Mild brain injury and anticoagulants

Less is enough

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Abstract

Background: Despite the higher theoretical risk of traumatic intracranial hemorrhage (ICH) in anticoagulated patients with mild head injury, the value of sequential head CT scans to identify bleeding remains controversial. 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. **Methods:** We retrospectively evaluated the clinical records of all patients on chronic anticoagulation treatment admitted to the emergency department for mild head injury. **Results:** A total of 344 patients were 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. **Conclusions:** Systematic routine use of a second CT scan in mild head trauma in patients taking anticoagulants is expensive and clinically unnecessary. *Neurol Clin Pract* 2017;7:296–305

Traumatic brain injury (TBI) is a common neurologic disorder with an important effect on health systems. In Europe, the incidence rate of TBI is 262:100,000, with an average mortality rate of 10.5:100,000 and an estimated total annual cost of €33 billion.^{1,2} In the United States, the estimated annual incidence is 1.7 million cases, with approximately 1,365,000 emergency department (ED) visits and an estimated cost of nearly \$16.7 billion per year.³ In clinical practice, TBI severity is generally estimated on the basis of the Glasgow Coma Scale (GCS), the duration of loss of consciousness, and the

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duration of posttraumatic amnesia. Mild TBI is defined by GCS ≥ 13 , loss of consciousness < 30 minutes, and posttraumatic amnesia < 24 hours.^{4–7} Approximately 80% of all TBI are classified as mild. Given this high incidence, the resulting economic and social burden is substantial.³

Delayed onset of an intracranial hematoma is a major concern for patients with mild TBI.⁸ Long-term oral anticoagulation is an independent risk factor for both immediate and delayed intracranial cerebral hemorrhage (ICH) in patients with TBI.^{9–11} In the United States, more than 6 million patients receive long-term oral anticoagulant (OAC) therapy, and from 2009 to 2014, OAC visits in patients with atrial fibrillation increased from 0.88 million to 1.72 million.¹² Thus, due to the increase in the use of anticoagulants and the high fall risk in the elderly population, brain injury in anticoagulated patients is a frequent challenge in the ED.

European guidelines suggest that all anticoagulated patients with head injury should undergo a CT scan and a period of routine observation, regardless of their clinical presentation.¹³ In the United States, the most commonly used clinical criteria to assess for CT indication (namely the New Orleans Criteria and the Canadian CT Head Rules) are not validated for patients on anticoagulant therapy.^{8,14,15} Major guidelines suggest that CT scans “should be considered in patients with coagulopathy” in cases in which there is no loss of consciousness or posttraumatic amnesia, but the guidelines also suggest that there are inadequate data to conclude that mild TBI patients on oral anticoagulation with negative CT scans could be safely discharged.¹⁶ Therefore, because limited data are available on the incidence and prevalence of delayed traumatic ICH (dtICH), the optimal management of these patients remains controversial.⁷

To assess the utility of a 48-hour observation protocol with 2 head CT scans at a 48-hour interval, we retrospectively examined the incidence of delayed ICH in all anticoagulated patients admitted to our ED over 5 consecutive years.

METHODS

Standard protocol approvals, registrations, and patient consents

This study was approved by the local ethical committee and written informed patient consent was received.

We reviewed the clinical records of all patients with TBI admitted to the ED of the San Paolo University Hospital in Milan, Italy, between March 2010 and August 2015 identified by the Emergency Room Discharge Dataset. Inclusion criteria were as follows: (1) age 18 years or older, (2) blunt head injury, (3) no loss of consciousness or loss of consciousness of less than 30 minutes, (4) no amnesia or less than 24 hours posttraumatic amnesia, (5) GCS 13–15 at admission, and (6) preinjury use of an anticoagulant medication (warfarin, low-molecular-weight heparin, or novel OACs [rivaroxaban, apixaban, dabigatran]). Patients with concomitant anticoagulant and antiplatelet treatment were included.

