Venous thromboembolism following prolonged cast immobilisation for injury to the tendo Achillis

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We report an audit of 208 patients with a mean age of 39 years (16 to 65) attending the Orthopaedic Assessment Unit at the Wellington Hospital between January 2006 and December 2007 with an injury of the tendo Achillis requiring immobilisation in a cast. Information on assessment of venous thromboembolism (VTE) risk, prophylactic measures and VTE events for all patients was obtained from the medical records. A VTE risk factor was documented in the records of three (1%) patients. One of the 208 patients received aspirin prophylaxis; none received low molecular weight heparin. In all, 13 patients (6.3%, 95% confidence interval 3.4 to 10.5) developed symptomatic VTE during immobilisation in a cast, including six with a distal deep-vein thrombosis (DVT), four with a proximal DVT, and three with a confirmed pulmonary embolus. This incidence of symptomatic VTE is similar to that reported following elective hip replacement.

We propose that consideration is given to VTE prophylaxis during prolonged immobilisation of the lower limbs in a cast, to ensure that the same level of protection is provided for patients undergoing elective hip replacement.

Prolonged cast immobilisation of the lower limb following injury is associated with an increased risk of venous thromboembolism (VTE), presenting as deep-vein thrombosis (DVT) and/or pulmonary embolism. A number of factors are likely to contribute to the risk, including the trauma itself, surgical intervention, and the subsequent prolonged period of immobilisation of the lower limb. Prophylaxis with low molecular weight heparin (LMWH) significantly reduces the risk of VTE during immobilisation of the lower limb, without an increased risk of major bleeding complications.

About one in six patients, not initially identified as being at high risk, will experience a VTE event following immobilisation of the lower limb in a POP cast if thromboprophylaxis is not administered. In most the event is an asymptomatic distal DVT, with the diagnosis made by radiological screening during a randomised controlled trial. Symptomatic VTE events generally present within the first four weeks of immobilisation, although DVT has been reported within 24 hours of application of the cast. The type of injury does not greatly influence the risk, which is similar for both tendon injuries and fractures.

In this study we investigated the incidence of symptomatic DVT and pulmonary embolism in a cohort of patients who had prolonged immobilisation of the lower limb in a cast for injury of the tendo Achillis. The assessment of risk factors for VTE, use of LMWH or aspirin prophylaxis and the clinical features of the VTE episodes are presented. The clinical significance of the findings is considered and compared with recommendations for prophylaxis for VTE in elective hip replacement surgery.

Patients and Methods
From the clinical database of patients presenting to the acute Orthopaedic Assessment Unit at Wellington Hospital, Capital and Coast District Health Board between January 2006 and December 2007, 237 patients aged 16 to 65 years with a confirmed injury of the tendo Achillis, including partial and complete rupture, laceration, chronic tendonitis and admission for surgical repair, were identified. All 208 patients were treated with immobilisation in a cast for longer than one week as an outpatient. Patients were excluded if they had a tendo Achillis injury that did not require cast immobilisation, if the diagnosis was not confirmed, or if their medical follow-up was outside the Capital and Coast District Health Board. Each patient was only included in the audit once, so repeat presentations were considered part of the initial event. From the electronic medical and clinic records, characteristics of the patients and their
management were documented, including basic demographic details, the nature of the injury of the tendo Achillis and approach to management, either conservative or operative. Documented risk factors for VTE were noted, as was the consideration for or administration of prophylactic LMWH or aspirin.

Patients who subsequently developed a DVT or pulmonary embolism were identified by review of their hospital medical records and the Capital and Coast District Health Board VTE database. This contains comprehensive clinical details of all patients aged 16 to 65 years attending the VTE Service which follows all community and hospital inpatient referrals in whom a diagnosis of DVT or pulmonary embolism was made. In order to be included, patients had an injury of the tendo Achillis, managed with cast immobilisation within four weeks of the onset of symptoms of the VTE event, and the clinical diagnosis of DVT or pulmonary embolism had to be confirmed either by Doppler ultrasound of the lower limb or by chest CT with pulmonary angiography. The characteristics of the VTE event were documented, including the site and extent of the DVT and/or pulmonary embolism. A pulmonary embolism was considered massive if associated with major proximal thrombus and hypotension (systolic BP < 90 mmHg) and submassive if a major proximal thrombus was present, together with electrocardiogram (ECG) evidence of right ventricular strain and/or a troponin T rise. Factors which may have contributed to the risk of VTE were documented, including thrombophilia status, coexisting medical illness, use of prothrombotic medication, and other reasons for prolonged immobility, such as seated travel for more than four hours.

This audit was approved by the Coast District Health Board Quality Assessment Unit.

**Statistical analysis.** The incidence of a VTE event was compared between the operative and non-operatively treated patients using chi-squared analysis. A p-value of < 0.05 was considered significant.

