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Fatal pulmonary embolism following elective total knee replacement using aspirin in multi-modal prophylaxis — A 12 year study

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ABSTRACT

Background: The National Institute for Health and Clinical Excellence (NICE) has issued guidelines on which thromboprophylaxis regimens are suitable following lower limb arthroplasty. Aspirin is not a recommended agent despite being accepted in orthopaedic guidelines elsewhere. We assessed the incidence of fatal pulmonary embolism (PE) and all-cause mortality following elective primary total knee replacement (TKR) with a standardised multi-modal prophylaxis regime in a large teaching district general hospital.

Methods: We utilised a prospective audit database to identify those that had died within 42 and 90 days postoperatively. Data from April 2000 to 2012 were analysed for 42 and 90 day mortality rates. There were a total of 8277 elective primary TKR performed over the 12 year period. The multi-modal prophylaxis regimen used unless contraindicated for all patients included 75 mg aspirin once daily for four weeks. Case note review ascertained the causes of death. Where a patient had been referred to the coroner, they were contacted for post mortem results.

Results: The mortality rates at 42 and 90 days were 0.36 and 0.46%. There was one fatal PE within 42 days of surgery (0.01%) who was taking enoxaparin because of aspirin intolerance. Two fatal PE's occurred at 48 and 57 days post-operatively (0.02%). The leading cause of death was myocardial infarction (0.13%).

Conclusions: Fatal PE following elective TKR with a multi-modal prophylaxis regime is a very rare cause of mortality.

1. Introduction

Fatal pulmonary embolism (PE) is still perceived by some to be a significant cause of death after lower limb arthroplasty. The National Institute for Health and Care Excellence (NICE) guidelines state that there are 25,000 preventable deaths per year from venous thromboembolism (VTE) across all specialities, highlighting orthopaedic surgery as a high-risk specialty [1]. They recommend the use of chemical thromboprophylaxis for 10–14 days following total knee replacement (TKR).

The incidence of fatal PE following TKR without thromboprophylaxis has been reported as 0.22–0.4% [2]. Figures such as these have led to the rapid expansion in mechanical and chemical thromboprophylaxis agents on the market. Whilst evidence in support of low molecular weight heparin (LMWH) has evolved over the past decade, so has peri-operative management with

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increasing regional anaesthesia, mechanical methods (anti-embolism stockings and foot pumps) and early (day 1) mobilisation [3]. It is therefore difficult to directly attribute all improvements in thromboembolic and mortality rates simply to one factor.

Aspirin is not recommended under NICE guidelines because it is perceived by some to have insufficient effect on VTE rates [1]. However, studies have not made direct comparisons with aspirin, almost all trialling enoxaparin, warfarin and more potent anti-coagulants against each other [4–9]. A recent meta-analysis was unable to find a clear benefit with potent anticoagulants when comparing results from studies utilising aspirin [10]. These papers have contributed to the re-introduction of aspirin into the American Academy of Orthopaedic Surgeons (AAOS) and American College of Chest Physicians (ACCP) guidelines, and questions are being raised by orthopaedic surgeons in the United Kingdom as well [11–14].

In the past, aspirin has been shown to decrease overall VTE rates [15–17], and with ongoing concerns about the risk to patients with regard to bleeding complications and infection rates following TKR, there is still a large body of orthopaedic surgeons who advocate the use of aspirin for chemical thromboprophylaxis [18–21]. With the emphasis on practising evidence based medicine, there is a need to investigate further the use of aspirin as a thromboprophylaxis agent.

We hypothesise that the use of aspirin as part of a multi-modal thromboprophylaxis regimen, does not lead to a significant higher risk of fatal pulmonary embolism or of increased mortality. This study presents our 12-year experience following elective primary TKR.

2. Materials and methods

Information was taken from a prospective audit database in which data was captured over a 12-year period from April 2000 to December 2012. Clinical coding was used to identify those patients who had undergone elective primary TKR and eventually deceased within 42 and 90 days. During this study period, we performed 8277 elective primary total knee replacements. The standard recommended multi-modal thromboprophylaxis regimen employed during this period was regional anaesthesia where possible (approximately 94%), mechanical prophylaxis (Flo-tron calf garment per-operatively, arteriovenous impulse boots until mobile and anti-embolism stockings for six weeks), mobilisation within 24 h, and 75 mg aspirin for four weeks (unless contra-indicated).

The only exceptions (<5%) were the small number of patients already receiving warfarin for medical co-morbidities, aspirin sensitivity or a past history of VTE, for whom warfarin, or occasionally LMWH, was used as the prophylactic agent. Case notes were reviewed to ascertain the causes of death and to confirm their thromboprophylaxis regimen. Where a patient had been referred to the coroner, the appropriate coroner's office was contacted for post-mortem results. Cause of death was taken from Part 1a of the death certificate.

3. Results

The mortality rates at 42 and 90 days were 0.36% and 0.46% respectively. There was a secular decrease apparent across the observational period from 0.28% and 0.56% (42 and 90 days respectively) in 2000–01, to 0.18% and 0.18% in 2011–12. There was one fatal PE within 42 days of surgery (0.01%), and two fatal PEs subsequently at 48 and 57 days (0.02%). The leading causes of death were myocardial infarction and lower respiratory tract infections (11 and eight respectively) (Table 1). The early death attributed to PE occurred in a patient receiving enoxaparin because of aspirin intolerance. Overall we identified three patients who had died receiving enoxaparin (0.04%), and one taking warfarin for atrial fibrillation (AF) (0.01%). Both of the patients with a fatal PE after 42 days were confirmed to have received aspirin as chemical thromboprophylaxis on case note review.

Table 1
Table of all causes of death following primary total knee replacement.

Cause of death	Number at ≤42 days	Number at >42 days
Pulmonary embolus	1	2
LRTI	5	3
IHD	3	
Myocardial infarction	9	2
Ischaemic bowel	3	1
Cerebrovascular disease	3	1
Fat embolism	1	
Coal workers' pneumoconiosis		1
Suicide	1	1
Decompensated liver disease[a]	1	
Ruptured AAA	1	
Acute biliary peritonitis[c]	1	
Septicaemia[b]	1	

LRTI — lower respiratory tract infection, IHD — ischaemic heart disease, AAA — abdominal aortic aneurysm.
[a] 1C was chronic autoimmune hepatitis.
[b] 1B was malignant lymphoma.
[c] 1B was cholecystitis.

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