Does Use of Oral Anticoagulants at the Time of Admission Affect Outcomes Following Hip Fracture

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Abstract

Purpose: The purpose of this study was to compare hospital quality outcomes in patients over the age of 60 undergoing fixation of hip fracture based on their anticoagulation status. Materials and Methods: Patients aged 60 and older with isolated hip fracture injuries treated operatively at 1 academic medical center between October 2014 and September 2016 were analyzed. Patients on the following medications were included in the anticoagulation cohort: warfarin, clopidogrel, aspirin 325 mg, rivaroxaban, apixaban, dabigatran, and dipyridamole/aspirin. We compared outcome measures including time to surgery, length of stay (LOS), transfusion rate, blood loss, procedure time, complication rate, need for intensive care unit (ICU)/step-down unit (SDU) care, discharge disposition, and cost of admission. Outcomes were controlled for age, Charlson comorbidity index (CCI), and anesthesia type. Results: A total of 479 hip fracture patients met the inclusion criteria, with 367 (76.6%) patients in the non-anticoagulated cohort and 112 (23.4%) patients in the anticoagulated cohort. The mean LOS and time to surgery were longer in the anticoagulated cohort (8.3 vs 7.3 days, \( P = .033 \) and 1.9 vs 1.6 days, \( P = .010 \)); however, after controlling for age, CCI, and anesthesia type, these differences were no longer significant. Surgical outcomes were equivalent with similar procedure times, blood loss, and need for transfusion. The mean number of complications developed and inpatient mortality rate in the 2 cohorts were similar; however, more patients in the anticoagulated cohort required ICU/SDU-level care (odds ratio \( = 2.364, P = .001 \), controlled for age, CCI, and anesthesia). There was increased utilization of post-acute care in the anticoagulated cohort, with only 10.7% of patients discharged home compared to 19.9% of the nonanticoagulated group (\( P = .026 \)). Lastly, there was no difference in cost of care. Conclusion: This study highlights that anticoagulation status alone does not independently put patients at increased risk with respect to LOS, surgical outcomes, and cost of hospitalization.

Keywords

hip fracture, anticoagulation, geriatric trauma, economics of medicine, surgical outcomes

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Introduction

With the aging population, an increasing number of elderly patients are being treated for hip fractures. Current estimates place this number above 300 000 hip fracture hospital admissions annually, which is expected to increase in the next decade.\(^1\) As this hip fracture population ages, an increasing number of patients have comorbidities requiring chronic anticoagulation medications. As care for hip fracture patients transitions from a fee-for-service model to a bundle payment model, efforts have been made to identify high-risk patients and to provide more high-quality resource-conscious care to these patients.\(^2\) Studies have demonstrated an increased time to surgery in patients on anticoagulant medications (warfarin and direct oral anticoagulants [DOACs])\(^3,4\); however, these studies have been less definitive about the hospital quality measures of these patients including length of stay (LOS) and complication rates.
rate.4-7 These studies have also largely focused on the more common anticoagulant drugs such as warfarin and clopidogrel, with no published literature on outcomes of patients on DOAC drugs including factor Xa inhibitors and direct thrombin inhibitors. In addition, to date, there have been no studies analyzing the influence of anticoagulant medications on discharge disposition or cost, which are 2 markers becoming increasingly important as hip fracture care becomes incorporated into the bundle payment of care system. Hip fracture patients treated with arthroplasty procedures are already incorporated into the Comprehensive Joint Replacement bundle and hip fractures treated with nonarthroplasty procedures will be included in the proposed optional Surgical Hip and Femur Fracture Treatment bundle.8,9 Under these bundle payment models, hospitals will be responsible for care through 90 days postdischarge including index admission costs, post-acute facility use, and readmissions. Understanding which patients are at risk to be high-cost patients who fall outside the reimbursement limits of the bundle will be essential in providing value-based care to these patients. In addition, it will also allow hospitals to engage in risk adjustment and to understand, plan, and possibly better negotiate for reimbursement based on their case mix. The purpose of this study was to compare the outcomes and cost of patients over the age of 60 undergoing hip fracture fixation based on their anticoagulation status on admission.

Patients and Methods

A total of 531 consecutive hip fracture patients were retrospectively analyzed from 1 academic medical center between a 2-year period (October 2014 and September 2016). Patients were included if they were aged 60 and older and had isolated hip fracture injuries. Included fracture patterns were intertrochanteric, subtrochanteric, and femoral neck hip fractures. Patients with associated fractures and those who were treated nonoperatively for their injuries were excluded from this analysis. Patient outliers who had hospital LOS greater than 4 standard deviations from the mean were excluded from all analysis. Patients on the following anticoagulants were included in the anticoagulated cohort: clopidogrel, warfarin, and factor Xa inhibitors including rivaroxaban and apixaban, dabigatran, dipyridamole/aspirin, and aspirin 325 mg. Patients who were not taking any of the aforementioned drugs at the time of admission made up the nonanticoagulated cohort.

