



## Outcomes of preinjury anticoagulation in patients with traumatic rib fractures



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### ABSTRACT

**Background:** Anticoagulant and antiplatelet agents (ACAP) have been shown to negatively affect trauma patients.

**Methods:** Outcomes in adults with rib fractures were reviewed. Pearson chi-square test was used for analysis. Multivariate logistic regression was used to adjust for potential confounders.

**Results:** Of the 1448 included patients, 149 (10.3%) took preinjury ACAP; these patients were significantly older than non-anticoagulated patients (72 vs. 54 years,  $P \leq 0.05$ ). There was no difference in pulmonary complications, ICU admissions or ICU LOS. The preinjury ACAP group had a significantly longer LOS (12.03 vs. 9.33 days,  $P = 0.004$ ), fewer pulmonary contusions (15.43% vs. 22.94%,  $P = 0.037$ ), and fewer thoracic drainage procedures (10.74% vs. 18.17%,  $P = 0.023$ ). Multivariate adjustment for possible confounders revealed that patients taking warfarin had a significantly longer LOS (+7.38 days). After adjustment there was no difference in mortality.

**Conclusion:** Preinjury ACAP use does not increase mortality or morbidity in patients with rib fractures.

**Summary:** We demonstrated that preinjury anticoagulation and antiplatelet agents do not increase mortality or morbidity in patients with rib fractures. However, they lead to a longer hospital length of stay, particularly in patients on warfarin.

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### Background

Rib fractures are present in more than 10% of all trauma admissions.<sup>1,2</sup> One-third of patients with rib fracture experience major adverse events after admission, such as pulmonary complications, emergent intubation, tracheostomy, or death.<sup>2</sup> Risk factors for adverse events in patients with rib fractures include advanced age, the number of fractured ribs, and presence of pre-existing conditions.<sup>3–5</sup>

Anticoagulant usage is highly prevalent. In 2004, there were nearly 31 million prescriptions written for warfarin alone in the United States.<sup>6</sup> The use of anticoagulants is expected to increase with the aging population and development of novel drugs that are easier for patients to use and providers to prescribe.

Several trials have shown that preinjury anticoagulant and antiplatelet agents (ACAP) lead to increased morbidity and mortality in trauma patients, particularly those with traumatic brain injuries and pelvic fractures.<sup>7–10</sup> These findings have led to the development of protocols and guidelines for determining an appropriate level of care, consultation, and follow-up imaging studies.<sup>11</sup>

Data on the effect of anticoagulants on patients with blunt chest trauma are limited.<sup>1</sup> The objective of our study was to determine the impact of various ACAP on mortality and morbidity of patients with rib fractures. These findings are important to provide guidance to clinicians in the management of rib fractures in the setting of preinjury anticoagulation.

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## Methods

Albany Medical Center Institutional Review Board approval (#4282) was obtained to conduct this study. We performed a retrospective study using the Albany Medical Center Trauma Registry to review all consecutive patients with rib fractures admitted to our level one trauma center from January 1, 2011 to December 31, 2014. All patients 18 years and older with at least one rib fracture caused by a blunt mechanism were identified. Outpatient medical records and medication reconciliation were used to establish anticoagulant and antiplatelet use.

Demographic characteristics assessed included age, sex, Injury Severity Score (ISS), and Glasgow Coma Scale (GCS) score. Outcomes evaluated were mortality (in-hospital death), pulmonary complications, associated thoracic injuries, hospital length of stay (LOS), admission to the intensive care unit (ICU), and thoracic drainage procedures. Pulmonary complications were defined as the presence of any of the following: empyema, pneumonia, hemothorax, pleural effusion, and intubation. Intubation was used as a surrogate for respiratory failure.

For patients with International Classification of Disease, Ninth edition (ICD-9) codes 807.08 and 807.18 (closed/open fracture of 8 or more ribs), and 807.09 and 807.19 (closed/open fracture of multiple ribs, unspecified), an imaging study was reviewed to record the exact number of rib fractures. ICD-9 codes were also used to identify subsequent pulmonary complications and associated thoracic injuries, including pneumonia (486), hemothorax (860.2), pleural effusion (511.9), empyema (510.9), thoracic drainage procedures (34.0–34.9), intubation (96.04), and pulmonary contusion (861.21). After identifying patients with pulmonary contusion from the registry, radiologists quantified the amount of pulmonary contusion according to the methodology described by Wagner and colleagues.<sup>12</sup>

Comorbidities present on admission were recorded using ICD-9 codes. The following comorbidities were assessed as potential confounders: tobacco use disorder (current or history of use) (158.2 and 305.1), morbid obesity (278.01), obstructive sleep apnea (327.23), chronic respiratory failure (518.83), chronic obstructive asthma (493.20), asthma (493.90), chronic airway obstruction (496), bronchitis (490), emphysema (518.1, 492.8, and 492.0), congestive heart failure (428.0), heart disease (416.8 and 429.9), chronic kidney disease (585.2–585.4, 585.6, 585.9, and 403.91), and anemia (285.9 and 280.9).

