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RESEARCH

THE EFFECT OF BLOOD TRANSFUSION AND TRANEXAMIC ACID ON LENGTH OF HOSPITAL STAY AND MORTALITY AFTER HIP FRACTURE SURGERY IN ELDERLY PATIENTS

ABSTRACT

Introduction: The timely and appropriate administration of the transfusion of blood and/or blood components may considerably improve patient outcomes of geriatric hip fractures. However, the transfusion requirement is not free of complications. The purpose of this study was to evaluate the outcomes of geriatric hip fracture patients who required transfusion and antifibrinolytic treatment.

Material-Method: This study included geriatric patients with a hip fracture who were admitted to our institution between 2017 and 2018. Patient outcomes were evaluated in respect of mortality and length of hospital stay according to the need for blood transfusion.

Results: The data of 502 patients were analyzed. In-hospital mortality was recorded for 20 patients (4%). A median of 2 units of red blood cells were used in 218 patients (43.4%), median 2 units of platelet concentrates were used in 4 patients (0.8%), and a median of 2 units of fresh frozen plasma were used in 29 patients (5.8%). Length of hospital stay, and intensive care unit stay were significantly higher for patients who received blood products ($p<0.05$). The inpatient mortality rates were similar for patients who received and did not receive blood products ($p>0.05$) but were significantly low in patients who received tranexamic acid (1.2% vs. 5.3% respectively, $p<0.05$).

Conclusion: Blood transfusion in geriatric hip fractures is often associated with long-term hospital and intensive care stays and mortality. In addition, the results of this study revealed that inpatient mortality is significantly low in elderly patients with hip fractures who administered TXA perioperatively.

Keywords: Blood transfusion; Geriatrics; Hip fractures; Tranexamic acid; Mortality; Length of stay

INTRODUCTION

Trauma is a major contributor to mortality worldwide, reportedly the cause of 4.9 million deaths in 2016 (1). In extremely severe cases, mortality associated with trauma may be as high as 40%, and one-quarter of these deaths are associated with uncontrolled blood loss and coagulopathy (2). Thus, the acute management of orthopedic traumatic injury also includes interventions using transfusion algorithms to achieve rapid homeostasis to prevent morbidity and mortality (3).

Exsanguination due to traumatic injury is accompanied and aggravated by a significant deterioration in the endogenous control of homeostasis, hypoperfusion, and shock, which are collectively referred to as acute traumatic coagulopathy (4). The trauma-induced release of mediators acts as an activator for several humoral mechanisms including coagulation, complement, and fibrinolysis, which play important roles in altered homeostasis and the development of systemic inflammatory response and multiple organ failure (5).

Hip and femur fractures may deteriorate hemostatic mechanisms and cause significant mortality and morbidity in geriatric patients (6). Although minimally invasive techniques such as intramedullary nailing (IMN) are used to reduce bleeding, implantation of extra-medullary fixation devices, or Hemi/total arthroplasty, which are related to more bleeding, may need to be performed depending on the fracture type or patient characteristics (7). In the absence of prophylactic measures, the postoperative incidence of venous thromboembolism (VTE) following a hip fracture is generally very high (40%–60%) (8). Prophylactic agents may cause bleeding while protecting against VTE. In addition to surgical interventions, the management of hip fractures also includes timely and appropriate transfusion of red blood cells (RBC), fresh frozen plasma (FFP), and platelet concentrates (9). Transfusion

of blood components is associated with improved patient outcomes (10). However, transfusion is also related to infection and morbidity in orthopedic procedures (11).

