

Are Sequential CT Scans Necessary in Patients on Warfarin with a Minor Head Injury and Initial Normal CT of the Brain?

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Abstract

Original Research Article

Background: TBI is one of the leading causes of death and disability in the US irrespective of age, race, gender, ethnicities and economical status and imparts a paramount effect on health system. There are insufficient data to conclude that mild TBI patients on oral anticoagulation with negative initial CT scans could be discharged safely: **Methods:** We conducted a retrospective study involving anticoagulated patients who had sustained minor head injury ((GCS on admission 13-15; ISS <15); a negative initial head CT scan at a level 2 Regional Trauma Center from October 2013 to December 2017. All patients admitted for at least 24 hours observation with a repeat CT scan performed before discharge; Preinjury use of anticoagulation (warfarin use for at least 1 week). **Results:** All 61 patients were on Coumadin and (9/61) took aspirin as an additional anticoagulant. The first CT scan was negative in all patients. The second CT scan, performed at ≥ 6 hours, was positive in 3/61 of the patients. 98% percent of the patients (60/61) had no neurological deterioration during their hospital stay. 92% of patients did not have a CT scan at time 3 or time 4 and 8% of patients (5/61) did have a scan during this period. Of the 5 patients undergoing a CT scan, 3 patients had a positive scan, showing some abnormality. Fifty-four percent of the patients (33/61) had a hospital stay of greater than 3 days. **Conclusion:** A mean 4 day hospital stay as was evident from our study comprising of elderly patient population would amount to \$16,304USD. Excluding the ancillary costs of labs and transport etc. Patients with a mild head injury, a therapeutic INR, and negative initial CT brain can be safely discharged home with close family monitoring, proper education and detailed instructions on when to return. **Keywords:** Minor TBI, Sequential CT scans, Anticoagulated.

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INTRODUCTION

TBI is one of the leading causes of death and disability in the US irrespective of age, race, gender, ethnicities and economical status and imparts a paramount effect on health system [1,2].

In the United States Traumatic Brain Injury (TBI) accounts for estimated 1.7 million cases with an estimated 1,365,000 Emergency Department (ED) visits and an estimated cost of approximately \$16.7 billion per year [3]. About 80% of all TBI are classified as mild thus resulting in a substantial social and economic burden. Mild TBI is defined by GCS >13, loss of consciousness <30 minutes, and posttraumatic amnesia <24 hours.

Delayed onset of an intracranial hemorrhage is a real concern for patients with mild TBI [4]. Long term oral anticoagulation is an independent risk factor for both immediate and delayed Intra Cerebral Hemorrhage (ICH) even in mild TBI patients[5-7]. In the US more than 6 million patients receive long term anticoagulation therapy and with the increase in elderly population this number has grown exponentially in recent years [8]. The percentage of Americans who will be on anticoagulation and antiplatelet therapy will continue to increase with the long-term trend towards longer life expectancies [9].

European guidelines suggest that all anticoagulated patients with head injury should undergo a CT scan and routine admission for observation irrespective of their clinical presentation [10]. There is not sufficient data to conclude that mild TBI patients on oral anticoagulation with negative initial CT scans can be discharged safely.

In our institution we follow a protocol of admitting any patient on warfarin and head injury for at least 24 hours observation. They get a non-contrast CT scan of the brain in the ED followed by a repeat scan at a 6-8 hour interval. We retrospectively looked at the patients admitted in our Regional level 2 trauma center over a 3 year period with mild /minor TBI on warfarin. All these patients had their initial head CT scan negative for any intracranial hemorrhage. We tried to answer the question whether a repeat CT does provide us with answers and whether these patients truly need admission. We reviewed the relevant literature and discuss the financial implications.

METHODS

Study design and setting

We conducted a retrospective chart review study involving anticoagulated (on warfarin) patients who had sustained minor head injury at a level 2 community Regional Trauma Center at Monroeville, Pennsylvania, from October 2013 to December 2017.

Selection of patient participants

Paper and electronic charts were selected using ICD codes and reviewed by the researchers. All data was de-identified prior to analysis. The study was approved by the IRB.

INCLUSION CRITERIA

Our inclusion criteria were strict in accordance to the abstract submission approved for the LECOM grant and IRB permission.

