Post-discharge symptomatic thromboembolic events in hip fracture patients

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ABSTRACT

INTRODUCTION The aim of this study was to audit referral rates for post-discharge symptomatic thromboembolic events following hip fracture surgery to assess the extent of the clinical problem and to initiate discussion on prolonged chemoprophylaxis.

PATIENTS AND METHODS All patients who underwent surgery for proximal hip fractures in one year (2001–2002) were followed up. Patient case-notes were used to identify all morbidity episodes within 3 months following discharge. Patients with suspected symptomatic thromboembolic episodes were investigated to confirm the diagnoses objectively. Reasons for hospital re-admission and causes of death were identified.

RESULTS A total of 267 patients who underwent surgery for proximal hip fractures were included in the study. Forty-three patients died during initial admission episode. Of the 224 patients discharged, 46 (20.54%) patients were referred back to hospital within 3 months, for unplanned emergency management. Of these, 8 patients (3.57%) were referred back for suspected thromboembolic events. Of these, 6 (2.67%) were referred with a clinical diagnoses of deep vein thrombosis (DVT) but only 1 patient (0.45%) was confirmed to have DVT. Two patients (0.89%) were referred with features of pulmonary embolism (PE). Both were confirmed on ventilation-perfusion scans and both patients died. One patient died following PE in the community. Thus, overall, 3 deaths (1.34%) following discharge were recorded to be due to pulmonary embolism.

CONCLUSIONS Suspected thromboembolic events constitute a major proportion of unplanned referrals back to the hospital. Three deaths due to delayed pulmonary embolism may justify prolonged universal chemoprophylaxis following hip fracture surgery.

KEYWORDS

Hip fracture – Femoral neck fracture – Thromboembolism – Pulmonary embolism

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Patients with proximal hip fractures constitute a high risk for thromboembolic complications.^{1,2} Reports have raised concerns about continued high incidence of post-discharge deep vein thrombosis (DVT), with associated morbidity and mortality.⁵ It has been suggested that these complications can be avoided by the continued use of DVT prophylaxis for an extended duration after discharge.⁵

Most of the studies showing efficacy of extended duration thromboprophylaxis have used venograms to detect prevalence of DVT.^{5–7} Concerns have been raised regarding correlation of a surrogate end-point-like venogram with clinically important thromboembolic events.^{8,9} Reports on efficacy of extended duration chemoprophylaxis show decreased prevalence of venographically detected DVT but have been unable to show similar beneficial effect on clinical events like pulmonary embolism⁹

Our unit protocol is to use low molecular weight heparin for thromboprophylaxis till discharge. This is the most popular

method of thromboprophylaxis in Great Britain.¹⁰ Before initiating any new thromboprophylaxis regimen, it is important to know through clinical audit if there is a problem with the existing method such as unacceptable rates of symptomatic thromboembolism. A suggested clinically relevant end-point is 'symptomatic thromboembolic event which leads to objective radiological confirmation and subsequent treatment'.^{9,11} The aim of this audit was to see if our protocol was associated with high rates of symptomatic thromboembolic events following hip fracture surgery. This would help assess the extent of the clinical problem and to initiate discussion on prolonged chemoprophylaxis.

Patients and Methods

The study was conducted at the Royal Oldham Hospital, UK in 2001–2003, after approval from the hospital audit department. All elderly (> 65 years) patients who

underwent surgery for proximal hip fractures (intracapsular and intertrochanteric neck of femur fractures) in one calendar year (July 2001 to June 2002) were included. Patients were excluded from the study if they had another major surgery including joint replacement surgery in the preceding 3 months. Other exclusion criteria were recent or current DVT, current warfarin therapy or presence of any contra-indication to chemoprophylaxis including recent haemorrhagic stroke, active bleeding ulcers or any allergies to heparin. As per our department policy, all these patients had received once-a-day low molecular weight heparin, starting 8 h postoperatively till discharge.

Our hospital is the sole provider of an anticoagulation service for the catchment population and we expect to see all patients referred for suspected thromboembolic complications. The hospital computerised logging system records all episodes of patient attendance, which could be through accident and emergency, out-patient clinics or ward admissions. At the time of the study, all patients with suspected thromboembolic events were admitted for investigations. All records were examined to identify any episodes of patient contact with the hospital services within 3 months of discharge after index operation. The information (including surgical details, risk factors, provisional diagnoses at the presentation, investigations performed, final diagnoses and treatment) was entered in a performa. The data were entered into a Microsoft's Excel spreadsheet programme and analysed. All patients with suspected DVT were assessed by colour Doppler ultrasonography and cases of suspected pulmonary embolism were confirmed by ventilation-perfusion scan or spiral computerised tomography (CT) scan.

