ORIGINAL CONTRIBUTION

Risk of Intracranial Hemorrhage in Ground-level Fall With Antiplatelet or Anticoagulant Agents

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ABSTRACT

Objectives: Anticoagulant and antiplatelet medications are known to increase the risk and severity of traumatic intracranial hemorrhage (tICH), even with minor head trauma. Most studies on bleeding propensity with head trauma are retrospective, are based on trauma registries, or include heterogeneous mechanisms of injury. The goal of this study was to determine the rate of tICH from only a common low-acuity mechanism of injury, that of a ground-level fall, in patients taking one or more of the following antiplatelet or anticoagulant medications: aspirin, warfarin, prasugrel, ticagrelor, dabigatran, rivaroxaban, apixaban, or enoxaparin.

Methods: This was a prospective cohort study conducted at a Level I tertiary care trauma center of consecutive patients meeting the inclusion criteria of a ground-level fall with head trauma as affirmed by the treating clinician, a computed tomography (CT) head obtained, and taking and one of the above antiplatelet or anticoagulants. Patients were identified prospectively through electronic screening with confirmatory chart review. Emergency department charts were abstracted without subsequent knowledge of the hospital course. Patients transferred with a known abnormal CT head were excluded. Primary outcome was rate of tICH on initial CT head. Rates with 95% confidence intervals (CIs) were compared.

Results: Over 30 months, we enrolled 939 subjects. The mean ± SD age was 78.3 ± 11.9 years and 44.6% were male. There were a total of 33 patients with tICH (3.5%, 95% CI = 2.5%–4.9%). Antiplatelets had a rate of tICH of 4.3% (95% CI = 3.0%–6.2%) compared to anticoagulants with a rate of 1.7% (95% CI = 0.4%–4.5%). Aspirin without other agents had an tICH rate of 4.6% (95% CI = 3.2%–6.6%); of these, 81.5% were taking low-dose 81 mg aspirin. Two patients received a craniotomy (one taking aspirin, one taking warfarin). There were four deaths (three taking aspirin, one taking warfarin). Most (72.7%) subjects with tICH were discharged home or to a rehabilitation facility. There were no tICH in 31 subjects taking a direct oral anticoagulant. CIs were overlapping for the groups.

Conclusion: There is a low incidence of clinically significant tICH with a ground-level fall in head trauma in patients taking an anticoagulant or antiplatelet medication. There was no statistical difference in rate of tICH between antiplatelet and anticoagulants, which is unanticipated and counterintuitive as most literature and teaching suggests a higher rate with anticoagulants. A larger data set is needed to determine if small differences between the groups exist.

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Anticoagulant and antiplatelet medications are used to treat and prevent thromboembolic diseases. However, the benefits of these agents must be weighed against the risk of increased bleeding propensity,[1,2] especially after trauma. Even a low-acuity mechanism such as a ground-level fall, which typically will not cause a life-threatening injury, may lead to significant morbidity and mortality in patients taking an anticoagulant or antiplatelet drug. Until 2009, the only available oral anticoagulant and antiplatelet agents were aspirin, clopidogrel, and warfarin. Since 2009, the FDA has approved the antiplatelet agents prasugrel and ticagrelor, the direct thrombin inhibitor dabigatran, and the direct Factor Xa inhibitors rivaroxaban apixaban, and edoxaban. Emergency departments (EDs) are seeing an increased number of patients taking a direct oral anticoagulants (DOAC), dabigatran, rivaroxaban, apixaban, or edoxaban.[3] Clinical trials and postmarketing reports with DOACs suggest a decreased overall bleeding risk as well as a lower rate of intracranial hemorrhage compared to warfarin.[3–7] However, these did not specifically investigate traumatic intracranial hemorrhage (tICH).

Head injury is a frequent chief complaint in ED patients, while ground-levels falls or fall of lesser height is a common mechanism in the elderly,[8] with an increased risk of tICH.[9] Anticoagulants clearly increase the risk and severity of tICH, even with minor head trauma. One retrospective analysis found a mortality of 50% from a tICH in patients taking warfarin.[10] Warfarin use has been associated with increased morbidity and mortality in patients who suffer a low-acuity mechanisms such as a simple fall.[11] tICH from the DOACs has the potential to be especially devastating because only dabigatran has an FDA-approved reversal agent.