- Patients above 18 years of age.
- Both male and female patients.
- Head injury with a blunt mechanism only.
- Minor or minimal head injury with a GCS on admission 13-15. ISS <15.
- Injury sustained within the previous 48 hours of admission.
- Patients with no focal neurodeficit and/or no evidence of cranial fracture
- All patients admitted for at least 24 hours observation with a repeat CT scan performed before discharge.
- Preinjury use of anticoagulation (only warfarin). Warfarin use for at least 1 week.
- (Warfarin and aspirin in combination were included in our study). Aspirin use alone was not sufficient for inclusion.

- Initial CT scan on admission was negative for any intracranial bleed.

EXCLUSION CRITERIA

- Hemodynamically unstable patients
- Polytrauma patients.
- Penetrating head injury, with or without calvarial fractures.
- History of structural brain abnormalities eg arteriovenous malformations, tumors or other space occupying lesions and previous intracranial surgeries.
- Patients taking aspirin and plavix combination, clopidogrel, heparin, enoxaparin, or dipyridamole.
- Patients taking any one of the newer antiplatelet (Prasugrel, Ticagrelor, Cangrelor, Glycoprotein IIb/IIIa inhibitors- Abciximab, Tirofiban and eptifibatide) or anticoagulant agents (Dabigatran etexilate, Apixaban, Rivaroxaban, Edoxaban)

DATA COLLECTION

We collected demographic data, mechanism of injury, symptoms on presentation, clinical findings on physical assessment, INR levels, CT scan results and neurosurgical interventions.

For the purpose of this project we used only minor or minimal head injuries. Minor head injuries are defined as those associated with loss of consciousness, amnesia or confusion and a Glasgow Coma Scale score of 13-15. Minimal head injuries are devoid of those symptoms or signs and a GCS of 15.

We looked also at return visits to the ED, hospital readmissions, delayed ICH within 2 weeks of admission and deaths. If a symptom/sign was not mentioned in the reviewed nursing/physician note we assumed that those were absent. We searched for patients who may have sought subsequent care at other institution within our network and for death. Our group of designated researchers collected our data. We used a standardized proforma data collection form enclosed.

Outcome measures

The primary outcome was to calculate the rate of delayed intracranial bleeds. We defined intracranial bleeding as the presence of subarachnoid, subdural, epidural or intraparenchymal hematoma in the final radiology report of the patients CT head. Delayed intracranial hemorrhage (ICH) was defined as brain bleed within 2 weeks of following an initial normal CT scan and in the absence of repeat head trauma.

STATISTICAL METHODS

All data analysis began with assessment of the normality of continuous variables using the Shapiro-Wilk test. Continuous normally distributed variables

were reported as means and standard deviations; non-normally distributed variables as medians with interquartile ranges [IQR]. Categorical variables were reported as counts and percentages. Fisher's exact test, or the Freeman-Halton extension of Fisher's exact test, was used to assess the association between categorical variables. Statistical analyses were performed using IBM-SPSS Statistics, version 24.0 (IBM Corp., Armonk, New York).

RESULTS

Sixty-one patients met inclusion criteria and 32 patients (52.5%) were women. Fifteen percent of the patients (9/61) were between the ages of 41 – 65; 85% (52/61) were age 66 or older. Glasgow Coma Score (GSC) was 14 in 13% of the patients (8/61) and 15 in 87% of the patients (52/61). Fall was the most common mechanism of injury (78% or 48/61 patients) and 98% of the patients (60/61) arrived at the hospital within 48 hours of injury.

All 61 patients were on Coumadin and only 15% of the patients (9/61) took aspirin as an additional anticoagulant. The first CT scan was negative in all 61 patients. The second CT scan, performed at ≥ 6 hours, was negative in 93% of the patients (52/61) and positive in 7% of the patients (3/61). Ninety-eight percent of the patients (60/61) had no neurological deterioration during their hospital stay. The one patient (1.6%) who had neurological deterioration later died of cardiac arrest. Ninety-two percent of patients (56/61) did not have a CT scan at time 3 or time 4 and 8% of patients (5/61) did have a scan during this period. Of the 5 patients undergoing a CT scan, 1 patient had a negative scan and 4 patients had a positive scan, showing some abnormality. Fifty-four percent of the patients (33/61) had a hospital stay of greater than 3 days; 19.7% of patients (12/61) had a hospital stay of 2-3 days and 26.2% of patients (16/61) had a hospital stay between 0 – 1 day.