The assessment included a noncontrast head CT (CT1), a neurologic examination, and an admission trauma laboratory panel with coagulation parameters (prothrombin time, partial thromboplastin time, and international normalized ratio [INR]), regardless of the severity of trauma. All patients with negative CT1 were admitted to the ED observation units for a 48-hour period of observation. Emergency physicians and nurses trained in the observation of head injury closely evaluated the patients every 2 hours. If patients developed new signs or symptoms, an urgent neurologic consultation was requested. At the end of this period, a second head CT (CT2) and a final neurologic examination were performed. We considered CT2 to be positive in the presence of any acute bleeding regardless of the amount (subarachnoid hemorrhage, subdural hematoma, epidural hematoma, intraparenchymal hemorrhage, or contusion of any size).

Finally, the patients were analyzed for diagnosis-related group codes reimbursement and the total cost of in-hospital observation on serial scanning.

In our population, the rate of dtICH identified by the repeated second CT was low (1.4%), and dtICH lacked clinical significance.

RESULTS

A total of 344 patients fulfilling the inclusion criteria were identified. Of these patients, 7 (2.0%) had positive CT1. Among the 337 with negative CT1 (table 1), 53 were excluded because they did not complete the protocol (22 refused observation and 31 did not receive the second CT scan). Of the remaining 284 patients, 275 were admitted soon after the injury and completed the 48-hour observation, and 9 entered the ED with a delay of 24 hours from injury. These 9 patients received CT1 at the moment of admission and CT2 at 48 hours after the trauma, with an in-hospital observation period of 24 hours.

During the observation period, ED physicians required additional neurologic evaluation for 14 patients secondary to the onset of headache or nausea or the suspicion of neurologic worsening. However, neurologic evaluation was negative in all cases; in 13 out of 14 patients, an additional CT was performed without ICH detection. All of these patients underwent CT2, and none had a positive CT2 at 48 hours.

None of the 284 patients received reverse anticoagulation therapy with prothrombin complex concentrate, desmopressin, or fresh frozen plasma.

At CT2, delayed traumatic ICH was identified in 4/284 (1.4%) patients. None of the patients exhibited neurologic deterioration; all patients had a GCS of 15 and unremarkable neurologic examinations, and only one patient reported mild headache. None of the patients required neurosurgical interventions; 3 were hospitalized and monitored with serial CT scans until dtICH resolved (between 3 and 7 days after trauma), and 1 patient was discharged home and was well 1 month later. The clinical data for these patients are reported in table 2.

The estimated direct cost of patient admission and serial CT scans for each patient who completed the 48-hour observation was €654 (\$693 USD); the cost for the 9 patients admitted with 24-hour delay was €454 (\$481 USD). Therefore, the total expense for this management was €183,936 (\$194,972 USD) per 284 patients (table 3).

DISCUSSION

Our retrospective study demonstrates that dtICH among anticoagulated patients with mild TBI is rare (1.4%, confidence interval 0.00385–0.03567). Despite the low clinical significance of the dtICH identified, the public health cost to admit, observe, and reimagine all patients was considerable (approximately €185,000 or \$194,972 USD over 5 years, with a cumulative hospital stay of 560 days). Notably, this study extended the in-hospital observation and serial head CT evaluations at 48 hours.

Several studies have investigated risk factors in patients with mild brain injury, and the guidelines to determine which patients with mild TBI should receive a CT scan, be admitted for observation, or be discharged home are continuously evolving.^{17–24} Long-term oral anticoagulation is a recognized independent risk factor for ICH after even mild head trauma.^{25–30} As a result, patients on OACs are usually included in the high-risk group, and there is a general agreement that these patients should undergo a head CT at presentation. However, controversy exists regarding their further management and the utility of serial CT scans to exclude delayed intracranial complications. Due to the increasing number of patients under anticoagulant therapy, we require more instruments to evaluate the small risk of a serious complication in large patient populations. In addition, the aging population has resulted in an important overlap in traumatic ICH risk due to the greater use of OACs in subjects >65 years of age and the major risk of falls in elderly people.

