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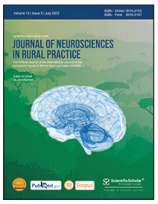

Original Article

Analysis of traumatic intracranial hemorrhage and delayed traumatic intracranial hemorrhage in patients with isolated head injury on anticoagulation and antiplatelet therapy

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ABSTRACT

Objectives: Anticoagulants and antiplatelet (ACAP) agents are increasingly and frequently used, especially in the elderly. The present study was carried out to assess the prevalence of delayed traumatic intracranial hemorrhage (dtICH) after a normal result on an initial head computed tomography (CT) in adults who were taking ACAP medication.

Materials and Methods: The present retrospective included all adult patients who arrived in the emergency department between January 2017 and January 2021 with a history of fall from the patient's own height, while being on ACAP medication with an isolated head injury. The Institutional Review Board approved the study with a waiver of consent. The primary outcome measures were prevalence of dtICH in patients who had initial normal CT scan brain and were on ACAP medication.

Results: There were 2137 patients on ACAP medication, of which 1062 were male, and 1075 were of the female gender. The mean age of the patients was 82.1 years. About 8.2% had positive first CT scans (176/2137), while 0.023 (27/1149) had dtICH. The most common positive finding on the CT scan was subarachnoid hemorrhage followed by subdural hemorrhage. Male gender positively correlated with increased risk for first CT being positive ($P = 0.033$). Patient's with comorbidity of cirrhosis and chemotherapy had higher risk of dtICH ($P = 0.47, 0.011$).

Conclusion: There was a very low (0.023%) prevalence of dtICH. Dual therapy or Coumadin therapy made up the majority of tICH. Cirrhosis and chemotherapy were associated with the risk of a repeat CT scan being positive with an initial CT scan negative.

Keywords: Anticoagulants, Antiplatelets, Traumatic brain injury, Intracranial hemorrhage, Coagulopathy, Computed tomography scan

INTRODUCTION

Anticoagulants and antiplatelet (ACAP) agents are frequently used in patients for the prevention of thromboembolic disease. ACAP medications use is on the rise, especially among the elderly.[1-3] While these medications are key to preventing long-term morbidity and mortality, they are associated with an increased risk of hemorrhage. It is thought that patients on ACAP medications are therefore at a higher risk of Intracranial hemorrhage (ICH) following a fall. Head injury is common with an increasing presence in the emergency department (ED). The prevalence of traumatic brain injury (TBI)-related ED visits had increased by 63% from 2006 to 2014. Hospital admission following falls is also on the rise as well, particularly among the elderly.[4] Falls are the most common cause of TBI, making up to 48% of all TBI-related ED visits. Earlier studies in patients on ACAP medications showed an increase in morbidity and mortality when compared to patients who are not on ACAP medications.[5-7] For example, one study found a 4–5 fold increase in traumatic intracranial injury when the patient is on oral anticoagulation medication.[7] Due to these earlier studies, many institutions have developed and studied the optimal protocols for the initial triaging of patients who present to the ED on ACAP medications following a fall.[8-10] The most recent guidelines put forth by the American College of Surgeons Committee on Trauma recommend that older patients that fall from any height on ACAP medication receive a limited trauma team activation.[11] The present study was conducted to assess the prevalence of delayed ICH

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(d-ICH) in patients on ACAP medications after a normal result on an initial head computed tomography (CT) scan.

MATERIALS AND METHODS

After the Institutional Review Board approval, including a waiver of consent, we performed a retrospective analysis from the Sarasota Memorial Hospital (SMH) trauma registry. The chart review and documentation of data followed the ethical standards of SMH. The retrospective analysis had two arms. In the retrospective chart review, we assessed all adult fall from patient's own height while being on ACAP medication with an isolated head injury. We looked into ED arrival dates between January 2017 and January 2021. The primary outcome was as follows: The prevalence of d-ICH in this population. Additional collected and reviewed information were patient demographics, vital signs, Glasgow Coma Score (GCS), loss of consciousness, comorbidities, injury details, ACAP medications, ACAP reversal agents, diagnosis, procedures, and complications. An abbreviated injury scale severity score of greater than two in areas other than the head or any transferred patient from another facility due to the possibility of there being incomplete information was excluded from the study. We defined it as a positive second CT scan head where the first head CT (HCT) scan was negative. To calculate the prevalence of d-ICH, we followed the patients who had negative HCT initially and were admitted for observation and an interval repeat HCT 12–24-h later.