The local health authority was contacted for data on patients who died in the community and causes of death were collected from patients' death certificates.

This methodology would miss asymptomatic patients who can only be identified through venographic studies but would identify symptomatic thromboembolic episodes which were subsequently confirmed radiologically. Patients who developed DVT while in hospital but became symptomatic later would also be picked up, giving an overall estimate of clinical load due to the post-discharge thromboembolic phenomenon.

Results

A total of 282 patients were operated for proximal hip fractures at our institution, in the period from 1 July 2001 to 30 June 2002. Of these, 15 patients were excluded as they were on current warfarin therapy either for previous thromboembolism (3 patients) or for other medical reasons (atrial fibrillation, 11; prosthetic valve, 1). Out of 267

patients included in our study, 101 had cemented hemiarthroplasty (bipolar hemiarthroplasty for physiologically younger patients) performed for displaced intracapsular fractures, 145 had dynamic hip screw fixation for intertrochanteric fractures, 14 had cannulated screw fixation for undisplaced intracapsular neck fractures and 7 patients had proximal femoral intramedullary nailing device used for unstable intertrochanteric fracture. The average age of patients was 80.5 years (range, 65–102 years); 75% of patients were females. Of the patients, 62% received spinal anaesthesia and the remainder general anaesthesia. The average hospital stay was 19 days.

During index admission, 36 patients were investigated for suspected DVT while positive Doppler scan for DVT was present in 14 patients (5.24%). A further 6 patients were investigated for suspected pulmonary embolism, which was confirmed by spiral CT scan in 4 patients. Two of these patients died later. Six patients had sudden deaths, which were thought to be due to pulmonary embolism on clinical grounds. Autopsy was done in only one of these patients which confirmed the diagnosis. Thus, a total thromboembolic complication rate of 24/267 (8.98%) and a fatal pulmonary embolism rate of 8/267 (2.996%) was noted during initial admission. A total of 43 out of 267 (16.1%) patients died during initial admission episode.

Of the 224 patients discharged, 46 (20.54%) patients were referred back to our hospital for unplanned emergency management. Eight patients (3.5% of discharges, or 17.39% of all referrals) were referred back for suspected thromboembolic episodes. Nine patients (4.01% of discharges or 19.56% of referrals) were referred back for further orthopaedic problems (re-fractures, 4; superficial infection, 2; deep infection, 2; and implant cut-out, 1). Other medical problems accounted for 19 referrals (8.48% of discharges or 41.30% of referrals: chest infection, 5; urinary tract infection, 4; cerebrovascular accident, 2; general deterioration, 2; myocardial infarction, 1; congestive cardiac failure, 1; inability to cope, 1; vomiting, 2; ischaemic foot, 1; incontinence, 1; morphine overdose, 1; inflammatory bowel disease, 1). Seven patients were admitted for investigation of, and management following, recurrent falls (3.12% of discharges or 15.21% of referrals).

Of 8 patients referred with suspected thromboembolic event, 6 were referred with a clinical diagnosis of DVT. Following investigations, only 1 patient (0.45% of discharges and 2.17% of referrals) was confirmed to have calf vein DVT. Two patients were referred with features of pulmonary embolism. Both were confirmed on ventilation-perfusion scans; both patients died. Thus, a total of 3 referred patients (6.52% of referrals, 1.33% of discharges) were confirmed to have thromboembolic complications following discharge. Twenty-three of our discharged patients died within 3 months of discharge; of these, 15 died in hospital, which

Table 1 Summary of the results

Total number of cases	267
Pre-discharge symptomatic and confirmed DVT	5.24%
Pre-discharge fatal PE	2.99%
Deaths during index admission	16.1%
Total discharged	224
Re-admission/referral rates	20.54%
Referral/re-admission for suspected symptomatic thromboembolism (including DVT and PE)	3.57%
Post-discharge symptomatic and confirmed DVT	0.45%
Post-discharge fatal PE	1.34%

included 2 deaths due to pulmonary embolism as mentioned above. Eight patients died in the community. In only one of these patients was pulmonary embolism mentioned as cause of death. Thus, overall, 3 deaths (1.34%) following discharge were recorded due to pulmonary embolism (see Table 1 for summary of the results)

Discussion

Patients undergoing surgery for hip fractures are known to be at high risk for venous thromboembolism, with comparatively high rates of deep venous thrombosis and pulmonary embolism.^{1,12} Besides the orthopaedic injury, their advanced age, medical co-morbidities and poor postoperative mobilisation, contribute to the high risk of thromboembolism.¹ Without prophylaxis, the incidence of DVT is approximately 50% in this population, with about 20% being proximal thrombosis. The prevalence of fatal pulmonary embolism has been reported to be up to 7.5% after proximal femur fractures.¹ Unfortunately, risk of thromboembolism persists for significant duration after surgery, despite thromboprophylaxis. Complications associated with thromboembolism are the source of major postoperative morbidity and mortality.^{13,14} With decreasing in-patient stay following surgery, the duration of prophylaxis may not be adequate. Research has shown that extended-duration thromboprophylaxis may reduce thromboembolism associated with hip fractures.⁵