Table 1 Patients with negative CT1^a (n = 284)

	Values
Age, y, mean (SD)	79.09 (11.62)
Sex, n (%)	
M	100 (35.2)
F	184 (64.7)
Mechanism of injury, n (%)	
Fall from standing	194 (68.3)
Syncope	31 (10.9)
Unclear	28 (9.8)
Aggression	5 (1.7)
Vehicle accident	4 (1.4)
Other	9 ^b (3.1)
Loss of consciousness, n (%)	
Yes	39 (11.3)
Uncertain	31 (9.0)
GCS, n (%)	
14	66 (23.2)
15	218 (76.7)
Amnesia (<24 h), n (%)	10 (3.5)
Cranial fractures, n (%)	5 (1.7)
Nasal	2 (0.7)
Zygomatic	2 (0.7)
Frontal	1 (0.3)
Anticoagulant agent, n (%)	
Warfarin	244 (85.9)
Acenocumarol	26 (9.1)
LMWH	8 (2.8)
Combined antiplatelet and OAC therapy, n (%)	5 (1.7)
Combined anticoagulant and LMWH, n (%)	1 (0.35)
INR range, ^c n (%)	
>4	22 (7.7)
3-4	41 (14.4)
2-3	123 (43.3)
1.2-2	65 (22.8)
<1.2	22 (7.74)
Missing	3 (1.05)

Abbreviations: GCS = Glasgow Coma Scale; INR = international normalized ratio; LMWH = low-molecular-weight heparin; OAC = oral anticoagulant.

^aHead CT on admission.

^bThree patients with accidental brain injury, 3 falls from stairs, 1 fall from a horse, 1 fall from a bicycle, and 1 epileptic seizure.

^cINR was not considered in patients on LMWH (n = 8).

Table 2 Characteristics of patients with a negative CT1^a and positive CT2^b

Age, y; sex	Injury mechanism/ LOC/amnesia	GCS/symptoms/ signs at admission	Medication	INR at admission	CT2 findings	GCS/symptoms/ signs at 48 hours	CT3 findings (hours from CT2)	OAC discontinued/ OAC reversal	Outcomes
42, M	Aggression/yes/ yes	14/Posttraumatic amnesia/no	Warfarin	2.93	Small intraparenchymal hematoma	15/Headache/no	Stable (24)	Yes/no	Hospitalized
98, F	Fall from standing/no/no	15/No/no	Acenocoumarol	2.22	Small intraparenchymal hematoma	15/No/no	Stable (24)	Yes/no	Hospitalized
82, F	Fall from standing/no/no	15/Headache vomiting/No	Warfarin	2.49	Small intraparenchymal hematoma	15/No/no	Negative (12)	Yes/no	Hospitalized
84, F	Car accident/no/ no	15/No/no	Warfarin	1.21	Hygroma with minimal subdural bleeding	15/No/no	Not performed	No/no	Discharged home

Neurosurgery was not performed on any of the patients.

Abbreviations: GCS = Glasgow Coma Scale; INR = international normalized ratio; LOC = loss of consciousness; OAC = oral anticoagulant.

^aHead CT on admission.

^bHead CT at 48 hours from injury.

Table 3 Cost analysis for the 48-hour in-hospital observation per patient

Intervention	Cost in Europe, €	Cost in United States, \$
Average cost for a noncontrast head CT ^a scan in the ED	127	464
Average cost for 24-hour hospital admission	200	3,612
Total cost (average cost for 48-hour hospital admission +2 noncontrast head CT scans in the ED) ^b	654	8,152

Abbreviation: ED = emergency department.

^aHead CT on admission.

^bIf an additional CT was performed (13 cases), the total and estimated costs would become, respectively, €781 and \$8,616 USD.

