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Clopidogrel: is a surgical delay necessary in fractured neck of femur?

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ABSTRACT

INTRODUCTION This paper assesses the outcomes of patients after surgery for a proximal femur fracture while on clopidogrel. It describes a single-centre retrospective observational study over a two-year period.

PATIENTS AND METHODS A total of 31 surgical patients were included in this study. Of these, 28 were on clopidogrel and 3 on dipyridamole. Patients were split into subgroups based on when surgery took place and the type of hip fracture. The 'early surgery' (<48 hours from admission to theatre) group contained 16 patients (51.6%) and the 'late surgery' (>48 hours) group composed 15 patients (48.4%). Type of surgery performed and pre-and postoperative haemoglobin (Hb) levels were recorded. Furthermore, the number of units of blood transfused per patient as well as complications before and after surgery were noted.

RESULTS A significantly larger mean Hb drop occurred in the early surgery group (3.2g/dl) compared with the late surgery group (2.3g/dl) (p=0.027). The mean length of inpatient stay was 21 days in the early and 23 days in the late group (p=0.456). A significantly larger Hb mean drop occurred in patients with extracapsular hip fractures (3.4g/dl; n=16) compared with patients with intracapsular fractures (2.3g/dl; n=15) (p=0.020). The extracapsular patients had longer stays in hospital: 24.5 days versus 19.8 days in the intracapsular group (p=0.521). There was no statistical difference in the 30-day mortality between the early surgery (3/16 deaths) and late surgery (2/15 deaths) groups (p=0.481).

CONCLUSIONS Patients with extracapsular fractures, treated with early surgery, appear to be most at risk of complications after surgery.

KEYWORDS

Clopidogrel – Dipyridamole – Orthopaedics – Femur – Hip fractures

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Hip fracture represents the most common cause of injury requiring hospitalisation in patients over the age of 65.[1] In the UK there are approximately 76,000 hip fractures a year and National Health Service costs amount to around £1.4 billion.[2] The incidence of concurrent medical co-morbidities among this group of patients is high, with 66% having an American Society of Anesthesiologists (ASA) grade of 3 or greater.[3] Preoperative assessment by orthogeriatricians is recommended to manage these patients[2–4] although it is recognised that less than 42% of hip fracture patients have any preoperative medical assessment.[5]

Increasing numbers of elderly patients are managed on long-term antiplatelet medications (clopidogrel or dipyridamole). These drugs are associated with an increased perioperative bleeding risk. Elective surgery recommendations state that all antiplatelets should be discontinued five to seven days before surgery to allow a reversal of the drug effect.[5] Current evidence recommends, where possible, that hip fracture patients should undergo surgery within 48 hours[6–9] to minimise perioperative risks. At present there is no official strategy for trauma patients on antiplatelet therapy. Current practice appears to vary, with no clear evidence base, between early surgery versus a 'haemoprotective' surgical delay[10] or operating immediately with perioperative platelet transfusion.

This study analyses the outcome of patients admitted at our institution who underwent different management strategies while taking clopidogrel or dipyridamole, focusing specifically on blood loss, length of stay and complication rates.

Methods

All patients admitted to the Royal Albert Edward Infirmary in Wigan who sustained a fractured proximal femur between 1 January 2008 and 31 December 2009 were reviewed. A total of 619 cases of neck of femur fracture were identified, of which 35 patients were taking clopidogrel or dipyridamole.

Data were collected on antiplatelet type and whether antiplatelet medication was stopped preoperatively. Admission time to hospital, time to surgery, type of surgery performed, anaesthetic technique, and pre-and postoperative haemoglobin (Hb) levels were recorded. Blood loss was calculated by subtracting postoperative from preoperative Hb levels in the immediate postoperative period. The number of packed red cell and platelet transfusions per patient (and

Table 1 Comparison between patients in the 'early surgery' and the 'late surgery' group

	Mean length of stay	Mean Hb drop	Complications before surgery	Complications after surgery	Total units of blood transfused	Inpatient deaths
Early surgery (*n*=16)	21.1 days	3.2g/dl	2	8	7	2
Late surgery (*n*=15)	22.9 days	2.3g/dl	4	5	7	2

Table 2 Comparison between patients with extra- and intracapsular hip fractures

Type of hip fracture	Mean length of stay (days)	Mean Hb drop (g/dl)	Complications before surgery	Complications after surgery	Total units of blood transfused	Inpatient deaths
Extracapsular (*n*=16)	24.5	3.4	2	9	17	2
Intracapsular (*n*=15)	19.8	2.3	1	6	13	2

when transfused) was recorded. Complications before and after surgery, including inpatient and outpatient mortality, were identified. Finally, the patients were matched in terms of age, sex, ASA grade and co-morbidities to assess the balance of the cohort. All data were collected either directly from case notes or from patient discharge summaries on our electronic patient record system.

