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Use of anti-platelet agents after traumatic intracranial hemorrhage

Keith Kerr[a], Christopher Wilkerson[b], Scott Shepard[a], HuiMahn Choi[a], Ryan Kitagawa[a,*]

[a] Vivian L. Smith Department of Neurosurgery, University of Texas Health Science Center at Houston, TX, USA
[b] University of Utah School of Medicine, Department of Neurosurgery, USA

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ABSTRACT

Objective: To evaluate the risk of hemorrhagic complications associated with starting anti-platelet therapy (APT) after acute traumatic intracranial hemorrhage (tICH) and to examine the frequency of thrombotic complications.

Patients and methods: We retrospectively identified all patients admitted to our institution with tICH that received APT during their initial hospitalization over a three-year period. We reviewed their demographics, hospital course, clinical indication and timing for initiation of APT, and complications.

Results: A total of 222 patients were identified. The median age and Injury Severity Score (ISS) was 61 and 21, respectively. Fifty (23%) patients required neurosurgical procedures. APTs were initiated due to a history of APT use in 91 patients (41%) and blunt cerebrovascular injury in 86 patients (38.6%).

The median time from injury to starting APT was 4 days. Immediate complications including new or worsening hemorrhage occurred in 1 (<1%) patient. Delayed hemorrhagic complications occurred in 6 (4.7%) patients.

Thrombotic events occurred in 21 (9.4%) patients prior to starting APT. Thirteen (5.8%) of these were potentially preventable.

Conclusion: The risk of immediate and delayed intracranial hemorrhages from initiating APT after tICH must be weighed against the morbidity of delaying indicated thrombotic prophylaxis. Our initial data indicates that hemorrhagic complications are infrequent, and thrombotic complications can have significant clinical consequences. Our retrospective review provides the first rates of complications for this patient population.

1. Introduction

Anti-platelet therapies (APTs) are frequently utilized medications, and are commonly indicated in patients with traumatic intracranial hemorrhage (tICH). Although venous thromboembolism prophylaxis after tICH has been studied, no data exist to guide clinicians on when it is safe to initiate APTs [1]. Indications for APTs include ischemic stroke prevention after blunt cerebrovascular injury (BCVI), acute myocardial infarction treatment, and secondary prevention of heart attack and stroke [2–6].

The prevalence of traumatic brain injury in individuals older than 65 years is growing, and more than 60% of this population takes aspirin [7]. Thus, clinicians must decide when to resume the APTs after tICH. Additionally, more BCVIs are being diagnosed as computed tomography angiography (CTA) is becoming routine in the polytrauma patient, with approximately 25–40% of these patients also having a tICH [3,4,8]. Treating BCVI with appropriate APT or anticoagulation is important, as untreated injuries carry a 10–50% risk of stroke with subsequent mortality rates of 30–50%. Prompt therapy may decrease the stroke risk to less than 10%, however, the treatment of BCVI must be weighed against the risk of traumatic hemorrhage progression [2,4,9].

We present our experience with patients who presented with tICH who received antiplatelet therapies during their hospital stay including the complications of starting APTs and of withholding them. Our primary objective was to determine the rate of intracranial hemorrhage in this patient population. Secondarily, we aimed to identify the frequency of thrombotic events, if the timing of APT initiation showed any relation to the development of hemorrhagic or thrombotic events, and which patient populations might be most susceptible to these complications. Although most institutional practices are based on personal experience and general guidelines, our data are the first to study these medications in the TBI population.

* Corresponding author at: Vivian L. Smith Department of Neurosurgery, The University of Texas Health Science Center at Houston, Medical School, 6400 Fannin # 2800, Houston, TX 77030, USA.
E-mail address: Ryan.S.Kitagawa@uth.tmc.edu (R. Kitagawa).

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2. Patients and methods

A retrospective chart review was performed for all TBI patients from 2010 to 2012 at Memorial Hermann Hospital at the Texas Medical Center in Houston, Texas. All patients with International Classification of Diseases (ICD) codes consistent with intracranial hemorrhage and claims demand management (CDM) codes for pharmaceutical antiplatelet therapy (aspirin or clopidogrel) on a single admission were included (Fig. 1).

We then excluded patients who received both antiplatelet and anticoagulation therapy (other than deep venous thrombosis prophylaxis) in the same hospital stay. We also excluded patients with spontaneous subarachnoid or intracerebral hemorrhages as well as patients with chronic, subacute, or acute-on-chronic subdural hemorrhages. Thus, only acute trauma patients were including in this study.

For the remaining patients, age, sex, race, mechanism of injury, Glasgow Coma Scale (GCS) score at presentation, past medical history including prior antiplatelet or anticoagulant use, initial imaging findings, Injury Severity Score (ISS), APT indication, type and dose of antiplatelet agent, surgical procedures, thrombotic events (myocardial infarction or ischemic stroke) prior to initiation of APT, length of hospital stay, length of intensive care unit (ICU) stay and mortality were recorded. The timing of APT initiation and its relationship to the patient's initial injury, stable radiographic findings, neurosurgical procedures, and thrombotic events were also noted.