Oxygen requirement was considered as the first recorded oxygen level in the emergency department. For non-ventilated patients, oxygen levels, with respect to the delivery device, were converted to a percentage of the fraction of inspired oxygen (FiO<sub>2</sub>), according to the American Association for Respiratory Care guidelines.<sup>13</sup> The number and type of blood products administered were recorded for each patient that received a transfusion. Additionally, data on open reduction and internal fixation of rib fractures were obtained from the hospital database.

Encountered ACAP were sorted into four groups: aspirin/dipyridamole, warfarin, clopidogrel, and miscellaneous agents (Supplemental Digital Content Table 1). The miscellaneous group

contained all patients on newer anticoagulants (e.g., rivaroxaban, apixaban, and dabigatran) and enoxaparin. In the case of polypharmacy, we established a hierarchy of ACAP based on the likely predominant pharmacologic impact. Consequently, one primary ACAP was identified (Supplemental Digital Content Table 2).

## Statistical analysis

Data were analyzed using the Pearson chi-square test. Analysis was performed using a commercially available statistical software package (Stata, version 14.0; StataCorp, College Station, TX). Multivariable logistic regression was used to adjust for potential confounders (e.g., the ISS and GCS score on admission, age, and pre-existing comorbidities), to assess the independent effect of various risk factors when  $P < 0.05$ .

## Results

Over the 4-year study period, 7283 trauma patients were admitted, with 1448 (23.9%) patients admitted with rib fractures resulting from a blunt trauma mechanism (Fig. 1). Preinjury ACAP were identified in 149/1448 patients (10.3%).

Of 149 patients on an ACAP, 53.69% (80 patients) were on aspirin or dipyridamole, 22.15% (33 patients) were on warfarin, 15.43% (23 patients) were on clopidogrel, and 8.72% (13 patients) were considered to be on miscellaneous agents. Less than 20% (29 patients) of patients were on two or three ACAP. Demographic characteristics, including the number of rib fractures and mechanism of injury, were similar between patients on ACAP and non-anticoagulated patients (N-ACAP), except for age, GCS score, ISS, and comorbidities (Table 1). Patients on ACAP were significantly older than N-ACAP patients (mean age, 71.86 vs. 53.54,  $P \leq 0.05$ ). Patients on ACAP presented to the hospital with less traumatic brain injury (GCS score, 14.24 vs. 13.44) and were found to have endured less severe trauma compared to N-ACAP patients (ISS, 16.71 vs. 19.49). There was no difference between the two groups with regard to the number of ribs fractured. There was no relationship between the number of ribs fractured and the presence or absence of preinjury ACAP. Most patients (1151 patients, 79.49%) underwent computed tomography of the chest during their admission work-up. There was a significant difference in comorbidities (ACAP vs. N-ACAP) for chronic airway obstruction (12.08% vs. 5.23%,  $P = 0.001$ ), congestive heart failure (14.77% vs. 2.39%,  $P < 0.001$ ), chronic pulmonary heart disease (2.68% vs. 0.69%,  $P = 0.015$ ), and stage III chronic kidney disease (2.68% vs. 0.15%,  $P < 0.001$ ) between the two groups.

When comparing outcomes, there was no difference in composite pulmonary complications, ICU admissions, ICU LOS, or rate of respiratory failure (Tables 2 and 3). Interestingly, patients on ACAP required fewer thoracic drainage procedures (10.74% vs. 18.17%,  $P = 0.023$ ) than N-ACAP patients, despite the increased likelihood of developing a pulmonary contusion (odds ratio, 1.215; 95% confidence interval, 0.731–2.019) after adjusting for age, GCS score, ISS, and comorbidities. Additionally, no significant difference was observed in the FiO<sub>2</sub> level, despite a trend toward a higher FiO<sub>2</sub>

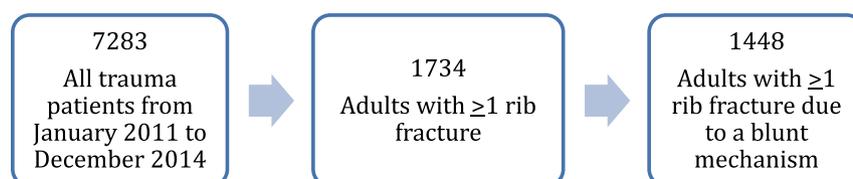


Fig. 1. Flow chart of population selection.