For statistical analysis, Kolmogorov–Smirnov testing was applied and, where appropriate, an independent samples t-test was run for significance in relevant groups. A Mann–Whitney U test was performed for comparison of data that were not normally distributed. All data analyses were performed using SPSS® v10.1 (SPSS Inc, Chicago, Illinois, US).

Results

A total of 35 patients sustaining a fractured neck of femur were admitted while taking clopidogrel or dipyridamole. Of these, 31 were managed surgically and 4 conservatively.

Of the 31 surgical patients, 28 were on clopidogrel and 3 were taking dipyridamole. Twenty-four of the patients (86%) had clopidogrel stopped on admission while dipyridamole was not stopped in any patient. Eight patients were dead at twelve months, four as inpatients within thirty days of surgery and four after discharge (returning under medical care for unrelated symptoms). Patients were split into two subgroups for comparison: those having early surgery (defined as <48 hours) (*n*=16; 51.6%) versus late surgery (defined as >48hours) (*n*=15; 48.4%). The mean age of the patients undergoing early surgery was 81.6 years versus 82.6 years in the late surgery group. The mean number of co-morbidities was four in patients having early surgery and five in those having late surgery. The mean ASA grade for all patients was 3.

Further subgroup analysis compared extracapsular versus intracapsular fracture cases. The extracapsular group had a mean age of 84.5 years while the intracapsular group had a mean age of 79.5 years. The mean number of co-morbidities in the extracapsular group was 4 and the intracapsular group was 5.

Early surgery vs late surgery

A comparison between the patients in the early surgery and later surgery groups is shown in Table 1. There was a significantly larger mean Hb drop in the early surgery group (3.2g/dl) compared with the late surgery group (2.3g/dl) (p=0.027). A total of seven packed red cell units were transfused across both groups, all after surgery. Perioperative platelet transfusion was performed in three patients to expedite surgery, with two units transfused per patient.

The early surgery group had two patients (12.5%) with a preoperative complication and eight (50%) with complications after surgery (two fatal). The late surgery group had four patients (26.7%) with preoperative complications and five (33.3%) with complication after surgery (two fatal). Five patients died in the early surgery group (two as inpatients) and three died in the late surgery group (two as inpatients). The mean length of stay was 21 (range: 5–58) days in the early group and 23 (range: 8–61) days in the late group (not significant; p=0.456).

Extra vs intracapsular hip fractures

A comparison between the patients with extra and intracapsular hip fractures is shown in Table 2. There was a significantly larger mean Hb drop in patients with extracapsular hip fractures (3.4g/dl; *n*=16) compared with that in patients with intracapsular fractures (2.3g/dl; *n*=15) (p=0.020). A total of 17 blood transfusion units were given to 7 patients in the extracapsular group, while only 13 units were transfused to 6 patients in the intracapsular group. No platelets were administered in the extracapsular group. However, three patients treated for an intracapsular fracture were given two units each and subsequently operated on after 48 hours. Two patients (12.5%) had preoperative complica-

tions in the extracapsular group compared with one (7%) in the intracapsular group. Nine patients (56%) had complications after surgery in the extracapsular group and six (40%) in the intracapsular group. Two patients died in each group. The extracapsular group had a longer stay in hospital: 24.5 days versus 19.8 days in the intracapsular group (not significant; p=0.521).

The results demonstrate that the extracapsular group had a longer stay on the wards along with a greater number of complications before and after surgery, also having more units of blood transfused, although these results were not significant.