Outcomes once a tICH is identified with an anticoagulant have been previously described; however, few studies have compared the rate of tICH from antiplatelet and anticoagulant agents including DOACs. One study attempted to ascertain the rate after closed head injury of warfarin versus clopidogrel only.[12] Additionally, traumatic mechanisms are heterogeneous and intuitively, a high-velocity mechanism would be expected to increase risk of internal injury. Our goal was to decrease heterogeneity by standardizing to low-acuity ground-level fall mechanism to study bleeding propensity and rate of tICH when taking an antiplatelet or anticoagulant. Additionally, most previous studies are limited to retrospective reviews or trauma registry analyses when attempting to ascertain rates as it is difficult to capture all subjects who fall and do not sustain a tICH. The objective of this study is to assess the rates of intracranial hemorrhage in ED patients on anticoagulants or antiplatelet agents who sustain a ground-level fall and receive cranial computed tomography (CT) imaging.

METHODS

This was a prospective, observational cohort study of consecutive patients presenting to the ED of an urban, university-affiliated, Level I trauma center, tertiary care hospital ED with an annual volume of 55,000 patients. Subjects were enrolled from June 2013 to November 2015. Subjects were identified by asking a screening question to the clinician during the index ED visit, the charts were abstracted without subsequent knowledge of the hospital course, and then outcomes were subsequently determined through medical records review. The project received expedited approval from the hospital's institutional review board.

Study Population

Consecutive adult patients (>18 years of age) who presented to the ED with a ground-level fall or lesser mechanism of injury were enrolled if they also had a CT head performed and had aspirin, clopidogrel, prasugrel, ticagrelor, warfarin, dabigatran, rivaroxaban, or enoxaparin identified on their ED medication reconciliation. Edoxaban was excluded because it had not received FDA approval at the initiation of this study. Patients transferred from an outside hospital with identified injuries or an injury that occurred greater than 24 hours prior to presentation were excluded. This population was chosen to calculate an accurate rate of tICH in patients taking an antiplatelet or anticoagulant medication who present to an ED de novo after their injury. The standard approach of the emergency medicine faculty at this ED is to obtain a head CT in patients who fall and are taking an anticoagulant or antiplatelet.

Patient Screening and Study Protocol

If a patient presented to our ED taking one of the above medications and had a CT head performed, the treating clinician was electronically asked the question "Did the patient fall from standing or lesser height?" during the admit/discharge process. The clinician

could answer "yes," "no," "uncertain," or decline to answer. This was accomplished using the ED "dashboard," a robust tracking and information system that collects clinical and operational data. The ED IS system generated daily reports of all subjects who met the above criteria and had a "yes," "uncertain," or empty response to the prospective question. A research assistant performed a confirmatory chart review of all patients in this screening log and included those who had a "yes" response. Those with an "uncertain" response or no clinician response were reviewed by the research assistant and included if there was a clear history of ground-level fall documented in the ED note. We have selected only the first visit of each subject for the current analysis.

A standardized data abstraction form was designed and the research assistant was trained on how to identify the necessary historical elements. The research assistant was aware of the study goals. The research assistant and the principal investigator communicated on a regular basis to clarify any potential study issues and resolved and discrepancies trough consensus review. For any subjects who had a tICH identified, the principal investigator (PI) conducted a secondary chart of review of inpatient course to further qualitatively describe interventions and outcome and confirm the research assistant's initial data abstraction. There was no other abstractor used to perform interrater reliability. Data were stored in a Redcap database.

Outcomes

The primary outcome was a tICH defined as a subdural or epidural hematoma, subarachnoid hemorrhage, or intraparenchymal hemorrhage identified on head CT interpreted by an attending neuroradiologist. The neuroradiologists were not part of the study team; rather, they were reading the studies as part of clinical care, and therefore there was no adjudication performed to determine a criterion standard read. The final CT read was reviewed by the PI and only definitive hemorrhages were considered positive; any equivocal studies were considered negative. Other abstracted data included patient demographics and comorbid conditions, mechanism of injury and related features including loss of consciousness (LOC), scalp injury, Glasgow Coma Scale at presentation, neurologic deficits, laboratory values, any interventions and disposition. At the completion of the study period, we searched the hospital electronic medical records for any deaths that occurred within 30 days of the index visit. These charts were reviewed by the PI to determine whether the cause of death was due to a delayed complication from the head trauma. Our health system practice is that even if a patient expires at an outside facility, there will often be a note within the hospital electronic records summarizing the events.