There was no statistically significant relationship between the patient's Glasgow Coma Score on admission and hospital length of stay, measured in days ($p = .36$) (Table 4). Seventy-five percent of patients (6/8) with a Glasgow Coma Score of 14 had a hospital stay of greater than 3 days compared with 51% of patients (27/53) with a Glasgow Coma Score of 15 (Table 4).

There was no statistically significant relationship between the patient's age category and hospital length of stay, measured in days ($p = .23$) (Table 5). Seventy-eight percent of patients (7/9) in the 41-65 age category had a hospital length of stay greater than 3 days compared with 50% of patients aged 66 years or older. There was not a statistically significant relationship between gender and Glasgow Coma Score ($p = .09$). For both groups, the majority of patients had a Glasgow Coma Score of 15. Ninety-percent of men

(26/29) had a Glasgow Coma Score of 15 and 84% (27/32) had a Glasgow Coma Score of 15. (Table 5)

There was no statistically significant relationship between result on the second CT scan and hospital length of stay, measured in days ($p = .81$) (Table 6). In patients with a negative CT scan at time points 3-4, 53% (30/57) remained in the hospital greater than 3 days. In patients with a positive CT scan at time points 3-4, 75% (3/4) remained in the hospital greater than 3 days. (Table 6)

Tables 1 thru 3 provide the demographic, mechanism of injury data, clinical and hospital length of stay data for the 61 study patients.

Table-1: Demographic characteristics of the study patients and mechanism of injury (n = 61)

Variable	Values
Age, years	
Mean (SD) (n = 53)	79.1 (11.2)
Median [IQR] (n = 53)	83.0 [17.0]
Range (n = 53)	50 - 97
Proforma Data Categories for Age (n = 61)	
18 – 40	0
41 – 65	9 (14.8)
66 and older	52 (85.2)
Sex (n = 61)	
Male	29 (47.5)
Female	32 (52.5)
Mechanism of Injury (n = 61)	
Fall	48 (78.7)
Motor vehicle collision	9 (14.8)
Found down in parking lot	1 (1.6)
Hit by car	1 (1.6)
Struck by car	1 (1.6)
Kicked in chest by horse	1 (1.6)
Glasgow Coma Score (n = 61)	
Mean (SD)	14.9 (.34)
Median [IQR]	15.0 [0]
Range of Values	14 - 15
Proforma Data Categories for GCS (n = 61)	
13	0
14	8 (13.1)
15	53 (86.9)
Time since Injury (Proforma Data Categories) (n = 61)	
<48 hrs.	60 (98.4)
≥ 48 hrs.	1 (1.6)

Values are reported as mean (SD), count (%), or median [interquartile range]

Table-2: Clinical characteristics of the study patients (n = 61) and Demographic and clinical characteristics of the 4 study patients with a positive CT scan

Variable	Values
CT Scan #1 Result (n = 61)	
Negative	61 (100)
Positive	0 (0)
Coumadin >1week (Y/N)	61 (100)
INR if Coumadin >1 week (n = 48)	
Mean (SD)	2.4 (.72)
Median [IQR]	2.4 [.9]
Range of values	1.5 – 5.1
Coumadin >1week not reported (n = 8)	
Coumadin >1week INR reversed results (n = 5)	
Mean (SD)	5.4 (4.4)
Median (IQR)	3.1 [6.75]
Range of values	2.0 – 12.80
Other Anticoagulants (n = 61)	
No	52 (85.2)
Yes – ASA	9 (14.8)
CT Scan #2 Result (>6 hrs.) (n = 61)	
Negative	57 (95.1)
Positive	3 (4.9)
If positive, list result	
New SAH	
Stable, thin hyper density in the inter Hemispheric fissure, favor dural Thickening over hemorrhage	
Small parenchymal + thin subdural	
Small left subdural	
Neuro deterioration (n = 61)	
No	60 (98.4)
Yes	1 (1.6)
If yes, list reason	
Patient died of cardiac arrest	

Values are reported as mean (SD), count (%), or median [interquartile range]

Table-2: (Cont'd) Clinical characteristics of the study patients (n = 61)

