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Worsening head bleeds in elderly blunt head trauma patients taking antithrombotics: Delayed CT head fails to change management

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ABSTRACT

Background: Most elderly trauma patients suffer blunt head injury and many utilize antithrombotic (AT) medications. The utility of delayed CT-head (D-CTH) in neurologically intact elderly patients using AT who have an intracranial hemorrhage (ICH) on presentation is unknown. We hypothesized that D-CTH would not alter clinical management and aimed to evaluate the role of D-CTH in this population.
Methods: A retrospective cohort study was performed. Patients ≥65 years sustaining blunt head injuries from January 2010 to July 2017 were identified using our level 1 trauma center database. AT-patients presenting with ICH who underwent D-CTH were included. Patients with worsened ICH were compared to those with stable to improved ICH on D-CTH. AT-patients were compared to a cohort of non-AT patients. Fisher's Exact and Mann-Whitney U tests were utilized and a power analysis conducted.
Results: 137 AT and 34 non-AT patients were identified. There was no difference in hemorrhage progression or appearance of new ICH. No patient had a change in management from D-CTH in either cohort. AT-patients were slightly older ($p < 0.001$), but cohorts were otherwise similar.
50 AT-patients with worsened ICH were compared to 87 with stable ICH. There was no difference in cohort demographics. Hemorrhage progression did not vary with type of AT used but did increase if multiple types of synchronous ICH were present ($p < 0.001$).
Conclusions: Our data supports abstaining from routine D-CTH of elderly ICH patients with an intact neurologic examination who are utilizing aspirin, clopidogrel or warfarin. Conclusions cannot be drawn regarding new oral anticoagulants (NOACs) given low enrollment. Further multicenter study is required to provide adequate power and detect small levels of management change.

Introduction

The elderly representan increasing proportion of the American population, as well as its trauma victims [1–3]. Many of these patients suffer blunt head injury after falls and many have comorbidities and pharmacologic obstacles distinct from their younger counterparts [4–6]. Nationally, nearly 50% of traumatic head bleed patients are using aspirin and approximately 20% are taking warfarin [7]. The literature detailing outcomes in these patients is mixed, and is largely scattered between neurosurgery and trauma surgery research endeavors [8,9].

It is generally agreed that elderly patients utilizing antithrombotic medication presenting with a negative first CT of the head do not need routine delayed CT of the head (D-CTH) as the risk of new bleeding is low [9]. How to manage the same patients presenting with a positive first CT of the head has not been settled as it is known that the progression rate of existing hemorrhage may be high [8,9]. In this medically fragile patient population, there is legitimate concern that minor bleeds could blossom into a surgical emergency. This idea has been used in trauma centers to justify the routine use of D-CTH in 6–24 h after an initial scan to monitor the progression of any intracranial hemorrhage. The data gleaned from this practice allows us to understand the natural history of these injuries, but we do not know what the common protocol of D-CTH accomplishes even if it identifies a worsening bleed.

At this time, this practice is not proven to alter any management and is largely based on clinical assumption rather than any research establishing benefit. Moreover, it is resource depleting and potentially expensive for the patient. Our hypothesis was that routine repeat head CT in an elderly patient taking antithrombotic medication with a stable neurologic exam would not change

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clinical management decisions. We aimed to detail the role of D-CTH in this population.

Methods

A retrospective cohort study was performed after obtaining appropriate approval from our institutional review board and a waiver of informed consent. We used our institutional trauma registry to identify patients ≥65 years who sustained blunt head injuries during a 90 month time frame from January 2010 to July 2017 Fig. 1. Inclusion criteria for the antithrombotic (AT) cohort consisted of all patients over the age of 65 on anticoagulant and antiplatelet therapy who were admitted to our level one trauma center with a traumatic ICH detected on initial CTH (I-CTH) and a GCS on presentation of 9 or greater. Patients were excluded from this cohort if they proceeded to neurologic surgery based upon I-CTH findings or if a change in neurologic status prompted a repeated CTH. This was determined based on chart review of event notes, radiology indications for imaging as noted in the final attending read, nursing documentation and neurosurgical documentation. Patients were also excluded if they had a GCS on arrival of <9, never underwent D-CTH, if ICH was felt by the neuroradiologist to be chronic in nature or if data regarding AT use was absent. Individuals were excluded if it was determined on admission that the patients were not surgical candidates. Patients were also excluded for known intrinsic coagulopathy such as Von Willebrand's disease or Cirrhosis.

