

Transfusion after Intramedullary Nailing of Hip Fractures

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Abstract

Introduction: Patients with unstable multi-fragmentary trochanteric fractures in comparison to those with simple intra-capsular and inter-trochanteric fractures have a larger amount of fractured metaphyseal bone from which bleeding can occur at the time of injury. A detailed analysis was performed comparing haemoglobin (Hb) in the pre and post-operative periods between patients requiring transfusion and those not. This was to determine if pre-operative blood loss caused a greater magnitude of fall in Hb concentration compared to post-operative blood loss, demonstrating if bleeding from the fracture as opposed to the surgery that patients had undergone was associated with the need for transfusion.

Methods: Retrospective review of patients undergoing third generation Gamma Nail (Stryker Trauma, Switzerland) fixation for unstable peritrochanteric fractures. Fracture type was classified according to the MÜller AO/OTA classification. Patients were excluded if they had prophylactic nailing for metastatic disease; had sustained a diaphyseal fracture; or if they had been on warfarin, had any previous documented anaemia or acute gastrointestinal haemorrhage. The pre and post-operative Hb was recorded, timing and volume of transfusion. The Hb levels were analysed using a repeated measures regression model. The mean arterial blood pressure (MAP), level of fitness prior to surgery according to the American Society Anaesthesiologists (ASA) grading and fracture type was defined for each patient.

Results: There were 51 patients with a mean age of 78 years after exclusions. 23 patients received a transfusion and 28 did not. The mean pre-operative Hb in the non-transfused group was 118.4 g/L, higher than the Hb in the transfused group, 95.9 g/L ($p < 0.00$). In comparison, in the 48 hour period after their operation, the mean Hb concentrations were comparable in both groups ($p=0.358$).

Conclusions: There was a significant difference in the starting Hb level between groups: in the group requiring transfusion patients were anaemic before surgery. The association of pre-operative anaemia with an unstable multi-fragmentary trochanteric fracture should alert clinicians that these patients are likely to require blood replacement.

Keywords: Transfusion; Intramedullary nail; Hip fracture; Osteoporotic fracture

Introduction

Patients with unstable peri-trochanteric proximal femur fractures typically undergo operative fixation with a cephalomedullary device, as standard dynamic hip screw fixation is considered to have a higher risk of failure, for instance: trochanteric fractures extending distal to the lesser trochanter or a reverse oblique pattern. The majority of acute blood loss sustained by patients with a fractured neck of femur is postulated as due to bleeding from the initial fracture, rather than from blood loss due to surgery [1,2,3]. And it has been recommended patients with a subtrochanteric fracture should have a repeat Hb after undergoing preoperative intravenous fluid rehydration, as they have been seen to have a larger drop in Hb compared to intertrochanteric and intracapsular fractures prior to surgery [4]. Unstable peri-trochanteric fractures may need to be considered differently in terms of an increased resuscitation requirement compared to patients with a generic neck of femur fracture.

A lack of consensus remains amongst the best approach for neck of femur patients in anticipation of their transfusion requirements: a protocol for cross-matching, universal group and save or unselective cross-matching [5,6,7]. In addition, several factors may influence the initial Hb level on admission, including: the timing after fracture and presence of pre-fracture dehydration and pattern of injury [1,3]. Those patients in greatest need for replacement of acute blood loss are also often not identified early [2]. Patients with trochanteric fractures treated by intramedullary nailing have been calculated to have the highest estimated total blood loss of all treated neck of femur patients [1]. To further examine this in a particularly at risk group, we undertook

a focused analysis of patients undergoing intramedullary nailing of unstable multi-fragmentary trochanteric fractures. The Hb levels in the pre and postoperative period between those patients requiring transfusion and those not were directly compared, to show whether intra-operative or pre-operative losses contributed more to the drop in Hb and requirement for transfusion.

Patients and Methods

All patients undergoing fixation of a hip fracture using a third generation Gamma Nail (Stryker Trauma, Geneva, Switzerland) over a 12 month period from August 2007 to August 2008 were identified from the hip fracture database. Patients were excluded if they had prophylactic nailing for metastatic disease; had sustained a diaphyseal fracture; had any previous documented anaemia or acute gastrointestinal haemorrhage. Patients were also excluded if they had been on warfarin since they would have undergone reversal of therapy on admission using vitamin K, which may cause a confounding factor in the analysis of Hb levels over time due to the delay whilst awaiting the international normalised ratio (INR) to fall to an acceptable level.

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Patients were separated into 2 cohorts: those requiring transfusion and those not. A retrospective observational review was performed with data collected on fracture classification, serial Hb measurements, patient co-morbidities and intra-operative as well as post-operative BP measurements.