Sample Size Justification

Since at the initiation of the study, we were unaware of data on the incidence and distribution of tICH when using these various agents in a population with homogenous mechanism of injury, no a priori power calculation was performed. Instead, we chose to enroll a consecutive sample of patients initially over 1 year. This time frame was extended further on interim review of data.

Data Analysis

Statistical analysis was performed using the IBM SPSS Statistics software package (version 20.0) and WinPepi.[13] Continuous variables with normal distribution are presented as means (±SD) and compared by one-way analysis of variance (ANOVA). The rate of tICH for each agent was reported with 95% CIs using exact or Wilson's tests. Dichotomous variables are compared with the use of the chi-square test or exact test as appropriate. Two-tailed values of $p < 0.05$ were considered statistically significant.

RESULTS

There were 4,539 patients screened who had a CT head performed and their medication list contained an anticoagulant or antiplatelet. On the question posed to clinicians during the disposition module, clinicians answered "yes" to ground-level fall for 1,282 (28.2%), "uncertain" to 324 (7.1%), and "no" to 1,537 (33.9%) and for 1,396 (30.8%) there was no response. Of the charts with an "uncertain" answer or no clinician response, 333 (19.4%) were enrolled after confirmatory chart review. Of these 1,069 visits, 130 were excluded because they represented a repeat ED visit for a fall (five of those visits sustained a tICH). The final enrollment was 939 subjects (21.5%). The subject flow diagram is presented in Figure 1.

Mean ± SD subject age was 78.3 ± 11.9 years and 44.6% were male. The vast majority of subjects in the study were taking aspirin (78.0%), followed by warfarin (24.0%). There were 141 (15.0%) subjects

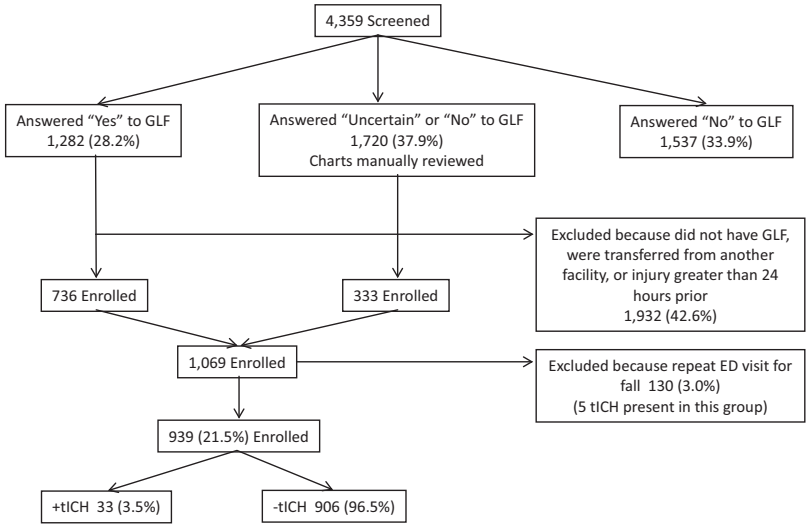

Figure 1. Flow of patients in study. GLF = ground-level fall; tICH = traumatic intracranial hemorrhage.

Table 1
Baseline Subject Characteristics

Characteristic	Antiplatelet Treatment, *n* = 668 (71.1%)	Anticoagulation Treatment, *n* = 180 (19.2%)	Combined Treatment, *n* = 91 (9.7%)	p-value*
Age (y)	78.3 ± 11.9	78.7 ± 12.5	78.1 ± 11.1	0.853
Male sex	298 (44.6)	74 (41.1)	47 (51.6)	0.54
Past medical history				
Hypertension	472 (70.7)	111 (61.7)	73 (80.2)	0.005
CAD/MI	215 (32.2)	45 (26.1)	49 (53.8)	<0.001
CHF	82 (12.3)	33 (18.3)	22 (24.2)	0.003
Dementia	127 (19.0)	22 (12.2)	10 (11.0)	0.03
Diabetes	196 (29.3)	37 (20.6)	35 (38.5)	0.01
Hyperlipidemia	150 (22.5)	36 (20.0)	24 (26.4)	0.49
CVA/TIA	78 (11.7)	23 (12.8)	16 (17.6)	0.28
Atrial fibrillation	69 (10.3)	109 (60.6)	53 (58.2)	<0.001
Previous history of intracranial bleeding	18 (2.7)	6 (3.3)	1 (1.1)	0.57