Patient demographics, health status, injury status, and procedure details were collected for each patient. Health status was evaluated using the Charlson comorbidity index (CCI). Injury status included fracture type. Procedure details included operation performed and anesthesia choice. For patients on warfarin, INR at the time of admission and at the time of procedure was recorded. There were no standardized approaches regarding delay of surgery for patients on anticoagulation medications. Patients on anticoagulation medications typically had their medications stopped at the time of admission, but anticoagulant management was left to individual physician clinical practice. Patient hospital quality measures and surgical outcomes were also extracted from each patient’s electronic medical chart. Hospital quality measures included LOS, time between presentation (as defined by arrival in the emergency department) and surgery, complications, transfusion requirement (packed red blood cells, fresh frozen plasma, and platelets), need for intensive care unit (ICU)/step-down unit (SDU) care, and inpatient mortality. Data regarding complications were gathered from hospital discharge summaries and progress notes, including sepsis, pneumonia, deep vein thrombosis/pulmonary embolism, acute myocardial infarction, acute kidney injury, stroke, hematoma, decubitus ulcer, urinary tract infection, acute respiratory failure, acute renal failure, and cardiac arrest. Surgical outcomes included procedure time, operative blood loss, and anesthesia choice.

Index hospital admission costs were obtained from the hospital finance department. Our institution considered these financial data proprietary information. Thus, all cost data are reported as a proportion of the mean total direct variable cost of care for the nonanticoagulated cohort of patients (“$”). Patient discharge disposition was also recorded.

Statistical Analysis

Differences between the 2 cohorts (nonanticoagulated and anticoagulated) were compared using independent t tests, χ2 analyses, and Fisher exact tests. Subanalyses were also performed for each of the different anticoagulant medication types. The effects of age, CCI, and anesthesia type were controlled for using analysis of covariance and hierarchical logistic regression models. A P value <.05 was considered significant. All statistical analyses were performed using SPSS version 23.0 software (SPSS, Inc, Chicago, Illinois).

Results

Of 531 consecutive hip fracture patients over the age of 60 analyzed, 479 (90.2%) met all inclusion criteria. Twenty-three patients were treated nonoperatively, 27 were excluded as they had additional orthopedic injuries, and 2 patients were removed as they were outliers as described in the Methods section. Of the 479 patients, 367 (76.6%) patients were in the nonanticoagulated cohort and 112 (23.4%) patients were in the anticoagulated cohort. There was no difference in fracture type or procedure type between the 2 groups (Table 1). The anticoagulated cohort was older compared to the nonanticoagulated cohort (83.8 [7.7] years vs 81.7 [9.9] years, P = .022). Mean CCI was greater in the anticoagulated cohort compared to the nonanticoagulated cohort (1.8 [1.3] vs 1.2 [1.6], P < .001). There was also a difference in anesthesia choice between the 2 cohorts, with a greater proportion of anticoagulated patients receiving general anesthesia (61.6% vs 83.9%; P < .001).

The anticoagulated cohort had a longer mean time to surgery (1.9 [1.1] days vs 1.6 [1.1] days, P = .010) and a longer total mean LOS (8.3 [4.7] days vs 7.3 [4.0] days, P = .033; Table 2). However, after controlling for age, CCI, and anesthesia type, patients on anticoagulation no longer had significantly longer
The mean total number of complications developed in the 2 cohorts was similar, with 1.3 (1.2) mean complications in the anticoagulated cohort compared to 1.1 (1.0) in the nonanticoagulated group (Table 3). The most common complications were acute anemia, urinary tract infection, and acute kidney injury (Table 4). Although the total number of complications was no different between the 2 cohorts, the incidence of sepsis and acute respiratory failure was greater in the anticoagulated group even when controlling for age, CCI, and anesthesia type. Patients on anticoagulation had nearly a 3 times greater risk of developing sepsis than the patients in the nonanticoagulated cohort (odds ratio [OR] = 2.998, 95% confidence interval [CI]: 1.036-8.673, P = .028). Subanalysis of the anticoagulated cohort demonstrates that the increased rate of sepsis among anticoagulated patients was largely due to the patients in the factor Xa inhibitor cohort in which 12.5% of these patients developed sepsis during their index admission. When controlling for age and anesthesia type, these patients were more than 5 times more likely to develop sepsis (OR = 5.108, 95% CI: 1.181-22.098, P = .029). Similarly, patients on anticoagulation had a 2 times greater risk of developing acute respiratory failure (OR = 2.021, 95% CI: 1.035-3.947, P = .039). No individual anticoagulant subgroup had a significantly increased risk of acute respiratory failure. Notably, there was no difference in inpatient mortality between the 2 cohorts.