A recently popularized approach for hemorrhagic control is the administration of the antifibrinolytic agent tranexamic acid (TXA), which inhibits the activation of plasminogen competitively (12,13). Evidence suggests that TXA is safe and effective to use for controlling blood loss without increasing the VTE in orthopedic procedures (14). Although there are studies in the literature on the use of transfusion and tranexamic acid in the management of blood loss in geriatric hip fractures, recent meta-analyses show that these studies do not reach a sufficient number to create conclusion (15,16). Based on the significant burden of hip and femur fractures in the geriatric population, appropriate management of orthopedic procedures and hemorrhagic control strategies in these patients are vital components of improved patient outcomes. In this study, we aimed to evaluate the outcomes of transfusion of blood components and administration of tranexamic acid (TXA) along with surgical interventions in geriatric patients with hip fractures regarding mortality and length of hospital stays with a high number of patients.

MATERIALS AND METHOD

This study was designed as a retrospective chart review. The target population of our study was the geriatric patients hospitalized in the orthopedic surgery department of our hospital between 2017 and 2018. The inclusion criteria of the study were patients age 65-110 years, patients treated for proximal femoral fracture (femoral neck, intertrochanteric, sub-trochanteric, and peri-prosthetic) and having complete hospital records. Patients were excluded from the study if they were scheduled for elective hip surgery, had a pathological fracture or any known hematological



Table 1. Demographic characteristics of the patients (n=502)

Characteristics	
Age (years), mean±SD	82.6±7.3
Sex, n (%)	
Male	184 (36.7)
Female	318 (63.3)
Diagnosis, n (%)	
Peritrochanteric fracture	305 (60.8)
Femoral neck fracture	179 (35.7)
Subtrochanteric fracture	14 (2.8)
Periprosthetic fracture	4 (0.8)
Comorbidities, n (%)	
Neurological diseases	10 (2)
Malignancies	4 (0.8)
Hypertension	305 (60.8)
Diabetes mellitus	67 (13.3)
Chronic obstructive pulmonary disease/asthma	222 (44.2)
Cardiovascular disease	41 (8.2)
Acute/chronic kidney failure	20 (4)

SD, Standard deviation

disorder. After exclusions, records of the remaining 502 patients were screened and included in the analyses.

The data collected for the study included the demographic and clinical characteristics of the patients in respect of the type of injury, surgical interventions, utilization of blood and blood components, and administration of antifibrinolytic agents (TXA). Analyses were performed to evaluate the effects of these characteristics on the length of hospital stay and in-hospital mortality.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS ver. 21 software (IBM Inc., Armonk, NY, USA). Descriptive data were presented as mean and standard deviation for

numerical variables, and frequency and percentage for categorical variables. Comparisons of data between independent prognostic subgroups were performed using the Mann–Whitney U test and Chi-square test for numerical and categorical variables, respectively. Preoperative to postoperative changes in blood counts were compared using the Wilcoxon test. A type I error level of 5% was considered the threshold for statistical significance.

RESULTS

This study included 502 patients, comprising 318 (63.3%) females and 184 (36.7%) males with a mean age of 82.6±7.3 years. In total, 305 patients (60.8%) had per-trochanteric fracture,

Table 2. Treatment-related characteristics of patients

Treatment-related characteristics	
Surgery, n (%)	
Intramedullary nailing	277 (55.2)
Partial hip arthroplasty	181 (36.1)
Total hip arthroplasty	17 (3.4)
Plate fixation	4 (0.8)
Dynamic hip screwing	3 (0.6)
ASA class, n (%)	
1	1 (0.2)
2	63 (13.5)
3	382 (82.2)
4	19 (4.1)
The total length of hospital stay (days), mean±SD	6.9±6.8
Length of ICU stay (days), mean±SD	3.1±5
Survival, n (%)	
Alive	482 (96)
Dead	20 (4)
Preoperatively	8 (1.6)
Postoperatively after intramedullary nailing	8 (1.6)
Postoperatively after partial hip arthroplasty	4 (0.8)

ASA, American Society of Anesthesiologists; ICU, Intensive care unit; SD, Standard deviation

179 (35.7%) had femoral neck fracture, 14 (2.8%) had sub-trochanteric fracture, and 4 (0.8%) had peri-prosthetic fracture. The distribution of comorbidities in the patients was as follows: hypertension in 305 patients (60.8%), chronic obstructive pulmonary disease /asthma in 222 patients (44.2%), diabetes mellitus in 67 patients (13.3%), cardiovascular disease in 41 patients (8.2%), acute/chronic kidney failure in 20 patients (4%), neurological disorders in 10 patients (2%), and malignancies in 4 patients (0.8%) (Table 1).

