



Analysis of The Risk Factors for Postoperative Allogenic Blood Transfusion Requirement in Intertrochanteric Femur Fractures

Analýza rizikových faktorů pro požadavek pooperační alogenní krevní transfuze u intertrochanterických zlomenin femuru

G. CANSABUNCU¹, A. TURGUT²

¹ Department of Orthopaedic and Traumatology, Bartın State Hospital, Bartın, Turkey

² Department of Orthopaedic and Traumatology, Tepecik Training and Research Hospital, İzmir; Turkey

ABSTRACT

PURPOSE OF THE STUDY

Hemoglobin (Hb) levels tend to decrease in patients after hip fractures. There are several factors that are responsible for this decrease in Hb levels. The primary aim in this study was to evaluate the risk factors of blood loss in patients with IFF and to determine the limits that may require allogeneic blood transfusion (ABT), and the secondary aim was to prevent unnecessary blood crossing outside these limits.

MATERIAL AND METHODS

119 patients with intertrochanteric femur fracture (IFF) were included in the study. The patients were divided into two groups according to the use of ABT in the postoperative period. Age, gender, fracture side, height, weight, body mass index (BMI), American Society of Anesthesiologist (ASA) score, preoperative hemoglobin (Hb) level, platelet (Plt) number, International Normalized Ratio (INR), prothrombin time (PT), activated partial thromboplastin time (aPTT) values, comorbid diseases, history of drug use, whether ABT was applied in the preoperative period or not, and the postoperative 1st day Hb levels were evaluated from the medical records. A p value below than 0.05 was accepted as statistically significant.

RESULTS

Advanced age [odds ratio (OR) 1.069, 95% confidence interval (CI) 0.372–3.202], unstable fracture type [OR 0.258, 95% CI 0.496–6.632], and hemoglobin level <11 g / dL [OR 5.574, 95% GA 0.312–65.278 was found to be an independent predictive risk factor for allogeneic blood transfusion requirement in the postoperative period.

DISCUSSION

There are several factors that are responsible for decrease in Hb levels in patients after hip fractures. The most important and most likely cause of these is the fracture itself. Other reasons are stated as type of fracture, time elapsed until the surgical treatment, preferred implants for treatment, advanced age, mean preoperative Hb value and anticoagulant drug usage in literature. Although the preoperative blood loss due to trauma is inevitable, unnecessary aggressive and/or inadequate treatments can be avoided if patients with higher bleeding risk and complication rate can be detected.

CONCLUSIONS

Advanced age, unstable fracture pattern and low preoperative Hb values should be considered as risk factors for the postoperative ABT requirements for patients with IFF.

Key words: intertrochanteric femur fracture, allogenic blood transfusion, blood loss hemoglobin level.

INTRODUCTION

Although intertrochanteric femoral fractures (IFF) are frequently seen in the elderly patient population, they constitute approximately 3% to 4% of all fractures (26). Conservative treatment of IFFs in elderly patients is known to increase disability and mortality rates by causing pressure sores, pulmonary system and urinary system infections (19). Surgical treatment is the current approach to reduce mortality, increase quality of life and preserve joint functions in these patients (14). Cephalomedullary nails are the preferred implants for most extra-capsular proximal femoral fractures (2, 24). Fixation method such as proximal femoral nail antirotation (PFNA) is frequently used in the treatment of IFF

because the procedure is less invasive, intraoperative blood loss is reduced and a reliable fixation opportunity is provided (13, 23). However, even with this treatment method, it has been reported that postoperative anemia develops in most of the patients and up to 41.6% of the patients require allogeneic blood transfusion (ABT) to replace the blood loss (8). It is important to determine the risk factors that may cause anemia in the postoperative period, as the decrease in the amount of hemoglobin in the perioperative period and the related ABT applied may increase mortality and morbidity in these patients. Some studies have been reported to determine the risk factors for preoperative and perioperative hemoglobin decrease (11,25). However, the criteria that may require ABT have not been determined yet.



The primary aim in this study was to evaluate the risk factors of blood loss in patients with IFF and to determine the limits that may require ABT, and the secondary aim was to prevent unnecessary blood crossing outside these limits.

