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Research Paper

Clinical outcomes for patients on antiplatelet and anticoagulants in thoracoabdominal trauma

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ABSTRACT

Introduction: Trauma outcomes can be greatly affected by antiplatelet and anticoagulant (AP/AC) use. The goal of this study was to compare outcomes in trauma patients on AP/AC undergoing emergent surgery for thoracoabdominal trauma at 35 level 1 and 2 trauma centers from 2014 to 2021.

Methods: This was a retrospective cohort study of 2460 adult patients with a chest, abdomen, or pelvis abbreviated injury score (AIS) of 2 or more who underwent surgery within 24 h of admission. These patients were segregated into four main cohorts based on antiplatelet/anticoagulation use: those not on AP/AC, those taking direct-acting oral anticoagulants (DOACs), those taking clopidogrel, and those taking warfarin. Patients were excluded if they had surgery >24 h after presentation, were dead on arrival, or had any other body system AIS score of 3 or higher.

Results: The mean injury severity score (ISS) in all four groups ranged from 16.3 to 18.6 ($p = 0.834$) with a mean time to operating room from 208 to 478 min ($p < 0.001$). Laparotomy was performed in 60 to 71 % ($p > 0.01$) of patients, regardless of AP/AC status, and thoracic procedures were performed in 3.1 to 9.3 % ($p = 0.42$) of patients. In-hospital mortality and hospice rates were highest in the clopidogrel group at 21.9 %, followed by warfarin at 13 %, DOACs at 15 %, and no AP/AC at 7.63 % ($p = 0.008$). Serious complications occurred in 61 % of patients on warfarin, 50 % of those on DOACs, and 44 % of those on clopidogrel. All of these groups demonstrated significantly higher complication rates than patients in the no AP/AC control group at 25 % ($p < 0.001$). Total transfusion of packed red blood cells and fresh frozen plasma did not differ significantly between the groups; however, 24-h platelet transfusion did. Patients on clopidogrel received 14 packs of platelets, while those on warfarin and DOACs received 8 and 13 packs respectively ($p = 0.011$). Patients on warfarin had the longest hospital length of stay (LOS) at 13 days and ICU LOS at 9 days, compared to those on DOACs (8 and 4), those on clopidogrel (7 and 3), and those not taking AC/AP (7 and 4) (hospital LOS $p = 0.03$, ICU LOS $p = 0.019$). Those on AC/AP were also noted to be significantly older than those on neither, with those taking these medications averaging out to be approximately 69 years old and those not on these medications averaging 37 years old ($p < 0.001$).

Conclusion: There was significantly higher mortality in patients on clopidogrel and increased length of stay and risk of serious complications in patients taking DOACs and warfarin. In patients on AP/AC there was also a significantly longer time to surgery than in those not taking either. Given these associations trauma surgeons should consider intervening sooner on patients taking AP/AC on admission, as the delay to intervention may contribute to the risks for trauma patients and result in worse outcomes as well as higher rates of mortality.

Introduction

As our trauma population in the United States becomes older and the use of antiplatelet and anticoagulant agents is increasingly more common in elderly patients, questions regarding outcomes of trauma surgery for patients on these agents have become more frequent, complex, and potentially consequential. Many studies investigating outcomes of surgery in injured patients on chronic antiplatelet and

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anticoagulant (AP/AC) therapies have been performed in efforts to improve outcomes for these patients [3-6,8,9].

One such study in 2022 by Narula et al [1] investigated how antiplatelets and anticoagulants affect trauma patients as a whole in regards to mortality and length of stay by retrospectively investigating over 2200 patients in their trauma registry. They concluded that patients on anticoagulants have a higher mortality rate and longer hospital length of stay, while those on antiplatelets did not. In the same year, Reina et al. [2] investigated whether preinjury anticoagulant use affected outcomes of patients with isolated blunt abdominal injuries who underwent non-operative management. This group used the American College of Surgeons (ACS) Trauma Quality Improvement Program (TQIP) database, which includes patients from >875 trauma programs within the United States. They analyzed >2700 patients from 2022, comparing outcomes in anticoagulated patients to those who were not anticoagulated. They found that anticoagulated patients had higher non-operative