The cohort of elderly patients not taking antithrombotics (non-AT) was created with the same inclusion and exclusion criteria aside from antithrombotic use and timing of admission Fig. 1. D-CTH was at the discretion of the trauma surgery and neurosurgery attending physicians prior to September of 2014 in this group. After this date, the protocol matched what it had always been for elderly AT patients. Thus only the non-AT patients accrued after this point were included in this study to avoid confounding in comparison for the AT and non-AT cohorts. Furthermore, patients were only included if their medication reconciliation had been completed and included no antithrombotic agents.

Electronic medical records were reviewed to determine outcomes and to collect mechanism of injury, age, sex, comorbidities, concurrent injuries, medications, laboratory values, and Glasgow Comas Scale (GCS) on presentation. The primary outcome was change in medical or surgical management based on D-CTH.

A patient was considered to have a change in management if the delayed imaging was performed on a routine scheduled basis and its findings were documented to have yielded any medical or surgical intervention that was previously unplanned. This included any surgical procedure (diagnostic or therapeutic) undertaken by neurosurgery as invasive intracranial pressure monitoring, cranial decompression or hematoma evacuation. This does not include

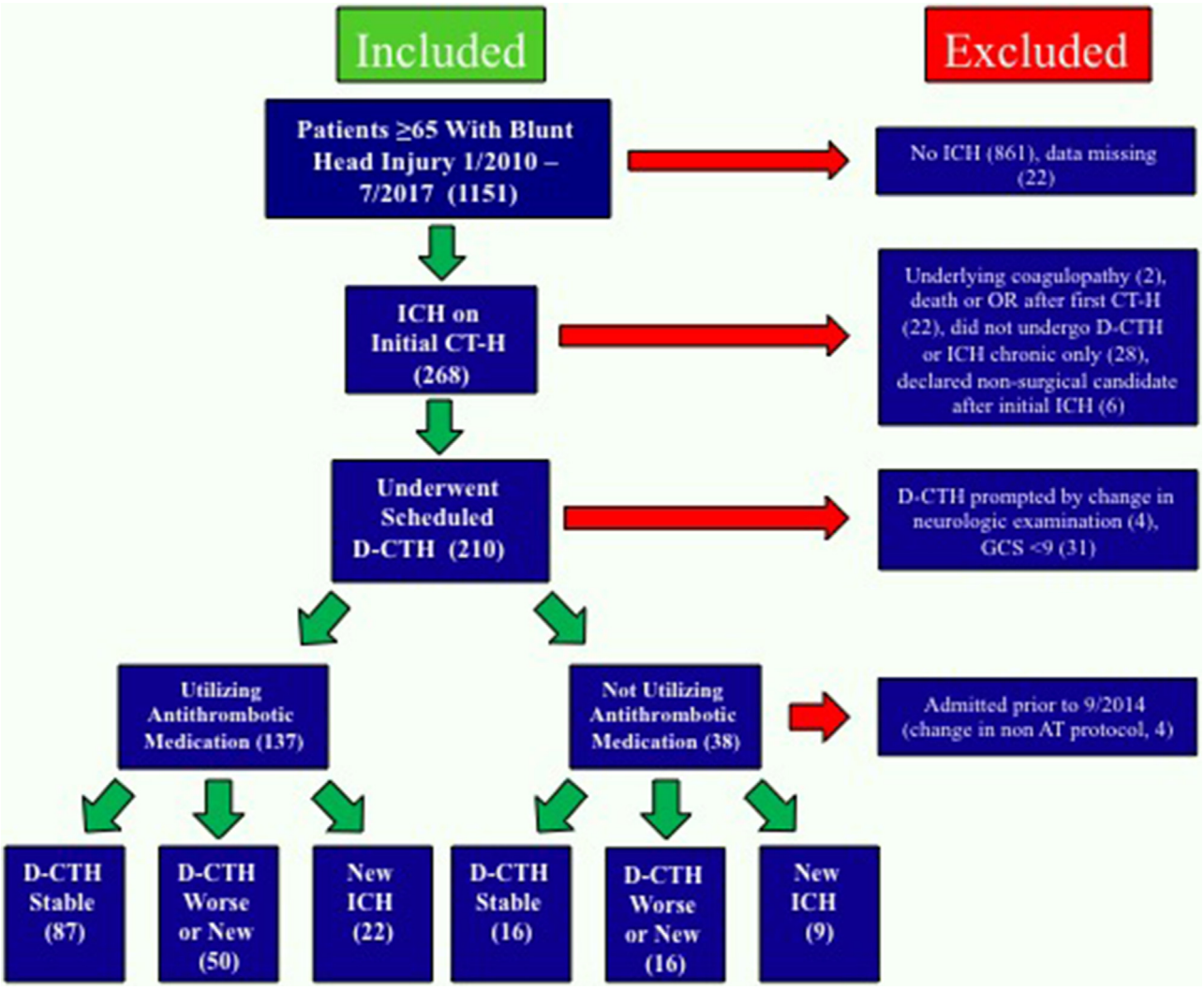

Fig. 1. Flow chart of study design including inclusion and exclusion criteria.

additional repeat CT of the head if that imaging or any subsequent imaging does not change any other medical or surgical management. Secondary outcomes included progression of initial ICH, appearance of new foci of bleeding and length of stay. The progression of bleeding, appearance of new ICH and the type of ICH endured were determined based on final CT reading by the attending neuro-radiologist. As this study is retrospective, the neuro-radiologists were not aware at the time of reading the films that the data would be included in our study.