**Results**

Of the 208 patients included in the study group, 205 (98.7%) had a partial or complete rupture of the tendo Achillis and three patients had other conditions affecting the tendon (Table I). The treatment was changed to operative intervention within seven days of presentation in 35 patients (16.8%) and a further ten patients (4.8%) had subsequent surgery for re-rupture or failure of the non-operative approach. Nevertheless in all 208 patients were treated in a plaster cast for more than one week. The mean duration of immobilisation could not be calculated from the case notes, however, the routine policy of the orthopaedic department following rupture of the tendo Achillis is a minimum of six to eight weeks of immobilisation in a
A specific VTE risk factor was documented in three patients (1.4%), at presentation, namely an imminent long-distance flight in two and pregnancy in the third. One of the travellers was prescribed aspirin and a compression stocking for the normal limb. After consideration, no prophylactic measures were prescribed for the pregnant woman or the other traveller.

No patient in the series received LMWH prophylaxis.

Of the 208 patients, 13 (6.3%, 95% confidence interval (CI) 3.4 to 10.5) developed a confirmed VTE event (Table III), all presenting with symptoms suggestive of a DVT and/or pulmonary embolism and who therefore underwent radiological investigation. No DVT was identified in an additional 22 cases in which ultrasound examination of the lower limb was performed to assess healing of the injury of the tendo Achillis or for investigation of symptoms suggestive of DVT.

The mean age of the patients with a VTE event was 44 (32 to 55) years, compared with 39 (16 to 65) years in those without.

Doppler ultrasound confirmed isolated distal DVT in six patients, and proximal DVT in four, of whom two had a high clinical probability of concomitant pulmonary embolism with symptoms of breathlessness and pleuritic chest pain, but did not undergo further radiological investigation (Table III). Three patients had a pulmonary embolism identified by CT with pulmonary angiography. In two of these the embolus was submassive, one with right ventricular infarction (troponin T level of 0.09 ng/ml; normal range < 0.03) and the other a saddle embolism with ECG changes of right ventricular strain but no rise in troponin T.

Approximately half the VTE patients could have been considered as at increased risk of VTE according to their history.
tory at presentation. This included a positive family history, BMI > 30 kg/m², significant medical comorbidity and planned long-distance travel (Table III). Another patient was considered at risk due to Factor V Leiden heterozygous status, discovered following diagnosis of the VTE event.

All VTE events presented between one and ten weeks after application of the cast, and there was a trend towards more proximal DVT and pulmonary embolism with increased duration of immobility (Table III). All patients with VTE received warfarin therapy with initial LMWH cover.

Of the 35 patients who underwent surgery within seven days of presentation of injury to the tendo Achillis, there was no case of VTE. The absolute risk difference between primary surgical intervention and conservative management was not statistically significant (p = 0.13, Fisher’s exact chi-squared test).

Discussion
In this series, a symptomatic DVT and/or pulmonary embolism was identified in 13 patients (6.3%) managed with cast immobilisation after injury to the tendo Achillis. The symptomatic VTE occurred in a population that was not routinely assessed for VTE risk and, apart from one patient, did not receive prophylaxis.

Our incidence of symptomatic VTE was higher than the 2.5% reported in the placebo groups of a recent Cochrane meta-analysis of randomised controlled trials (RCTs) of LMWH prophylaxis in lower limb cast immobilisation. This difference is likely to be partly due to the study design of the RCTs, which excluded patients at high risk of VTE. Also, all RCTs included in the meta-analysis employed early routine screening for DVT, which led to the identification of asymptomatic DVT in 17.1% when no prophylaxis was provided. Some trials specifically reported that full anticoagulation treatment was initiated after the diagnosis of asymptomatic VTE was made. This would have reduced the risk of a symptomatic event due to subsequent thrombus extension or embolisation. It is therefore likely that the incidence of symptomatic VTE reported in RCTs involving patients with immobilisation of the lower limb in a cast cannot be generalised to the unselected population of patients presenting in routine clinical practice, where the incidence is likely to be considerably higher, as shown in our study. Indeed, our incidence of symptomatic VTE may well be an underestimate, as some patients may not have reported or been investigated for symptoms suggestive of DVT if these were considered to be arising from injury of the tendo Achillis itself.

There was a relationship between the duration of cast immobilisation and the extent of the thrombosis. All six cases of isolated distal DVT presented in patients who had a cast for no more than four weeks. Conversely, the seven cases of proximal DVT and/or pulmonary embolism had immobilisation for between four and ten weeks. This difference has not previously been noted and suggests the risk of a proximal DVT and pulmonary embolism might increase as the period of immobilisation lengthens.

