf) DVT

If calf DVT (in the posterior tibial, peroneal, gastrocnemius or soleus veins) was found at Day 7, the patient was given therapeutic doses of LMWH (subcutaneous enoxaparin 1 mg/kg or dalteparin 100 IU/kg 12-hourly) or warfarin (to maintain an INR of 2.0–3.0), according to the preference of the surgeon, for a further 7 days.

On Day 14, a second bilateral ultrasound scan was performed on patients with previous thrombi who were available for testing at the Mater Hospital. (Patients who lived too far away to return to the hospital had arrangements made with their local doctor to organise a scan elsewhere and provide follow-up.)

If the second scan showed that the calf thrombus was the same size, was smaller, or

2 Pre-discharge prevalence of DVT and pulmonary embolism after hip or knee replacement surgery (total *n* = 5999)

	After THR (*n* = 3028)	After TKR (*n* = 2441)	After bilateral TKR (*n* = 530)	Total
Total number of patients with DVT	263/3028 (8.9%)	627/2441 (25.6%)	196/530 (36.9%)	1086/5999 (18.1%)
Patients with distal DVT	217/263 (82.5%)	596/627 (95.1%)	190/196 (96.9%)	1003/1086 (92.4%)
Patients with proximal DVT	46/263 (17.5%)	31/627 (4.9%)	6/196 (3.1%)	83/1086 (7.6%)
Patients with contralateral DVT (ie, in non-operated leg)	55/263 (20.9%)	56/627 (8.9%)	n/a	
Proportion of deep-vein thrombi larger at Day 14 despite 7 days' treatment*	7.0%	10.0%	7.0%	
Proportion of deep-vein thrombi same size, smaller or absent at Day 14 after 7 days' treatment*	93.0%	90.0%	93.0%	
Symptomatic in-hospital pulmonary embolism (*n* = 115)	37/3028 (1.2%)	68/2441 (2.8%)	10/530 (1.9%)	115/5999 (1.9%)
Patients with three or more deep-vein thrombi	13/263 (4.9%)	75/627 (12.0%)	35/196 (17.9%)	

DVT = deep vein thrombosis. THR = total hip replacement. TKR = total knee replacement.
* Based on 528 (49%) patients with thrombus.

had disappeared, LMWH or warfarin was stopped and the patient was instructed to take 100 mg of aspirin daily for 1 month, unless there were contraindications. If the thrombus had increased in size, therapeutic doses of LMWH or warfarin were continued for a further week, when the ultrasound scan was repeated on Day 21.

If the third ultrasound scan showed the calf thrombus was shrinking, LMWH or warfarin was stopped and aspirin given, as above. If the thrombus had grown by Day 21, warfarin was begun in patients who had previously been taking LMWH (LMWH was stopped once the INR was between 2.0 and 3.0), and was continued in the 12% of patients already taking warfarin. Warfarin treatment was then continued for 3–6 months, or until the DVT had disappeared.

Proximal (thigh) DVT

If proximal DVT (in the popliteal, superficial femoral or common femoral veins) was found on ultrasonography on Day 7, LMWH and warfarin were used as described above for the extending calf DVT. A V/Q scan was also performed on these patients.

Pulmonary embolism

Patients with symptoms and signs suggestive of PE (eg, chest discomfort, arrhythmia or hypoxia) had a chest x-ray and V/Q scan as a primary investigation, with computed tomographic pulmonary angiography performed if the diagnosis was uncertain. If PE was diagnosed, warfarin was used in the same way as described for the extending calf DVT or the proximal DVT. Follow-up ultrasonography and V/Q scans were done as necessary.

Statistical analysis

All results were recorded daily, entered into a database, and reviewed at 3-monthly intervals throughout the study.

Odds ratios for the differences in risk of DVT between patients receiving different forms of chemical and physical prophylaxis were calculated using standard χ^2 methods.[18] *P* values were 2-sided ($\alpha = 0.05$). Although a small number of patients had knee replacements at different times in the course of the study, the proportion of "double counting" in the TKR group was small (3%) and was not considered significant.

RESULTS

Population characteristics

The total number of patients included in our study was 5999. Of the preoperative medical disorders, cardiac disease was the most common, followed by respiratory disease, then renal disease.