Details on positive and negative head CT scans were verified with the documented reports of the radiologist available in the medical records. The head CT scan was considered positive if there was evidence of acute ICH attributable to trauma, including epidural subdural, intraventricular, and subarachnoid hemorrhage. A negative head CT scan was defined as a CT scan with no findings of acute ICH. Patients with a negative first head CT scan were admitted and a repeat CT head was done after 24 h. CT scan positive after 24 h which was negative initially was considered for delayed traumatic intracranial hemorrhage (dtICH) cohort.

Descriptive statistics were used to compare the means of the variables. Logistic regression analysis was conducted to compare the impact of different variables on the occurrence of dtICH. Statistical significance was set at $P < 0.05$. Statistical analysis was performed using R Statistical Software.

RESULTS

Demographics

The present study included 2137 patients who presented with a history of trauma and were on ACAP medication. The mean age of the patients was 82.1 years (Range: 68; 36–104 years; median 83 years) with a male: female of 0.98. Hypertension, congestive heart failure, diabetes mellitus, cerebrovascular accident, and chronic obstructive pulmonary disease were common comorbidities, while cirrhosis and alcohol intake were not frequent in these patients. The majority had GCS ≥14; 1705 patients had a GCS of 15. One thousand two hundred and sixteen patients had a length of hospital stay of 1 day, 236 patients had 2 days, 157 patients had 3 days, 281 patients had more than 3 days, and length of hospital stay was not available for 247 patients. The demographic details of age and gender are presented in [Table 1]. [Table 2] shows the details of the comorbidities and risk factors, and [Tables 3 and 4] shows the details of the parameters of age, GCS, heart rate, systolic and diastolic blood pressure, oxygen saturation, and international normalized ratio (INR). The data are skewed and does not follow normal age, GCS, and INR distribution. For initial (tICH) –- the prevalence of tICH was 8.2% (176/2137), the prevalence of neurosurgical intervention was 0.28% (6/2137), the prevalence of reversal agents was 3% (65/2137), and dual therapy or Coumadin therapy made up the majority of tICH 51% (91/176). For dtICH, the prevalence of dtICH was 0.023% (27/1149), the prevalence of neurosurgical intervention was 0.2% (3/1122), – prevalence of reversal agent was 0.5% (7/1282), and only one patient was reversed on Eliquis, and this was a part of a clinical trial. Details of ACAPs are presented in [Table 5].

Second CT scan

Second plain CT head was performed in selected patients (1281), of which 151 had positive findings while 1149 had negative CT. Twenty-seven patients had a second CT scan as positive, with a negative first CT scan. One hundred and twenty-four patients had both first and second CT scan positive three patients required surgery after the second head CT scan, one underwent percutaneous drainage of subdural hematoma, and two underwent craniotomy and evacuation of subdural hematoma. Like the first CT scan, the typical positive findings were subarachnoid hemorrhage and subdural hematoma, while intraparenchymal hematoma was less common. Ten patients had contusion of the cerebrum,

Table 1: Age distribution.

Age range	Number
(0, 10.0)	0
(10.0, 20.0)	0
(20.0, 30.0)	0
(30.0, 40.0)	3
(40.0, 50.0)	9
(50.0, 60.0)	56
(60.0, 70.0)	166
(70.0, 80.0)	571
(80.0, 90.0)	966
(90.0, 100.0)	353

20 had a traumatic subarachnoid hemorrhage, and 22 had a subdural hematoma. The number of patients with a positive second head CT scan where the first CT scan was negative is shown in [Table 6].

DISCUSSION

The level of trauma activation in these patients is institutionally dependent. It is important to monitor and manage trauma activation criteria to prevent overutilization of resources as well as the significant expense associated with the medical treatment of falls.[12] The management of ACAP trauma patients commonly includes a CT of the head (CTH) to assess for ICH at the time of presentation. If the initial CTH shows no ICH patients; even with only minor head trauma, are usually admitted for observation as well as an interval repeat CTH within 24 h to assess for d-ICH.[13-15] The practice of this is again institutionally dependent with no current nationally accepted guidelines recommending repeat CTH after an initial negative CTH in trauma patients that are on ACAP medications to access d-ICH. Rates of d-ICH in these patients range from 2.1% to 2.5%.[14] There is an integral need to understand the frequency of d-ICH in patients taking ACAP medications to improve patient care and reduce hospital spending.