By institutional policy, all AT patients aged ≥65 who suffer a head injury undergo a CT of the head without contrast as part of their initial trauma evaluation. Patients with an identified ICH on the I-CTH then receive a scheduled non-contrast CT of the head (D-CTH) approximately 6–12 h after the first scan is completed. The treatment protocol below is the same regardless of the type of bleed. These patients are admitted to the surgical intensive care unit for hourly neurologic examination by trauma-trained intensive care nurses. They are eligible to be transferred to the medical surgical floor after 24 h. Physician to physician neurosurgical consultation is immediately made and imaging reviewed by the neurosurgical attending. This also became our standard of care for non-AT ICH patients in 2014 though it had always been our standard for our AT patients. Patients with ICH are given seven days of levetiracetam. All antithrombotic medications are held in the setting of ICH and are not restarted during the admission. Patients with a positive initial CT scan and taking an anti-platelet medication are given a transfusion of a pack of platelets. Other coagulopathy is also corrected with available reversal agents, including fresh frozen plasma for warfarin with INR followed to normalcy and prothrombin complex concentrate as a one time dose for factor Xa inhibitors. Idaricizumab was not available as an antidote to the direct thrombin inhibitor dabigatran during this study. Reversal was done at the discretion of the attending neurosurgeon. The primary indicators of coagulopathy not dictated by antiplatelet agents were partial thromboplastin time (PTT) and prothrombin time (PT) with international normalized ratio (INR). Doses were not repeated after D-CTH.

All CT scans were evaluated based on the findings confirmed by attending neuroradiologists. A patient was considered to have an intracranial hemorrhage (ICH) if any of the following injuries were seen on initial head CT: subarachnoid hemorrhage (SAH), subdural hematoma (SDH), epidural hematoma (EDH), intraventricular hemorrhage (IVH), or cerebral contusion/intraparenchymal hemorrhage (IPH). D-CTH when compared with the I-CTH was classified as either improved or stable versus worsened hemorrhage. We also noted new hemorrhage foci in worsened studies.