The patients in the anticoagulated cohort also had an increased need for ICU/SDU-level care, with 34.8% of the cohort requiring this advanced level of care compared to 19.1% in the nonanticoagulated cohort (P = .001). When controlling for age, CCI, and anesthesia type, patients in the anticoagulated cohort were over 2 times more likely to require this advanced level of care compared to their nonanticoagulated counterparts (OR = 2.364, 95% CI: 1.433-3.900, P = .001). Subanalysis of the anticoagulated cohort demonstrates that the increased need for this advanced level of care was largely due to patients in the warfarin cohort in which 40.5% of patients required ICU/SDU-level care. When controlling for age, CCI, and anesthesia type, these patients were nearly 3 times more likely to require ICU/SDU-level care (OR = 2.998, 95% CI: 1.424-6.314, P = .026). When controlling for age, CCI, and anesthesia type, anticoagulant status was not independently responsible for this increase. Lastly, with respect to index admission costs, there was no difference in total index admission cost of care between the 2 cohorts. The total cost of care (direct variable costs) for the anticoagulated cohort was $1.07x (0.58x) compared to $x (0.51x) in the nonanticoagulated cohort (P = .201). This lack of difference in cost was observed when compared to the nonanticoagulated cohort (Table 3).

time to surgery (P = .103) and LOS compared to the nonanticoagulated cohort (P = .300). Notably, when performing subanalysis of the anticoagulated cohort, patients on warfarin had a significantly longer time from admission to surgery compared to the nonanticoagulated cohort (2.3 [1.4] days vs 1.6 [1.1] days, P < .001; Table 3). The mean INR for patients on warfarin on admission was 2.3 (0.7); the mean INR for these patients at the time of procedure was 1.6 (0.3). Twelve of these patients received Fresh Frozen Plasma (FFP) prior to surgery to reverse the effects of warfarin, 3 received a combination of vitamin K and FFP, and 11 patients received vitamin K only. The remaining 11 were given no reversal agent. There were no differences with respect to LOS for the other anticoagulant subgroups when compared to the nonanticoagulated cohort after adjustment (Table 3).

When comparing surgical outcomes, there was no difference in procedure time nor blood loss between the 2 groups (Table 2). This lack of difference in procedure time and blood loss was maintained when each anticoagulation subgroup was compared to the nonanticoagulated cohort (Table 3). The mean number of units of packed red blood cells transfused was also similar (0.9 [1.3] units in the nonanticoagulated cohort vs 1.1 [1.6] units in the anticoagulated cohort, P = .125). There was however a greater number of FFP units transfused in the anticoagulated cohort (0.3 units vs 0.0 units, P = .001). All of the FFP transfusions observed in the anticoagulated group, but one were for patients on warfarin. As such when the warfarin subgroup was compared to the anticoagulated cohort, there was a difference in FFP transfusions (0.8 [1.2] units vs 0.0 [0.3] units, P < .001). There was no difference seen when the other anticoagulation subgroups were compared to the nonanticoagulated cohort (Table 3).
even when comparing each anticoagulated subcohort to the nonanticoagulated cohort.

Discussion

This study demonstrates that when controlling for age, comorbidities, and anesthesia choice, operative hip fracture patients on anticoagulation fared no worse compared to those patients not on anticoagulation with respect to LOS, surgical blood loss, total complication rate, and post-acute care facility use. Furthermore, these hospitalizations were no costlier to the hospital than those of patients not on these anticoagulant medications. However, there were some observed differences, particularly with respect to need for ICU/SDU-level care during their admission, the development of certain complications such as sepsis and acute respiratory failure, and as expected, the need for fresh frozen plasma. Although these patients on anticoagulation were more likely to have comorbidities, and therefore, may inherently be at risk for longer LOS and increase post-acute care facility use, surgeons and hospital administrators should not use anticoagulation status alone as a measurement of risk when assessing patients on admission or consider anticoagulation to be an additive risk factor in these patients with comorbidities, particularly in the new bundle payment model of care.