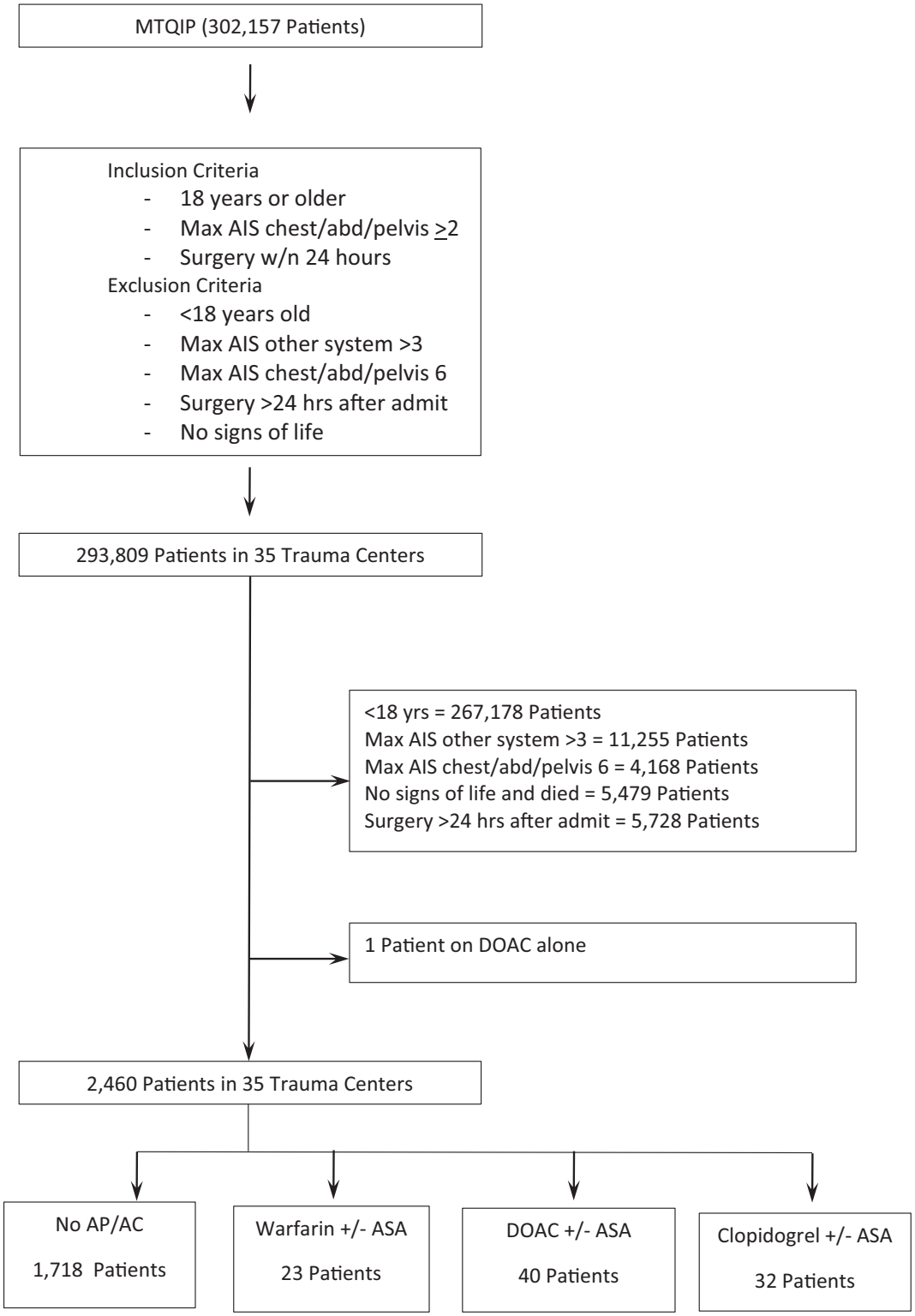

Fig. 1. Inclusion and exclusion criteria.

management failure rates; increased incidence of cardiac arrest, acute kidney injury, and myocardial infarction; higher mortality rates; and longer ICU and hospital length of stay.

These studies prompt an additional question: do patients who require operative intervention for trauma have worse outcomes if they are taking antiplatelet or anticoagulant medications than patients who are not? While other researchers have sought to answer this question in all trauma patients, we were specifically interested in the differences in outcomes associated with body regions where non-compressible hemorrhage can lead rapidly to death without surgical intervention; namely the thoracoabdominal region. To this end, the goal of this study was to determine the effect that preinjury antiplatelet and anticoagulant use has on clinical outcomes following emergent surgery, specifically for patients with thoracoabdominal trauma. We hypothesized that those on AP/AC agents had higher rates of mortality or discharge to hospice, higher rates of serious in-hospital complications, and longer length of stay in the hospital and the ICU.

