Injury, Int. J. Care Injured 50 (2019) 2040–2044

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Impact of oral anticoagulation on proximal femur fractures treated within 24 h – A retrospective chart review

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ARTICLE INFO

Article history:
Accepted 6 September 2019

Keywords:
Hip fracture
Anticoagulation
Early surgical care
Geriatric trauma

ABSTRACT

Background: About one third of all patients with proximal femur fractures take oral anticoagulation like aspirin (ASS), direct platelet aggregation inhibitors like Clopidogrel and Ticagrelor (PAI), vitamin-K-antagonists like Warfarin (VKA) and direct oral anticoagulants like Rivaroxaban, Dabigatran and Apixaban (DOAC). The management and timing of fracture stabilization of these patients is a rising challenge in orthopedic trauma. Our objective was to determine the effect of oral anticoagulation on patients with proximal femur fractures, which received a proximal femur nail antirotation (PFNA) within 24 h after trauma.

Material and methods: A retrospective chart review of 327 patients (mean age 80 ± 13 years; 223 women and 104 men) with sub- or intertrochanteric fractures between January 2013 and December 2017 was performed. All patients underwent surgery in the first 24 h after admission. Solely patients without or with only one type of oral anticoagulation were included. There were 74 patients with ASS, 30 with PAI, 52 with DOAC and 25 with VKA medication. All patients taking VKA received high dose Vitamin K or coagulation factors to normalize INR prior to surgery. Primary outcome measures were transfusion rate and pre- and postoperative hemoglobin (Hb) difference. Secondary outcome measures were mortality and complications like infection, hematoma and acute cardiovascular events.

Results: Patients undergoing treatment with DOAC had a 3.4-fold increased risk for intraoperative blood transfusion. The risk for blood transfusion for patients taking ASS, PAI or VKA did no differ from the control group. Patients without an intraoperative blood transfusion on oral anticoagulation showed no increase in pre- and postoperative Hb-difference compared with controls. Anticoagulation showed no significant effect on complication rates and mortality in patients operated within the first 24 h.

Conclusion: Early surgical care of proximal femur fractures is safe even in patients with anticoagulant medication. All patients should be preoperatively prepared for possibly intraoperative transfusion, especially patients on DOAC.

Background/Introduction

With the fast growth of the elderly population the number of proximal femur fractures is rising. In addition, these patients are often treated for chronical cardiovascular illnesses [1,2] such as coronary heart disease, hypertension, cerebrovascular disease and atrial fibrillation with anticoagulant medications [3,4]. The attending surgeon has to decide for each case whether to continue, modify, bridge or even counteract the anticoagulation therapy, if surgery is necessary. For most patients on platelets inhibitors like Aspirin (ASS), Clopidogrel or Ticagrelor (PAI) the indication is a secondary prevention therapy after myocardial infarction. After myocardial infarction treated with a coronary stent therapy platelets inhibitors are critical to prevent stent thrombosis and therefore medication has to be continued perioperatively [5]. Furthermore, the effects of these drugs last about 7–10 days [6]. Direct oral anticoagulants like Rivaroxaban, Dabigatran and Apixaban (DOAC) have shorter effects with a half-life about 7–15 h. It is dependent on renal function [7–10] and takes 24–48 h for the factor Xa-activity to return to normal [11]. No antidote for DOAC is available except Idarucizumab for Dabigatran [12]. In comparison, effects of vitamin-K-antagonists like Warfarin (VKA) can be reversed slowly with vitamin-k or immediate with prothrombin complex concentrates. The most common indications for DOAC or VKA range from mechanical heart valves to atrial fibrillation, a recent thromboembolic event or an elevated CHADS2 score. Therefore, if the medication is discontinued, bridging therapy is necessary. The effect of each

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https://doi.org/10.1016/j.injury.2019.09.011
0020-1383/

anticoagulant can be reversed with discontinuing the medicine and time, but delaying the surgery increases the risk of pulmonary embolism, prolongs the hospital stay and increases the mortality [13–17]. Delay of the operation for more than 48 h showed higher postoperative complications like urinary infections, decubitus ulcers, acute pulmonary edema and myocardial ischemia [18,19]. The current S2 guideline of German traumatology society recommends the treatment of proximal femur fractures within 24 h. Still, surgery for patients taking oral anticoagulant medication is often delayed [20–23]. For this retrospective study, we identified 327 patients with a proximal femur fracture operated within 24 h with a PFNA to evaluate the effects of the different kinds of oral anticoagulation.