In the last decade, there has been increasing literature on hip fracture care for anticoagulated patients. However, most of this focuses on patients on warfarin and clopidogrel, with no studies on the outcomes of hip fracture patients on DOACs. The relationship between anticoagulation and time to surgery has been analyzed by several groups. One recent study by Tran et al of several thousand hip fracture patients in Canada demonstrated that those on warfarin and DOACs had a median time to surgery of 40 hours compared to a time to surgery of 26.2 hours for nonanticoagulated patients. They also noted that patients in the DOAC group had even longer median time to surgery (66.9 hours) compared to patients on warfarin (39.4 hours). Another large study from the United Kingdom also demonstrated this delay in surgery for patients on warfarin compared to those not on anticoagulation (46 hours compared to 24 hours). In contrast, analysis of patients on clopidogrel demonstrated that they have similar mean times to surgery as those patients not on anticoagulation (1.66 days compared to 1.55 days). In our cohort, there was no difference in time to surgery between the nonanticoagulated patients and the anticoagulated patients as a whole. However, when subanalysis was performed, the time between admission to surgery was significantly longer in the warfarin group with a mean TTS of 2.3 days. The time to surgery for patients in the other anticoagulant subcohorts was similar to that of the time to surgery in the nonanticoagulant group. Notably, the time to surgery in our DOAC group was much less than the nearly 67 hours mean time to surgery reported by Tran et al. As there are not yet orthopedicspecific guidelines regarding these medications due to their recent introduction on the market, this may reflect different practices between different surgeons.

The current studies on LOS for hip fracture patients on anticoagulant medications do not present a definitive relationship between these factors. Four large studies analyzing patients on warfarin have been performed, with 2 citing a longer LOS for these anticoagulated patients and 2 citing no association. The largest study performed by Lawrence et al was the only study that controlled for factors such as age and American Society of Anesthesiologists (ASA) score. However, all of these studies were performed in Europe and had LOS much greater than the average hip fracture LOS of about 8 days in the United States. For example, the study by Lawrence et al cited a median LOS of 15 days for the anticoagulated group compared to 13 for the nonanticoagulated cohort. One of the only studies on patients on clopidogrel by Collinge et al demonstrated that while the preoperative LOS was equivalent between patients on clopidogrel and those not on the drug, the postoperative LOS was greater for patients on clopidogrel by 1 day. However, this group did not control for comorbidities, simply noting that the clopidogrel group had a significantly higher ASA score. To date, there have been no studies demonstrating the outcomes of patient on DOACs with respect to LOS, given the recent introduction of these medications on the market. Notably, in our analysis, patients on factor Xa inhibitors had the longest mean LOS with a mean of 9.3 days.

In this study, we report equivalent surgical outcomes between patients on anticoagulants and those not on these...
Table 3. Hospital Quality Measures and Surgical Outcomes for the Nonanticoagulated and Anticoagulated Cohorts (Divided Into Anticoagulant Cohorts).a

| P Value | P Value | P Value | P Value |
|---------|---------|---------|---------|
| (Adjusted) | (Adjusted) | (Adjusted) | (Adjusted) |
| None | Warfarin | Clopidogrel | Factor Xa |
| (n = 365) | (n = 37) | (n = 36) | (n = 4) |
| Time from admission to surgery, mean (SD), days | 1.6 (1.1) | 2.3 (1.4) | <0.01 (0.001) | 1.6 (0.8) |
| Length of stay, mean (SD), days | 7.3 (4.0) | 8.8 (4.8) | 0.07 (1.38) | 7.8 (4.4) |
| Procedure time, mean (SD), minutes | 75.7 (32.7) | 72.4 (46.3) | 835 (682) | 765 (28.0) |
| Blood loss, mean (SD), mL | 156.0 (108.8) | 161.3 (137.7) | 710 (445) | 176.8 (144.7) |
| Units of FFP transfused, mean (SD) | 2.0 (0.3) | 0.0 (0.2) | <0.01 (0.001) | 0.0 (0.2) |
| Units of platelets transfused, mean (SD) | 0.0 (0.1) | 0.1 (0.2) | 3.3 (176) | 6.4 (846) |
| Number of complications, mean (SD) | 1.1 (0.0) | 1.2 (1.3) | 4.8 (377) | 4.6 (97) |
| aControlled for age, CCI, and anesthesia choice.