Though much work has been done on thromboembolism following arthroplasty, there is little literature about thromboembolism and its consequences in the setting of hip fracture. Our study is significant in that it looks at the clinical burden of post-discharge thromboembolism in the setting of a district hospital. In our study, 24.7% of patients died in the time from injury to 3 months following discharge. This compares with 18% 90-day mortality seen in an East

Anglian audit.¹⁵ In our study, radiologically confirmed DVT was noted in 5.24% of in-patients while deaths due to fatal PE were seen in 2.99% of in-patients. Of all referrals following discharge, 17.39% were for suspected thromboembolic episodes. Six patients were referred back for suspected DVT but only 1 patient was confirmed to have DVT on radiological examination. This suggests a high index of suspicion among referring general practitioners but poor accuracy of clinical examination in diagnosing DVT. This contrasts with radiological confirmation of diagnoses in both patients referred with clinical diagnoses of PE. Most of the symptomatic DVT and fatal PE episodes were recorded while patients were in hospital. This may be due to long duration of in-hospital stay for these patients (19 days in our study). Only 1 case of confirmed DVT was noted after discharge but 3 cases of fatal PE (1.34%) were recorded following discharge from the hospital. This suggests that most of thromboses remain silent till they present in a catastrophic manner with a pulmonary embolism.

Our study estimated rates of post-discharge thromboembolic events based on clinical grounds and subsequent confirmation by radiological tests. This methodology would miss asymptomatic patients who can only be identified by using techniques like venograms for every patient. However, our aim was to establish the extent of clinical problem due to thromboembolism following hip fracture surgery. We feel that, on the basis of three pulmonary embolism related deaths within 3 months of operation, there may be clinical grounds for extended-duration chemoprophylaxis.

The choice of the thromboprophylactic agent remains debatable. The Pulmonary Embolism Prevention (PEP) trial showed that extended-duration aspirin use produced a proportional reduction in pulmonary embolism of 43% and in symptomatic deep vein thrombosis of 29%.¹⁵ Aspirin also has the advantage of low cost and ease of administration. In fact, the Scottish Intercollegiate Guidelines Network in 2002 recommended that all hip-fracture patients should be prescribed aspirin for 35 days following injury.¹⁶ However, use of aspirin is associated with a small, but significant, risk of increased bleeding.^{15,17} Warfarin has been shown to be more effective than aspirin for extended-duration thromboprophylaxis in hip fracture patients, with similar bleeding rates.¹⁸ In a cohort study of 897 hip-fracture surgery patients who received peri-operative prophylaxis with enoxaparin for about 5 weeks, objectively confirmed, symptomatic, thromboembolic events occurred in only 7 patients (0.8%), with no cases of PE. However, major bleeding was encountered in 5% of patients.¹⁹ In different clinical trials, low molecular weight heparin (LMWH) has been shown to be consistently more effective than aspirin without the increased bleeding risk.¹⁷ We are not aware of any clinical trials which have directly compared the use of LMWH and

warfarin in hip fracture patients.¹⁷ The synthetic pentasaccharide fondaparinux, which is a selective Factor Xa inhibitor, has been shown to be more effective than LMWH in hip fracture patients.²⁰ A recent, double-blinded clinical trial⁵ compared extended-duration prophylaxis with fondaparinux with placebo. Venography, performed after 4 weeks of prophylaxis, documented DVT in 1.4% of the extended-prophylaxis patients and in 35.0% of placebo recipients. The rates of symptomatic thromboembolism were 0.3% and 2.7%, respectively. Bleeding rates were not significantly different.⁵ The American College of Chest Physicians recommends that patients undergoing hip fracture surgery be given extended prophylaxis for 28–35 days after surgery. The recommended options are fondaparinux, LMWH, or warfarin.¹⁷ The National Institute for Health and Clinical Excellence in a recent draft for consultation on venous thromboembolism has also recommended that fondaparinux or low molecular weight heparin should be continued for 4 weeks after hip fracture surgery.²¹ We feel that the choice of the anti-thrombotic agent can be decided after consultation locally and local protocols should be established.

Conclusions

This study has shown that post-discharge thromboembolism is a real problem in hip fracture patients and measures to prevent its sequelae should be instituted.