Variable	Values							
CT Scan #3 – 4, if any, results								
No	56 (91.8)							
Yes	5 (8.2)							
If yes, list result								
CT-3: Negative								
MRI day #3 for syncopal workup showed hemorrhagic contusion. CT-3: hemorrhagic contusion left frontal lobe, CT-4: stable hemorrhagic contusion								
CT 3: evolving, but no new hemorrhage								
CT 3-4: evolving left SAH without new hemorrhage								
Neuro Intervention								
No	61 (100)							
Yes	0							
ID	CT Result	Age	Sex	GCS	Aspirin	Neuro Decline	Hospital LOS (days)	Readmission
4	New SAH	≥66	Female	15	No	No	>3 days	No
43	Small parenchymal & thin subdural	41 – 65	Male	15	Yes	No	0 – 1	No
50	Small left subdural	≥66	Male	14	No	Yes	>3 days	No

Values are reported as mean (SD), count (%), or median [interquartile range]

Table-3: Length of hospital stay and hospital readmission (n = 61)

Variable	Values
Length of hospital stay (days) (n = 54)	
Mean LOS (SD)	4.0 (3.3)
Median LOS in days [IQR]	3.0 [5.0]
Range of values (days)	1 - 14
Proforma Data Categories for LOS (days)	
0 - 1	16 (26.2)
2 - 3	12 (19.7)
>3	33 (54.1)
Hospital readmission	
No	60 (98.4)
Yes	1 (1.6)
If yes, list reason	
11 days later for extremity weakness. MRI showed small acute infarct with no hemorrhagic transformations	

Values are reported as mean (SD), count (%), or median [interquartile range]

Table-4: Categories of the Glasgow Coma Score * Hospital Days Cross Tabulation

			Hospital days			Total
			0 - 1	2-3	>3 days	
GCS Category	14	Count	2	0	6	8
		% within GCS_CAT	25.0%	0.0%	75.0%	100.0%
		% of Total	3.3%	0.0%	9.8%	13.1%
	15	Count	14	12	27	53
		% within GCS_CAT	26.4%	22.6%	50.9%	100.0%
		% of Total	23.0%	19.7%	44.3%	86.9%
Total		Count	16	12	33	61
		% within GCS_CAT	26.2%	19.7%	54.1%	100.0%
		% of Total	26.2%	19.7%	54.1%	100.0%

Table-5: Age Category * Hospital days Crosstabulation

			Hospital days			Total
			0 - 1	2-3	>3 days	
Age Category	41 - 65	Count	2	0	7	9
		% within Age Category	22.2%	0.0%	77.8%	100.0%
		% of Total	3.3%	0.0%	11.5%	14.8%
	≥66	Count	14	12	26	52
		% within Age Category	26.9%	23.1%	50.0%	100.0%
		% of Total	23.0%	19.7%	42.6%	85.2%
Total		Count	16	12	33	61
		% within Age Category	26.2%	19.7%	54.1%	100.0%
		% of Total	26.2%	19.7%	54.1%	100.0%

Table-6: CT-2 result (≥ 6 hrs.) * Hospital days Crosstabulation

			Hospital days			Total
			0 - 1	2-3	>3 days	
CT-2 Result	Negative	Count	15	12	30	57
		CT-2 Result	26.3%	21.1%	52.6%	100%
		% of Total	24.6%	19.7%	49.2%	93.4%
	Positive	Count	1	0	2	3
		CT-2 Result	33.3%	0.0%	66.6%	100.0%
		% of Total	1.6%	0.0%	3.3%	4.9%
Total		Count	16	12	33	61
		CT-2 Result	26.2%	19.7%	54.1%	100%
		% of Total	26.2%	19.7%	54.1%	100%

STUDY LIMITATIONS

This study has several limitations: 1) the study has a small sample size and small event rate; 2) data on patient comorbidities was not reported and comorbidities may be a determinant of hospital length of stay, 3) the study may have benefitted from a comparison group of patients on Coumadin at a hospital with characteristics similar to AGH; 4) this was a single-center study with a small sample size conducted at an academic medical center and generalizability of results may be limited.

DISCUSSION

Trauma in the elderly is one of the most challenging problems healthcare providers confront on a regular basis in the 21st century. Elderly people are at particular risk due to increased fall risk, increased frailty, associated comorbidities, polypharmacy and anticoagulation use [11]. The number and rate of TBI related hospitalizations amongst patients 75 or older have increased per CDC from 359.6/100, 0001 population in 2007 to 454.4 in 2013. The annual direct medical costs for TBI treatment in the United States according to a published report amounts to \$4billion USD [12]. This amount increases to \$56.3billion USD if the cost of lost productivity is added [13].