MATERIAL AND METHODS

Local ethical committee approval was obtained for the study (2020/17-2). A total of 137 patients who were treated with PFNA for IFF in single department of Orthopedics and Traumatology between January 2018 and April 2020 were retrospectively evaluated.

Patients with pathological fractures, metastatic disease, multiple fractures, polytrauma, and patients required an open reduction were excluded from the study. As a result, 119 patients were included in the study. The patients were divided into two groups according to the use of ABT in the postoperative period. Age, gender, fracture side, height, weight, Body mass index (BMI), American Society of Anesthesiologist (ASA) score, pre-operative hemoglobin (Hb) level, Platelet (Plt) number, International Normalized Ratio (INR), Prothrombin time (PT), activated partial thromboplastin time (aPTT) values, comorbid diseases, history of drug use, whether ABT was applied in the preoperative period or not, and the postoperative 1st day Hg levels were evaluated from the medical records.

ABT was applied to the patients whose Hb level was below 9.0 g/dL in the preoperative period. In the post-operative period, the American Academy of Orthopedic Surgeons recommends that transfusion should not be performed in patients with hip fractures unless the Hb levels fall below 8 g/dL or show symptoms (15). Accordingly, in our study population ABT was applied to the patients with a Hb level below 8 g/dL and also to the patients with symptoms such as severe weakness, pallor, chest pain, tachycardia (≥ 100 min), hypotension (systolic blood pressure <90 mmHg) although Hb level is above 8 g/dL.

All procedures were performed in the lateral decubitus position on the standard operating table. Closed reduction was achieved by applying manual longitudinal

traction and internal rotation. Single type of implant (Cytroscopic-PFNA, Bursa, Turkey) was used in all patients.

For deep venous thrombosis (DVT) prophylaxis, a single daily dose of enoxaparin sodium 4000 IU (Clexane 4000 anti-Xa IU / 0.4 ml®, Sanofi Aventis) was used in all patients. Hemoglobin levels were evaluated by total blood counting for all patients on postoperative day one.

Statistical analysis

Statistical package for Social Sciences version 24 (IBM SPSS Corp, Armonk, NY, USA) was used for the statistical analysis. The Shapiro-Wilk test was used to evaluate the normality of groups. For the normally distributed continuous data, t-test was used. If the distribution of data was not normal, Mann-Whitney U test was used to compare the groups. Categorical data was analyzed by using Fisher exact or chi-squared tests. Binary logistic regression analysis was performed including the variables with a p-value ≤ 0.20 to evaluate the important factors on ABT. MedCalc Statistical Software version 15.8 (MedCalc Software bvba, Ostend, Belgium; <https://www.medcalc.org>; 2015) was used for the ROC curve analysis. A p-value below than 0.05 was accepted as statistically significant.

RESULTS

The patients were divided into two groups according to the necessity of transfusion as non-ABT (n: 62) and ABT (n: 50). The mean age was 75.4 ± 11.7 years in the non-ABT group and 80.6 ± 9.9 years in the ABT group ($p = 0.008$). Non-ABT consisted of 42 women, 22 men, and ABT group consisted of 41 women and 9 men ($p = 0.032$). There was no significant difference between the two groups in terms of BMI and the time to death (Table 1). The average amount of preoperative Hb was 12.0 ± 1.2 g/dL in the non-ABT group and 11.2 ± 1.2 g/dL in the ABT group ($p < 0.001$). When the post-operative Hb amounts were compared, the mean value was 10.4 ± 0.8 g/dL in the non-ABT group and 8.7 ± 1.1 g/dL in the ABT group ($p < 0.001$) (Table 1).

Table 1. Analysis of the effect of continuous variables on postoperative transfusion