Few studies have addressed the occurrence of dtICH among anticoagulated patients, which ranges from 0.6% to 6%.³¹⁻³⁷ Our data are consistent with the majority of the published literature (table 4), with the exception of the publication by Menditto et al. that reported a higher incidence of delayed ICH (6%).³² As highlighted by Chauny et al.,³⁸ this finding could be due to a selection bias; Menditto et al. describe a population of patients involved in motor vehicle accidents (74%), whereas the majority of the patient populations in the other publications had falls from standing (73%–89%).³¹⁻³⁸

Table 4 Risk of delayed intracranial hemorrhage in OAC patients in previous studies

Study design	Population	Outcomes	Key results
Prospective, observational			
Twenty-four-hour observation and a repeat head CT scan prior to discharge³¹	A total of 137 adult patients on preinjury anticoagulation therapy with mild head injury and normal initial head CT; 3 patients were on both anticoagulant and antiplatelet therapy	Presence of ICH on repeat CT, neurologic deterioration, neurosurgical intervention, and death	Delayed ICH was identified in 2 patients (1.4%); both were on concomitant antiplatelet and anticoagulant therapy; no patients exhibited neurologic deterioration or required neurosurgical intervention
Prospective, observational			
Twenty-four-hour observation and a repeat head CT scan prior to discharge³²	Ninety-seven patients >14 years old with mild head injury and preinjury anticoagulation	Presence of immediate intracranial hemorrhage, presence of delayed intracranial hemorrhage, neurosurgical intervention, or death	Delayed ICH identified in 5 of 87 patients receiving repeated CT scans (6%); 1 out of 5 exhibited neurologic deterioration and required surgery, 3 were hospitalized, and 2 were discharged because ICH was minimal; 2 patients who were discharged after completing the study protocol returned 2 and 8 day later with symptomatic SDH; neither required surgery
Retrospective review			
Twenty-four-hour observation and a repeat head CT scan prior to discharge³³	A total of 211 adult patients on preinjury oral anticoagulation with mild traumatic brain injury and a normal initial head CT scan; patients must have been on oral anticoagulant for >1 week with an INR >1.1	Presence of intracranial hemorrhage on repeat head CT scan, neurologic deterioration, neurosurgical intervention, or death	Five of 211 patients were found to have delayed ICH on repeat head CT scans, but in retrospect, only 2 of these patients had initially negative head CT scans (0.9%); these patients deteriorated at 19 or 28 days after trauma from delayed ICH

Continued

Table 4 Continued

Study design	Population	Outcomes	Key results
Retrospective review			
Twenty-four-hour observation and a repeat head CT scan prior to discharge ³⁴	Seventy-four adult patients on preinjury oral anticoagulation with mild head injury	Presence of intracranial hemorrhage on repeat CT scan	None of the 74 anticoagulated patients (0%) exhibited delayed ICH at CT2
Retrospective review ³⁵			
Medical record reviewed up to 60 days from the initial trauma	A total of 183 adult patients on preinjury oral anticoagulation with mild head injury	Presence of intracranial hemorrhage on repeat head CT scan (performed at 0–60 days), neurologic deterioration, neurosurgical intervention, or death	Five of 183 (2.7%) patients were found to have delayed ICH on repeat head CT scan, and 2 of these patients died as a consequence; the second CT scan was performed in 3 cases in the first 24 hours from TBI, in 1 case at 24 hours and in 1 case at 8 days
Retrospective review			
Six-hour observation and a repeat head CT scan prior to discharge ³⁶	A total of 424 adult blunt head trauma patients on anticoagulant or antiplatelet therapy and a normal initial head CT scan; 289 patients were on warfarin, 25 on both anticoagulant and antiplatelet therapy	Presence of intracranial hemorrhage on repeat CT at 6 hours, neurologic deterioration, or readmission	Delayed ICH was identified in 4 of 362 patients who received repeat head CT scan (1%); 5 were on warfarin and 2 were on both warfarin and aspirin; none of the delayed ICH cases was found to be clinically significant
Prospective, observational, multicenter			
Fourteen-day follow-up assessed in 930 patients by telephone survey (843 patients) or by electronic medical records review ³⁷	A total of 768 adult patients with blunt head trauma and preinjury warfarin use; initial CT scan was obtained in 1,000 patients (93%)	Presence of immediate intracranial hemorrhage, presence of delayed intracranial hemorrhage, neurosurgical intervention, or death	Delayed ICH was identified in 4 of 687 patients on preinjury warfarin (0.6%); of the 4 patients with delayed ICH, 2 died from extensive ICH; one of these 2 patients was previously discharged home without an initial CT scan
Abbreviations: ICH = intracranial cerebral hemorrhage; INR = international normalized ratio; OAC = oral anticoagulant; TBI = traumatic brain injury; SDH = subdural hematoma.			