Patients older than 65 years account for approximately 10% of ED visits and 30% of admissions for traumatic brain injury [14]. In elderly patients suffering a fall, long-term anticoagulation has been shown to increase not only the incidence of ICH compared to those not on anticoagulation, but to also increase mortality in those with ICH. The rate of preinjury warfarin use has been increasing in trauma patients in the US, (2.3% in 2002 to 4.0% in 2006); especially in patients older than 65 years.

Smith *et al.* [15] in their systematic review wanted to synthesize the best available evidence on the impact of pre injury anticoagulation therapy in the elderly adult patients with traumatic brain injury (TBI). They concluded that the use of preinjury anticoagulation increased risk of mortality in the older adult trauma patient diagnosed with traumatic brain injury [15].

Although clinical decision rules such as the Canadian CT Head Rule, the New Orleans criteria, and the NEXUS-II criteria exist to help determine which head injury patients require a head CT scan, these rules do not apply to anticoagulated patients. Studies in patients taking warfarin who suffer minor head injury have shown incidences of ICH ranging from 6.2% to 29%, leading some authors to conclude that most patients should undergo routine cranial CT scanning on presentation. (CT in Head injury patients) is used to predict intracranial traumatic CT findings in patients with minor head trauma. CHIP looks at age, GCS <15,

if GCS deteriorates 1 hour after patient presents to the hospital, if there is skull injury, post-traumatic amnesia, pedestrian/cyclist hit by motor vehicle, ejection from a motor vehicle, vomiting, use of anticoagulants, post-traumatic seizure, fall from any elevation, persistent anterograde amnesia, neurologic deficit or loss of consciousness. If any of these criteria are met the patient is no longer low risk and a head CT is considered using clinical judgement. CHIP was the most relevant to this study due to the large number of patients over the age of 65 and on anticoagulants.

Laura Campiglio *et al.* [16] in their research article retrospectively evaluated the clinical records of all patients on chronic anticoagulation treatment admitted to the emergency department for mild head injury. Out of a total of 344 patients included, and 337 (97.9%) had a negative CT1. CT2 was performed on 284 of the 337 patients with a negative CT1 and was positive in 4 patients (1.4%), but none of the patients developed concomitant neurologic worsening or required neurosurgery. This study evaluated the utility of 2 sequential CT scans at a 48-hour interval (CT1 and CT2) in patients with mild head trauma (Glasgow Coma Scale 13–15) taking oral anticoagulants. The authors concluded that systematic routine use of a second CT scan in mild head trauma in patients taking anticoagulants is expensive and clinically unnecessary [16].

Chauny *et al.* [17] in a meta-analysis estimating the risk of delayed intracranial hemorrhage 24 h after head trauma in patient's anticoagulated with vitamin K antagonist and normal initial CT scan. EMBASE, Medline, and Cochrane Library were searched using controlled vocabulary and keywords and both retrospective and prospective observational studies were included. Outcomes included positive CT scan 24 h post-trauma, need for surgical intervention, or death. The pooled estimate of the incidence of intracranial hemorrhage on the second CT scan 24 h later was 0.60% (95% CI 0-1.2%) and the resulting risk of neurosurgical intervention or death was 0.13% (95% CI 0.02-0.45%). The authors concluded that a repeat CT scan in the emergency department 24 h later is not necessary if the first CT scan is normal. Special care may be required for patients with serious mechanism of injury, patients showing signs of neurologic deterioration, and patients presenting with excessive anticoagulation or receiving antiplatelet co-medication [17].

Smits *et al.* [18] compared the cost difference between using selective computed tomographic (CT) strategies with that of performing head CT for all patients with minor head trauma. This study used either the Canadian CT head rule (CCHR) or CT in head injury patients (CHIP) rule. Their study concluded that the United States could save \$120 million and \$71 million dollars if the CCHR or CHIP rule was used,

respectively [18]. Along with the radiation exposure risks of repeated CT scans, the financial burden of repeat CT scans and a longer hospital stay is immense. Per head CT scan series, a patient is exposed to 3-7 rads, which is noteworthy over the course of many repeated CT scans [19].

Hospital admission or extension in LOS in the hospital to accommodate multiple CT scans can result in multiple transports, radiation exposure, and allocation of personnel all amounting to wastage of valuable resources. Evidence based literature shows when the hospitals reduce appropriately the length of stay (LOS) unnecessary risks and harms can be largely avoided.