	Non-transfused (n:62) [mean±std. dev. (min–max)]	Transfused (n:50) [mean±std. dev. (min–max)]	p value
Age (years)	75.4 ± 11.7 (41–101)	80.6 ± 9.9 (49–100)	0.008
Body mass index (BMI)	27.8 ± 4.1 (18.5–41.4)	26.6 ± 3.9 (19.5–39.1)	0.114
Time to surgery (days)	2.4 ± 1.3 (1–7)	2.4 ± 1.4 (0–7)	0.783
Preoperative hemoglobin (g/dL)	12.0 ± 1.2 (8.5–14.3)	11.2 ± 1.2 (7.8–14)	<0.001
Postoperative hemoglobin (g/dL)	10.4 ± 0.8 (8.2–12.9)	8.7 ± 1.1 (6.6–11.7)	<0.001
Platelet ($10^3/\text{mL}$)	212.8 ± 64 (46–423)	216.8 ± 74.4 (123–524)	0.930
International normalized ratio (INR)	1.0 ± 0.2 (0.1–1.9)	1.0 ± 0.4 (0.8–3.4)	0.294
aPTT (sec)	23.5 ± 3.9 (17.3–34.8)	22.6 ± 3.8 (17.6–39.8)	0.143
PT (sec)	12.9 ± 2.5 (9–25.6)	14.3 ± 10.2 (10.6–79.5)	0.942



Table 2. Analysis of the effect of categorical variables on postoperative transfusion

	Non-transfused (n:62)	Transfused (n: 50)	p value
Type of the fracture (stable/unstable)	30/32	14/36	0.022
Gender (female/male)	40/22	41/9	0.032
Fracture side (right/left)	25/37	23/27	0.340
Diabetes (present/absent)	15/47	9/41	0.288
Hypertension (present/absent)	15/47	11/39	0.483
Neurologic disease (present/absent)	9/53	9/41	0.403
Cardiac disease (present/absent)	7/55	4/46	0.401
Use of anticoagulant drugs (present/absent)	9/53	10/40	0.302
Preoperative transfusion (present/absent)	3/59	2/48	0.601
Preoperative hemoglobin value (<11 g/dL/≥11 g/dL)	11/51	22/28	0.002
Preoperative transfusion (present/absent)	3/59	2/48	0.060
ASA grade (<3/≥3)	25/37	14/36	0.150

When the groups were compared in terms of fracture type, 32 (51.6%) patients in the non-ABT group and 36 (76.0%) in the ABT group had an unstable fracture pattern ($p = 0.022$). No significant difference was found between the groups in terms of comorbid factors such as diabetes, hypertension, neurological disease, and cardiac disease (Table 2). Again, no difference was found in terms of anticoagulant drug use, coagulation markers such as INR, aPTT, and PT (Table 1). While three patients in the non-ABT group required transfusion in the preoperative period, this number was found to be two in the ABT group ($p = 0.601$).

When all parameters with a p value less than 0.05 were included into the multivariate regression analysis;

advanced age [odds ratio (OR) 1.069, 95% confidence interval (CI) 0.372–3.202], unstable fracture type [OR 0.258, 95% CI 0.496–6.632], and hemoglobin level <11 g/dL [OR 5.574, 95% GA 0.312–65.278] was found to be an independent predictive risk factor for allogeneic blood transfusion requirement in the postoperative period (Table 3).

ROC curve was created for these independent risk factors. Preoperative hemoglobin value, in terms of predicting allogenic blood transfusion after hip fracture surgery; the area under the curve (AUC: 0.692) reached with the cut-off point Hb ≤10.7 g/dL (Fig. 1).

DISCUSSION

It is well known that Hb levels tend to decrease in patients after hip fractures (10). There are several factors that are responsible for this decrease in Hb levels. The most important and most likely cause of these is the fracture itself. Another major reason is the surgical approach applied for treatment (21). Although the preop-

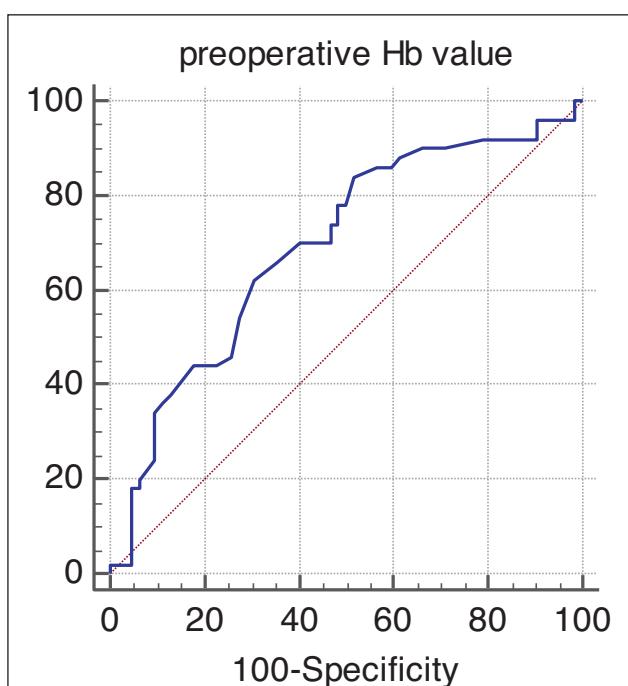


Fig. 1. The receiver operating characteristic curve analysis of the preoperative hemoglobin value predicting allogeneic blood transfusion requirement.