Data are reported as mean ± SD or *n* (%).
CAD/MI = coronary artery disease/myocardial infarction; CHF = congestive heart failure; CVA/TIA = cerebrovascular accident/transient ischemic attack
*Chi-square and ANOVA.

taking aspirin in combination with another agent. There were 668 (71.1%) subjects taking an antiplatelet agent and 31 (3.3%) taking a DOAC. The mean (±SD) international normalized ratio (INR) in subjects taking warfarin was 2.97 (±2.0), 19 (8.4%) did not have their INR checked during the index visit for the fall, 45 (20.0%) had an INR < 2.0, 15 (6.7%) had an INR < 1.5, and 15 (6.7%) had an INR > 5.0. Baseline subject characteristics are presented in Table 1.

Subject clinical findings and outcomes are presented in Table 2. Patients taking an antiplatelet were more likely to have had a LOC or show external signs of head trauma. The vast majority of subjects (99%) had an intact mental status on presentation. There was no difference in ED disposition or death rate between antiplatelet and anticoagulants.

Among the patients enrolled, there were 33 (3.5%, 95% CI = 2.5%–4.9%) tICH identified. Antiplatelets had a rate of tICH of 4.3% (95% CI = 3.0%–6.2%), compared to anticoagulants, which had a rate of 1.7% (95% CI = 0.4%–4.5%). Aspirin without other agents had the highest point estimate rate of tICH at 4.6% (95% CI = 3.2%–6.6%). When aspirin was used in combination with clopidogrel, the rate was 3.9% (95% CI = 0.5%–13.2%). Warfarin without other agents had a rate of 2.1% (95% CI = 0.05%–5.6%). There

Table 2
Subject Findings and Outcomes

Finding and Outcome	Antiplatelet Treatment, *n* = 668 (71.1%)	Anticoagulation Treatment, *n* = 180 (19.2%)	Combined Treatment. *n* = 91 (9.7%)	p-value*
Head strike recorded	407 (60.9)	102 (56.7)	62 (68.1)	0.19
LOC	120 (18.0)	18 (10.0)	3 (3.3)	<0.001
External signs of head trauma	277 (41.5)	62 (34.4)	28 (30.8)	0.05
Laceration	110 (16.5)	26 (14.4)	11 (12.1)	0.49
Abrasion	109 (16.3)	18 (10.0)	13 (14.3)	0.11
Hematoma	129 (19.3)	36 (20.0)	8 (8.8)	0.04
Mental status on presentation				
Awake and alert	661 (99.0)	179 (99.4)	91 (100)	0.53
Confused	52 (7.8)	15 (8.3)	3 (3.3)	0.28
Agitated	10 (1.5)	2 (1.1)	0	0.72
Lethargic	12 (1.8)	2 (1.1)	1 (1.1)	0.91
Unresponsive	1 (0.1)	0	0	1.00
Neurologic deficit noted	155 (23.2)	30 (16.7)	9 (9.9)	0.004
Disposition from ED				
Discharged home	267 (40.0)	68 (37.8)	43 (47.3)	0.82
ED observation	83 (12.4)	22 (12.2)	9 (9.9)	
Admission to floor	308 (46.1)	86 (47.8)	38 (41.8)	
Admission to ICU	10 (1.5)	4 (2.2)	1 (1.1)	
Deaths				
Within 7 days	8 (1.2)	0	0	0.34
Within 30 days	23 (3.4)	3 (1.7)	4 (4.4)	0.35
tICH on CT	29 (4.3)	3 (1.7)	1 (1.1)	0.13

Data are reported as *n* (%).
ICU = intensive care unit; LOC = loss of consciousness; tICH = traumatic intracranial hemorrhage.
*Chi-square or exact test analysis.

were no statistically significant differences between the various treatment groups. The mean INR in subjects taking warfarin and sustaining a tICH was 3.3 with a range of 2.5 to 4.7 (mean INR without ICH was 2.97, p = 0.58), suggesting that the bleeding was less likely from overanticoagulation. Of note, most subjects (81.5%) who had a tICH from aspirin were taking the low dose (81 mg). Out of the 33 tICH, 12 (36.4%) were described as "small," "punctate," or "tiny." There were no tICH found in the DOAC group; however, overall numbers were low (31). The rate of tICH by agent and combination of agents is in Table 3.