Regarding treatment, 277 patients (55.2%) had undergone IMN, 181 (36.1%) had partial hip arthroplasty, 17 (3.4%) had total hip arthroplasty, 4

(0.8%) had plate fixation, and 3 (0.6%) had dynamic hip screw. Approximately 75.7% of the patients were classified as ASA 3 and the mean length of hospital stay was 6.9±6.8 days (1–65 days). For the duration of hospitalization, the mean length of intensive care unit (ICU) stay was 3.1±5.0 days (0–61 days) for all. In-hospital mortality was recorded for 20 patients (4%), of which 8 (1.6%) died preoperatively, 8 (1.6%) postoperatively after IMN, and 4 (0.8%) after partial hip replacement surgery (Table 2).

The mean values of pre- and postoperative hemoglobin and hematocrit values were 12±1.9 mg/dl and 37.5% (±25%), and 9.6±1.3 mg/dl and



Table 3. Blood counts and transfusion of blood and blood components

Hemoglobin (mg/dL), mean±SD	
Preoperative	12±1.9
Postoperative	9.6±1.3
P	<0.001
Hematocrit (%), mean±SD	
Preoperative	37.5±25
Postoperative	28.7±4
P	<0.001
Red blood cell transfusion, n (%)	218 (43.4)
Number of transfusions, median (min-max)	2 (1-8)
Platelet concentrate transfusion, n (%)	4 (0.8)
Number of transfusions, median (min-max)	2 (2-3)
Fresh frozen plasma transfusion, n (%)	29 (5.8)
Number of transfusions, median (min-max)	2 (1-7)

SD, Standard deviation

28.7% (±4%), respectively. Both the hemoglobin ($p<0.001$), and hematocrit ($p<0.001$) levels were decreased significantly in the postoperative period compared to the preoperative period. A median of 2 units of RBC (range: 1–8 units) were used in 218 patients (43.4%), median 2 units of platelet concentrate (range: 2–3 units) were used in 4 patients (0.8%), and median 2 units of FFP (range: 1–7 units) were used in 29 patients (5.8%) (Table 3).

When the patient outcomes were compared according to the received blood components, the length of hospital stay and ICU stay were significantly higher for patients who received RBCs ($p<0.001$ for both) and FFPs ($p=0.001$ for the hospital stay, $p=0.018$ for ICU stay). When the patient outcomes were evaluated in respect of survival, the inpatient mortality rates were similar for the patients who received and did not receive RBCs ($p=0.216$), platelet concentrates ($p=1.0$), and FFPs ($p=0.324$). When the outcomes were compared between patients with and without TXA

use, the total length of hospitalization ($p=0.721$) and length of ICU stay ($p=0.918$) were found to be similar, but inpatient mortality rates were significantly lower in patients who received TXA (1.2% vs. 5.3%, $p=0.026$) (Table 4).

When treatments were grouped according to the utilization of blood components and TXA, 170 patients (33.9%) received only blood components, 53 patients (10.6%) received both blood components and TXA, 112 patients (22.3%) received only TXA, and 167 patients (33.3%) did not receive any type of blood components or TXA. The comparisons of patient outcomes between treatment groups revealed that the total length of hospital stay was significantly longer for patients who received both treatments and shorter for patients who only received TXA ($p<0.001$). The length of ICU stay was significantly higher for patients who only received blood components ($p<0.001$). The lowest mortality rates were observed in patients who received both blood components and TXA (0%) and patients who

only received TXA (1.8%), and the highest rates were observed in patients who received neither treatment (7.2%) (p=0.042) (Table 5).

