Factors influencing mortality in patients on antiplatelet agents presenting with proximal femoral fractures

Rohit Maheshwari, Mehool Acharya, Maureen Monda, Radhakant Pandey
Department of Trauma and Orthopaedics, University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester, United Kingdom

ABSTRACT

Purpose. To identify factors predicting one-year mortality in patients on clopidogrel presenting with proximal femoral fractures.

Methods. 9 men and 22 women aged 64 to 97 (mean, 81; standard deviation, 8) years who had been taking clopidogrel for ischaemic heart disease (n=15), cerebrovascular disease (n=6), or both (n=10) presented with proximal femoral fractures. The time from injury to operation, type of anaesthesia, treatment method, and postoperative complications were reviewed. One-year mortality was analysed using the Kaplan-Meier curve. Factors predicting one-year mortality were identified.

Results. The fracture configurations of the 31 patients included intracapsular femoral neck fracture (n=17), intertrochanteric fracture (n=13), and subtrochanteric fracture (n=1). 30 of the patients underwent hemiarthroplasty (n=16), dynamic hip screw fixation (n=9) or intramedullary hip screw fixation (n=5). The remaining patient underwent conservative treatment owing to metastatic prostate cancer. Of the 30 patients who underwent surgery, clopidogrel was discontinued at least 7 days prior to surgery, with the mean delay to surgery being 8.4 (range, 2–16) days. No patient had excessive blood loss at operation, although 7 patients received a blood transfusion postoperatively. 13 (43%) patients developed postoperative complications. The one-year mortality was 26% (8/31). Univariate analysis showed that factors predicting one-year mortality were spinal anaesthesia (p=0.04), postoperative blood transfusion (p=0.03), postoperative complications (p=0.03), and delay to surgery (p=0.03). Multiple regression analysis showed that delay to surgery (p=0.03) was the only independent predictor of one-year mortality, with a hazard ratio of 1.357 (95% confidence interval, 1.03–1.79).

Conclusion. Surgery should be performed as soon as possible in medically fit patients having proximal femoral fractures who are taking clopidogrel, as delay to surgery is associated with increased one-year mortality.

Key words: clopidogrel; femoral neck fractures; mortality
Mortality in patients on antiplatelet agents with proximal femoral fractures

INTRODUCTION

The number of proximal femur fractures in the United Kingdom is about 57 500 per year and is expected to increase to around 70 000 by 2020.1 Most patients presenting with such fractures are aged >65 years.1 They have a high prevalence of atherosclerotic vascular disease and often take antiplatelet agents.2,3 Clopidogrel bisulfate is an adenosine diphosphate inhibitor that works by antagonising its binding to platelet receptors, irreversibly impairing platelet clotting function by decreasing platelet aggregation and thrombus formation.3 It is used as routine secondary prevention therapy for myocardial infarction and is commonly substituted for aspirin in patients intolerant of this.

There are no universal guidelines on discontinuing clopidogrel preoperatively in patients having proximal femoral fractures.4–6 Delaying surgery in this group of patients (usually having multiple co-morbidities) may have adverse effects.4,5 We aimed to identify factors predicting one-year mortality in patients on clopidogrel treated for proximal femoral fractures.

MATERIALS AND METHODS

Between February and December 2006, 9 men and 22 women aged 64 to 97 (mean, 81; standard deviation, 8) years who had been taking clopidogrel for ischaemic heart disease (n=15), cerebrovascular disease (n=6), or both (n=10) presented with proximal femoral fractures. The time from injury to operation, type of anaesthesia, treatment method, and postoperative complications were reviewed.

The primary outcome measure was one-year mortality, which was analysed using the Kaplan-Meier curve. Factors predicting one-year mortality were identified using univariate analyses. Significant factors were then entered into a multiple regression analysis model to identify independent factors predicting one-year mortality.

