The incidence of fatal pulmonary embolism after primary hip and knee replacement in a consecutive series of 4253 patients

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We studied 4253 patients undergoing primary joint replacement between November 2002 and November 2007, of whom 4060 received aspirin only as chemical prophylaxis; 46 were mistakenly given low molecular weight heparin initially, which was stopped and changed to aspirin; 136 received no chemoprophylaxis and 11 patients received warfarin because of a previous history of pulmonary embolism. We identified the rate of clinical thromboembolism before and after discharge, and the mortality from pulmonary embolism at 90 days. The overall death rate was 0.31% (13 of 4253) and the rate of fatal pulmonary embolism was 0.07% (3 of 4253).

Our data suggest that fatal pulmonary embolism is not common following elective primary joint replacement, and with modern surgical practice elective hip and knee replacement should no longer be considered high-risk procedures.

In April 2007, the National Institute of Health and Clinical Excellence (NICE) published guidelines on thromboprophylaxis for in-patients undergoing surgery. These encouraged orthopaedic surgeons to use low-molecular weight heparin (LMWH) for thromboprophylaxis and to avoid the use of aspirin. This advice was based on the belief that the two main complications of venous thromboembolism, namely fatal pulmonary embolism and post-thrombotic syndrome, are common and that there is good evidence to support the view that reducing the rate of deep venous thrombosis (DVT) will reduce the overall death rate from fatal pulmonary embolism. The studies used to create these guidelines used surrogate rather than clinical endpoints, and assumed that reducing the incidence of venographically-detectable DVT would also lead to a reduction in the clinical endpoints of fatal pulmonary embolism and post-thrombotic syndrome. The NICE guidelines also included two assumptions which we believe are incorrect: first, that chemical and/or mechanical prophylaxis will reduce these two complications, and secondly, that orthopaedic operations, in particular elective hip and knee replacement, are high-risk procedures in this respect.

The NICE guidelines contain certain emotive statements, such as: ‘each year over 25,000 people in England die from VTE contracted in hospital. This is more than the combined total deaths from breast cancer, AIDS and road traffic accidents and more than 25 times the number of people who die from MRSA’. It is implied that if all orthopaedic surgeons in the United Kingdom were to adopt the NICE guidelines and use LMWH for patients undergoing total hip replacement (THR) and total knee replacement (TKR), there would be a significant reduction in mortality. We question whether clinical experience supports this. Published data from the National Joint Register for England and Wales for the years 2003 to 2006 record that the mortality for primary THR at one year was 1.9% (0.7% at 90 days). It does not state how many of those patients died from pulmonary embolism, but when examining controls of patients within the community of the same age and gender, the mortality for patients undergoing surgery was 50% less than for those who did not have surgery. In other words, patients having THRs are less likely to die than age- and gender-matched controls. It does, therefore, seem unlikely that the adoption of LMWH could produce any further significant reduction in observed mortality in this patient group.

The National Joint Registry has also reported death rates up to one year after surgery in four subgroups of patients undergoing THR: those who received no prophylaxis (1446); those who received only chemical prophylaxis (19 484); those who received only mechanical prophylaxis (13 183); and those who received both chemical and mechanical prophylaxis (42 204).
No difference in mortality was revealed at one year or at any time during the first year between any of the groups. Comparable results were revealed for TKR, except that the overall mortality at one year was 1.6% (0.5% at 90 days) and the observed mortality was 33% that of age- and gender-matched controls.

A meta-analysis including 130,000 patients carried out by Murray, Britton and Bulstrode showed a fatal pulmonary embolism rate of 0.1% to 0.2% and an overall death rate of 0.3% to 0.4% irrespective of pharmacological agent. Another meta-analysis carried out by Freedman et al included 10,929 patients and showed no significant differences in rates of fatal pulmonary embolism or all-cause mortality between the various prophylactic agents. These meta-analyses included studies dating back as early as the 1960s, when the incidence of fatal pulmonary embolism was as high as 2.3%, and it was thought that thromboprophylaxis probably did help reduce the incidence of pulmonary embolism.

Recently the reported incidence of fatal pulmonary embolism has been much lower, at between 0% and 0.2%. This is probably due to a combination of spinal anaesthesia, improved surgical technique and early mobilisation, rather than the result of any thromboprophylaxis. In order to reflect current practices, Sharrock et al reviewed publications over the last nine years and performed a meta-analysis of 28,038 patients which showed that pulmonary embolism occurs despite the use of anticoagulants, and that LMWH is associated with the highest all-cause mortality of all the prophylactic agents.

We wished further to investigate the effect of aspirin prophylaxis on the rate of fatal pulmonary embolism after hip and knee arthroplasty.

Patients and Methods
We analysed the prospectively-collected data on 4,253 consecutive patients who had a primary total hip or knee replacement between November 2002 and November 2007. In total, 2,050 patients had a TKR and 2,203 a THR. The mean age of the patients was 71 years (31 to 93) in the TKR group and 68 years (19 to 93) in the THR group. Every patient was treated at a specialist centre under the care of a single surgeon (DEB). Data were recorded prospectively on a database in the Orthopaedic outcomes department by a designated team of outcomes assessment nurses. Data were complete and accurate for peri-operative and 90-day morbidity and mortality for all patients.

Our standard practice was to give 150 mg aspirin from day one post-operatively for a period of six weeks. If there were contraindications to the use of aspirin then the patient received no chemical prophylaxis. If they had a previous history of treated pulmonary embolism they were given warfarin. A small number of patients (46; 1.1%) had LMWH prescribed by an anaesthetist, but as soon as the orthopaedic team was made aware of this it was stopped and changed to aspirin. Spinal anaesthesia was used for all patients wherever possible. A standard posterior approach was used for THR and a vertical midline incision and medial parapatellar approach for TKR. Whenever possible, patients were mobilised either on the day of surgery or the first post-operative day.

