

Screening for venous thrombosis by ultrasonography before hospital discharge after major joint surgery

What is the evidence?

Venous thrombosis and pulmonary embolism continue to be significant complications of hip or knee replacement surgery. Seven to 10 days of anticoagulant prophylaxis starting before or soon after surgery fail to prevent 20%–30% of venous thromboembolic events. It is this residual thrombosis rate that provides a spur for adding pre-discharge screening to routine prophylaxis, with the aim of detecting and treating silent thrombosis before it progresses to clinical disease.

In this issue of the Journal, O'Reilly and colleagues (page 154) report on routine venous ultrasound examination performed on almost 6000 patients before discharge from hospital 6–7 days after major joint surgery.¹ Within this large cohort, subclinical deep vein thrombosis (DVT) was detected in 9%, 26% and 37% of patients after hip, knee or bilateral knee replacement, respectively. This was despite intensive in-hospital prophylaxis using an anticoagulant (mostly low-molecular-weight heparin) plus intermittent calf com-

pression and the use of elastic stockings. Thrombosis was proximal (affecting the popliteal, femoral or iliac veins) in 1.5%, 1.3% and 1.1% of patients after hip, knee or bilateral knee replacement, respectively.

When considering how best to use this information, we should ask several questions.

First, is ultrasonography reliable for detecting subclinical DVT? Although it is preferred for investigating clinically suspected disease, opinions are divided about its value in screening for subclinical thrombi, which are often no more than a few centimetres long. Ultrasonography is observer-dependent, and screening by this method has not been validated through large, blinded comparisons with the "gold standard" of bilateral venography. However, an excellent systematic overview of ultrasonography² has reported a positive predictive value for subclinical proximal DVT of over 80% if disease prevalence is low and the false positive

rate is no more than 5% (results with calf DVT were less impressive). So the 1%–1.5% proximal DVT rate reported by O'Reilly et al is probably valid.

Second, are the DVT rates seen by O'Reilly et al consistent with previously reported results of routine venography? The answer is yes. Overall DVT rates 5–10 days after hip replacement in people given warfarin, low-molecular-weight heparin, fondaparinux (a specific inhibitor of activated factor X) or ximelagatran (an oral thrombin inhibitor) have been shown to be about 20%, 10%, 4%, and 8%, respectively, while proximal DVT rates are about 5%, 2%, 1.5%, and 3%, respectively.^{3,4} Reported rates of DVT after knee replacement are also consistent.^{3,4} If anything, the rate of proximal DVT found by O'Reilly et al is on the low side, perhaps because they combined chemical with physical prophylaxis and/or because ultrasound examination is less sensitive for detecting proximal DVT than is venography.

Third, does ultrasonographic screening at discharge bring any clinical benefit? We just do not know. Logic suggests it should, but attempts to validate the value of pre-discharge screening by randomised trials have failed. Perhaps the trials were underpowered to detect real but small reductions in rates of venous thromboembolism. Or perhaps it is a wrong assumption that new thrombus formation is not a problem once patients leave hospital.

We now know that thrombosis risk after major joint (especially hip) surgery persists for at least 4–6 weeks and that duration of prophylaxis is a major determinant of success. The rates of venous thromboembolism (subclinical, symptomatic and confirmed) in randomised comparisons are substantially reduced by persisting with preventive therapy until 4–5 weeks after a hip fracture or hip replacement rather than stopping (as in the study by O'Reilly et al) when patients are discharged from hospital.^{3,5,6} Hence, the recent recommendation by the American College of Chest Physicians (ACCP) for at least 10 days' prophylaxis after major joint surgery, extending to 28–35 days after hip arthroplasty or hip fracture.³ The obvious explanation for reduced rates of venous thromboembolism is suppression of late thrombus formation. More intriguing is the apparent resolution of small venous thrombi formed soon after surgery — an effect best seen in one of the fondaparinux trials (the "PENTHIFRA-Plus" trial),⁵ in which the venographically detected thrombosis rate with ongoing prophylaxis was negligible (1.4%) 4 weeks after hip fracture surgery and well below the 8.3% rate previously found after 7 days of preventive therapy.⁶ (The latter rate is similar to the 9% DVT rate observed by O'Reilly et al after 1 week of intense prophylaxis.) By contrast, the thrombosis rate after 4 weeks among PENTHIFRA-Plus trial patients given a placebo following 1 week of fondaparinux therapy was 35%,⁵ a figure much higher than the 8.3% observed after 7 days in the earlier trial.⁶

The high DVT rates observed by O'Reilly et al confirm that in-hospital prophylaxis alone is not enough. Many would argue that extended prophylaxis is likely to be the simplest, cheapest and perhaps safest solution. Even if pre-discharge screening for sub-clinical disease might pre-empt the need for continued prophylaxis, there remain significant questions of resource availability, cost and possible harm. Ultrasound examination alone, if done in all patients and followed by further testing in the 9% or 26% of patients with thrombosis after unilateral hip or knee surgery, would cost (at current Medicare Benefits Schedule rates) about \$200 000 per 1000 patients.

The approach of O'Reilly et al was to treat all clots, regardless of their extent or position, with full doses of an anticoagulant for at

least 2 weeks. This includes silent clots in the soleus or gastrocnemius muscle veins whose natural history is uncertain and perhaps mostly benign.⁷ But any decision to use anticoagulant therapy must balance potential benefit with likely bleeding risk. In this case, both remain unknowns, as the authors do not report on treatment complications.

Evidence-based recommendations by expert groups are not prescriptions, and require judgement when applied to clinical practice. Even so, we should note the recent, firm (Grade 1A) recommendation by the 7th ACCP Conference on Antithrombotic and Thrombolytic Therapy³ against routine screening for DVT after major joint surgery, based on the lack of any demonstrable clinical effectiveness or cost-effectiveness of such screening.

Alexander S Gallus

Director of Pathology Services, SouthPath
Flinders Medical Centre, Bedford Park, SA
alexander.gallus@flinders.edu.au

Competing interests: The author has received consulting fees for participating in clinical trial steering committees (from Sanofi, Bristol-Myers Squibb, Bayer and Organon) and expert committees (from AstraZeneca, Bayer and CSL).

- 1 O'Reilly RF, Burgess IA, Zicat B. The prevalence of venous thromboembolism after hip and knee replacement surgery. *Med J Aust* 2005; 182: 154-159.
- 2 Kassai B, Boissel JP, Cucherat M, et al. A systematic review of the accuracy of ultrasound in the diagnosis of deep venous thrombosis in asymptomatic patients. *Thromb Haemost* 2004; 91: 655-666.
- 3 Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126(3 Suppl): 338S-400S.
- 4 Weitz JI, Hirsh J, Samama MM. New anticoagulant drugs: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126(3 Suppl): 265S-286S.
- 5 Eriksson BJ, Lassen MR; PENTHIFRA Surgery Plus (PENTHIFRA-Plus) Investigators. Duration of prophylaxis against venous thromboembolism with fondaparinux after hip surgery: a multicenter, randomized, placebo-controlled, double-blind study. *Arch Intern Med* 2003; 163: 1337-1342.
- 6 Eriksson BJ, Bauer KA, Lassen MR. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med* 2001; 345: 1298-1304.
- 7 Macdonald PS, Kahn SR, Miller N, Obrad D. Short-term natural history of isolated gastrocnemius and soleal vein thrombosis. *J Vasc Surg* 2003; 37: 523-527.