This study investigated the prevalence of ICH early and delayed after TBI. In addition, we reported the comorbidities that might have a higher risk of intracranial pathology development in the first CT scan or observation scan, or scans done later. This study also presents the correlation of these variables with the outcome in patients with TBI on ACAP medication. TBI is a challenging problem adding to the mortality, morbidity, and socioeconomic burden.[16] While the most typical cause for TBI in lower and middle-income countries is road traffic accidents; the epidemiology has changed in high-income countries. There has been an increase in the longevity and geriatric population is at higher risk of fall, common causes of TBI include falls in elderly patients who already have comorbidities, and many are on ACAP medication for various reasons.[17,18] This changing epidemiology, lack of guidelines, and variable presentation of patients with TBI who are taking ACAP medication are a common challenge for neurosurgeons. The clinical course of these patients often gets complicated due to anticoagulant use or coagulopathy due to other comorbidities.[19,20] Hughes *et al*.[21] reported a lower incidence of delayed tICH with the use of warfarin as compared to direct oral anticoagulants. In a meta-analysis of eleven studies, it was found that the use of warfarin increased the mortality risk from blunt trauma head by 2 times,[22] while in another study, it was found that

Table 2: Details of risk factors.

Risk Factors	No	Yes
Anticoagulant	-	2137
Adv dir limiting care	1866	271
Alcoholism	2085	52
ASA	2112	25
Baby ASA	1663	474
Bleed disorder	2107	30
Chemotherapy	2108	29
CHF	1723	414
Cirrhosis	2131	6
COPD	1909	228
CVA	2018	119
Dementia	1726	411
Dependent Health	1065	1072
Diabetes mellitus	1699	438
Dis cancer	2128	9
Hypertension	447	1690
Mental personality	2088	49
Myocardial infarct	2123	14
Peripheral disease	2022	115
Renal failure	2085	52
Smoker	2053	84
Steroid use	2031	106
Substance abuse	2106	31
Add ADHD	2134	3

ASA: Acetyl salicylic acid, CHF: Congestive heart failure, CVA: Cerebrovascular accident, COPD: Chronic obstructive pulmonary disease, ADHD: Attention deficit hyperactivity disorder

Table 3: Details of vital parameters including INR.

Parameter	Mean	Median	Min	Max	Range	Standard deviation
Age	82.09691	83	36	104	68	9.480435657
GCS	14.713483	15	3	15	12	0.92243738
Heart rate	81.247646	79	2	165	162	15.82987359
Resp rate	17.77736	18	3	75	72	3.286483252
Systolic BP	149.26303	149	49	260	211	27.29584766
Diastolic BP	83.212036	82	30	171	141	18.07618678
Oxygen saturation	97.554041	98	67	100	33	2.931419957
INR	1.4736368	1.12	0.06	14.84	14.78	0.867565244

GCS: Glasgow Coma Score, BP: Blood pressure, INR: International normalized ratio

Table 4: Correlation *P*-values of different variables.

Variable	Correlation with outcome *P* value	Correlation with first head CT as positive *P*-value	Correlation with second head CT as positive *P*-value	Correlation with third head CT as positive *P*-value
Gender	0.996	0.033	0.245	0.725
Bleeding disorder	0.997	0.312	0.748	0.991
Cirrhosis	0.998	0.047	0.057	0.994
Smoking	0.997	0.974	0.983	0.99
Chemotherapy	0.997	0.28	0.011	0.0378
Heart rate	0.577	0.383	0.864	0.0285
Oxygen saturation	0.608	0.684	0.58	0.524
Respiratory rate	0.935	0.898	0.442	0.372
Systolic BP	0.262	0.316	0.351	0.962
Diastolic BP	0.991	0.351	0.5	0.273
Length of hospital stay	0.983	0.0001	0.0001	0.0021
First Head CT positive	0.997		0.0001	
Second Head CT positive	0.999			

BP: Blood pressure, CT: Computed tomography

Table 5: ACAP Details.