Methods

Institutional and prior ethical committee approval for the use of data in this study was obtained.

Between January 2013 and December 2017, 327 patients with per- or subtrochanteric fractures treated within 24 h after admission were identified. Exclusion criteria included patients, who ultimately did not have surgery, patients with the need of regular blood transfusions, patients for whom the proximal femur fracture was not the admitting diagnosis, patients with 2 or more anticoagulant medication and patients requiring other surgical procedures in addition to the PFNA. After excluding the patients with these conditions, we identified 412 patients of which 327 were treated within 24 h. From the 85 patients treated after 24 h 36 had a medical condition, which had to be treated before surgery and 49 were delayed because of organizational reasons like missing operating room capacity. The 327 patients which were treated within 24 h were treated with a proximal femoral nail antirotation with a perforated blade (Fa. DePuy Synthes) allowing augmentation with Traumacem V + Cement (Fa. DePuy Synthes). All procedures were performed or supervised through experienced attending orthopedic trauma surgeons.

In this retrospective study, clinical records including patient charts, laboratory results and anesthesia protocols were reviewed. Patient charts were reviewed for oral anticoagulation like acetylsalicylic acid (ASS), direct platelet aggregation inhibitors like Clopidogrel and Ticagrelor (PAI), vitamin-K-antagonists like Warfarin (VKA) and direct oral anticoagulants like Rivaroxaban, Dabigatran and Apixaban (DOAC). ASS and PAI were continued during the hospital stay. VKA and DOAC were bridged with heparin and continued at the 7 Day after surgery. The primary outcome measures were rate of transfusion, pre- to 24 -h postoperative HB-difference and postoperative hematoma requiring revision surgery during the hospital stay, but at least for 7 days. Only red blood cell transfusions were evaluated. Decision for blood transfusion was made individually for every patient based on the factors Hb < 8 g/dl with accompanying hypertension, tachycardia or dizziness. The secondary outcome measures were mortality and surgical complications like deep vein thrombosis, cardiac infarction, stroke, pneumonia, urinary tract infection, acute renal failure and deep tissue infection.

Data analysis was performed with IBM SPSS Statistics (V12.0) and Microsoft Excel (V15.2). Demographic characteristics are described as mean and standard deviation. For the primary outcome measures, logistic regression was performed considering all variables related to the blood transfusion rate, HB-difference and hematoma requiring revision surgery. Also for the secondary outcome measures logistic regression was performed considering all variables related to postoperative complications and hospital and 1-year mortality.

Results

Patient population

For 327 patients, the medical records were reviewed. General factors like age, gender, the American Society of Anesthesiologists Classification (ASA) and type of anticoagulation were evaluated (Table 1). For statistical purposes age was classified in 3 groups (<65 years; 65–85 years; >85 years).

Perioperative factors like AO-classification, grouped operating time, grouped time to surgery, rate of blood transfusions and complications is shown in Table 2. For statistical purposes the operating time (<45 min; 45–90 min; >90 min) and the time to surgery (<6 h; 6 h–18 h; >18 h) where classified in 3 groups.

Transfusion

The rate of blood transfusion was investigated in dependence of the grouped age, AO-type of the fracture, type of anticoagulation, ASA-classification, grouped operating time, grouped time to surgery and surgical approach. Overall 74 out of 327 patients needed a blood transfusion (Fig. 2). For patients taking DOAC the risk for the need of blood transfusion was significantly, 3.4-fold increased. If operated in the first 6 h after admission, the risk was significantly lowered by the factor 2. If the operating time exceeded 90 min the risk of transfusion was significantly increased by the factor 5.5. Time to surgery (Fig. 1) showed no significant difference between diverse types of anticoagulation. Low Hb-values at admission increased the risk of a blood transfusion significantly.