Cohorts were created based on classification of ICH on the D-CTH. Those using AT with improved or stable ICH on D-CTH were compared with those with worsened and/or additional ICH on D-CTH. Patients taking antithrombotics were also compared to a cohort of patients ≥65 who did not take antithrombotic medications, presented with ICH on I-CTH and underwent D-CTH. Antithrombotic medications identified included the anti-platelet agents of aspirin, clopidogrel, dipyridamole and the anticoagulants warfarin, dabigatran and rivaroxiban.

General demographic and clinical comparisons of outcomes were performed using Fisher's Exact and Mann Whitney U tests. Statistical significance was defined as a p-value of less than 0.05. A power analysis was also completed for rate of ICH progression and change in management.

Results

Elderly patients using antithrombotics presenting with ICH versus elderly patients presenting with ICH without antithrombotic use

137 elderly blunt head trauma patients taking antithrombotic medications with ICH on initial CTH and meeting inclusion criteria presented to our institution during the study period. They were compared with 34 patients not using AT Table 1. Mechanism of injury was not different between cohorts Fig. 2. 76% in the AT group and 81% of the non-AT cohort suffered falls ($p = 0.762$).

The mean age of the AT group was significantly higher (82 years vs 76 years, $p < 0.001$). Presenting median and mean GCS, median injury severity scores (ISS), abbreviated injury scores (AIS) of the head and length of stay were not different Table 1. Progression of

Table 1
Comparative demographics of the 137 elderly patients taking antithrombotics and the 34 elderly patients who took no antithrombotics. There were no significant differences between the groups aside from a higher average age and GCS in the cohort taking antithrombotics. Interquartile ranges (IQR) are shown for median values and standard deviation (SD) for mean values.

Demographic	Antithrombotic Cohort (N = 137)	Non-Antithrombotic Cohort (N = 34)	Significance
Age in Years (Mean)	82 SD 8.7	76 SD 8.4	<0.001
ISS (Median)	17 Q1 11, Q3 21 IQR 10	17 Q1 10, Q3 21 IQR 11	0.711
Initial GCS (Median)	15 Q1 14, Q3 15 IQR 1	15 Q1 14, Q3 15 IQR 1	0.395
AIS Head (Median)	4 Q1 3, Q3 4 IQR 1	4 Q1 3, Q3 4 IQR 1	0.653
Length of Stay in Days (Median)	5 Q1 3, Q3 8 IQR 5	7 Q1 3, Q3 10.75 IQR 7.75	0.105
Progression of Intracranial Hemorrhage	N = 50 37% 95% CI 30%–46%	N = 17 50% 95% CI 33%–67%	0.178
New Intracranial Hemorrhage	N = 22 16% 95% CI 11%–23%	N = 9 26% 95% CI 13%–44%	0.211
Change in Management after Delayed CT	N = 0 0% 95% CI 0%–3%	N = 0 0% 95% CI 0%–10.3%	1.000

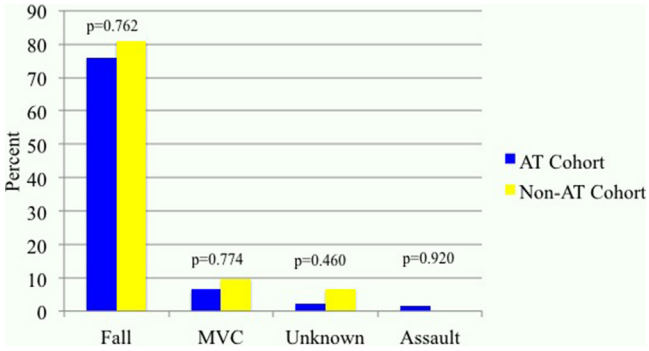

Fig. 2. There was no difference in the mechanism of injury elderly cohorts with and without antithrombotic use.

hemorrhage and appearance of new hemorrhagic focus was also no different between cohorts Table 1. No patient in either cohort had change in management from D-CTH Table 1.

Elderly patients using antithrombotics with worsened D-CTH versus those with stable to improved D-CTH

137 patients were on AT and 50 (37%) experienced worsened appearance of their ICH on D-CTH and 87 (63%) had stable to improved appearance on D-CTH Table 2. Age was not significantly different between cohorts, nor was presenting GCS, ISS, AIS or length of stay Table 2.