DISCUSSION

This study evaluated the outcomes of geriatric patients with hip fractures in respect of the need for blood and blood components to emphasize the related morbidity and mortality rates and the importance of administration of TXA to reduce transfusion requirement. Less than half of the patients needed RBC transfusion, and only 5.8%

whereas this increased to 21.2% in 2008–2010. During the past two decades, clinicians have used two major strategies for blood transfusion, namely restrictive and liberal strategies. These strategies (restrictive and liberal) have used hemoglobin threshold levels as ≤ 8 g/dL and ≤ 10 g/dL for transfusion, respectively (12). The liberal regimen suggests that utilizing an upper threshold for RBC transfusion provides an increased oxygen supply and circulatory stability, which eventually results in a shorter rehabilitation period (17). However, transfusion is not free of risk and has the potential to

Table 4. Patient outcomes (length of hospital stay and mortality) according to transfusion of blood and components

	RBC transfusion			Platelet concentrate transfusion			FFP transfusion			TXA		
	+	-	p	+	-	p	+	-	p	+	-	p
The total length of hospital stay, mean±SD	7.9±7.7	6.1±5.9	<0.001	7±0	6.9±6.8	0.165	11.1±9.6	6.6±6.5	0.001	6.9±5.6	6.9±7.3	0.721
Length of ICU stay, mean±SD	3.4±3.9	2.7±5.6	<0.001	3	3.1±5	0.332	3.7±2.9	3±5.1	0.018	2.8±2.8	3.1±5.7	0.918
Number of deaths, n (%)	6 (2.8)	14 (4.9)	0.216	-	20 (4)	1.0	2 (6.9)	18 (3.8)	0.324	2 (1.2)	18 (5.3)	0.026

RBC, Red blood cell; FFP, fresh frozen plasma; ICU, Intensive care unit; SD, Standard deviation

and 0.8% of patients needed transfusion of FFP and platelet concentrations, respectively. The length of hospital stay, and ICU stay were significantly longer for those received RBCs and FFPs. The statistical analyses revealed that the utilization of TXA had no significant effect on the length of hospitalizations, but the mortality rates were significantly low among these patients.

Over recent decades, there has been an increase in the proportion of patients receiving a blood transfusion during major orthopedic surgeries. A previous study by Browne et al. reported that 18.1% of patients received a blood transfusion during hip and knee surgeries in 2005,

increase postoperative unfavorable events such as infections and cardiovascular events (18). We have not evaluated the postoperative complications per se, but the total length of hospitalization and ICU stays were significantly higher among patients who received RBC or FFP. However, this could also be associated with the clinical severity of the patients because those who received transfusions would most likely be the patients with more complicated surgeries. In a study by Monsef et al, two-thirds of the patients were aged > 60 years, and it was reported that blood transfusion extended hospital stay after total hip arthroplasty (19). The current study findings supported the evidence in the literature that transfusion might be associated



with a prolonged hospital stay (12). On the other hand, the current study results also showed that the inpatient mortality rates were similar for the patients who received and did not receive blood components. This demonstrates that when transfusions are applied properly on time to those who need it, the mortality rates can be equalized. In the study of Smeets et al, patients who received erythrocyte transfusion had a significantly longer hospital stay and more postoperative cardiac complications (20). In the meta-analyses of studies investigating blood transfusion in major

et al also showed that TXA reduced hospital and ICU stays after total knee replacement surgery (22).