Hb-level and -difference

Hb-difference was investigated in dependence of the grouped age, AO-type of the fracture, type of anticoagulation, ASA-classification, grouped operating time, grouped time to surgery and surgical approach. Out of these factors, only the grouped operating time and type of anticoagulation had a statistical significant effect. If operating time exceeded 90 min, the Hb-difference was significantly higher. ASS, PAI and DOAC showed no statistical significant effect on Hb-difference. Patients undergoing treatment with VKA had a significantly lower postoperative Hb-difference. The Hb-difference of each anticoagulant is shown in Fig. 3.

The Hb-value at admission shows Fig. 4. The lowest mean value was measured for patients undergoing treatment with DOAC with $112 \pm 2{,}0$ and the highest for patients without anticoagulant medication with $122 \pm 2{,}0$. This difference was significant. There was no significant difference in Hb at admission for ASS, PAI and VKA.

Table 1
General factors.

Variable	Mean/Count	Range/%
Age [years]	80,7	20–102
gender		
male	104	31,8%
female	223	68,2%
ASA		
1	6	1,8%
2	30	9,2%
3	218	66,7%
4	73	22,3%
5	0	0%
Type of anticoagulation		
none	146	44,6%
ASS	74	22,6%
TAI	30	9,2%
VKA	25	7,6%
DOAC	52	15,9%

Table 2
Perioperative factors.

Variable	Mean/Count	Range/%
AO-classification		
31A1.1-3	109	33,3%
31A2.1-3	143	43,7%
31A3.1-3	75	22,9%
Classified operating time		
<45 min	131	40,1%
45–90 min	161	49,2%
>90 min	35	10,7%
Time to surgery [min]	503	74–1439
none	489	75–1431
ASS	445	140–1300
TAI	509	74–1402
VKA	601	257–1426
DOAC	572	138–1439
Rate of blood transfusion		
yes	74	23,1%
no	253	76,9%

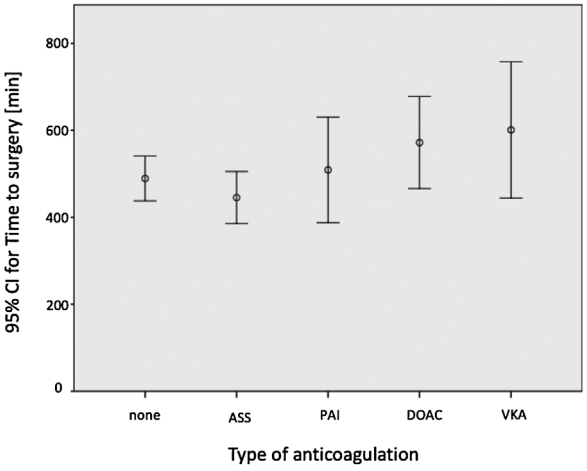

Fig. 1. Time of surgery depending on oral anticoagulant.

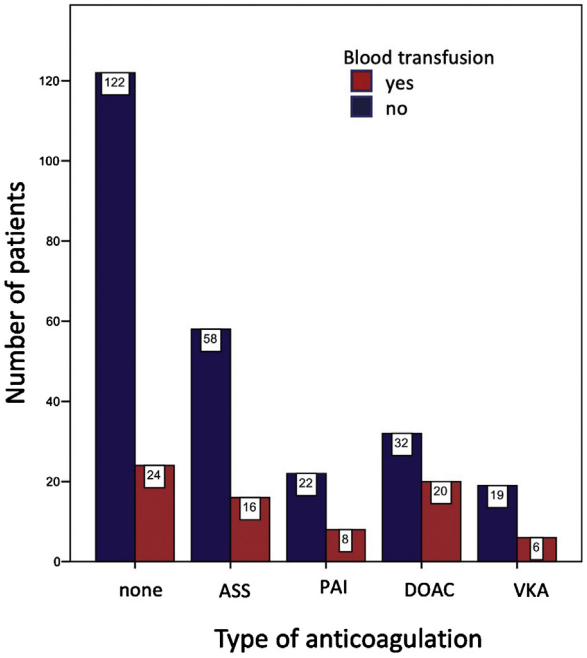

Fig. 2. Transfusion rate for anticoagulant medications.