**Table 1**  
Patient characteristics.

Characteristic	ACAP group	N-ACAP group
n	149	1299
Age* (years)	71.86 (69.72–74.00)	53.54 (52.54–54.55)
Male sex, n (%)	94/149 (63.08%)	902/1299 (69.44%)
Average ISS (95% CI)	16.71 (15.43–17.99)	19.49 (18.98–20.00)
Average Chest IS (95% CI)	2.75 (2.62–2.88)	2.96 (2.92–3.02)
Average GCS score (95% CI)	14.24 (13.83–14.65)	13.44 (13.24–13.64)
Mechanism of Injury	n (%)	n (%)
MVC	55 (36.9%)	564 (43.4%)
MCC	9 (6.0%)	220 (16.9%)
Assault	2 (1.3%)	30 (2.3%)
Fall	76 (51.0%)	410 (31.6%)
Pedestrian crash	4 (2.7%)	45 (3.5%)
Struck by foreign object	3 (2.0%)	29 (2.2%)
Number of rib fractures**	n (%)	n (%)
1 rib	26 (17.45%)	216 (16.63%)
2 ribs	19 (12.75%)	164 (12.63%)
3 ribs	16 (10.74%)	159 (12.24%)
4 ribs	22 (14.77%)	168 (12.93%)
5 ribs	20 (13.42%)	143 (11.01%)
6 ribs	13 (8.72%)	139 (10.70%)
7 ribs	8 (5.37%)	84 (6.47%)
8 ribs	15 (10.07%)	113 (8.70%)
9 ribs	3 (2.01%)	29 (2.33%)
10 ribs	3 (2.01%)	15 (1.15%)
11 ribs	0 (0%)	18 (1.39%)
12 ribs	1 (0.67%)	17 (1.31%)
13 ribs	3 (2.01%)	10 (0.77%)
14 ribs	0 (0%)	10 (0.77%)
15 ribs	0 (0%)	2 (0.15%)
16 ribs	0 (0%)	2 (0.15%)
17 ribs	0 (0%)	7 (0.54%)
18 ribs	0 (0%)	1 (0.08%)
20 ribs	0 (0%)	1 (0.08%)
22 ribs	0 (0%)	1 (0.08%)

\*Age,  $P = 0.000$ .\*\*Distribution of rib fractures,  $P = 0.932$ .

GCS, Glasgow Coma Scale; ISS, Injury Severity Score; CI, confidence interval; ACAP, anticoagulant and antiplatelet agents; N-ACAP, non-anticoagulated; MVC, motor vehicle crash; MCC, motorcycle or bicycle crash.

level for ventilated patients on ACAP. In-hospital mortality was significantly lower in the ACAP group than in the N-ACAP group (1.34% vs. 5.54%;  $P = 0.027$ ). After adjusting for the GCS score, ISS, and age, there was no significant difference in mortality between the two groups. Although the number of ribs was significantly associated with pulmonary complications and mortality, the number of rib fractures was not associated with anticoagulation use; therefore, it was not adjusted as a confounder.

Patients on ACAP had a significantly longer LOS than N-ACAP patients (12.03 vs. 9.33 days,  $P = 0.004$ ) (Table 3). After multivariate

adjustment, patients on ACAP stayed an average of 3.26 days longer than N-ACAP patients did. Increased LOS was mostly affected by patients who were on warfarin at the time of injury. Compared to N-ACAP patients, those on warfarin had a significantly longer LOS after multivariate adjustment (7.38 days longer; 95% confidence interval, 3.79–10.98).

Patients on ACAP were more likely to receive a transfusion than N-ACAP patients were, although the two groups received similar quantities of blood products on average (Table 4). Patients on ACAP received fresh frozen plasma (FFP) more frequently than N-ACAP patients (16.11% vs. 9.62%,  $P = 0.014$ ). There was no significant difference in the frequency of packed red blood cells (PRBC) or platelet transfusion between the two groups. Compared to N-ACAP patients, those on ACAP received fewer units of PRBC (2.33 vs. 3.98,  $P = 0.026$ ), FFP (3.13 vs. 3.77,  $P = 0.240$ ), and platelets (1.17 vs. 2.14,  $P = 0.108$ ). Of note, only two patients in the study population, both of whom were not on any pre-injury anticoagulation drug, received cryoprecipitate. Open reduction and internal fixation of ribs was performed in only three patients in the ACAP group versus 34 patients in the N-ACAP group.

