

# Risk of Delayed Intracerebral Hemorrhage in Anticoagulated Patients after Minor Head Trauma: The Role of Repeat Cranial Computed Tomography

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## ABSTRACT

**Context:** Patients receiving anticoagulant medications who experience minor head injury are at increased risk of an intracerebral hemorrhage (ICH) developing, even after an initial computed tomography (CT) scan of the brain yields normal findings. Conflicting evidence exists regarding the frequency at which delayed bleeding occurs.

**Objective:** To identify the frequency of delayed traumatic ICH in patients receiving warfarin or clopidogrel.

**Design:** We performed a retrospective observational study of adult trauma encounters for anticoagulated patients undergoing head CT at 1 of 13 Kaiser Permanente Southern California Emergency Departments (EDs) between 2007 and 2011. Encounters were identified using structured data from electronic health and administrative records, and then records were individually reviewed for validation of results.

**Main Outcome Measures:** The primary outcome measure was ICH within 60 days of an ED visit with a normal head CT result.

**Results:** Our sample included 443 (260 clopidogrel and 183 warfarin) eligible ED encounters with normal findings of initial head CT. Overall, 11 patients (2.5%, 95% confidence interval [CI] = 1.4%-4.4%) had a delayed ICH, and events occurred at similar rates between the clopidogrel group (6/260, 2.3%, CI 1.1%-5.0%) and warfarin group (5/183, 2.7%, CI 1.2%-6.2%).

**Conclusion:** Trauma patients in the ED who are receiving warfarin or clopidogrel have approximately a 2.5% risk of delayed ICH after an initial normal finding on a head CT.

## INTRODUCTION

Emergency medicine currently emphasizes the role of the emergency physician as steward over limited health care resources. Optimizing the use of computed tomography (CT) is a key area of emphasis for emergency physicians to eliminate unnecessary risk and to improve affordability.<sup>1-3</sup> Targeting this goal, the American College of Emergency Physicians emphasized the use of validated decision rules to guide CT use in the evaluation of Emergency Department (ED) patients with traumatic head injury.<sup>4</sup> Many of these rules have been studied extensively, but all are intended to help assess the initial need for head CT, and few address the needs of specific high-risk groups.<sup>4-9</sup> Patients receiving

anticoagulant medications, such as warfarin or clopidogrel, are one group that could benefit from further investigation. Although imaging in these patients is generally recommended at initial evaluation, there is conflicting evidence regarding the frequency (rates between 0% and 6%) of delayed intracerebral hemorrhage (ICH) and the potential need to repeat CT in this group.<sup>10-12</sup>

The number of anticoagulated patients visiting EDs is expected to increase with the increasing age of the population.<sup>13</sup> If a substantial percentage of these patients who experience minor head injury are at risk of delayed ICH, they will incur the necessary expense of extended observation or admission, and repeat CT scanning. There is a need to better understand the

frequency of delayed bleeding for patients visiting community EDs after head trauma in order to better inform future emergency medicine policies and practices.

The goal of this investigation was to identify the frequency of delayed traumatic ICH in ED patients receiving warfarin or clopidogrel after a normal result of an initial head CT scan.

## METHODS

### Study Design and Setting

We performed a retrospective observational study of Kaiser Permanente Southern California (KPSC) ED encounters for head injury from 2007 to 2011. Our study uses structured data from KPSC for 13 affiliated community EDs.