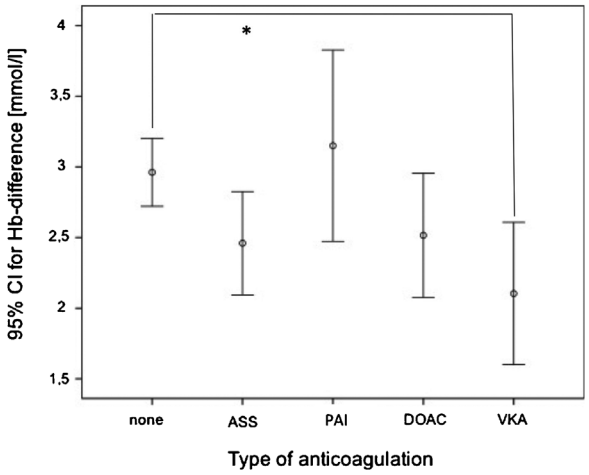

Fig. 3. Hb-difference pre-/and postoperative for different anticoagulants. * Hb-difference was significantly lower in patients taking VKA. ($p < 0.05$).

Hematoma

Occurrence of a postoperative hematoma with the need of surgical revision was investigated in dependence of the grouped age, AO-type of the fracture, type of anticoagulation, ASA-classification, grouped operating time, grouped time to surgery and surgical approach. Overall 21 patients needed revision surgery, because of postoperative hematoma. From the investigated factors, only ASA-classification showed a significant effect.

1-Year mortality

Only 122 patients could be reviewed retrospectively for 1 year. 26 of these patients died within the first postoperative year. Grouped age, type of anticoagulation, ASA-classification, grouped operating time, grouped time to surgery were investigated for statistical significance. Out of these factors, only ASA-classification and age showed a significant effect. 47% of ASA 4 patients died within a year. Patients over 85 years of age had a mortality of 33% within the first year.

Discussion

For patients with a proximal femur fracture, which are also undergoing anticoagulation therapy, timing of surgery is critical.

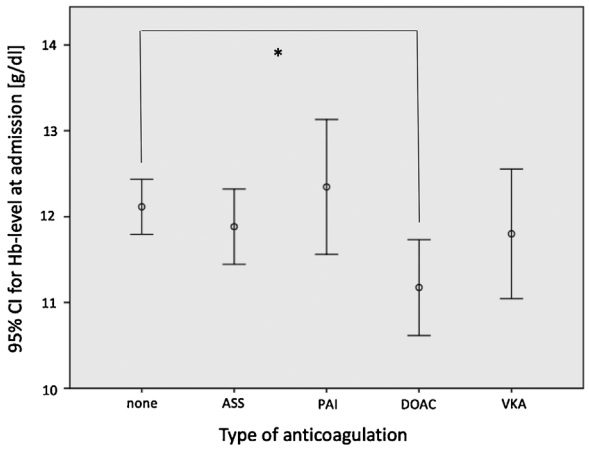

Fig. 4. Hb-level at admission for different anticoagulants. * Hb-level was significant lower for patients taking DOAC. ($p < 0.05$).

The attending surgeon has to decide for each type of anticoagulation whether to continue or counteract to assure optimal conditions for surgery. The most common type of anticoagulation is platelet inhibition with ASS. Devereaux et al. showed that administration of ASS before and during the postsurgical period had no significant effect on the rate of death and nonfatal myocardial infarction, but increased the risk of major bleeding [24]. In comparison, Collinge et al. could not find an increased risk for patients taking ASS undergoing hip fracture repair [25]. We also could not discover an increase in transfusion rate, Hb-difference or postoperative complication rate for patients treated with ASS.

For patients undergoing treatment with TAI there are studies reporting higher transfusion rates [26,27], lower postoperative Hb-levels [28,29]. Compared to those studies we could not show differences in the rate of blood transfusion, Hb-difference and postoperative complications between the groups. This is in line with two large metaanalysis [30,31]. Compared to all mentioned studies our time to surgery was even shorter. In line with these metaanalysis, surgery should not be delayed for patients taking ASS or TAI.