Methods

Using the Michigan Trauma Quality Improvement Program (MTQIP) database, which includes 35 Level 1 and Level 2 trauma centers, we performed a retrospective observational study of trauma patients who presented between 2014 and 2021 with thoracoabdominal injuries requiring surgical intervention, which included any procedures performed in the operating room, interventional radiology suite, or at bedside in the ICU.

Our inclusion criteria were all patients 18 years or older with a chest, abdomen, or pelvis abbreviated injury severity score (AIS) of 2 or more who underwent surgery within 24 h of admission. The AIS score is an anatomically based, internationally accepted tool for ranking injury severity, that ranges from 1 for minor to 6 for fatal. According to this scoring system, a patient with a chest, abdomen, or pelvis AIS score of 2 or greater would indicate more severe injury in that body region. Our exclusion criteria were patients who were <18 years of age; those who had surgery >24 h from admission; those with max chest or abdomen AIS score of 6 (determined to be non-survivable); those with no signs of life at initial evaluation, defined as a Glasgow Coma Scale (GCS) 3, pulse 0, and systolic blood pressure 0; or those with max head, face, neck, abdomen, spine, upper extremity, or lower extremity AIS score of 3 or more. (Fig. 1). AIS scores of 3 or greater in other body regions were excluded because that would indicate life-threatening injuries outside of the thoracoabdominal area.

Four main cohorts were created for comparison. Our first group, those not on any antiplatelet or anticoagulation medications, were used as our reference group ($n = 1718$). The remaining three groups were those taking direct oral anticoagulants (DOACs, such as anti-Xa or direct thrombin inhibitors) and not on warfarin or clopidogrel ($n = 40$); those on warfarin not taking DOACs or clopidogrel (23), and those on clopidogrel and not DOACs or warfarin ($n = 32$). Of note, the database does not provide information on how long the patient had been taking the medication on evaluation in the trauma bay. The database also does not indicate whether patients fell within a therapeutic range on these medications.

Our primary outcomes were in-hospital mortality and rate of discharge to hospice. Secondary outcomes were defined as the amount of blood products received within 24 h of admission; hospital and ICU length of stay; and rates of serious in-hospital complication. Serious in-hospital complications were defined as adult respiratory distress syndrome (ARDS), pneumonia, pulmonary embolism, intubation, acute renal failure, stroke, lower extremity deep vein thrombosis, septic shock, extremity compartment syndrome, decubitus ulcer, or enterocutaneous fistula.

Descriptive statistics were performed across and between cohorts on all variables analyzed for each emergent surgery type, respectively. Specifically we calculated the mean and standard deviation of numeric data, except for ICU and hospital length of stay, where we calculated the median and interquartile range, and count and percent of categorical data. We performed t- and Chi-square tests to compare variables analyzed by cohort and subgroups for continuous and categorical data, respectively, and Mann-Whitney *U* tests to compare ICU and Hospital days. Fisher's Exact test was used instead of t- and Chi-square tests where appropriate for small sample sizes.

A logistic regression was performed to evaluate our primary outcomes, where in-hospital mortality and rate of discharge to hospice were regressed into AP/AC status (i.e., each cohort), patient age, race, diabetes, CVA, hemiparesis, dementia, stroke, smoker status, ISS, and intubation status. We excluded vitals from this model because the outcome lacked variation in these variables.

To address our secondary outcomes, we performed a series of separate logistic regressions, regressing the amount of blood products (i.e. frozen plasma, platelets, and blood units) received within 24 h of admission and the presence of serious complication following emergent surgery into the same patient characteristics as above. These were treated as response variables and separate Poisson regressions whereas hospital and ICU length of stay were treated as response variables using the aforementioned predictors. Predictors were dropped from a given model if they lacked sufficient within strata samples to compute adequate parameter estimates. Logistic regressions were repeated as above by evaluating subgroups as our main predictor variable instead of cohorts.