In subjects with tICH, more patients had a LOC with 10/33 (30.3%) recorded compared to 131/906 (14.5%) who had LOC without ICH (p = 0.012). In subjects with tICH, 29/33 (87.9%) had external signs of head trauma compared to 338/906 (40.6%) who had external signs of head trauma without tICH (p < 0.001).

The characteristics of subjects with tICH are presented in Table 4. Most tICH (66.7%) had a subdural component. Medical interventions included a prothrombin complex concentrate (Profilnine or Kcentra depending on which was available during the study period) for three patients taking warfarin, as well as vitamin K and fresh-frozen plasma. Five subjects who were taking aspirin received a platelet transfusion. Two subjects required a craniotomy. Most (72.7%) of subjects with a tICH were discharged home or to a rehabilitation facility, while four (12.1%) subjects died. Of the subjects with tICH who died, three were taking aspirin, one was taking warfarin, and one received a craniotomy.

There were eight (0.9%) deaths within 7 days and 30 (3.2%) deaths within 30 days of the initial ED visit. Of these 30 deaths, four subjects had a tICH identified on initial CT head. In subjects who had no tICH on initial CT head, one subject who had an initial fall described without head strike and taking 325 mg of aspirin sustained a spontaneous and nonsurvivable subdural hemorrhage (SDH) 30 days later. There were no other delayed tICH or tICH-related mortality identified in the subjects who expired who had an initial CT head without tICH.

Table 3
Rate of tICH by Agent

Agent	Subjects with tICH	Total Subjects	Proportions, % (95% CI)*
Aspirin alone†	27	591	4.6 (3.2–6.6)
Aspirin + clopidogrel‡	2	52	3.9 (0.5–13.2)
Aspirin + warfarin + clopidogrel§	1	8	12.5 (0.6–48.0)
Warfarin alone‖	3	143	2.1 (0.05–5.6)
Aspirin + enoxaparin	0	4	
Aspirin + warfarin	0	66	
Clopidogrel alone¶	0	21	
Prasugrel	0	1	
Ticagrelor	0	1	
Dabigatran	0	18	
Rivaroxaban	0	10	
Apixaban	0	3	
Enoxaparin alone	0	11	
Antiplatelet	**29**	**668**	**4.3 (3.0–6.2)**
Anticoagulant	**3**	**180**	**1.7 (0.4–4.5)**
Combined	**1**	**91**	**1.1 (0.1–5.3)**

INR = international normalized ratio; tICH = traumatic intracranial hemorrhage.
*Wilson's or exact test.
†Aspirin dose: 22 (81.5%) taking 81 mg; five (18.5%) taking 325 mg.
‡Aspirin dose for both subjects was 325 mg.
§Aspirin dose 81 mg, INR = 2.5.
‖INR range was 2.9–4.7.
¶All clopidogrel doses 75 mg.

DISCUSSION

In this study, we calculated the rates of tICH among patients with a ground-level fall who are taking antiplatelet or anticoagulant therapy, including the DOACs. Nishijima et al.[12] prospectively determined rate of tICH with blunt head injury, but only in patients taking warfarin or clopidogrel and did not standardize the mechanism of injury; however, most subjects did have a similar fall mechanism. That study found a 12% rate of tICH in patients taking clopidogrel, compared to 5.1% for warfarin. Of those with a tICH, 64% had a GCS of 15. This population had only a 4% concomitant aspirin use.[12]

The rate of tICH in anticoagulated patients in the literature is quite variable. It has been reported as low as 0% when there is no LOC and minor trauma.[14] Some studies place the rate between 15 and 25%,[15–17] while one study found a rate as high as 60%.[18] However, these studies are difficult to extrapolate from as they are retrospective or based on trauma registries and are composed of heterogeneous mechanisms of injury. Our study found a much lower rate of tICH with anticoagulation, most likely because our methods were not subject to the selection bias of retrospective and trauma center–based studies, as well as limited injury mechanism to a ground-level fall. Thus, our rate of tICH more likely approximates a true rate of anticoagulated patients commonly presenting to an ED without a major traumatic mechanism of injury.