Forty-eight per cent of the patients were men (mean age, 67 years; range, 19–100 years). Among the 19% of men who had DVT, the mean age was 68 years (range, 26–100 years); the mean age of men without DVT was 67 years (range, 19–100 years).

The mean age of female patients was 69 years (range, 17–100 years). Among the 17% of women with DVT, the mean age was 72 years (range, 32–100 years); the mean age of women without DVT was 66 years (range, 17–100 years).

Prevalence of DVT

The number of patients developing DVT within 7 days postoperatively was 263/3028 (8.9%) after THR, 627/2441 (25.6%) after TKR, and 196/530 (36.9%) after bilateral TKR (Box 2).

Progress of DVT

Follow-up ultrasonography at Day 14 postoperatively was performed in the 528 (49%) patients with DVT who were able to return as outpatients for follow-up or (in rare cases) were still inpatients. The behaviour of thrombi was similar for THR, TKR and bilateral TKR patients, with thrombi extending (in spite of appropriate treatment) in 7%–10% of patients, unchanged in 7%–13%, shrinking in 48%–60%, and resolved in 25%–30%.

Prevalence of in-hospital symptomatic pulmonary embolism

Non-fatal. Of 250 V/Q scans performed, 115 (1.9%) were positive for PE (Box 2).

Fatal. Three fatal pulmonary emboli occurred among the 5999 patients in the study (a prevalence of 0.05%). The three deaths were all after knee replacements.

One man, aged 75, with a history of PE after appendicectomy and herniorrhaphy as a young man and an uneventful TKR in 1991, had a TKR in 1998 during our study. Multiple pulmonary emboli were detected on Day 7 postoperatively, associated with massive DVT. He died on Day 23.

A second man, aged 84, with a history of mild chronic obstructive airway disease, developed a pulmonary infection after a TKR during our study. An initial V/Q scan was negative, but a second scan late in the illness was positive. He also suffered a myocardial infarction and died on Day 36.

A third man, aged 76, a chronic smoker with bronchiectasis, collapsed 5 days after bilateral TKR and could not be resuscitated. PE was thought to be the probable cause of death.

3 Proportion of patients with DVT after 7 days, according to whether they received intermittent calf compression (ICC) or no calf compression*

	With ICC	Without ICC	Odds ratio (95% CI)	*P*
After THR	6.9%	17.5%	0.34 (0.26–0.45)	< 0.0001
After TKR	23.2%	42.1%	0.41 (0.32–0.52)	< 0.0001
After bilateral TKR	34.5%	58.5%	0.37 (0.21–0.66)	0.0011

DVT = deep vein thrombosis. THR = total hip replacement. TKR = total knee replacement.
*ICC was not introduced until June 1996 (15 months after the beginning of the study).

4 Proportion of patients with DVT after 7 days, according to whether they received warfarin or low-molecular-weight heparin (LMWH)*

	Warfarin	LMWH	Odds ratio (95% CI)	*P*
After THR	12.5%	8.6%	1.49 (0.94–2.38)	< 0.0115
After TKR	35.5%	23.6%	1.79 (1.43–2.24)	< 0.0001
After bilateral TKR	47.1%	33.9%	1.73 (1.14–2.61)	0.0118

DVT = deep vein thrombosis. THR = total hip replacement. TKR = total knee replacement.
*The choice of anticoagulant was made by the surgeon rather than randomly assigned.

Association between PE and DVT

Twenty (17%) of the 115 patients with symptomatic in-hospital PE had proximal DVT, 63/115 (54%) had calf DVT, and 30/115 (27%) had no DVT on ultrasonography during their in-hospital stay of 7 days. This does not show that calf DVT causes PE, but does show that many symptomatic in-hospital pulmonary emboli are associated with either calf DVT or no DVT at all.

Risk of DVT

Risk of any DVT after different types of surgery. The risk of DVT was greater after TKR than THR (odds ratio [OR], 3.64; 95% CI, 3.12–4.26; $P < 0.001$), and much greater after bilateral TKR than THR (OR, 6.17; 95% CI, 4.97–7.66; $P < 0.001$). The risk was also greater after bilateral TKR than TKR (OR, 1.69; 95% CI, 1.39–2.07; $P < 0.001$). The cumulative risk of DVT for two TKRs in the one patient, weeks or months apart, was greater than for bilateral TKR.