All previous studies for patients on anticoagulation (warfarin and clopidogrel) have demonstrated that these patients are at no greater risk for inpatient mortality, thromboembolic events, or bleeding complications.5,10,12 In our study, although we noted there was no difference in the total number of complications, there was an increased incidence of acute respiratory failure and sepsis in the anticoagulated group in addition to increased need for ICU/SDU care. These particular complications have not been included in the aforementioned complication analyses. The incidence of sepsis was largely comprised by the factor Xa inhibitor group, and the need for ICU/SDU-level care was largely comprised by the warfarin group. Although the small number of patients in the anticoagulation subgroups limits the significance of these findings, surgeons should be mindful that anticoagulated patients may be at risk for these particular complications and of needing advanced level of care during their index admission, particularly those on warfarin and factor Xa inhibitors. Further evaluation of this relationship between sepsis and respiratory failure and these specific anticoagulation medications with larger cohorts is warranted.

To our knowledge, no study has investigated the usage of ICU stay, discharge disposition, or cost in anticoagulated hip fracture patients. A better understanding of these measures is crucial to provide more cost-effective care to hip fracture patients, particularly in light of the bundle payment model. The ICU care often leads to longer hospital admissions and greater room and board costs. The ICU/SDU utilization rate in this study is consistent with the reported 20% ICU care rate noted in a previous analysis by Donegan et al.13 As our study included ICU and SDU care, the 35% and 19% rates presented in this analysis in the anticoagulated and nonanticoagulated cohorts, respectively, were as expected slightly higher than the previously reported ICU care rate. As room and board contributes to approximately 30% of the index cost of admissions, better identification of patients at risk for high utilization of these services and analysis of triage protocols for these hip fracture patients are needed to provide more cost-effective care.14 Discharge disposition is also becoming increasingly important as the reimbursement for hip fracture care shifts to a bundle payment model with hospitals responsible for care through 90 days postdischarge. The cost of post-acute care contributes significantly to the 90-day costs of hip fracture patients, with some studies citing that post-acute care consumes up to 45% of the bundle payment cost.15 As trauma
patients cannot be optimized prior to admission, identifying at-risk patients from the onset of admission in order to provide additional resources for these higher-risk patients is crucial for cost-effective care. As opposed to viewing anticoagulation status as an independent and additional level of risk, providers should instead be mindful of the underlying comorbidities of the patient on anticoagulation during risk assessment.

The observed impact of comorbidity on the outcome of hip fracture patients has been reported with studies demonstrating that patients with comorbidities such as hypertension and heart disease have an increased risk of readmission and mortality within 6 months of hospital discharge.16 As expected, CCI has been noted to be consistently higher in anticoagulated patients. Even while not controlling for CCI, our hip fracture patients on anticoagulation with higher CCI did not have more costly admissions than the nonanticoagulated cohort. However, there has been a study demonstrating increased cost among patients with greater CCI.17 In this study, LOS was used as a proxy for cost. Direct costs for individual patients were not analyzed; instead, the authors calculated a difference in cost based on the difference in LOS seen in patients with greater CCI using an average cost/day. To our knowledge, our study is the first study to directly compare patient cost data.

Limitations to this study include the generalizability of these results as the patient cohort was from 1 urban academic medical center. However, although only 1 center was included, this academic medical center encompasses an orthopedic specialty hospital, a tertiary care referral center, and a level 1 trauma center. As such, the cost and LOS figures presented in this study should be generalizable to many hospitals in the United States. Furthermore, although we did not see significant differences in cost of care between cohorts, the substantial variability observed in our cost data may have contributed to this finding. Second, we did not control for socioeconomic factors in this analysis, which may have played a role in several factors, particularly LOS and discharge location. Third, whereas INR can be checked for patients on warfarin to detect the level of anticoagulation on admission, there is no lab value to monitor whether the patients are therapeutic on the nonwarfarin anticoagulant medications used in this study. Lastly, the number of patients in each anticoagulation subgroup is small, particularly the factor Xa inhibitor and the direct thrombin inhibitor groups. However, as there are currently no orthopedic studies analyzing the outcomes of patients on these newer anticoagulant drugs, these data are necessary for orthopedic surgeons to be able to properly triage and treat patients on these medications.

After controlling for age, CCI, and anesthesia type, patients on anticoagulation had similar LOS, surgical outcomes, total complication rates, and admission costs to those patients not on anticoagulation. Of note, although there was no difference in the total number of complications, patients taking factor Xa inhibitors and warfarin may experience a heightened incidence of sepsis and need for ICU/SDU care, respectively. Although many of these patients have comorbidities that place them at increased risk for poor outcomes, this study highlights that initiatives aimed at providing more resource-conscious and cost-effective care should not use anticoagulation status as an independent or additive risk marker for these patients.

**Authors’ Note**

Investigation performed at NYU Langone Health, New York, New York, and Jamaica Hospital Medical Center, Queens, New York.
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