RESULTS

The fracture configurations of the 31 patients included intracapsular femoral neck fracture (n=17), intertrochanteric fracture (n=13), and subtrochanteric fracture (n=1). 30 of the patients underwent hemiarthroplasty (n=16), dynamic hip screw fixation (n=9) or intramedullary hip screw fixation (n=5). The remaining patient underwent conservative treatment owing to metastatic prostate cancer.

Of the 30 patients who underwent surgery, clopidogrel was discontinued at least 7 days prior to surgery, with the mean delay to surgery being 8.4 (range, 2–16) days. The American Society of Anesthesiologists grade was 2 in 6 patients, 3 in 18, and 4 in 6. 16 patients had general anaesthesia with or without a regional block, whereas 14 patients had spinal anaesthesia.

No patient had excessive blood loss at operation, although 7 patients received a blood transfusion postoperatively. Their mean postoperative haemoglobin level was 8.9 (range, 7.3–10.8) g/dl. In all 31 patients, the mean pre- and post-operative haemoglobin levels were 11.7 (range, 9.1–15.5) and 9.9 (range, 7.3–12.7) g/dl, respectively.

13 (43%) patients developed postoperative complications (Table). No patient receiving spinal anaesthesia developed spinal haematoma. The one-year mortality was 26% (8/31, Fig.). Univariate analysis showed that factors predicting one-year mortality were spinal anaesthesia (p=0.04), postoperative blood transfusion (p=0.03), postoperative complications (p=0.03), and delay to surgery (p=0.03). Multiple

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchopneumonia</td>
<td>6</td>
</tr>
<tr>
<td>Clostridium difficile diarrhoea</td>
<td>2</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2</td>
</tr>
<tr>
<td>Fixation failure</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
</tr>
</tbody>
</table>

Figure One-year mortality
regression analysis showed that delay to surgery (p=0.03) was the only independent predictor of one-year mortality, with a hazard ratio of 1.357 (95% confidence interval, 1.03–1.79).

**DISCUSSION**

In our hospital, 5% of patients admitted with proximal femoral fractures were taking clopidogrel regularly for secondary prevention of myocardial infarction and stroke. With an ageing population, this percentage is likely to increase.

The risks of clopidogrel and other antiplatelet agents include increased surgical bleeding and the development of spinal haematoma in patients undergoing spinal or epidural anaesthesia. The American College of Chest Physicians guidelines recommend withholding antiplatelet agents at least 5 days prior to elective surgical procedures. With regard to clopidogrel, the American Society of Regional Anaesthesia guideline recommends that neuraxial anaesthesia not be administered until this drug has been discontinued for a minimum of 7 days. Nonetheless, there are no consensus guidelines for the management of such patients presenting with a proximal femoral fracture. Our hospital’s policy was to discontinue clopidogrel on admission and delay surgery for 7 days to reduce any risk of increased bleeding.

Patient age and co-morbidities are considered to affect mortality, whereas anaesthetic technique per se has minimal impact on mortality. Short-term mortality is reduced with the use of regional anaesthesia, but no conclusion can be drawn on long-term mortality. In our study, spinal anaesthesia was predictive of increased one-year mortality, but was not an independent predictor. Patients were relatively hypotensive during spinal anaesthesia, which may affect the postoperative recovery and outcome. Blood transfusion and postoperative complication were also predictive of increased one-year mortality. Blood transfusion correlates positively with postoperative complication (Pearson’s correlation=0.3, p=0.04), but it was not an independent predictor of mortality. Patients receiving blood transfusion may be at higher risk of developing postoperative complications. In another study, postoperative transfusion was associated with a significantly increased risk of mortality and infection in hip fracture patients at ≥4 months. Alternatively, patients developing postoperative complications may endure delayed rehabilitation and thus may undergo transfusion to improve their rehabilitation potential.

As delay to surgery was the only independent predictor of mortality, we recommend that medically fit patients presenting with proximal femoral fractures who are taking clopidogrel should undergo surgery without undue delay. Platelet transfusion should be available in the event of major bleeding.

**REFERENCES**