Table 3. Binary logistic regression analysis of the factors those are effective on postoperative transfusion

	p value	Odds ratio	95% confidence interval
Gender (male)	0.872	1.092	1.020–1.120
Age (↑)	0.006	1.069	0.372–3.202
Type of fracture (unstable)	0.006	0.258	0.496–6.632
Hemoglobin level (<10 g/dL)	0.269	4.513	0.098–0.680
Hemoglobin level (<11 g/dL)	0.046	5.574	0.312–65.278
Hemoglobin level (<12 g/dL)	0.116	4.553	1.032–30.118
Hemoglobin level (<13 g/dL)	0.546	1.912	0.686–30.212



erative blood loss due to trauma is inevitable, unnecessary aggressive and/or inadequate treatments can be avoided if patients with higher bleeding risk and complication rate are detected. In our study, in which we aimed to determine the main risk factors to predict the need for postoperative ABT requirement in patients presenting with IFF, it was observed that; advanced age, unstable fracture pattern and lower Hb levels at presentation were the major risk factors for postoperative ABT requirement.

Compared to femoral neck fractures among hip fractures, blood loss is greater in trochanteric region because the IFF is in the extra capsular area where the fracture originates from cancellous bone (21). Wu et al. evaluated preoperative blood loss in hip fractures. The authors reported that the total blood loss in extra capsular fractures was higher than in intracapsular fractures (25). It has been reported that a decrease in the amount of hemoglobin level in the perioperative period increases mortality rates and is associated with deterioration in quality of life and joint functions (17, 18). Yet another study showed that; complications (such as pneumonia and anemia) and postoperative mortality rates were higher in IFF than femoral neck fractures (16). Considering the above literature, it can be thought that this is because blood loss is higher in IFF than femoral neck fractures. In a study in which isolated IFF was evaluated, it was reported that patients with AO 31 A2.2-A2.3 (unstable) fracture pattern had a higher rate of decrease in Hb levels compared to the AO 31 A1.1-A2.1 (stable) group (12). In our study, there were 36 (76.0%) unstable fractures in the ABT group and 32 (51.6%) in the non-ABT group ($p = 0.022$). The binary logistic regression analysis showed that the unstable fracture pattern had a significant effect on postoperative ABT requirement ($p = 0.006$).

Considering the time elapsed until the surgical treatment of the fracture, it has been reported that the possibility of postoperative ABT requirement increases in patients with long surgical intervention due to repetitive movements of the fracture ends, open medullary canal and regional hemorrhage (27). In their study, Luo et al. concluded that the Hb levels were lower and the preoperative ABT rates were higher in patients with a surgical intervention duration longer than 5 days. Therefore, they argued that delayed surgical intervention may increase the amount of preoperative blood loss (14). On the other hand, there are studies stating that the time from injury to surgical intervention has no effect on preoperative ABT requirements (5,7). In our study, no significant difference was found between the two groups in terms of the time from injury to surgery ($p = 0.783$). In line with this result, we think that the time to surgery has no effect on ABT requirement. However, it should be kept in mind that when the time to surgical intervention prolongs, this may lead to decubitus ulcers, urinary infections, venous thrombosis, pneumonia, and cardiovascular events (20).

Cephalomedullary nails are the preferred implants for most proximal extra-capsular proximal femur fractures (2, 24). Although studies indicated that intramedullary fixation methods increased the amount of blood loss due to the opening of the medullary canal and proximal femoral reaming (6, 7), we preferred to use cephalomedullary nails to treat the fracture in 68 (60.7%) of the patients who had unstable fracture patterns to achieve a stable fixation.