Each patient was reviewed at six weeks after a THR and three months after a TKR and then at one year. There was no loss to follow-up. Adverse incidents were recorded by the outcomes nurses at each review. DVT was classified as either distal (‘below knee’) or proximal (‘above knee’). Proximal DVT was defined as thrombus located in either the popliteal, femoral or iliac veins. At our hospital proximal DVT is treated with warfarin for three months. But distal DVT is not treated. A clinical diagnosis of DVT was confirmed by duplex ultrasonography or venography, and a pulmonary embolism was confirmed by a ventilation/perfusion scan. A confirmed pulmonary embolism was treated with warfarin for six months. Fatal pulmonary embolism was confirmed from the post mortem record or death certificate. Any deaths of unknown cause that occurred within three months of operation were considered to be the result of pulmonary embolism.

Results
Of the 2,050 TKR patients, 1966 (95.9%) received aspirin only, 50 (2.44%) received no thromboprophylaxis, 29 (1.41%) received LMWH initially in hospital but were discharged on aspirin if tolerated, and five (0.24%) patients received warfarin because of a history of previous pulmonary embolism. Of the 2,203 hip replacements, 2,094 (95.1%) patients received aspirin only, 86 (3.90%) received no thromboprophylaxis, 17 (0.77%) received LMWH initially in hospital but were discharged on aspirin if tolerated, and six patients (0.27%) received warfarin because of a history of previous pulmonary embolism.

Within 90 days of surgery, 14 patients (0.33% of procedures) had a confirmed proximal DVT and started treatment. Of these, 11 were given aspirin, two had no thromboprophylaxis, and one had LMWH and aspirin. A total of 28 patients (0.66% of procedures) had a non-fatal symptomatic pulmonary embolism, of whom 27 were given aspirin and one LMWH and aspirin. In all, 13 patients died (0.31% of procedures); five after a THR (0.23%, all THRs) and eight after a TKR (0.39%, all TKRs). All had received aspirin as thromboprophylaxis. A total of five deaths occurred while an in-patient, of which three were due to myocardial infarction. One patient developed an acute abdomen post-operatively and was transferred to a general surgical unit, but died as a result of a bowel infarction after a mesenteric vessel thrombosis. One patient developed a chest infection and subsequently died in intensive care, and eight patients died after initial discharge from hospital (Table I).

In the whole series, only three deaths (0.07%) could be attributed to pulmonary embolism, one after a THR (0.05% all THRs) and two after a TKR (0.1% all TKRs).
Two patients died suddenly at home and did not undergo a post mortem examination, and one died of respiratory failure after a pulmonary embolism, which was demonstrated at post mortem.

Complications related to bleeding were low; 14 patients in the TKR group developed a haematoma, three of which required evacuation and lavage. The others were observed until resolution; none became infected. Of these patients, three were on warfarin. In all, eight patients bled for longer than expected and 49 had prolonged serosanguinous ooze. In the THR group, complications were less frequent. One patient developed a haematoma which required a washout and two patients bled extensively, one of whom was re-explored. A further 29 patients had prolonged serosanguinous ooze. Two patients had a gastrointestinal haemorrhage, one of whom died.

Discussion

This study has shown that our overall death rate (0.31%) at 90 days is low and compares favourably with 90-day mortality rates quoted in the recent literature (0% to 0.67%). The fatal pulmonary embolism rate (0.07%) suggests that this is a rare event after elective total joint replacement if aspirin is given. That no deaths occurred in the 4.5% of patients who did not receive aspirin is not statistically significant. Although some medical complications of aspirin therapy may not have been recorded owing to a focus on the surgical complications, it would appear that aspirin is a relatively safe drug with a low complication rate despite the fact that it has the potential to cause gastrointestinal ulceration and bleeding in a small proportion of patients. It is easy to administer and is inexpensive. It also has the advantage of reducing arterial occlusion. It does not cause major wound haemorrhage, unlike LMWH, which can cause significant post-operative bleeding in a small number of patients.

In conclusion, we found that the omission of LMWH thromboprophylaxis and/or mechanical prophylaxis in our series of 4253 patients undergoing total joint replacement resulted in only three deaths from pulmonary embolism at 90 days post-operatively. We do not believe that the introduction of LMWH would produce any significant clinical reduction in proximal DVT or fatal pulmonary embolism. It has been stated that to provide strong evidence of any potential benefit would require a study of approximately 30 000 patients in each arm of a prospective randomised controlled trial to clearly demonstrate a significant reduction in the rate of fatal pulmonary embolism. With the small incidence rate of fatal pulmonary embolism we report, 67 500 patients would be required in each arm. This would provide 80% power to detect a difference in death rates of 0.07% vs 0.035%. Therefore, if the NICE guidelines were implemented in full specifically for elective primary hip and knee replacement, it is difficult to see how they could have any significant impact on the rate of fatal pulmonary embolism. We believe that with modern surgical and anaesthetic practice, fatal pulmonary embolism is no longer common, but still continues to occur despite the use of anticoagulants. Our study suggests that the use of aspirin is reasonable: it has also been shown to be effective in other centres. We have not studied post-thrombotic syndrome in any detail but are unaware of it as a major issue in our clinical practice. However, in studies which look at the incidence of post-thrombotic syndrome after joint replacement, there is no obviously increased risk of developing post-thrombotic syndrome after either symptomatic or asymptomatic DVT. These studies included relatively small numbers of patients, and we feel that this area is worthy of further study.

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References