We found no tICH in patients anticoagulated with a DOAC, although overall numbers of these patients included in our study was quite low (3%) in our data set and there is a broad CI around our estimate. Given the low number of DOAC patients, it is unreliable to draw any conclusions regarding risk of traumatic bleeding with these agents. A previous retrospective analysis by Beynon et al.[19] of patients with mild head injury with tICH included only six subjects taking rivaroxaban, but found an increased rate of rebleeding and mortality compared to nonanticoagulated and antiplatelet therapy only subjects. Another retrospective analysis of all patients sustaining a ground-level fall found a much higher rate of tICH and mortality in patients taking dabigatran compared to warfarin or no anticoagulant. However, the dabigatran group only had five subjects, most of whom were taking concomitant warfarin, aspirin, or clopidogrel.[20] Comparing the results of these studies to ours is

Table 4
Characteristics of Patients With tICH

Characteristic	*N* = 33
Location	
Subdural	13 (39.4)
Subarachnoid	9 (27.3)
Subdural + intraparenchymal	1 (3.0)
Subdural + subarachnoid	6 (18.2)
Subdural + subarachnoid + intraparenchymal	2 (6.1)
Intraparenchymal	2 (6.1)
Epidural	0
Other CT characteristics	
Midline shift	2 (6.1)
Intraventricular blood present	2 (6.1)
Signs of herniation	1 (3.0)
Medical interventions	
Vitamin K	2 (6.1)
Fresh-frozen plasma	1 (3.0)
Packed red blood cells	2 (6.1)
Platelets	5 (15.2)
DDAVP	1 (3.0)
Prothrombin complex concentrate	3 (9.1)
Endotracheal intubation in ED	1 (6.1)
Surgical intervention	
Intraventricular drain	0
Craniotomy	2 (6.1)
Disposition from hospital	
Discharged home	15 (45.5)
Discharged to rehabilitation facility	9 (27.3)
Discharged to long-term care facility	4 (12.1)
Transferred to another acute care hospital	1 (3.0)
Death	4 (12.1)

Data are reported as *n* (%).

challenging as they are retrospective and often start with patients identified with a tICH, resulting in a selection bias. Additionally, they contradict findings of clinical trials and other postmarketing analyses[3] that suggest a decreased overall bleeding risk with DOACs, although extrapolating to patients sustaining injury is also difficult. Therefore, we suggest further prospective collection of data with DOACs to understand the true traumatic hemorrhage propensity in this population.

One of the most striking findings in our data was that there was no statistical difference in the tICH rate between antiplatelet medications and anticoagulants (the 95% CIs overlapped). We were expecting to find a statistically higher rate of tICH with the anticoagulants, which would be consistent with commonly held beliefs and teaching. Although not commonly discussed in the literature, aspirin has been associated with increased morbidity and mortality in patients with tICH. In a case-control study of patients admitted to a trauma service with intracranial injury, 47% taking aspirin died compared to 33% taking warfarin and 8% controls.[21] Another case-control study of patients with tICH found those taking aspirin, clopidogrel, or both had a 23% mortality rate compared to 9% in nonanticoagulated controls.[22] A retrospective review of patients with head injury taking an anticoagulant or antiplatelet found a 15% rate of tICH with warfarin compared to 25% with aspirin.[17] However, these results are not universal; a retrospective analysis of elderly patients with tICH found an increase risk if in-hospital death with warfarin compared to antiplatelets.[23]

It is not clear and somewhat counterintuitive that antiplatelets may have a similar traumatic bleeding propensity as anticoagulants; however, there may be a mechanistic explanation. After a vascular injury, the first step in hemostasis is platelet activation and aggregation. These steps are inhibited by agents such as aspirin and clopidogrel. Only after the platelet plug is formed can the clotting cascade form a fibrin clot and stabilize the platelet plug. Thus, one may hypothesize that early after an injury, platelets are more important in preventing extravascular extravasation of blood than the coagulation cascade. Additionally, there may be vascular bed–specific hemostasis variability in cerebral vasculature response to injury. Another potential explanation is that the antiplatelet effects of available agents cannot be easily measured such as with warfarin; thus, some patients may have excessive platelet inhibition and thus increased bleeding propensity even with typical dosing.