The mortality of elderly patients with a hip fracture is as high as 32.5% in males and 21.9% in females at one year after fracture (23). In the current study, the lowest inpatient mortality rates were observed in patients who received both blood components and TXA, and patients who only received TXA whereas the highest rates were observed in patients who received neither of the treatments. This reveals that patients receiving TXA appear to have low mortality rates regardless

Table 5. Patient outcomes (length of hospital stay and mortality) according to transfusion of blood and components

	Only blood components (n=170)	Blood components and TXA (n=53)	Only TXA (n=112)	None (n=167)	P
Total length of hospital stay, mean±SD	7.6±7.7	9.2±7.4	5.8±4.1	6.1±6.8	<0.001
Length of ICU stay, mean±SD	3.6±4.3	2.9±2.2	2.8±3.0	2.7±6.9	<0.001
Number of deaths, n (%)	6 (3.5)	-	2 (1.8)	12 (7.2)	0.042

ICU, Intensive care unit; SD, Standard deviation

orthopedic procedures, no significant differences have been detected between restrictive and liberal transfusion regimens (21).

In this study, the total length of hospital stay was significantly longer for patients who received both blood transfusion and TXA and shorter for patients who only received TXA, whereas the length of ICU stay was significantly longer for patients who only received blood components. This shows that for patients who need blood transfusions, the duration of hospital stay cannot be reduced, including those given TXA. However, the use of TXA may reduce the duration of ICU stay in patients who need blood transfusion., Leite

of the need for transfusion. Mortality was highest in patients who did not need a transfusion and did not receive TXA. These results demonstrated that patients who were not indicated for blood transfusion and who did not receive TXA were the ones with the highest in-hospital mortality rates. This can be explained by the hidden blood loss of the patients. Smith et al showed that hidden blood losses affect mortality in hip fractures (24) and TXA was reported to prevent hidden blood loss in geriatric patients with hip fractures (25). Optimal transfusion indications for the elderly trauma patients can be studied further because of this hidden blood loss and anemia of these

patients. Puckeride et al remarked on the delayed treatment of anemia in elderly patients with hip fractures and as this study suggests, there seems to be a need for revision of the routine transfusion indications for elderly patients with hip fractures (26). Besides, although mortality can be related to the several comorbidities of elderly patients, TXA can be used for elderly patients with hip fractures to reduce in-hospital mortality.

There is currently no consensus on the practice guidelines for transfusion in orthopedic surgeries. This situation has therefore resulted in considerable variation in the rates of transfusions in different centers. A study by Cobain et al. (14) evaluated the epidemiology of transfusion in the United States, England, Australia, and Denmark, and reported that orthopedic surgeries used 6%–13.8% of all allogeneic and autologous packed RBCs, and the distribution of these transfusions was not even, as the utilization of blood components varied significantly between the centers. Boralessa et al (27) evaluated the use of blood in orthopedic surgeries in the United Kingdom in 2009 and reported that transfusion rates for total hip arthroplasty ranged from 0% to 100% among the evaluated hospitals, and only 47% of the hospitals had a transfusion protocol. Another study by Chen et al (28) evaluated the blood transfusion rates after primary total joint arthroplasties in the USA in 2013 and reported that the rates varied between 4.8% and 63.8% for total knee arthroplasties, and 4.3% and 86.8% for total hip arthroplasties. In the current study, 43.4% of patients received RBC

transfusion, which is a rational rate according to the literature data.

Besides the promising results observed about the survival benefit of TXA among geriatric patients who underwent surgical treatment due to hip fracture in this study, several limitations should also be considered when interpreting our results. First, the retrospective design of this study limited the assessments of these patients for both short- and long-term outcomes regarding extra complications other than the duration of hospitalization or mortality. Second, the effects of the history of baseline medications and other treatments on outcomes could not be assessed due to the unavailability of adequate data in patient records, which may alter the results about the TXA and transfusions. Nevertheless, the large sample size may be considered as a strength of the study, and promising results should worth evaluation in future researches.

CONCLUSION

Surgical treatment of the geriatric hip fracture is frequently related to significant blood loss, which may result in significant morbidity or mortality risk. Although blood transfusion is an essential component in the management of these patients, the results of this study revealed that it is related to longer hospital and intensive care unit stays. And although the mortality can be related with several comorbidities of these patients, in-hospital mortality is significantly low in elderly patients with hip fracture who administered TXA perioperatively.

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