Discussion

According to our results, patients on clopidogrel/dipyridamole having early hip fracture surgery have significantly greater blood loss compared with those patients on clopidogrel/dipyridamole whose hip surgery is delayed for 48 hours or more. Similarly, patients on clopidogrel/dipyridamole with extracapsular hip fractures have significantly greater blood loss compared with those patients with intracapsular fractures. Our results show there were more complications after surgery in the early surgery group and the extracapsular group, when compared with the late surgery and intracapsular groups.

It is generally accepted that patients sustaining a fractured neck of femur should undergo surgery within 48 hours to prevent perioperative complications. Our data do not support this assumption for those patients taking clopidogrel/dipyridamole. According to our data, there was no significant difference in 30-day mortality for those patients having early versus late surgery. This concurs with the data from the Scottish national study.[10] Furthermore, in our study more patients developed complications after early surgery compared with patients whose surgery was delayed for more than 48 hours although these results were not significant (p=0.481).

Patients requiring extracapsular hip fracture surgery have significantly greater blood loss than patients undergoing intracapsular surgery. Additionally, they have longer hospital stays, have more complications before and after surgery, and also have more units of blood transfused after surgery although these differences were not significant. The 30-day mortality for extra and intracapsular fracture groups was identical.

The limitations of this study are that this is a single-centre study of small size. We cannot control patient age, co-morbidities, operative surgeon, operative technique or anaesthetic technique. It is likely these variables will have a significant influence on the patients' blood loss and overall outcome. When evaluating the blood loss, this study only used the drop in Hb and did not calculate an actual blood loss in millilitres. Although intravenous fluid and dehydration can affect pre and postoperative Hb levels,[11] we assume the intravenous fluids given before and after surgery are generally constant, along with the dehydration levels of each patient on admission.

Conclusions

Despite these limitations, important conclusions can still be drawn from these results and guidance can be offered on the appropriate management of hip fracture patients while on clopidogrel/dipyridamole. It would appear the extracapsular neck of femur patient treated with early surgery is most at risk of bleeding and postoperative complications. In this patient group, platelet administration prior to the first skin incision to reduce the rate of blood loss and postoperative complications might be considered. While delaying surgery for these patients is considered controversial,[8,12,13] we have not found any significant medical disadvantage, which concurs with the Scottish national study.[10,14] We note that the UK National Institute for Health and Clinical Excellence is currently without a policy regarding these patients[15] and we aim to offer assistance in the matter with this study.

Appendix

Complications before and after surgery in the 'early surgery' group

Early surgery	Complications before surgery	Complications after surgery
1	Urinary tract infection	Wound oozing; chest infection – patient died
2	Fast atrial fibrillation – patient died	Wound oozing
3		Wound oozing
4		Wound infection
5		Confusion; urinary tract infection
6		Anaemia; exacerbation of congestive cardiac failure
7		Chest infection; myocardial infarction
8		C2 peg fracture – patient died

Complications before and after surgery in the 'late surgery' group

Late surgery	Complications before surgery	Complications after surgery
1	Chest infection	Wound oozing; cerebrovascular accident – patient died
2	Confusion	Wound infection
3	Other: haematuria (Hb dropped to 7.9g/dl; required transfusing)	Chest infection; pseudo bowel obstruction; mild wound oozing
4	Cerebrovascular accident	Wound haematoma
5		Wound oozing – patient died

Complications before and after surgery in the 'extracapsular hip fracture' group

Extra-capsular	Complications before surgery	Complications after surgery
1	Other: haematuria (Hb dropped to 7.9g/dl; required transfusing)	Hyponatraemia 119mEq per litre
2	Fast atrial fibrillation	Urinary tract infection; leg swelling
3		Exacerbation of congestive cardiac failure
4		Wound oozing – patient died
5		Wound bleeding excessive
6		Sudden myocardial infarction (after atrial fibrillation) – patient died
7		Chest infection; pseudo bowel obstruction; mild wound oozing
8		Wound oozing
9		Myocardial infarction; transferred to intensive care unit

Complications before and after surgery in the 'intracapsular hip fracture' group

Intra-capsular	Complications before surgery	Complications after surgery
1	Confusion	Wound oozing
2	Cerebrovascular accident	Wound infection
3		Confusion; urinary tract infection
4		Cerebrovascular accident; left thigh swelling – patient died
5		C2 peg fracture – patient died
6		Chest infection

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