The clinical significance of the VTE events is illustrated by the submassive pulmonary embolism in two patients. Such events are life-threatening, particularly in association with right ventricular infarction, in which the risk of death may be as high as 20%. The clinical significance is also suggested by the 1.4% rate of proven pulmonary embolism observed in our study, which is comparable with the 1.1% to 1.5% rate of pulmonary embolism complicating elective hip replacement. Although such comparisons are limited by the small number of patients, they suggest that the risk of clinically significant pulmonary embolism with immobilisation in a cast following injury to the tendo Achillis is similar to that for elective hip replacement.

We observed that documentation of specific risk factors for VTE, or consideration of any form of prophylaxis, was seldom undertaken in the orthopaedic management of the patients in this study, in contrast to the observation that VTE risk factors are commonly present in such patients. Importantly, prophylaxis with LMWH was not given to any of the 208 patients, regardless of the presence of other risk factors for VTE. Likewise, aspirin was not prescribed in any patient, apart from one in whom it was recommended, along with compression stockings, during long-distance air travel.

The inability to provide prophylaxis may relate to the lack of recognition by orthopaedic surgeons managing injury to the tendo Achillis, of the risk of VTE from prolonged immobilisation in a cast and the significant reduction in the risk that can be achieved with extended LMWH therapy. The efficacy and safety of prophylaxis with LMWH in reducing the risk of VTE in patients with prolonged immobilisation in a cast for lower limb injury is well established. The Cochrane meta-analysis of extended LMWH prophylaxis reported a significant 51% reduction in the incidence of VTE, with the level of protection being similar for both tendon injuries and lower limb fractures. This reduction in risk is similar to that observed with LMWH prophylaxis for elective hip replacement, and is not associated with an increased risk of major bleeding complications.

These findings suggest that current international guidelines may need modification to reflect this evidence base, and to ensure that patients in casts are given the same level of VTE protection as those undergoing elective hip replacement. The North American (ACCP) and Scottish (SIGN) guidelines recommend that individual clinicians may choose whether to provide LMWH prophylaxis for patients with immobilisation of the lower limb in a cast, with the options including no prophylaxis, in-hospital prophylaxis, or prophylaxis that is continued after discharge from hospital. In contrast, these guidelines recommend that all patients undergoing elective hip or knee replacement surgery should be routinely considered for LMWH prophylaxis for seven to 15 days after operation and continued for four to five weeks in high-risk patients. One potential limitation of the use of LMWH prophylaxis for patients who are immobilised in a cast is the requirement to administer a prolonged course of
up to ten weeks, and this may be difficult to supervise on an outpatient basis, particularly in centres without a dedicated community-based anticoagulation service.

To our knowledge, the efficacy of aspirin as a VTE prophylactic agent has not been specifically investigated in relation to prolonged immobilisation in a cast. Antiplatelet agents have been demonstrated to reduce the risk of VTE across a range of other orthopaedic, general surgical and medical settings.16-19 Although there are potential advantages of aspirin over LMWH therapy, including cost, comfort and simplicity of administration, this is counterbalanced by reduced efficacy. Owing to a lack of evidence regarding its efficacy as a prophylactic agent in this setting, it was not endorsed by the 2008 ACCP guidelines for prophylaxis during immobilisation in a cast,14 although the SIGN guidelines regard aspirin as a reasonable alternative when LMWH is contraindicated.15

Other emerging options include the direct thrombin inhibitor dabigatran etexilate and the Factor Xa inhibitor rivaroxaban. Randomised controlled trials suggest that they are at least as effective as and have a similar safety profile to LMWH in reducing VTE after elective hip and knee replacement.20-27 Both drugs have the advantage of oral administration, thereby avoiding repeated subcutaneous injection. Both agents were approved in 2008 by the European Union as an alternative to LMWH for VTE prevention, although at present their use is solely following elective hip and knee replacement.

Another potential approach in the management of immobilisation in a cast is early weight-bearing, physiotherapy and gentle mobilisation, although this has not been assessed as a prophylactic measure for VTE. Randomised controlled trials of different pharmacological and non-pharmacological prophylactic measures are a priority to provide evidence-based guidelines for the prevention of VTE during immobilisation in a cast.

In summary, in our patients immobilised with a cast in the treatment of an injury to the tendo Achillis there was an increased risk of DVT formation and development of a pulmonary embolism. Consideration should be given to LMWH prophylaxis being administered routinely to patients requiring prolonged immobilisation in a cast in this setting. This approach may be preferable to the selective use of prophylaxis in high-risk patients, as only about half of the patients (seven) who developed a VTE had identifiable risk factors at the time of the injury. Consideration may also be given to other preventative measures, such as aspirin, direct thrombin and Factor Xa inhibitors and early mobilisation through physiotherapy. However, endorsement of such approaches must await the outcome of further clinical trials.

Supplementary material
A further opinion by D. Warwick is available with the electronic version of this article on our website at www.jbjs.org.uk

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References


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