Current studies showed, that patients undergoing VKA treatment didnt have a higher rate of blood transfusion or lower postoperative Hb-levels [32], but had a significant delay in time to surgery [33]. The Hb-difference was significantly lower and there was not an increased rate of transfusion in our study even with average time to surgery of 10 h. All patients with VKA treatment were substituted either with Vitamin K or prothrombin complex concentrate under laboratory controls. A possible explanation for the lower Hb-difference might be the preoperative optimization of coagulation. It has to be determined in further studies, if it is possible to reduce blood loss with Vitamin K or prothrombin complex concentrate in patients without anticoagulant medicine. In comparison, no higher rates for thrombosis or cardiac complications could be seen in substituted patients.

Patients on anticoagulation with DOAC often experience longer delays in time to surgery [33–35]. Only a few current studies describe complications and outcome after early surgical care of hip fractures in patients treated with DOAC. Franklin et al. found a higher readmission rate in patients undergoing DOAC treatment, but no difference in Hb-levels or rate of transfusions [35]. In line with these results, Schermann et al. found no significant changes in Hb-levels, rate of transfusion or mortality. In both studies time to surgery was above 24 h. Mullins et al. compared patients under treatment with DOAC with patients without anticoagulant medication as matched pairs with the factor time to surgery. Average time to surgery in this study was about 19 h with a range of 7–64 hours. Mullins et al. found no difference in Hb-Difference and rate of blood transfusions and concluded, that a delay of surgery will not reduce perioperative bleeding or increase mortality. In our study the average time to surgery for patients on DOAC was about 10 h with a range of 2–24 h. With this short time to surgery the rate of transfusion was significantly increased. Also, the Hb-value at admission was significantly lower in this group. Still, the rate of postoperative complications was not increased and overall mortality was only significantly affected by age and high ASA-classification. The timing of surgery remains a critical decision for the attending surgeon. We found, that surgery within 6 h might prevent intraoperative blood transfusion without dependence on oral anticoagulation. Delay of surgery might dissolve the effects of oral anticoagulants, but increases the risk of pulmonary embolism, urinary infections, decubitus ulcers, myocardial ischemia and therefore prolongs the hospital stay [18,19]. There is also evidence the delaying the operation increases the mortality [13–17].

Therefore, in our Level-I trauma center proximal femur fractures are treated as soon as possible despite anticoagulant medication. All patients are preoperatively prepared for intraoperative transfusions. Patients taking VKA are substituted with Vitamin K or if necessary are given prothrombin complex concentrates to prevent a delay of surgery. In this study, no postoperative complications could be seen in early surgical care of proximal femur fractures.

This study benefits from several strengths. The outcome measures rate of transfusion, Hb-difference and postoperative hematoma, requiring revision surgery, are verifiable and of clinical relevance. This is the first study, which reports on the 4 main oral anticoagulants in patients with proximal femur fractures operated within 24 h. Furthermore, compared to other studies there was no significant difference in time to surgery. The average time to surgery was about 8,3 h and therefore very short. Cofounders like fracture classification, approach, operating time, age and ASA have been considered.

The study has certain limitations. The lack of specified transfusion criteria means, that transfusion may be cofounded by the preference of the attending anesthesiologist. The time to surgery was measured starting with the admission of the patient. Time, that passed between the fall und admission to the hospital, could not be evaluated. Also, time between the fall and preoperative hemoglobin measurement could not be evaluated. In all patients, hemoglobin was measured the first postoperative day, due to different admission times the interval between pre- and postoperative blood sample was variable. Due to the retrospective design, mortality could only be investigated in patients with readmission in the hospital within 1 year. Therefore, for the investigation of mortality, only a small sample size could be considered so mortality should be evaluated in further prospective studies. The high rate of revision surgery for postoperative hematoma should be evaluated in further studies, because no dependency on the evaluated factors could be seen. We only investigated proximal femur fractures, if these finding can be transferred for all hip fractures must be evaluated in further studies.

Conclusion

Early surgical care of proximal femur fractures showed no increase in postoperative complications in this retrospective study and proved to be safe even in patients with anticoagulant medication. All patients should be preoperatively prepared for possibly intraoperative transfusion, especially patients on DOAC.

Source of funding

No author is affiliated to any of the supporting companies or received or will receive any form of payment related to this study.

Declaration of Competing Interest

The authors declare that there is no conflict of interest. No company had influence in the collection of data or contributed to or had influence on the conception, design, analysis and writing of the study. No further funding was received.

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