### Selection of Patients

Structured data routinely collected at KPSC comprising claims data and information from electronic health records were queried to create our sample. Our sample was limited to the following inclusion criteria: ED encounters for trauma (International Classification of Diseases, Ninth Revision [ICD-9] Codes 800-800.06, 802-803.09, 804.01, 804.5, 850-850.12, 850.5, 850.9, 870-873.8, 925.1, 959.01, and 959.09), receipt of a head CT scan (ICD-9: 87.0x and 87.1x; Current Procedural Terminology Codes 0042T, 70450, 70460, 70470, 70480-70482, 70486-70488, and 70494), and currently prescribed warfarin (and had an international normalized ratio above 1.2 on the day of the ED visit) or clopidogrel as listed in our pharmacy records. Patient variables such as demographics, medication (clopidogrel or warfarin), mechanism of injury, initial and follow-up head CT findings, and

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outcome (mortality) were entered into the database by a research assistant. The principal investigator (CS) reviewed the database and, when necessary, patient charts to confirm these variables. We excluded pregnant patients and those with an ICH identified on initial CT. Those who were not KPSC members were also excluded because of inadequate follow-up to identify delayed bleeding.

### Outcome Measures and Follow-Up

The primary outcome for our study was delayed ICH, with mortality as a secondary outcome. We defined ICH as subarachnoid hemorrhage, subdural hematoma, epidural hematoma, or intraparenchymal hemorrhage or contusion. A delayed hemorrhage was defined as any hemorrhage that was identified within 60 days of an ED encounter for evaluation of head trauma, after analysis of an initial head CT scan had determined no bleeding. Among those patients confirmed to have an initial CT scan with normal results, the medical record was reviewed up to 60 days from the initial trauma to determine if any repeated scans or mortality had occurred. If a patient had an initial normal CT finding, and at a subsequent visit a repeated CT yielded abnormal results, the chart was reviewed to ensure no new trauma had occurred.

The KPSC institutional review board approved the study.

## RESULTS

### Characteristics of Subjects

Initially, 1050 subjects were included in the study. However, 559 subjects were excluded because of incomplete data (466 patients did not experience trauma leading to their CT scan, and 93 patients did not have a CT report available), resulting in 491 eligible ED encounters. Of these patients, 290 were receiving clopidogrel, and 201, warfarin. Patients had a mean age of 79.2 years, and 47.5% were female. Among patients with an initial head CT scan, 31% underwent follow-up CT. The median time from initial CT to follow-up CT was 1 day (Table 1).

### Main Results

Of the 491 encounters, 48 demonstrated ICH on the initial CT scan,

**Table 1. Demographics of 491 adult patients receiving warfarin or clopidogrel and evaluated for head trauma<sup>a</sup>**

Demographic	Value
Female sex (%)	47.5
Age (years)	
Mean (SD)	76.6 (11.9)
Median	79.2
Time to follow-up CT (days)	
Median	1
Mean	4.7
Mechanism of injury (%)	
Fall from standing	88
Fall from elevation	1
Auto collision	10
Motorcycle collision	1

<sup>a</sup> Evaluated in 1 of 13 Kaiser Permanente Southern California Emergency Departments. CT = computed tomography; SD = standard deviation.

leaving 443 patients with an initially normal CT result. Eleven of these 443 patients (2.5%, 95% confidence interval [CI] = 1.4%-4.4%) experienced a delayed ICH: 6 (2.3%, CI 1.1-5.0%) in the clopidogrel group and 5 (2.7%, CI 1.2-6.2%) in the warfarin group (Table 2). Four of the 11 patients with a delayed bleed died because of ICH. The 11 patients with delayed ICH are described in Table 3.

## DISCUSSION

Our results for delayed hemorrhage show that patients receiving anticoagulant or antiplatelet medications have an overall risk of delayed ICH of 2.5% (2.7% for warfarin and 2.3% for clopidogrel). These results are higher than reported rates of delayed ICH compared with a report in 2012, which showed no patients who were receiving clopidogrel and 0.6% of patients receiving warfarin had delayed bleeding,<sup>11</sup> but are lower

than the 6% risk in a smaller prospective study.<sup>12</sup> Numerous factors such as differences in patient demographics or trauma severity may contribute to these differences. Compared with the study by Nishijima and colleagues,<sup>11</sup> our patients had a similar mean age (75 vs 77 years for our study patients). Our study had slightly higher rates of ICH on initial CT (9.8% vs 7.0%), which may indicate that our population had more severe trauma. In addition, our follow-up period was 60 days in an attempt to be more sensitive and capture any delayed bleeding, compared with the former study, which used 14 days.