Various studies have shown that advanced age may be a risk factor for the need for ABT in patients with IFF (7, 14). In our study, it was observed that the mean age of the patients in the ABT group (80.6 ± 9.9) was higher than the non-ABT group (75.4 ± 11.7). In addition, advanced age was found to be a risk factor for postoperative blood transfusion requirement in our logistic regression analysis ($p = 0.006$). Similarly, Swain et al. reported that patients aged 80 years and over had higher transfusion needs in their study (22).

In our study, the mean preoperative Hb value of the non-ABT group was 12.0 ± 1.2 g/dL and this value was 11.2 ± 1.2 g/dL in the ABT group ($p < 0.001$). According to the result of logistic regression analysis, preoperative Hb value below 11 g/dL increased the postoperative ABT requirement risk 5.5 times. Moreover, the preoperative Hb value of 10.7 g/dL was found to be a strong predictive risk factor for postoperative ABT requirement. In a study, Adunski et al. reported that patients with preoperative Hb > 12 g/dL could undergo surgery without crossing the blood (1). We should recommend making the erythrocyte suspensions ready for the patients with a preoperative Hb lower than 11 g/dL, however it is not possible for us to make a conclusion such as "the patients with a preoperative Hb level higher than 12 g/dL should not need transfusion after the surgery".

In our study, no difference was found between the groups according to the anticoagulant drug usage, INR, aPTT and PT values in terms of postoperative transfusion. Although similar results were found in the literature (4, 7). There are also studies showing that the use of preoperative anticoagulants increases post-operative ABT and mortality (3, 9). The literature is not clear on this subject.

CONCLUSIONS

The strength of our study can be accepted as using the same type of implant in all surgical interventions, applying the same anesthesia approaches and transfusion criteria in a single center. Analysis of retrospective data and not calculating the amount of perioperative bleeding amount can be considered as the weaknesses of this study.

In conclusion, advanced age, unstable fracture pattern and low preoperative Hb values should be considered as risk factors for the postoperative ABT requirements for patients with IFF fractures.