The two complication types include hemorrhage progression due to the use of APTs and thrombotic complications including myocardial infarctions (MIs) and cerebrovascular accidents (CVA) not attributable to cerebral herniation. Thrombotic events were considered preventable if an indication for APT was present prior to the event but the medication was withheld due to perceived risk of intracranial hemorrhage.

Hemorrhagic progression due to APTs included immediate complications (less than 7 days), intermediate complications (7–14 days), and delayed complications (greater than 14 days). These complications were either radiographic only or clinical if the patients treatment course was altered such as with new surgery. The Glasgow Outcome Score (GOS) at the time of discharge from the hospital was also recorded.

All statistics were performed using SPSS version 21. A two tailed test of statistical significance was set at $P < 0.05$.

3. Results

3.1. Patient participant identification

A total of 1016 patients hospitalized with intracranial hemorrhage that received APT were identified. Of those, 794 were excluded because their hemorrhage was non-traumatic, or they received concomitant anticoagulation therapy other than subcutaneous deep vein thrombosis prophylaxis (Fig. 1). Thus, 222 patients remained. Although the patient population was heterogeneous, the two largest groups included 86 BCVI patients requiring prophylaxis to prevent ischemic stroke, and 91 patients who were previously taking APT for a past medical history of arteriosclerosis. Other indications included seven acute myocardial infarctions after their presenting TBI, five peripheral arterial injuries, 20 patients with thrombocytosis, five patients with strokes unrelated to vascular injuries and eight patients with no indication listed.

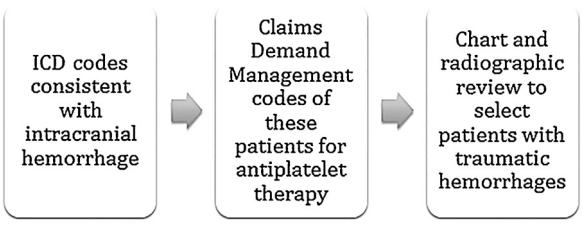

Fig. 1. Patient selection flow diagram.

3.2. All patients – descriptive and outcome data

The median patient age was 61 years (range 16–94 years) with a 2:1 male to female ratio (Table 1). The median ISS score for the entire population was 21 (range 4–50), and 34% of patients had severe TBI (GCS score <9) on presentation. A total of 50 (23%) patients required neurosurgical intervention prior to beginning APT.

For all patients, the most common form of APT was aspirin 325 mg. The median interval between primary injury to initiation of APT in all patients was 4 days (range 0–34 days), and the median time from neurosurgical procedure to initiation of the total population was 5 days (range 6–34 days). The median interval from stable CT scan to initiation of APT in all patients was 3 days (range 2–25 days) (Table 1 and Fig. 2). Overall, there was one radiographic hemorrhagic complication, and six clinical complications. None of these were acute, 2 were intermediate and 4 were long term. There were 21 total thrombotic events including 7 myocardial infarctions and 14 strokes. Thirteen of these events were considered preventable. The median GOS at discharge was 4, with 10 mortalities (5%).

3.3. Blunt cerebrovascular injury – descriptive and outcome data

The 86 BCVI patients had a median age of 36.5 years (range 16–92 years) and 54 (63%) were male. Motor vehicle collisions were the most common mechanism of injury (52%). 53 patients (62%) patients presented with severe TBI on presentation, and the median

Table 1
Patient characteristics

	All patients	Blunt cerebrovascular injury	Prior prophylactic antiplatelet therapy
	Demographics		
Population	222	86	91
Males	142 (64%)	54 (63%)	56 (62%)
Age (median)	61	36.5	77
	Presenting condition		
GCS severe (3–8)	75 (34%)	53 (62%)	7 (8%)
GCS mild/moderate (9–15)	147 (66%)	33 (38%)	84 (92%)
ISS[a] (median)	21	29	16
Prior APT/ACT	98 (44%)	28 (33%)	91 (100%)
Required neurosurgical procedure	46 (21%)	29 (34%)	9 (10%)
	Antiplatelet therapy data		
Aspirin 81 mg	81 (36%)	22 (26%)	40 (43%)
Aspirin 325 mg	111 (50%)	64 (74%)	21 (23%)
Clopidogrel 75 mg	13 (6%)	0 (0%)	13 (14%)
Aspirin and clopidogrel	17 (8%)	0 (0%)	17 (19%)
Days from injury to initiation (median)	4	3	3
Days from procedure to initiation (median)	5	3	9
Days from stable scan to initiation (median)	3	3	3
Days of APT (median)	6	8.5	5

[a] ISS for 210 (95%) patients of the total population.
Percentages are of the indicated population or subpopulation.