Results

Patients on AP/AC were significantly older and more likely to have multiple medical comorbidities including COPD, diabetes, history of stroke, and pneumonia (Table 1). Patients on clopidogrel were more likely to be older than those on warfarin, DOACs, or those not taking AP/AC. Injury severity score (ISS) did not vary significantly between the groups with the average ranging from 16.4 to 18.9 ($p = 0.80$). Despite the similarity in ISS, those on warfarin (65 %) and DOACs (59 %) had

Table 1
Patient demographics.

Variable	No AP/AC	Warfarin	DOAC	Clopidogrel	*p*-value
Age (SD)	37 (15.8)	69 (16.8)	68 (12.9)	69 (10.5)	<0.001
Male, %	77	48	69	81	0.007
ISS, %					
5–15	46	48	38	41	0.94
16–24	29	35	36	34	0.95
25–35	20	17	18	22	0.95
> 35	5	0	8	3	0.94
Max AIS >2, %					
Chest	35	57	54	38	0.03
Abdomen	76	48	72	72	0.12
Comorbidities, %					
Diabetes	4	22	26	38	<0.001
Pneumonia	6	17	15	9	0.012
COPD	2	17	15	13	<0.001
CVA hemiparesis	0.1	13	13	3	<0.001
CVA history	0.4	0	5	0	0.028
Smoker	38	17	21	25	0.01
Injury type, %					
Bowel	28	5	5	14	<0.001
Rib	38	64	55	41	0.015
Procedure type, %					
Bowel	46	30	21	31	0.002
Bronch	2	0	8	9	0.02
Solid Organ	19	26	36	28	0.021
Bronchoscopy	2	0	8	9	0.02
Tracheostomy	1	17	5	0	0.001
Minutes to procedure	209	479	322	332	<0.001

higher chest AIS scores than those in the clopidogrel (44 %) or no AP/AC groups (45 %) ($p = 0.03$). Patients not taking antiplatelets or anticoagulants were more likely to have bowel injuries (28.3 %) and bowel related procedures (46 %) when compared to patients taking warfarin (4.6 % and 30 %), DOACs (5.3 % and 20.5 %), and clopidogrel (13.8 % and 31 %, $p < 0.001$ and $p = 0.002$ respectively) who also had abdominal trauma. Rib fractures were significantly more common in the warfarin group at 64 %, DOAC group at 55 %, and clopidogrel group at 41 % when compared to the no AP/AC group at 38 % ($p = 0.015$). Solid organ injuries that required some form of intervention were more common in patients on warfarin at 26 %, DOACs at 36 %, and clopidogrel at 28 % when compared to the no AP/AC group at 19 % ($p = 0.021$).

There was also a significant difference in time to intervention seen in these cohorts. When patients were not on antiplatelet or anticoagulant medications, the average time to intervention was 209 min. Average time to intervention in patients on DOACs and clopidogrel was 322 and 332 min respectively. Warfarin patients were delayed significantly longer than the other three cohorts, with an average of 479 min before intervention ($p < 0.01$).

Discussion

Many studies, including those by Narula and Reina et al [1,2] have investigated outcomes in trauma patients taking clopidogrel, warfarin, or DOACs prior to injury. However, there remains a paucity of literature on patient outcomes in those taking AP/AC who sustain thoracoabdominal trauma requiring surgical intervention in the first 24 h, allowing this to be the first study of its kind.

In contrast to Narula's study [1] which demonstrated higher rates of mortality in patients taking warfarin and DOACs, we found that use of preinjury clopidogrel increased mortality and platelet use in the first 24 h while warfarin and DOAC use trended toward higher mortality (Table 2). Warfarin was significantly associated with higher risk of serious in-hospital complications, as well as increased hospital and ICU length of stay. It is a well-known phenomenon in both clinical practice as well as in the literature that antiplatelet and anticoagulant agents can lead to more complications in trauma care. How these medications affect patient outcomes when emergent trauma surgery is required has largely remained unstudied until this paper.

As expected, most patients on AP/AC agents are significantly older than those not taking either medication. Their age alone inherently puts them at higher risk of poor outcomes due to the likelihood of comorbid conditions, as well as a greater risk of frailty. They are also at greater risk of rib fractures due to bone deterioration related to aging. Therefore, the findings of greater rib fractures in this population is not surprising. These rib fractures can also lead to greater rates of complications such as respiratory failure that can require interventions such as tracheostomy, even early in the hospital course. What was unexpected in these results were the number of patients requiring tracheostomy within the first 24 h. This procedure is not commonly done early in a patient's hospital course and may have included patients requiring emergent cricothyroidotomy, though this information cannot be gleaned from retrospective review of the database.