References

1. Adunsky A, Lichtenstein A, Mizrahi E, Arad M, Heim M. Blood transfusion requirements in elderly hip fracture patients. *Arch Gerontol Geriatr.* 2003;36:75–81.
2. Brandt E, Verdonschot N. Biomechanical analysis of the sliding hip screw, cannulated screws and Targon1 FN in intracapsular hip fractures in cadaver femora. *Injury.* 2011;42:183–187.
3. Chechik O, Thein R, Fichman G, Haim A, Tov TB, Steinberg EL. The effect of clopidogrel and aspirin on blood loss in hip fracture surgery. *Injury.* 2011;42:1277–1282.
4. Collinge CA, Kelly KC, Little B, Weaver T, Schuster RD. The effects of clopidogrel (Plavix) and other oral anticoagulants on early hip fracture surgery. *J Orthop Trauma.* 2012;26:568–573.
5. Dai CQ, Wang LH, Zhu YQ, Xu GH, Shan JB, Huang WC, Wei LH, Zhou FL, Li Y. Risk factors of perioperative blood transfusion in elderly patients with femoral intertrochanteric fracture. *Medicine.* 2020;99:e19726.
6. Foss NB, Kehlet H. Hidden blood loss after surgery for hip fracture. *J Bone Joint Surg Br.* 2006;88:1053–1059.
7. Hou G, Zhou F, Tian Y, Ji H, Zhang Z, Guo Y, Lv Y. Predicting the need for blood transfusions in elderly patients with peritrochanteric femoral fractures. *Injury.* 2014;45:1932–1937.
8. Hou GJ, Zhou F, Zhang ZS, Ji HQ, Tian Y. [Analysis of the blood loss in perioperative period of femoral intertrochanteric fracture in old patients treated with different internal fixations]. Beijing Da Xue Xue Bao Yi Xue Ban. 2013;45:738–741.
9. Kragh AM, Waldén M, Apelqvist A, Wagner P, Atroshi I. Bleeding and first-year mortality following hip fracture surgery and pre-operative use of low-dose acetylsalicylic acid: an observational cohort study. *BMC Musculoskelet Disord.* 2011;12:254.
10. Kumar D, Mbako AN, Riddick A, Patil S, Williams P. On admission haemoglobin in patients with hip fracture. *Injury.* 2011;42:167–170.
11. Li B, Li J, Wang S, Liu L. Clinical analysis of peri-operative hidden blood loss of elderly patients with intertrochanteric fractures treated by unreamed proximal femoral nail anti-rotation. *Sci Rep.* 2018;8:3225.
12. Lin PH, Chien JT, Hung JP, Hong CK, Tsai TY, Yang CC. Unstable intertrochanteric fractures are associated with a greater hemoglobin drop during the perioperative period: a retrospective case control study. *BMC Musculoskelet Disord.* 2020;21:244.
13. Liu Y, Tao R, Liu F, Wang Y, Zhou Z, Cao Y, Wang H. Mid-term outcomes after intramedullary fixation of peritrochanteric femoral fractures using the new proximal femoral nail antirotation (PFNA). *Injury.* 2010;41:810–817.
14. Luo X, He S, Li Z, Li Q. Quantification and influencing factors of perioperative hidden blood loss during intramedullary fixation for intertrochanteric fractures in the elderly. *Arch Orthop Trauma Surg. (Epub 2019)* 2020;140:1339–1348.
15. Roberts KC, Brox WT, Jevsevar DS, Sevarino K. Management of hip fractures in the elderly. *J Am Acad Orthop Surg.* 2015; 23:131–137.
16. Roche JJW, Wenn RT, Sahota O, Moran CG. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ.* 2005;331(7529):1374.
17. Sanz-Reig J, Salvador-Marín J, Peréz-Alba JM, Ferrández-Martínez J, Orozco-Beltrán D, Martínez-López JF. Risk factors for in-hospital mortality following hip fracture. *Rev Esp Cir Ortop Traumatol.* 2017;61:209–215.
18. Sim YE, Sim SD, Seng C, Howe TS, Koh SB, Abdullah HR. Pre-operative anemia, functional outcomes, and quality of life after ipH fracture surgery. *J Am Geriatr Soc.* 2018;66:1524–1531.
19. Simunovic N, Devereaux PJ, Sprague S, Guyatt GH, Schemitsch E, Debeer J, Bhandari M. Effect of early surgery after hip fracture on mortality and complications: Systematic review and meta-analysis. *CMAJ.* 2010; 82:1609–1616.
20. Smekta R, Endres HG, Dasch B, Maier C, Trampisch HJ, Bonnaire F, Pientka, L. The effect of time-to-surgery on outcome in elderly patients with proximal femoral fractures. *BMC musculoskeletal disorders.* 2008;9:171.
21. Smith GH, Tsang J, Molyneux SG, White TO. The hidden blood loss after hip fracture. *Injury.* 2011;42:133–135.
22. Swain DG, Nightingale PG, Patel JV. Blood transfusion requirements in femoral neck fracture. *Injury.* 2000;31:7–10.
23. Tang P, Hu F, Shen J, Zhang L, Zhang L. Proximal femoral nail anti-rotation versus hemiarthroplasty: A study for the treatment of inter-trochanteric fracture. *Injury.* 2012;43:876–881.
24. Vaquero J, Munoz J, Prat S, Ramirez C, Aguado HJ, Moreno E, Perez MD. Proximal Femoral Nail Antirotation versus Gamma3 nail for intramedullary nailing of unstable trochanteric fractures. A randomised comparative study. *Injury.* 2012;43:47–54.
25. Wu JZ, Liu PC, Ge W, Cai M. A prospective study about the pre-operative total blood loss in older people with hip fracture. *Clin Interv Aging.* 2016;11:1539–1543.
26. Xu Y, Geng D, Yang H, Wang X, Zhu G. Treatment of unstable proximal femoral fractures: comparison of the proximal femoral nail antirotation and gamma nail 3. *Orthopedics.* 2010;33:473.
27. Zhang PX, Xue F, An S, Gu HY, Lu H, Xu XD, Fu ZG, Zhang DY, Jiang BG. Clinical analysis of obvious and hidden blood loss in inter-trochanter fracture patients treated with proximal femoral nail anti-rotation and dynamic hip screw. *Journal of Peking University Health Sciences.* 2012;44:891–894.

Corresponding author:

Gökhan Cansabuncu
Department of Orthopaedic and Traumatology
Bartin State Hospital
Bartin, Turkey
E-mail: cansabuncu@gmail.com