Of note, Connolly et al.[24] published a recent meta-analyses of 19 randomized clinical trials comparing rate of SDH in patients taking vitamin K antagonists (VKA), antiplatelet monotherapy, or a DOAC. For SDH, VKA therapy had an OR of 3.0 compared to antiplatelet therapy, 2.9 compared to oral direct factor Xa inhibitors, and 1.8 for direct thrombin inhibitors. The rate of SDH on VKA therapy was found to be 2.9 per 1000 patient-years. Even though these results are different from ours, this study used pooled data from large clinical trials in which SDH was not a primary or secondary outcome and did not limit to solely tICH.[24]

Subjects in our data set who sustained a tICH were more likely to have LOC or external signs of head trauma. Previous studies suggest that patients who sustain minor head injury are more likely to have a tICH

if they have a history of LOC or external signs of head trauma.[25,26] However, of our subjects with tICH, 70% did not have an LOC and 12% did not have external signs of head injury suggesting that these findings are not sensitive enough to reliably rule out a tICH with a ground-level fall in a patient taking anticoagulant or antiplatelet therapy. Even though we found an overall 3.5% rate of tICH in patients with a ground-level fall, clinical outcomes were overall good. The vast majority (72.7%) of subjects with tICH were eventually discharged home or to a rehabilitation facility. The rate of neurosurgical intervention and death from the tICH itself was very low (0.4%) in the population as a whole.

LIMITATIONS

This study had several limitations. We did not include a control group that was not taking any anticoagulant or antiplatelet medication. Therefore, our results can only be interpreted as comparators between various therapies and not against the larger population in general. We did not include a control group as people do not reliably present to an ED after minor head trauma without LOC; thus the rate of tICH with our methods in a control group would have been biased higher than expected for the general population. Conversely, patients taking anticoagulants are acutely aware of risks of tICH and more likely to seek care than those taking an antiplatelet; as such we may have missed healthy patients taking aspirin who did not present to the ED. This selection bias would actually result in an underestimation of the true tICH antiplatelet rate. It is also possible that there were different rates of image acquisition for patients on anticoagulant therapy compared to antiplatelet therapy, which would have influenced the hemorrhage rate if more CT scans were ordered in one group. While in general, the threshold is very low for obtaining imaging in all elderly patients who fall, the potential for selection bias remains. Future studies may enroll all patients and include some element of clinical follow-up in patients who do not receive a CT head; however, this approach was outside the scope of this investigation. Finally, it is possible that there was a lower threshold to obtain a CT in patients on oral anticoagulants compared to antiplatelet agents, which would result in the oral anticoagulant group having a comparably lower rate of tICH due to selection bias.

Even though patients were identified prospectively, we used medical record review to abstract data such as head CT findings, laboratory values, clinical characteristics, and outcomes; therefore, our study shares limitations common to all record reviews such as reliability of subjective data. However, the primary outcome was tICH on CT head, which is objective data that should not be affected by records review. Clinical characteristics such as presence of LOC or signs of external head trauma are more subjective and may have been impacted. Also, 40% of screened subjects had "uncertain" or no response to the prospective screening tool and those charts required manual review to determine if a ground-level fall was present.

It is possible that in some subjects, especially in the five with intraparenchymal hemorrhage, the bleed preceded the fall. However, three of those subjects also had a subdural component, and all five had physical examination findings of head trauma; while not definitive, it does suggest a traumatic bleed. Except for subjects taking warfarin, we were unable to confirm that the subjects were taking the anticoagulant or antiplatelet medication at the time of their injury as serum concentrations of the medications were not obtained as part of routine clinical care.

Our results also did not show statistical significance. We did not calculate a power analysis as our methods, isolation to homogenous mechanism of low-acuity ground-level fall, and comparator groups were unique. As the similar rate of tICH with antiplatelet and anticoagulants is counterintuitive, and there were insufficient subjects taking DOACs to determine their risk of tICH, we suggest that our methods should be validated on a larger population across several centers and community hospitals. Additionally, prescription patterns of the DOACs compared to warfarin and newer antiplatelet agents such as ticagrelor are changing; thus these results may not reflect current usage and future larger data sets could provide novel insight.[3]

CONCLUSION

The rate of traumatic intracranial hemorrhage was 3.5% in subjects with a ground-level fall taking an antiplatelet or anticoagulant medication. There was no statistical difference in the rate of traumatic intracranial hemorrhage when comparing patients taking antiplatelet agents with anticoagulant agents, which was unanticipated and counterintuitive. A clinically significant traumatic intracranial hemorrhage was rare in our population with only 0.2% requiring neurosurgical intervention and 0.4% mortality. Most subjects with a

traumatic intracranial hemorrhage were discharged home or to a rehabilitation facility. Further data are needed to determine if direct oral anticoagulants share a similar risk to warfarin given the low rate of direct oral anticoagulant use in this data set and to validate if there is truly a similar rate of traumatic intracranial hemorrhage from aspirin low-dose monotherapy as with anticoagulants.

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