## Discussion

In this study, all patients with rib fractures on preinjury ACAP had an increased duration of hospitalization. Patients on warfarin had a greater increase in LOS, even after multivariate adjustment. To our knowledge, this is the largest study evaluating the impact of preinjury ACAP on patients with rib fractures.

Results similar to ours have been shown in other studies on the effects of preinjury anticoagulation on trauma patients. In a study of 1121 geriatric falls, Coleman et al. demonstrated that there was a higher LOS among patients on anticoagulation ( $6.3 \pm 6.2$  vs.  $4.9 \pm 5.2$ ,  $P = 0.001$ ) and an even higher LOS ( $7.2 \pm 6.8$  vs.  $5.0 \pm 5.3$ ,  $P = 0.001$ ) in patients on warfarin.<sup>14</sup> Maung et al. showed similar results among trauma patients with various mechanisms of injury.<sup>15</sup>

An increased LOS in patients on ACAP is likely related to, and exacerbated by, the anticoagulant effect itself and the reason why these patients are receiving ACAP: age. There is a linear relationship between age and comorbidities, including those requiring anticoagulation. For example, the prevalence of atrial fibrillation increases from 0.1% among adults younger than 55 years to 9.0% in persons aged 80 years and older.<sup>16</sup> Our data showed that patients on ACAP were significantly older than N-ACAP patients; therefore, one can speculate that patients on ACAP have more comorbidities and require more time for management of these conditions. The difference in LOS is simply the additional time necessary to stop, reverse, and restart ACAP under observation. The significantly longer LOS seen with patients on warfarin is likely related to its

**Table 2**  
Patient outcomes.

	ACAP group	N-ACAP group	P-value (chi-square test)	Adjusted <sup>a</sup> ACAP (OR, 95% CI)
Mortality	2 (1.34%)	72 (5.54%)	0.027*	0.101 (0.021–0.487)
Pulmonary complications	24.16%	22.27%	0.600	–
Empyema	1 (0.67%)	13 (1.00%)	0.697	–
Pneumonia	13 (8.72%)	67 (5.16%)	0.071	–
Hemothorax	6 (4.03%)	59 (4.54%)	0.774	–
Respiratory failure	14 (9.40%)	143 (11.01%)	0.549	–
Thoracic drain	16 (10.74%)	236 (18.17%)	0.023*	0.663 (0.384–1.144)
Pulmonary contusion	23 (15.43%)	298 (22.94%)	0.037*	1.215 (0.731–2.019)
Admitted to ICU	67 (44.97%)	538 (41.42%)	0.405	–

CI, confidence interval; OR, odds ratio; ACAP, anticoagulant and antiplatelet agents; N-ACAP, non-anticoagulated; ICU, intensive care unit.

\* $P < 0.05$ .<sup>a</sup> Multivariate adjustment was performed for age, Injury Severity Score, Glasgow Coma Scale score, and comorbidities.

**Table 3**  
Pulmonary complications and length of stay in the ACAP subgroups.

	Pulmonary Complications	Total LOS (days) (p-value)	Unadjusted Difference in LOS (days)	Adjusted difference in LOS (days)
N-ACAP	22.27%	9.33	Reference	Reference
Aspirin/dipyridamole	21.25%	11.24 (0.128)	1.91	2.29
Warfarin	24.24%	15.85(<0.01)	6.52(<0.01)	7.38(<0.001)
Clopidogrel	34.78%	10.87 (0.501)	1.54	2.13
Miscellaneous agents	23.08%	9.23 (0.975)	−0.95	1.14

Multivariate adjustment was performed for age, Injury Severity Score, Glasgow Coma Scale score, and comorbidities. ACAP, anticoagulant and antiplatelet agents; N-ACAP, non-anticoagulated; LOS, length of stay.