In our population, the rate of dtICH identified by the repeated second CT was low (1.4%), and dtICH lacked clinical significance; only one patient reported a mild headache, and no patients exhibited neurologic deterioration or GCS worsening or required neurosurgical intervention. Unexpectedly, although statistical analysis could not be performed due to the small sample size of CT2-positive patients, in our series, supratherapeutic INR does not seem to predict delayed ICH: 3/4 of CT2-positive patients exhibited a therapeutic INR of 2–3, and one patient had a near-normal INR. None of the 63 patients (22.1%) with supratherapeutic INR developed bleeding. On the contrary, the mechanism of injury seems to influence the risk of delayed ICH (figure): 1/5 of patients with aggression and 1/4 of patients involved in road traffic accident were CT2-positive, whereas the 2 remaining patients with delayed ICH represented 2 of the 194 who fell from standing.

This was a single-center study and our population consisted predominantly of geriatric patients who had falls from standing (68.3%) with a possible selection bias for very mild TBI. This bias is consistent with the low incidence of immediate ICH (2.0%) compared with reports in the literature in patients on OACs (7.0%–9.7%).^{39,40} However, we describe a uniform population, and our findings are consistent with the scenario of an average ED without a second-level trauma center.

Figure Temporal bleeding at CT2

Detection of a small temporopolar bleeding at CT2 in a 42-year-old patient admitted after mild traumatic brain injury due to assault. He was under anticoagulant therapy with warfarin. International normalized ratio at admission was 2.93.

According to the literature, to achieve a zero-miss rate for dtICH, the timing of CT2 must be extended up to a month. As the national health systems debate over cost containment, resources allocation, and optimization in acute care settings, this approach should not be considered unviable or unsustainable. Rather, it is safe and reasonable to clinically observe these patients for 24 hours and then discharge them under reliable caregiver supervision with written instructions regarding the identification of neurologic deterioration. We underline, however, the importance of clinical judgment; a prolonged observation or a second CT should be considered in patients with a higher risk of delayed bleeding (e.g., severe mechanism of trauma, commotio brain injury, high INR levels, or concomitant antiplatelet therapy) and those without social support.

Finally, in our study, the estimated direct cost for patient admission and serial CT scans was €654 (\$693.24 USD). Therefore, with different management, a total of €185,736 (\$196,880 USD) could have been saved. In the United States, considering the average cost of \$464 USD for a noncontrast head CT scan and the average cost of \$3,612 USD for 24-hour hospital admission, the 48-hour protocol assessed in our study would have cost approximately \$8,152 USD per patient.⁴¹

The utility of a 48-hour in-hospital observation in patients with mild head injuries on OACs followed by a repeated CT scan is questionable. These patients could be safely discharged after a 24-hour observation with correct surveillance at home or monitored in the ED without systematically using a second CT scan in the absence of clinical signs of brain bleeding to substantially save resources.

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AUTHOR CONTRIBUTIONS

L. Campiglio: study concept and design, acquisition of data, analysis and interpretation of data, writing the paper. F. Bianchi: analysis and interpretation of data. C. Cattalini: acquisition of data, study supervision. D. Belvedere: acquisition of data, study supervision. C.E. Rosci: acquisition of data, study supervision. C.L.M. Casellato: acquisition of data, study supervision. M. Secchi: acquisition of data, study supervision. M.C. Saetti: acquisition of data, study supervision. E. Baratelli: acquisition of data, study supervision. A. Innocenti: acquisition of data, study supervision. I. Cova: acquisition of data, study supervision. C. Gambini: acquisition of data, study supervision. L. Romano: acquisition of data, study supervision. G. Oggioni: acquisition of data, study supervision. R. Pagani: acquisition of data, study supervision. M. Gardinali: analysis and interpretation of data, critical revision of manuscript for intellectual content. A. Priori: analysis and interpretation of data, critical revision of manuscript for intellectual content, study design and supervision, writing the manuscript.

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