In our centre, Gamma Nail fixation is used for unstable multi-fragmentary and subtrochanteric fractures, through a small incision over the tip of the greater trochanter [8]. A standard closed reduction manoeuvre is performed on a traction table to reduce the fracture, before initial reaming of the proximal femur to allow insertion of the nail under image intensifier guidance and subsequent proximal lag screw and distal locking screws. For replacement of acute blood loss, the trigger for transfusion in this institution is a Hb level of 80 g/L or less with or without the presence of symptomatic anaemia, in accordance with established transfusion guidelines [9,10] and the British Committee for standards in haematology [11]. In patients who tolerate anaemia poorly, such as those over the age of 65, with cardiovascular or respiratory disease, transfusion is indicated for a Hb concentration of < 80 g/L; whilst in younger patients without associated co-morbidities transfusion is indicated at a Hb concentration of < 70 g/L [11].

Serial Hbs were analysed using a repeated measurements regression model with time category, transfusion or not, and the time-transfusion interaction as factors in the model. In order to compare the Hb levels in the model, data was aggregated and analysed according to time categories: time category 0 represented pre-operative measurements; time category 1 represented days 1-2 after operation; category 2 represented days 3-5, and time category 3 represented day 6 and beyond. Significance testing of coefficients in the regression model was done by Wald Chi squared test. The mean arterial pressure in mm Hg was derived from the lowest recorded intra-operative BP and the lowest recorded BP during the initial 4 hour recovery period for patients on the ward. Student's t test was used to test for a significant difference between the transfusion and non-transfusion groups as this was parametric data with standard normal distribution. To test for a significant difference between the two groups in the non-parametric ordinal data of the ASA grading of fitness for surgery, and AO/OTA classification [12] of fractures, Mann Whitney U Test was used.

Results

Fifty two patients were identified and one excluded because they had been on warfarin. The 51 remaining patients were allocated into 2 cohorts: 23 requiring transfusion and 28 not transfused. A total of 68 units of blood were given in the transfusion group, with a median 2 Units of blood transfused to each patient. Overall for the whole group, the Transfusion index (Ti), a measure of the average number of units of blood transfused per procedure [6], was 1.33. The majority of patients (19/23) received their blood transfusion in the early peri-operative period within 72 hours of surgery. The demographic characteristics of the two cohorts are presented in Table 1. The majority of patients in both cohorts were female, and the average age was 77 years in the group requiring transfusion, and 79 years in the non-transfusion group. The level of surgical complications was similar in both. In the non-transfused group one patient had a wound haematoma treated conservatively, and 2 suffered late failures of their gamma nails over a follow up period of 1 year. One patient had revision to a total hip replacement with a Reef femoral stem (DePuy, Indiana, USA) for cut out of the lag screw. The other patient underwent revision intramedullary nailing for non-union. In the patients requiring transfusion there was one surgical complication of continued bleeding from the wound post-operatively,

Patient Group	No Transfusion (No Tx)	Transfusion (Tx)
Patients	28	23
Mean Age (Range)	79 (51-95)	77 (34-96)
Male : Female	4 : 24	4 : 19
Consent Form 1	85%	80%
Surgical Complications	3	1
Medical Complications	6	6
Median Length hospital stay (Range)	11 (4-60)	16 (5-51)
Deaths	3	0

Table 1: Patient demographics and characteristics.

which required treatment by angiography and embolisation. There were 3 deaths in the non-transfusion group due to: cerebrovascular accident, abdominal sepsis and pneumonia. None of the patients who received a transfusion suffered an adverse reaction to blood transfusion.