**Table 4**  
Transfusion requirements.

	N-ACAP, %	ACAP, %	Aspirin/dipyridamole, n	Warfarin, n	Clopidogrel, n	Miscellaneous Agents, n
Any blood product <sup>a</sup>	20.40%	31.54%	–	–	–	–
PRBCs	12.24%	18.12%	9	9	6	3
FFP	9.62%	16.11%	8	19	4	1
Platelets	6.00%	8.72%	3	4	1	0

ACAP, anticoagulant and antiplatelet agents; N-ACAP, non-anticoagulated; PRBCs, packed red blood cells; FFP, fresh frozen plasma.

<sup>a</sup> Blood products include PRBCs, FFP, and platelets.

pharmacokinetic properties, particularly its relatively long half-life.<sup>15</sup> The increased LOS associated with use of ACAP has obvious implications on the health care system, as patients with coagulopathy or platelet dysfunction incur further costs for reversal, monitoring, and as demonstrated in this study, an increased transfusion requirement. At the same time, one could argue that a more aggressive approach to reverse anticoagulation with the use of more potent agents (e.g., tranexamic acid, prothrombin complex concentrate, factor VIIa, etc.) coupled with more stringent monitoring with thromboelastography (TEG), could reduce the LOS. Future investigations should evaluate the cost-benefit relationship of this approach, as well as possible thromboembolic complications. The lack of difference in mortality between ACAP and non-ACAP is not consistent with that reported in the literature on pre-injury anticoagulation in trauma patients<sup>8–10,14,15,17</sup> and patients with blunt chest trauma.<sup>17</sup> Additionally, our study demonstrated that the ICU admission rate and ICU LOS do not fit with current standards. This could be explained by the fact that the decision to admit patients to the ICU was primarily determined by respiratory function and severity of rib fractures as opposed to the presence of anticoagulant or antiplatelet drugs which defined our two cohorts. Patients on ACAP and N-ACAP had the same distribution of rib fractures, and they experienced the same pulmonary complications and respiratory failure rates.

Blunt trauma can lead to shearing across the lungs unique liquid–gas interface and tissue planes of varying densities, causing diffuse interstitial hemorrhage.<sup>18</sup> The inhibition of clot formation will predispose patients on ACAP to higher rates of bleeding complications, which has been previously well documented in traumatic brain injury and pelvic fractures.<sup>9,10</sup>

We did not observe an increased rate of pulmonary complications, including pulmonary contusions, which is counterintuitive. There were significantly less drainage procedures and pulmonary contusions in the ACAP group compared to those without anticoagulation. It is unlikely that ACAP protect patients from bleeding complications, and that the explanation for this observation may be due to unaccounted differences between the two populations, other than the ISS, GCS score, and number of rib fractures. It is very possible that providers at our center may be more cautious when considering placing a thoracic drain in an anticoagulated patient. To our knowledge, no data explain the lower propensity for bleeding with increased age, which was the

only significant difference between the two groups. Other than bias in our study, the lower rate of thoracic drainage procedures and pulmonary contusion in patients on ACAP could possibly be explained by the use of reversal agents, warranting further investigation.

Patients with rib fractures on preinjury ACAP should be assigned a higher index of risk on rib fracture management protocols. The next steps after this study include the development of management guidelines and the subsequent development of a prospective study to evaluate the effect of risk stratification on outcomes in this patient population.

There are multiple limitations to this study, including its retrospective design and relatively small ACAP sample population. The study was underpowered to detect smaller differences in outcomes as well as specific outcomes related to individual anticoagulants. Our study did not consider noncompliance and sub-therapeutic drug levels, which could introduce error in the analysis. Future studies would benefit from adherence to follow up to accurately report on death post discharge.

Our data demonstrate a high likelihood that the observed increase in LOS is due to the effect of ACAP. Clinicians should strive to identify these agents early in the care of trauma patients. Proper monitoring of coagulation and platelet function with coagulation studies, TEG, and platelet function tests should be performed. Likewise, chest tube output, hemoglobin trends, and vital signs should be monitored to assess for hemorrhaging. If bleeding is suspected, every effort should be made to aggressively reverse anticoagulation as early as possible. Although not captured in our data, reversal agents should include factor VIIa, prothrombin complex concentrate, and regimens to reverse newer oral anticoagulants.

## Conclusions

We demonstrated that preinjury anticoagulation and antiplatelet agents do not increase mortality or morbidity in patients with rib fractures. However, they lead to a longer hospital length of stay, particularly in patients on warfarin. This indicates a requirement for higher use of hospital resources. Therefore, patients with rib fractures on pre-injury anticoagulation drugs should be stratified to a higher risk tier for appropriate management.

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Marcel Tafen served as a lecturer for Synthes. All other authors declare no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.amjsurg.2018.06.007>.

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