When considering type of antithrombotic used, differences did not arise between the group with worsened ICH and those with stable to improved ICH Table 3. Arrival INR of the worsened group averaged 3.49 and was 2.72 in those with stable to improved D-CTH, but this was not significant. There were no significant differences between cohorts for use of clopidogrel, dabigatran, rivaroxaban or any other identified antithrombotics, though overall use of other drugs was low in our subjects during this study period Table 3.

In evaluation of type of presenting ICH, differences arose. Those with multiple types of ICH present on admission had significantly increased proportion of worsened D-CTH ($p = <0.001$) Table 4. There were no significant differences in proportion with worsened D-CTH regarding individuals presenting with any singular type of ICH Table 4.

As this is a subset of the elderly AT patient cohort, it was again noted that no change in management occurred. Of note, the significance identified in the AT cohort regarding multiple synchronous hemorrhage types was not found in the non-AT cohort but enrollment was quite low Table 5.

Discussion

Elderly blunt head trauma, especially in the setting of antithrombotic use, is a topic of prime importance in contemporary trauma research. It has been largely established that younger adult patients who did not utilize antithrombotics and present with mild head injury and ICH do not benefit from routine repeat imaging [10–12]. Furthermore, these patients may experience a decreased length of stay if managed only with serial neurologic examination [13].

Research has also established that elderly patients with mild injury, reliable neurologic exams and no ICH on first scan do not have a change in management from D-CTH, even when they are using antithrombotics [9]. The data lags behind significantly in the elderly population presenting with ICH and using anticoagulants or antiplatelet agents. We do know that these same patients, when they present with a bleed on first CT, show a high rate of radiologic worsening on D-CTH. [8,9,14], Prior studies have shown that anticoagulant users are more likely to have progression of initial intracranial hemorrhage and a higher likelihood to experience a new hemorrhagic focus on D-CTH when compared to non-users [8,9]. In recent studies, though, antiplatelet users did not show significant increase in progression or new bleed on follow-up scans [8,9].

The scant existing research evaluating these elderly patients using antithrombotics typically fails to comment on whether or not the high rate of worsening on D-CTH has any clinical relevance [14]. Studies in younger patients not utilizing antithrombotics have concluded that radiologic worsening does not carry clinical consequences or significance [12]. Despite this, it has long been known that quickly identifying operative candidates can improve outcomes, leading to a risk-averse strategy of repeated imaging in most trauma centers [15]. The specific and unique needs of the elderly trauma patient and the high cost of healthcare make this a very important, and very relevant, topic for study [16]. Only two prior studies which were either more limited in scope or sample size have previously addressed this issue.

One similar study did not evaluate antithrombotics beyond aspirin, but utilized an elderly population slightly younger than ours with mild injury and ICH on first scan. They did track some management changes. Joseph et al published an experience in

Table 2
Demographics of elderly patients taking antithrombotics comparing those with worsened delayed CT of the head with those who had a stable or improved delayed CT of the head. Interquartile ranges (IQR) are shown for median values and standard deviation (SD) for mean values.

Demographic (n = 137)	Worsened Intracranial Hemorrhage (N = 50)	Stable-Improved Intracranial Hemorrhage (N = 87)	Significance
Age in Years (Mean)	81 SD 7.4	82 SD 9.4	0.849
ISS (Median)	17 Q1 13.5, Q3 24.25 IQR 10.75	17 Q1 10, Q3 24.25 IQR 14.25	0.085
AIS Head (Median)	4 Q1 3, Q3 4 IQR 1	4 Q1 3, Q3 4 IQR 1	1.000
Initial GCS (Median)	15 Q1 14, Q3 15 IQR 1	15 Q1 14, Q3 15 IQR 1	0.904
Length of Stay in Days (Median)	6 Q1 3, Q3 9 IQR 6	4 Q1 3, Q3 7 IQR 4	0.142
Change in Management after Delayed CT	N = 0 0% 95% CI 0%–7.1%	N = 0 0% 95% CI 0%–4.2%	1.000

Table 3
Elderly patients using antithrombotic medications divided by type of antithrombotic used and whether or not the delayed CT of the head was worsened or stable/improved.