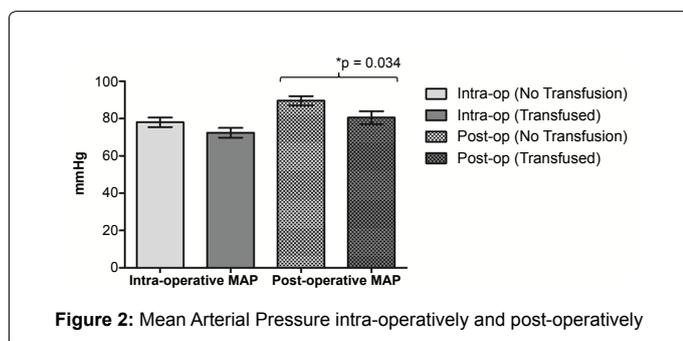
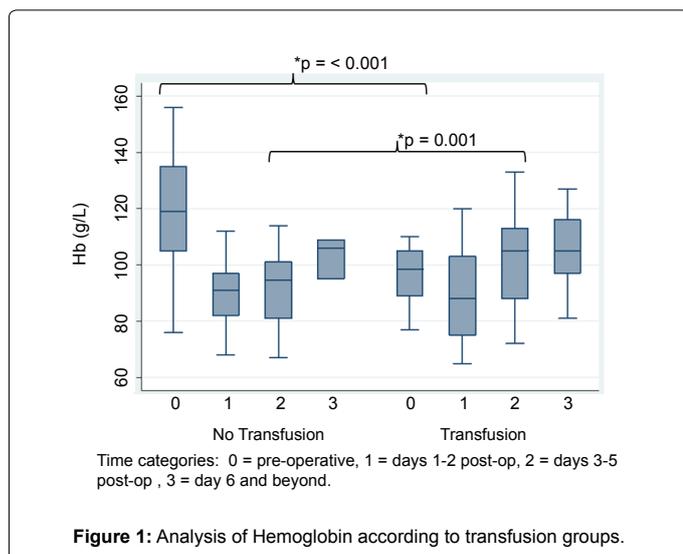
In the analysis of Hb levels by time categories (Figure 1), a significant difference was found in the pre-operative mean Hb (time category 0) between the groups: patients in the non-transfusion group had a higher mean Hb of 118.4 g/L compared to 95.9 g/L in those requiring transfusion ($p < 0.00$). In the early 48 hour post-operative period, the mean Hb was comparable in both ($p=0.358$). At days 3-5, a significantly lower mean Hb was measured in the non-transfused patients: 90.8 g/L compared to 105.5 g/L in those transfused ($p=0.001$) due to the effects of replacement of haemoglobin.

The mean arterial pressure is displayed for both groups in Figure 2. Intra-operatively there was no significant difference seen in MAP of patients requiring transfusion and those not transfused. During their operation, 16 patients received either phenylephrine or ephedrine to treat hypotension associated with anaesthesia: 7 in the transfusion group and 9 in the non-transfusion group. However, in theatre recovery and during the postoperative period on the ward, no patient received phenylephrine or ephedrine in either group. A significantly lower MAP was seen in the transfused patients postoperatively on the ward, with a mean of 80.6 mmHg (SEM 3.4) compared to 89.6 mmHg (SEM 2.5) for the non-transfused group ($p=0.034$). This provides evidence these patients had signs of altered haemodynamic response, albeit without major circulatory compromise requiring inotropic or vasopressor support, and this justifies the clinical decision at the time to transfuse them.

In terms of medical co-morbidities that might cause the patients to tolerate anaemia poorly, 9 patients had an existing history of ischaemic heart disease: 4 in the transfused and 5 in the non-transfused group. The groups were examined to see if there was any difference between them in the ASA grading (Figure 3) which might suggest a difference in their physiological response to trauma or blood loss. Analysis of the ASA grading showed there was no significant difference in the level of pre-morbid illnesses ($p=0.102$). Similarly, a comparison of AO/OTA classification of the fracture types (Figure 4) showed these were broadly similar between the groups ($p=0.292$).

Discussion

Several studies have observed that patients with extra-capsular neck of femur fractures sustain a greater drop in Hb compared to those with intra-capsular fractures following surgery [3,5,13]. This larger drop has been attributed to the type of operation that patients' have had: cephalomedullary devices and dynamic hip screws for trochanteric fractures have a greater calculated total blood loss [1] and transfusion index, compared to hemiarthroplasty or cannulated screws

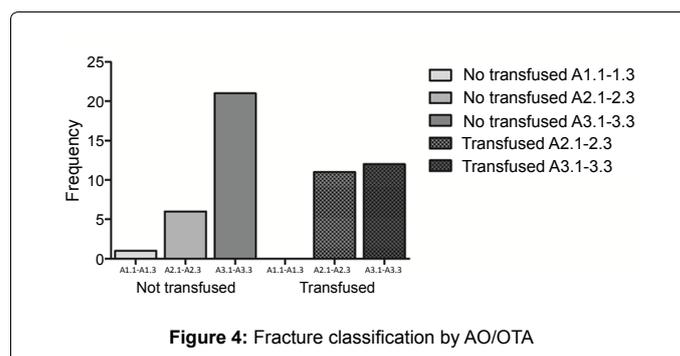
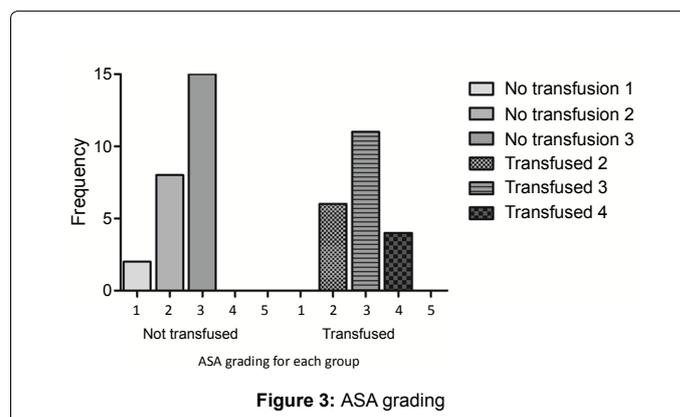


for intra-capsular fractures [5,6,14]. However, the differences are not fully explained by surgery alone [3]. There is also an additional unmeasurable blood loss sustained in neck of femur fracture patients: due to trauma, anticoagulation and bleeding from other sources [1,15]. In one study, 16% of patients with a two part trochanteric fracture required transfusion whilst 58% of those with a comminuted trochanteric fracture required transfusion [2].