Risk of thigh DVT after different types of surgery. Thigh DVT was much more likely after THR than either TKR (OR, 4.19; 95% CI, 2.59–6.77; $P < 0.001$) or bilateral TKR (OR, 6.89; 95% CI, 2.88–16.47; $P < 0.001$).

Risk of any DVT after different types of prophylaxis. The risk of DVT was much less in patients who had intermittent calf compression in the first 7 days postoperatively than patients who did not (Box 3).

The majority of patients (88%) were given LMWH prophylaxis for the first 7 days postoperatively, with only 12% given warfarin. The risk of DVT was greater in patients taking warfarin than those taking LMWH (Box 4). However, this result should be interpreted with caution, as the choice of anticoagulant was made by the surgeon rather than randomly assigned.

There was no excess of bleeding, infection or wound complication associated with prophylactic anticoagulation therapy.

DISCUSSION

The principal strengths of our study were that it involved a large cohort of consecutive patients in a single institution over a period of nearly 7 years. We also had the advantage of retaining, throughout the study, the same radiologist (I A B) to supervise ultrasound scans and the same chief ultrasonographer.

A limitation of our study was that it did not have controls to enable comparison between different forms of management. Thus, for example, no conclusions can be drawn from our study about whether ultrasonography is as effective as venography for detecting DVT, or whether LMWH is better than warfarin for prophylaxis.

Also, patients without DVT on ultrasound at Day 7 were not restudied for DVT. Although we think it is uncommon, it is possible some of these patients may have developed new thrombi after leaving hospital on Day 7, in which case we may have underestimated the prevalence of DVT.

The 6th American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy reviewed numerous studies of VTE involving various prophylactic measures.[15] In 30 trials of LMWH prophylaxis (involving a total of 6216 patients), total DVT prevalence after THR was 16.1%, and in 13 trials (involving a total of 1740 patients) total DVT prevalence after TKR was 30.6%. The corresponding prevalences in our study — 8.9% and 26.9%, respectively — were lower than the ACCP prevalences.

Chemical and physical prophylactic measures may have an additive effect on VTE reduction, and this may account for the lower prevalence of VTE in our patients, all of whom received both forms of prophylaxis.

Our patients were studied by ultrasonography, while the patients in the ACCP review were studied by venography. It has been said that ultrasonography is less sensitive than venography, and, in a 1995 meta-analysis, Wells et al concluded, for that reason, that ultrasonography had limitations as a screening test after orthopaedic surgery.[16] However, the studies on which that conclusion was based were done between 1982 and 1993. In 1994, Oishi et al found that, for detection of DVT after THR and TKR, ultrasonography had 100% sensitivity, 98% specificity and 98% accuracy in men and 88% sensitivity, 98% specificity and 97% accuracy in women.[19] Since then, ultrasound technology has improved, and calf DVT can be well seen and measured to the nearest centimetre.

The ACCP review did not recommend routine ultrasonography at the time of hospital discharge or during outpatient follow-up in asymptomatic THR or TKR patients. It quoted the study of Leclerc et al,[17] who concluded that "pre-discharge compression ultrasound cannot be justified". However, that study used a "limited ultrasound method that [had] been shown to be sensitive to proximal vein thrombosis in symptomatic patients", suggesting that the method was insensitive for detecting distal DVT.

Leclerc et al found that only 3/1936 (0.2%) of THR and TKR patients who received in-hospital LMWH prophylaxis had asymptomatic DVT on pre-discharge ultrasonography. Of our 4874 THR and TKR patients taking prophylactic LMWH, 719 developed DVT (14.8%). In view of the huge discrepancy between the data of Leclerc and colleagues and ours, we believe that their ultrasonography technique may have been inadequate for detecting calf DVT. This would have resulted in a much lower prevalence of total DVT than in our study, where 82%–97% of deep-vein thrombi were

in the calf. Leclerc et al also excluded patients with a previous history of VTE, whereas we had no exclusions.