Antithrombotic	Worsened Intracranial Hemorrhage (N = 50, 36%)	Stable-Improved Intracranial Hemorrhage (N = 87, 64%)	Significance
Warfarin (N = 25)	N = 13 52% 95% CI 34%–70%	N = 12 48% 95% CI 30%–67%	0.124
Aspirin (N = 107)	N = 36 34% 95% CI 25%–43%	N = 71 66% 95% CI 57%–75%	0.274
Clopidogrel (N = 27)	N = 6 22% 95% CI 10%–41%	N = 21 78% 95% CI 59%–90%	0.130
Dabigatran (N = 2)	N = 2 100% 95% CI 29%–100%	N = 0 0% 95% CI 0%–71%	0.263
Rivaroxaban (N = 5)	N = 1 20% 95% CI 2%–64%	N = 4 80% 95% CI 36%–98%	0.794
Other (N = 2)	N = 1 50% 95% CI 9%–91%	N = 1 50% 95% CI 9–91%	1.000

Table 4
Patients taking antithrombotics divided by type of presenting intracranial hemorrhage and tracked by whether delayed CT of the head was worsened or stable/improved.

Intracranial Hemorrhage Type	Worsened Intracranial Hemorrhage (N = 50, 36%)	Stable-Improved Intracranial Hemorrhage (N = 87, 64%)	Significance
SAH (N = 61)	N = 26 42% 95% CI 30%–54%	N= 35 58% 95% CI 46%–70%	0.247
IVH (N = 12)	N = 8 67% 95% CI 38%–86%	N = 4 33% 95% CI 14%–61%	0.054
IPH (N = 37)	N = 16 43% 95% CI 29%–59%	N = 21 57% 95% CI 41%–71%	0.423
EDH (N = 2)	N = 2 100% 95% CI 29%–100%	N = 0 0% 95% CI 0%–71%	0.263
SDH (N = 82)	N = 35 43% 95% CI 33%–53%	N = 47 57% 95% CI 47%–67%	0.096
Multiple Types (N = 44)	N = 27 61% 95% CI 47%–74%	N = 17 39% 95% CI 26%–53%	<0.001

Table 5
Patients not taking antithrombotics divided by type of presenting intracranial hemorrhage and tracked by whether delayed CT of the head was worsened or stable/improved.

Intracranial Hemorrhage Type	Worsened Intracranial Hemorrhage (N = 17, 50%)	Stable-Improved Intracranial Hemorrhage (N = 17, 50%)	Significance
SAH (N = 20)	N = 12 60% 95% CI 36%–81%	N = 8 40% 95% CI 19%–64%	0.296
IVH (N = 4)	N = 2 50% 95% CI 7%–93%	N = 2 50% 95% CI 7%–93%	1.000
IPH (N = 12)	N = 6 50% 95% CI 21%–79%	N = 6 50% 95% CI 21%–79%	1.000
EDH (N = 2)	N = 1 50% 95% CI 9%–91%	N = 1 50% 95% CI 9%–91%	1.000
SDH (N = 26)	N = 13 50% 95% CI 30%–70%	N = 13 50% 95% CI 30%–70%	1.000
Multiple Types (N = 14)	N = 7 50% 95% CI 23%–77%	N = 7 50% 95% CI 23%–77%	1.000

which 72 patients on pre-hospital low-dose ASA therapy were matched to a similar group not on any antithrombotic therapy [17]. Both cohorts were admitted for observation and repeat head CT 6 h after the initial scan. Their findings in this aspirin only population were quite similar to our findings in our overall antithrombotic group Fig. 1. There was no difference in progression of the initial findings on repeat head CT (25% in ASA versus 16.6% in no-ASA), earlier repeat head CT due to neurological decline (0% versus 1.4%) and neurosurgical intervention as a result of findings on repeat imaging (1.4% vs 1.4%) [17]. Overall, there was no difference in neurosurgical intervention or mortality amongst the two groups (5.6% versus 2.8%), and the authors concluded routine serial head CT in patients with ICH on low-dose aspirin therapy is not warranted and should be performed only in the setting of neurological deterioration [17].