References

1. Della Valle CJ, Mirzabeigi E, Zuckerman JD, Koval KJ. Thromboembolic prophylaxis for patients with a fracture of the proximal femur. *Am J Orthop* 2002; **31**: 16–24.
2. Thromboembolic Risk Factors (THRIFT) Consensus group. Risk of and prophylaxis for venous thromboembolism in hospital patients. *BMJ* 1992; **305**: 567–74.
3. Eriksson BI, Lassen MR, and the PENTasaccharide in Hip-FRActure Surgery Plus (PENTHIFRA Plus) Investigators. Duration of prophylaxis against venous thromboembolism with fondaparinux after hip fracture surgery: a multicenter, randomized, placebo-controlled, double-blind study. *Arch Intern Med* 2003; **163**: 1337–42.
4. Bergqvist D, Benoni G, Bjorgell O, Fredin H, Hedlundh U, Nicolas S *et al.* Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* 1996; **335**: 696–700.
5. Comp PC, Spiro TE, Friedman RJ, Whitsett TL, Johnson GJ, Gardiner Jr GA *et al.* Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. Enoxaparin Clinical Trial Group. *J Bone Joint Surg Am* 2001; **83**: 336–45.
6. Dahl OE, Andreassen G, Aspelin T, Muller C, Mathiesen P, Nyhus S *et al.* Prolonged thromboprophylaxis following hip replacement surgery – results of a double blind, prospective, randomised, placebo-controlled study with dalteparin (Fragmin). *Thromb Haemost* 1997; **77**: 26–31.
7. Planes A, Vochelle N, Darmon JY, Fagola MA, Bellaud M, Huet Y. Risk of deep-venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind randomised comparison of enoxaparin versus placebo. *Lancet* 1996; **348**: 224–8.
8. Ricotta S, Iorio A, Parise P, Nenci GG, Agnelli G. Post discharge clinically overt venous thromboembolism in orthopaedic surgery patients with negative venography – an overview analysis. *Thromb Haemost* 1996; **76**: 887–92.
9. Warwick D, Samama MM. The contrast between venographic and clinical endpoints in trials of thromboprophylaxis in hip replacement. *J Bone Joint Surg Br* 2000; **82**: 480–2.
10. Watts AC, Brenkel IJ. A postal survey of current thromboprophylactic practices of consultant orthopaedic surgeons in the treatment of fracture of the hip. *J Bone Joint Surg Br* 2005; **87**: 296–300.
11. Levine M, Gent M, Hirsh J, Leclerc J, Anderson D, Weitz J *et al.* A comparison of low-molecular weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. *N Engl J Med* 1996; **334**: 677–81.
12. Gillespie W, Murray D, Gregg PJ, Warwick D. Risks and benefits of prophylaxis against venous thromboembolism in orthopaedic surgery. *J Bone Joint Surg Br* 2000; **82**: 475–9.
13. Todd CJ, Freeman CJ, Camilleri-Ferrante C, Palmer CR, Hyder A, Laxton CE *et al.* Differences in mortality after fracture of hip: the East Anglian audit. *BMJ* 1995; **310**: 904–8.
14. Vajanto I, Kuokkanen H, Niskanen R, Haapala J, Korkala O. Complications after treatment of proximal femoral fractures. *Ann Chir Gynaecol* 1998; **87**: 49–52.
15. PEP Pulmonary Embolism Prevention (PEP) Trial Collaborative Group. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin. *Lancet* 2000; **355**: 1295–302.
16. Scottish Intercollegiate Guidelines Network (SIGN). Prevention and management of hip fracture in older people: a national clinical guideline. Jan 2002; SIGN Publication No. 56. Available at <<http://www.sign.ac.uk>> (Accessed 16 April 2003).
17. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW *et al.* Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; **126** (Suppl): 338S–400S.
18. Powers PJ, Gent M, Jay RM, Julian DH, Turpie AG, Levine M *et al.* A randomized trial of less intense postoperative warfarin or aspirin therapy in the prevention of venous thromboembolism after surgery for fractured hip. *Arch Intern Med* 1989; **149**: 771–4.
19. Thaler HW, Roller RE, Greiner N, Sim E, Korninger C. Thromboprophylaxis with 60 mg enoxaparin is safe in hip trauma surgery. *J Trauma* 2001; **51**: 518–21.
20. Eriksson BI, Bauer KA, Lassen MR, Turpie AGG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med* 2001; **345**: 1298–304.
21. National Institute for Health and Clinical Excellence. *Venous Thromboembolism: the prevention of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients undergoing orthopaedic surgery and other high-risk surgical procedures*. Full guideline draft. 2006. Available at: <<http://www.nice.org.uk>> (Accessed 3 October 2006).