Several studies have evaluated the incidence of delayed intracranial hemorrhage (dICH) following an initial normal CT scan. This factor can obviously affect patient disposition. Studies found a rate of 0.6-6% of delayed ICH for warfarin [7, 20-25]. Our incidence rate was 4.91 % (3/61) is consistent with majority of published literature. Menditto *et al.* [21] does report a high incidence of dICH (6%). Chauny *et al.* [17] points out that the higher value can be attributed to a selection bias with 74% of the patient population were victims of MVC; this is in contrast to the other publications where the majority (73%-89%) were falls from a standing position.

Despite the low clinical significance of the dICH, the cumulative public health burden of admission cost, observation and reimaging was considerable. Campiglio *et al* calculated a cost of \$194,972 USD over a 5 year period. With a cumulative hospital stay of 560 days [16] A recent study published in 2014 from Manchester Royal Infirmary, UK did an extensive MEDLINE search from 1946 to august 2013 [26]. They reviewed the 7 papers they thought were directly relevant to their search questions. They had a simple 3 part question.” *In (adult patients on warfarin with a minor head injury) does a (normal CT scan) allow (safe discharge home)?*”

Menditto *et al.* [21] Analyzed the management of minor head injury in patients receiving warfarin with a 24-hour observation protocol with a repeat head CT prior to discharge. Their case series enrolled 97-patients who were anticoagulated with warfarin who had an initial negative CT scan for any intracranial lesions after minor head trauma. 5/87 (6%) patients had a new hemorrhage on repeat CT scan with 1 patient requiring neurosurgical intervention. Two patients who were discharged after 24-hours later were readmitted for bleeding but did not require surgical intervention. This study concluded that the risk of delayed hemorrhage was greater if the INR was greater than 3.0 (RR 14) [21].

Kaen *et al.* [20] followed the Italian guidelines in that all patients with minor head injuries were admitted for 24 hours of observation with a repeat CT scan prior to discharge. They observed that 2/127 (1.4%) (INR 3.1 & 2.88) of patients had delayed intracranial hemorrhage (DICH) without the need for neurosurgical intervention. This study concluded that patients could be managed with strict neurologic observation without routinely performing a repeat CT scan. They advise the use of repeat scan for patients who develop new clinical symptoms [20].

Peck *et al.* [23] conclusions aligned with the previous study as they advised that warfarinised patients should have an initial head CT and a period of observation of signs and symptoms of neurologic deterioration. If the initial head CT is negative and the neurologic examination is normal or unchanged the patient can be safely discharged without a second head CT. In their study, they had 4 patients who had a positive DICH with a repeat CT scan 6-hour after the initial scan. 3 of the 4 patients were eventually discharged without intervention. 1 of the 4 patients died of cardiac disease following an orthopedic procedure [23].

Nishijima *et al.* [22] identified delayed traumatic intracranial hemorrhage (DICH) in 4 of 687 (0.6%) patients receiving warfarin after minor blunt head injury. The timeframe of when to repeat the CT scan was left up to the clinician’s discretion. Due to the low incidence of DICH, they recommended that a patient can be discharged from the emergency department after a normal CT scan with appropriate education [22].

Rendell and Sultan [26] concluded that observation is unnecessary following a normal CT scan in warfarinised head injuries. This is in direct contrast to an earlier European guideline which suggested that all anticoagulated patients with head injury should be admitted for a period of routine observation. They questioned the conventional guideline that advised CT scan for all patients with coagulopathy, admission for observation for 24 hours and a second CT scan prior to discharge. They even questioned the utility of repeat CT scan in such scenario with a low risk of DICH in published articles particularly with an initial INR <3 and a normal initial CT scan. The risk of DICH has been quantified as reassuringly small percentage in these studies.

Swap *et al.* [25] performed a retrospective observational study (2007-2011) of adult anticoagulated (warfarin and clopidogrel) patients undergoing head CT following minor TBI. This study was conducted at one of the Southern California Kaiser Permanente hospitals. The main outcome measured was ICH within 60 days of an ED visit with a normal initial head CT scan. The aim of the study was to evaluate the risk of delayed ICH

in anticoagulated patients after minor head trauma. They concluded that ED patients with an initial negative head CT scan have a 2.5% risk of delayed bleeding (11/443 patients).