To our knowledge, the rate of change in clinical management based on repeat CT scan has never been reported in this patient population and is unknown. This may be related to the need for an insurmountable number of patients. In our study, no change in clinical management in either group was noted and the study was 82.0% powered to detect a 15% difference in change in management. In order to detect a 1% change in management, similar to that in the ASA-only cohort discussed above, or 1 in 100 patients, a total sample size of 1560 patients would be required to reach 80% power.

In a much smaller study, Uccella et al evaluated 5 patients on antithrombotics with a mild TBI (GCS 14–15) and ICH on initial CT scan [18]. All of them underwent repeat head CT scan but none had neurological deterioration or required neurosurgical intervention [18]. The authors conclude that in the setting of a GCS of 15 and long-term anticoagulation, patients who suffer an traumatic ICH require only a diagnostic initial head CT and only an appropriate observation period before discharge [18].

Our study adds to these two preceding it by providing a larger sample size and a wider range of antithrombotic medications in the study group. We did not identify any change in management based upon D-CTH. The rate of progression after traumatic ICH has been studied in multiple settings, with rates ranging from 25% to 63% [17,19,20]. Although elderly patients taking AT medications are included in these samples, the rates are not specific for that subgroup. In this study, patients taking AT progressed 37.2% of the time, compared to those not taking AT progressing 50% of the time. This difference was not statistically significant and the sample size was low in the non-AT cohort.

The authors believe the sample needed to adequately power this comparison at a single institution over a reasonable amount of time is too burdensome for this select patient group. To detect a 10% change in progression at 80% power, each group would have to be more than 387 patients.

Of note, our study is retrospective and limited to only one trauma center. Our patient population is urban and of diminished socioeconomic status. Newer anticoagulant and antiplatelet medications were a rarity in this group during this study period, though globally most patients in America remain on aspirin and warfarin [7]. Our study did not have enough patients to draw conclusions about antithrombotics beyond aspirin, clopidogrel and warfarin. Enrollment for patients with less common ICH types was similarly low, such as EDH. Greater patient numbers are required to elucidate differences in the behavior of bleed types beyond IPH, SDH, SAH and synchronous ICH.

Regardless, there is no current data to adequately support the clinical utility of routine repeat CT scans in this overall population. While ionizing radiation exposure may be clinically insignificant in the very elderly, avoidance of unnecessary imaging is of certain importance in reducing healthcare costs for the patient (a charge of more than $4350 at our institution) and reducing healthcare service utilization in the hospital; freeing up radiologists, the CT scanner itself for more needing patients and the time of nurses and ancillary staffing that could be used elsewhere. In general, the increased utilization and cost of limited health care resources should be discouraged when clinical benefit is not discernible.

Conclusion

The data obtained from this study support abstaining from routine repeat head CT scanning for the management of elderly trauma patients with an intact neurologic examination who are utilizing aspirin, clopidogrel or warfarin. As in any clinical setting, medicine is an art in addition to a science. Clinical suspicion may still warrant use of D-CTH on a case-by-case basis and we anticipate this to be especially true in patients who do not have a reliable neurologic examination. Our study applies primarily to patients with an intact GCS and reliable neurologic examination on the above medications.

Ultimately, our results are compelling and echo the findings of similar studies in different populations. A prospective randomized and multicenter effort would be of substantial value to confirm our results with adequate power as we can conclude only that no large change in management exists for this unique group. The complex issue of elderly trauma and the ever-increasing array of antithrombotics being developed mandates continued research going forward. We encourage the publication of other institution's experiences in an effort to consolidate information and ideally modify current practice guidelines to provide safe and more resource-effective care.

Conflict of interest statement

This was completed in its entirety at Hahnemann University Hospital in partnership with the Drexel University College of Medicine in Philadelphia, Pennsylvania. No author has any conflict of interest to disclose and no funding was obtained.

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