Type ACAP	Number
Plavix, BASA	34
Eliquis	29
Coumadin	22
Plavix	19
Xarelto	11
Eliquis, BASA	8
Coumadin	8
Eliquis	8
Coumadin, BASA	8
Xarelto, BASA	5
Xarelto	4
Pradaxa	4
Eliquis, BASA	4
Jantoven	3
Brilinta, BASA	3
Coumadin, BASA	2
Plavix	2
Lixiana (Xa inhibitor)	1
Unknown type	1
Coumadin, plavix	1
Plavix, BASA	1
Lovenox 40 mg SQ, BASA	1
Eliquis (2.5 mg BID)	1
Eliquis (2.5 mg BID), BASA	1
Eliquis, Plavix	1
Eliquis, Cilotazol	1
Eliquis, Brilinta	1
Coumadin, Plavix	1
Effient, BASA	1
Aggrenox	1
Eliquis, BASA	1
Xarelto, Brilinta	1

ACAP: Anticoagulants and antiplatelet

Table 6: Two by two table for dTICH.

	Second head CT positive	Second head CT negative	Total
First head CT positive	124	8	132
First head CT negative	27	1122	1149
Total	151	1130	1281

dTICH: Delayed traumatic intracranial hemorrhage, CT: Computed tomography

the use of antiplatelet agents increased the risk of progression of tICH by 2 times and is an independent risk factor for increased morbidity and vegetative states.[23]

In a study by Della Pepa *et al*.[24] involving 4667 patients with mild TBI, 15.38% of patients with positive CT scans were on oral anticoagulants, and they found that only oral anticoagulants were significantly associated with the progression of ICH. The authors found that the most common intracranial pathology was a subdural hematoma, with intraparenchymal hematoma being less common in that study. Furthermore, the surgery was mainly required for subdural hemorrhage. Our study findings are similar to that study. However, traumatic subarachnoid hemorrhage was also widespread in our study and not frequently reported in the previous studies. Our study also provides clinical implications of oral anticoagulants or antiplatelets on the progression of intracranial hematoma, hospital stay, and outcome. In a study involving 230 patients on antiplatelet or anticoagulants, the authors found that antiplatelet use was significantly more associated with the progression of the ICH than the anticoagulants.[25] In our study, we found that dual therapy or the use of coumadin therapy was present in more than 50% of the patients.

A meta-analysis of nine studies and 14,545 patients found that patients on antiplatelet drugs had 1.5 times higher risk of ICH following a TBI than those not on antithrombotics.[26] In contrast, Scotti *et al*. reported that though both antiplatelets and warfarin increased the odds of ICH, only warfarin was associated with the risk of hematoma progression.[27] Single antiplatelet agents were not associated with poor outcomes.[27] In our study, only 27 patients had positive findings on CT scan when the initial CT scan was negative. This suggests that though they are at risk of hematoma progression, there may be not a significant increase or new findings on repeat CT scans, and hence, the requirement of repeat CT scans needs to be judged on individual case merit. A large multicentric study involving 33,710 patients concluded that anticoagulant effects on TBI are inconsistent and unrelated to hematoma progression or mortality.[28]

Several new findings reported in the present study were not reported earlier. Our study found that the male gender has a higher risk for CT scans to show positive findings. This contrasts with Koiso *et al*.,[29] who found that the female gender was more associated with hematoma progression and poor outcomes. Among all the variables, we found that only cirrhosis was significantly associated with positive findings on the first CT scan and chemotherapy for subsequent scans. This suggests that patients who have received chemotherapy and are on ACAP medication are at higher risk of hematoma progression and should be closely monitored with repeat CT scans.

Limitations

The major limitation of this study is that it is retrospective in nature. Although we have performed multivariate regression analysis, the inherent biases of a retrospective analysis could not be obliterated. Other limiting factors are that we have not assessed many other factors such as clinical profile, including posttraumatic amnesia, and seizures, as predictors of abnormal CT scans. The data in our study are skewed concerning gender and GCS and presents limitations. In additoin, there is a need further define the timings to perform a repeated CT scan, particulary who have sustained minor trauma.

CONCLUSION

The prevalence of tICH was 8.2% and 0.023% for initial and delayed traumatic intracranial hemorrhage. Dual therapy or Coumadin therapy made up the majority of tICH. None of the comorbidities affected the outcome. Male gender was positively associated with an increased risk of tICH in the first CT scan. Cirrhosis and chemotherapy were associated with the risk of repeat CT scan being positive with the initial CT scan negative. Further study is required to identify patients based on comorbidity and anticoagulant type who are at risk of repeat CT scan being positive and need prolonged observation.

Declaration of patient consent

The Institutional Review Board (IRB) permission obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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