The results here show the patients transfused in the peri-operative period were significantly more anaemic before surgery compared to those who did not require transfusion. This indicates the greatest contribution to blood loss was from injury as opposed to surgery. Had there been greater blood loss sustained from surgery, this would have manifested as differing levels of anaemia between the groups post-operatively. However this was not observed, and by days 3-5 the cohort of patients who needed transfusion had recovered to a significantly higher Hb, after receiving blood. In the initial 4 hours after surgery the haemodynamic effects of acute blood loss, in terms of a significantly reduced mean arterial pressure, was also seen in these same patients who required a transfusion. Consequently, the presence of anaemia in the pre-operative period is an early indicator of the need for blood replacement when these patients undergo surgical fixation. Whilst allogeneic transfusion is generally safe there remain potential disadvantages to use of a liberal transfusion policy. This is due to the risk of transfusion reaction from clerical error [16], transfusion related modulation of the immune system [17], the economic costs and theoretical risk of disease transmission. Further work is required in terms of strategies for conservation of blood in the traumatised elderly.

One option for reducing the need for transfusion in neck of femur patients may be the use of intravenous iron therapy or recombinant preoperative erythropoietin [18,19]. However, concerns exist for the potential for adverse drug reaction as well as the possible increased incidence of venous thromboembolism.

Some limitations are worth noting in this study. One weakness was that the grade of surgeon, length of operation and measurement of any blood loss intra-operatively was not investigated. The primary outcome was reduction in Hb level before and after surgery, and the magnitude of fall in Hb concentration. However without knowledge of the pre injury Hb level, an analysis of aggregated serial Hb levels over time provides only a surrogate indicator of when blood loss occurred. It is apparent that the difference in Hb levels between the groups occurred prior to surgery then at the time of operation. An attempt was made to control the confounding variables in the exclusion criteria, including excluding those patients known to have a previous documented history of anaemia. Ideally, knowledge of the pre injury Hb level would have allowed the effects of dehydration, iatrogenic haemodilution and the full extent of pre-existing anaemia to be shown in a longitudinal analysis of Hb concentration over time. Numerous difficulties exist in accurate assessment of intra-operative blood loss, and there is a considerable difference in the amount of observed blood suctioned from the wound and collected from swabs during an operation, compared to the calculated total amount of blood loss derived from the patient's Hb concentration, gender, height and weight [1]. An alternative measurement might have been to use the haematocrit (Hct) or packed cell volume, although this traditionally has not been seen as a reliable index of acute blood loss, due to the delay in interstitial fluid shift into the vascular space following haemorrhage. Hct is also affected by chronic renal disease, iron deficiency anaemia and the degree of hydration. There is growing interest in its role as a marker for transfusion requirement in major trauma [20] however in



the context of this study, for the purposes of examining acute blood loss and the response to blood replacement, the Hb concentration was more accurate. The small size of the study cohort was a limitation, and since a retrospective analysis of patients was performed, the sample size was not determined beforehand. Whilst an association between pre-operative anaemia and transfusion rather than causality is proven here, we think this study further adds to the current body of evidence.

The transfusion index for patients in this study was 1.33, comparable to previously reported values of 1.17 Units and 1.58 Units for intertrochanteric fracture fixation [5,6]. Placing this in context, the British Committee Standards in Haematology guidelines for surgical blood order recommend that for procedures where more than 30% of blood is used ($T_i > 0.3$) cross matching rather than group and save should be used [21]. In the group requiring transfusion, the median number of Units transfused per patient was 2, similar to findings in an overall study of blood transfusion in femoral neck fractures, with a value of 2.57 Units seen previously [13].

Patients with neck of femur fracture are frail, elderly, vulnerable to the effects of anaemia and hypovolaemia and have an altered physiological response to trauma [22]. The amount of blood loss which a patient can safely tolerate depends on their physiological status, and elderly patients with pre-existing coronary heart disease do not endure acute blood loss as well as younger healthy individuals [15]. We recommend that clinicians intending to use a cephalomedullary nail to fix an unstable neck of femur fracture should be aware of preoperative anaemia, as it is associated with an increased need for transfusion. Such recognition may avoid prolonged low mean arterial blood pressure postoperatively if patients are transfused early, and thus exposing these patients to the potential for circulatory compromise.

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