Detection and significance of DVT

The question of whether calf DVT is clinically significant is fundamental to the decision as to whether pre-discharge imaging for DVT should be done. It should only be done if the benefits outweigh the disadvantages. Venography, the method used in previous research studies, is not suitable for routine evaluation, especially in large studies like ours. It is time-consuming, uncomfortable, and can cause thrombosis and allergic reactions.

Ultrasonography is safe, comfortable and accurate, but to justify its routine use one would have to feel that DVT (which, in our case, mostly means calf DVT) is a serious enough disorder to warrant detection and treatment. DVT can cause postphlebitic syndrome, but little is known about the prevalence or severity of this condition after calf DVT. The other complication of DVT is PE, but it is not known whether calf DVT can actually cause PE.

DVT and pulmonary embolism

Presumably, if PE occurs without any DVT being found in the leg, the PE has either come from the pelvis, or a thrombus from the leg has completely embolised to the lung. However, if a patient has calf DVT and PE, it is possible there may have been an additional thrombus in the pelvis or thigh that embolised completely, leaving the patient with PE and calf DVT. We believe it is also possible, especially when there is extensive calf DVT, that some of the calf thrombus may become detached and cause PE with residual calf DVT.

It may be that with intensive prophylaxis over the years, the pattern of leg DVT is changing, with a higher proportion of calf thrombi than previously. This was suggested by Ciccone et al in 1998.[20] In a number of studies in the early 1990s, the proportion of calf deep-vein thrombi relative to total deep-vein thrombi in patients not receiving prophylaxis was 30%–50% after THR and 70%–75% after TKR.[15] In our study, with prophylaxis, the total prevalence of DVT was much lower (18.1%), and the proportion of calf thrombi was higher (83% after THR and 95% after TKR). It may be that, with current technology, we can better detect calf DVT, or it may mean that prophylaxis not only reduces the prevalence of total thrombi but also results in a preponderance of calf thrombi. We know that calf thrombi can extend, and if they become thigh thrombi would be more likely to cause PE.

In assessing whether a deep-vein thrombus in the leg will embolise, the total length of thrombus may be important. The mean total length of thrombus in our patients was 10 cm, but the mean total thrombus length in those with symptomatic in-hospital PE was 19 cm, suggesting that total thrombus length may be important in embolisation.

Management and length of follow-up

Planes et al found that the risk of late DVT after THR is high until Day 35 post-operatively if prophylaxis is not continued after leaving hospital.[21] A study by White et al found that the median time of diagnosis of symptomatic DVT is Day 17 after THR and Day 7 after TKR.[22] Comp et al showed that a 4-week course of enoxaparin prophylaxis after THR gave therapeutic benefit, reducing the incidence of VTE without compromising safety (however, a similar benefit was not seen in TKR patients).[23]

Given the uncertain behaviour of post-operative deep-vein thrombi, we believe that pre-discharge ultrasonography is helpful. It assists in planning post-discharge VTE management, an important point in our situation, where many patients face long trips home by car or plane, often to small centres with limited medical facilities. There is some evidence that ultrasonography will detect nearly all deep-vein thrombi by Day 7: in 200 consecutive THR and TKR patients showing no DVT on ultrasound at Day 7 managed with the same protocol as ours in a similar hospital in Sydney the prevalence of DVT on ultrasound at Day 90 was only 1% (Michael McGrath, Vascular Physician, St Vincent's Hospital, Sydney, personal communication). This would suggest that post-discharge "symptomatic" DVT is almost always visible on ultrasonography by Day 7. Whatever the case, the concept of "symptomatic" and "asymptomatic" DVT is flawed, as nearly all patients have pain and swelling in the leg (especially the calf) after THR or TKR, making accurate, early clinical diagnosis of DVT impossible.

Further studies comparing the VTE status of all patients at 90 days postoperatively with their status at 7 days would help in understanding the pathogenesis of VTE after lower-limb joint replacement.

Finally, while many deep-vein thrombi are relatively harmless, some are associated with PE, which, in rare instances, can be fatal. The dilemma is in knowing which thrombi are the dangerous ones.

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COMPETING INTERESTS

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