The length of time to operative intervention for thoracoabdominal trauma patients on warfarin, DOACs, and clopidogrel was also significantly longer. It is unclear what the cause of this delay is but could be due to awaiting reversal agent administration prior to intervention. Regardless of the reason, this delay may contribute to the increased mortality associated with clopidogrel use, as well as the higher complication rates and longer length of stay seen in warfarin and DOAC patients. Decreasing time to OR may be associated with lower rates of mortality, serious complication rates, and ICU and hospital length of stay in patients on chronic AP/AC. Methods of definitive hemorrhage control could include laparoscopy, laparotomy, or even interventional radiology techniques for definitive bleeding management.

This study has all of the limitations inherent in a retrospective database study. Many studies have investigated the outcomes of traumatically injured patients on aspirin. One such study performed by Ivascu et al [10] in 2008 looked at head injured patients on aspirin, clopidogrel, or both and their outcomes. They found that use of either aspirin, clopidogrel, or both had high mortality rates in the setting of intracranial injury. Another limitation of the study is the inability to isolate aspirin use from each of these cohorts to determine its unique effect on mortality. Similarly, it is not possible to know the aspirin dose for any of the patients in the study, which may influence the patient's outcomes.

We also were unable to evaluate individual patient ROTEM or TEG results that may have been important in the decision-making process for both transfusion needs as well as surgical interventions. Along this same vein, while we could determine how many patients received fresh frozen plasma and platelets and at what volume over the first 24 h, we are unable to evaluate if patients received certain reversal agents such as prothrombin complex concentrate (K-Centra, Bebulin, or Profilnine), anti-inhibitor coagulant complex (FEIBA), or Vitamin K. The timing of administration and the clinical need for these reversal agents could have contributed to delays in intervention or the ultimate outcomes we see in AP/AC patients. While many new reversal agents, such as idarucizumab for dabigatran, andexanet for apixaban and rivaroxaban exist, they are often costly and complex to give. Investigating patterns of use is being considered for a follow up study. Many patients may require restarting their AP/AC for treatment of their underlying hypercoagulable diseases as soon as sufficiently recovered from surgery and monitored resumption of these agents could have affected the length of stay. Future studies may also provide benefit by evaluating the outcomes from these decisions.

Table 2
Outcome variables analyzed by cohort.

	No AP/AC	Warfarin	DOAC	Clopidogrel
Death (%)	7.6	13	15	21.9
	(Reference)	1.04	1.08	2.22
		(0.27–4.09)	(0.37–3.13)	(0.83–5.94)
Complications	25.2	61	50	44
(%)	(Reference)	2.51	1.40	1.22
		(1.01–6.24)	(0.67–2.88)	(0.56–2.67)
Plt in 24 h	383	8	13	14
	(Reference)	2.92	1.80	3.00
		(1.06–8.06)	(0.81–4.00)	(1.30–6.87)
Hosp LOS (d)	7	13	8.5	7
	(Reference)	1.25	0.84	0.95
		(1.12–1.41)	(0.76–0.94)	(0.84–1.06)
ICU LOS (d)	4	9	4	3
	(Reference)	1.48	0.87	0.93
		(1.27–1.72)	(0.76–1.00)	(0.79–1.08)

Conclusion

This study demonstrates worse outcomes for patients on AP/AC requiring operative intervention after thoracoabdominal trauma, revealing that there may be a window of opportunity to improve outcomes. Given the higher mortality in patients on clopidogrel and the higher rates of complications and length of stay in patients taking warfarin and DOACs, trauma surgeons should consider earlier operative or radiological interventions on these patients to mitigate these risks.

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Ethics approval

This paper meets all research ethical standards.

CRediT authorship contribution statement

Jason Hecht is responsible for the idea and Rola Bazzi and Victoria Sharp reviewed the data from the MTQIP (Michigan Trauma Quality Improvement Program) data base. Victoria Sharp developed the abstract and manuscript for this paper and these were reviewed and primarily edited by Jason Hecht. Victoria Sharp presented the data at the Academic Surgical Congress in Houston.

Declaration of competing interest

The authors have no conflict of interest to disclose.

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