Our retrospective study started with over 1877 head injury patients who were admitted to the trauma service. By utilizing our strict inclusion and exclusion criteria, we narrowed it down to a target population of 61 patients who fulfilled all our inclusion criteria. Ultimately, by using strict inclusion and exclusion criteria, we were able to ensure homogeneity amongst the sample population, reduce confounding, and increase the likelihood of finding a true association between exposure/intervention and outcomes. This, in turn, optimized the internal and external validity of the study. With our homogenous target population and limited confounding variables that our strict inclusion and exclusion criteria helped to create, we believe our study and data to be easily reproducible and to show little variability from facility to facility that choose to utilize similar criteria to ours.

Our study did have its own limitations. Our patient pool being restricted to patients from a single Level 2 Regional Trauma Center may not be total representative of all gamuts of patient populations. Being a retrospective study, there was no ability to standardize certain study factors, such as including an exact time frame in which the repeat CT scans were completed or whether or not the patient's INR was reversed. Lastly, the study did not consider other pro-coagulable or anti-coagulable disorders including malignancy or liver disease.

This study could be expanded into a larger scale, multi-center trial including all anticoagulation and/or antiplatelet agents which would allow for a larger population study to increase randomization. A larger population might include more patients with supra-therapeutic INRs to see if this had a significant association with increased risk of delayed ICH. Also, there is a need for additional research on the benefits of reversing a supra-therapeutic INR in preventing delayed ICH. *Alrajhi et al.* study of 176 patients showed that patients with and without intracranial bleeding found no significant differences in INR but did not evaluate delayed hemorrhage [27].

A larger study with a greater population and resources could also allow investigation into the different types of anticoagulation/anti-platelet medications as it could impact future protocols.

The major bleeding risk is increased with antiplatelet therapy along with warfarin compared to warfarin alone. Combination of aspirin and warfarin has a hazard ratio (HR) of 1.83 which increases to 3.08 with a combination of clopidogrel and warfarin [28]. We

excluded clopidogrel or any of the new generation anticoagulants from our study.

Nishijima et al. [22] in their study on immediate vs delayed ICH, showed that 12% of those receiving Clopidogrel had an immediate ICH vs. 5.1% of those on Warfarin. However, 0% of the Clopidogrel patients had a delayed ICH where 0.6% of the Warfarin patients did [22]. This evidently shows that all anticoagulant/antiplatelet drugs are likely to have different incidence in causing delayed intracranial hemorrhages. This evidently shows that all anticoagulant/antiplatelet drugs are likely to have different risk factors and incidence in causing delayed intracranial hemorrhages, so this study solely focusing on Warfarin with or without aspirin is somewhat limited[22].

According to relevant literature to achieve a zero miss rate for dICH the timing may need to be extended significantly. However with the present day National Health Systems debate over resource allocations and cost containment in acute care settings this approach may not be a sustainable concept. In the United States the average cost for a non-contrast head CT scan \$464 USD and \$3612 USD for 24 hour hospital admission. A mean 4 day hospital stay as was evident from our study comprising of elderly patient population would amount to \$16,304USD. This excludes the ancillary costs of labs and transport etc. Some of the elderly patients because of their comorbidities and frailty needed advanced care unit bed (Stepdown/PCU) (\$3739 USD/day) or room in the Intensive care unit (@ cost \$4305 USD)[29].

CONCLUSION

We believe that with proper education and family support, patients that have a mild head injury, a therapeutic INR, and negative CT scan can be safely discharged home with close monitoring, provided they have stable family support, and detailed instructions on when to return. Following this protocol can save the patient excess radiation exposure as well as is a cost saving strategy for the health system and patients.

However, there is no substitute for sound clinical judgment as each patient presents a unique clinical scenario and risk profile for a delayed intracranial hemorrhage and each patient should be treated on its individual merit.

Bullet Points

- Obtain an initial CT scan in the ED for all anticoagulated patients even if their neurological examination is normal.
- Consider reversal of anticoagulation if the examination is abnormal or the patient is altered prior to getting the head CT followed by admission.

- If the initial CT along with the patient's clinical examination is normal, the patient can be potentially discharged with follow up provided a reliable caregiver is present. Proper education of the patient and the caregiver is of paramount importance with clear instructions for return precautions and follow up.
- If the patient follow-up is questionable admission is warranted.

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