In our cohort, only 31% of patients had a follow-up CT scan performed. This may reflect that during the study period, it was not standard practice to rescan anticoagulated patients with trauma. For patients who were not rescanned, any clinically significant rebleed should be identified during chart review. However, it is possible that patients in whom clinically insignificant hemorrhages developed would not seek medical attention, and thus such hemorrhages could have been missed in our follow-up.

Of the 11 patients who had ICH observed on subsequent imaging, 4 of them died as a result. This represents a small percentage (0.9%) of the overall group who initially had a normal head CT result after trauma; however, the potential for death is an important consideration when physicians decide who needs further evaluation or follow-up imaging after trauma. As emergency physicians interpret the evidence to guide their management of anticoagulated patients with head trauma, patient outcomes—not radiographic findings—should be most important.

Our findings give community emergency physicians further information to

**Table 2. Computed tomography findings for anticoagulated patients with minor head trauma**

CT finding	Clopidogrel (n = 290)	Warfarin (n = 201)	Total (N = 491)
ICH on initial CT	30	18	48
No ICH	254	178	432
Delayed ICH	6	5	11

CT = computed tomography; ICH = intracranial hemorrhage.

Patient	Age, years	Sex	Mechanism of injury	Medication	INR	Findings of repeat CT	Days between initial and follow-up CT	Mortality
1	69	Male	Fall	Clopidogrel		SDH/EDH	0	No
2	81	Male	Assault	Warfarin	1.6	IPH/SDH	0	Yes
3	87	Male	Syncope/fall	Warfarin	2.8	SDH	0	No
4	73	Female	Fall	Clopidogrel		SDH	0	No
5	87	Female	Fall	Warfarin	2.1	SAH/SDH/EDH	8	Yes
6	51	Male	Fall	Clopidogrel		IPH	27	No
7	89	Male	Syncope/fall	Warfarin	1.3	SDH	0	No
8	80	Female	Fall	Warfarin	4.1	SDH	1	No
9	75	Male	Fall	Clopidogrel		SDH/SAH	5	Yes
10	84	Male	Fall	Clopidogrel		SDH	54	No
11	85	Male	Fall	Clopidogrel		IPH	2	Yes

CT = computed tomography; EDH = epidural hematoma; INR = international normalized ratio; IPH = intraparenchymal hemorrhage; SAH = subarachnoid hemorrhage; SDH = subdural hematoma.

allow for informed and shared decision making between a physician and an anticoagulated patient who has a head injury and a normal initial head CT finding. Physicians have not yet established an agreed-on risk threshold; for some, 2.5% is too high a risk to omit repeated imaging, whereas for others this may be a small risk to warrant the costs, inconvenience, and risks associated with further observation and repeated imaging.

As with the need for repeat imaging, there are currently no consensus guidelines to recommend the timing of patient follow-up or when the patient can resume anticoagulant therapy. For those who do not receive repeat imaging, we recommend follow-up within 24 to 48 hours, and we generally advise that patients discontinue anticoagulant medications until they can be reevaluated. Given that delayed hemorrhage can occur more than 24 hours after the initial injury, the potential risks of restarting warfarin or clopidogrel therapy should be weighed carefully with the indication for the medication.

Our study has some important limitations. The study was retrospective, which inherently creates the possibility of selection bias. In addition, because of the retrospective nature of the study and the limitations of the program that we used to select subjects, a large percentage of subjects were excluded from the study because they either had missing CT data (because the initial scan was performed at a non-Kaiser Permanente facility) or, on

chart review, were identified as not having minor trauma. This may have resulted in sampling or exclusion bias.

## CONCLUSION

In our sample, patients receiving warfarin or clopidogrel who experience minor head trauma and have normal findings of initial CT have approximately a 2.5% risk of development of ICH and a 0.9% risk of death caused by delayed ICH. ❖

## Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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