Aspirin for primary prevention of stroke in traumatic cerebrovascular injury: association with increased risk of transfusion

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OBJECTIVE Blunt traumatic extracranial carotid or vertebral artery injury (i.e., traumatic cerebrovascular injury [TCVI]) occurs in 1%–2% of all blunt trauma admissions, carries a 10% risk of thromboembolic ischemic stroke, and accounts for up to 9600 strokes annually in the US. Screening CT angiograms (CTAs) of patients with trauma has become ubiquitous in recent years, and patients with initially asymptomatic TCVI are commonly treated with antiplatelet agents to prevent stroke. Prophylaxis with antiplatelets is thought to be safer than anticoagulation, which carries a significant risk of hemorrhage in patients with trauma. However, the risk of hemorrhagic complications due to antiplatelets has not been assessed in this population.

METHODS This is a retrospective cohort study of patients in whom a screening CTA was obtained after admission for blunt trauma at a Level 1 trauma center. Patients with CTAs indicating TCVI were treated routinely with 325 mg aspirin daily. The risk of transfusion > 24 hours after admission was compared according to CTA findings (CTA+ or CTA– for positive or negative findings, respectively) and aspirin treatment (ASA+ or ASA– for treatment or no treatment, respectively).

RESULTS The mean overall transfusion amount (number of units of packed red blood cells [PRBCs]) was 0.9 ± 2.1 for CTA+/ASA+ patients ($n = 196$) and 0.3 ± 1.60 for CTA–/ASA– patients ($n = 2290$) ($p < 0.0001$). In adjusted models, the overall relative risk (RR) of PRBC transfusion was 1.70 (1.32–2.20) for CTA+/ASA+ patients compared with CTA–/ASA– patients. Among age groups, participants whose ages were 50–69 years had the greatest significantly elevated RR (1.71, 95% CI 1.08–2.72) for CTA+/ASA+ patients compared with CTA–/ASA– patients.

CONCLUSIONS Treatment with aspirin for the prevention of stroke in patients with initially asymptomatic TCVI carries a significantly increased risk of PRBC transfusion. Future studies are needed to determine if this risk is offset by a reduced risk of ischemic stroke.

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KEYWORDS stroke; blunt trauma; dissection; antiplatelets; hemorrhage; primary prevention; vascular disorders

EXTRACRANIAL traumatic cerebrovascular injury (TCVI) is present in 1%–2% of patients admitted after high-energy blunt trauma, such as motor vehicle crashes and falls.^{15,18,37} Research has reported that 10%–20% of patients with TCVI have an ischemic stroke,^{5,16,37} and that TCVI may be the primary cause of up to 9600 ischemic strokes in the US per year.¹⁴ TCVI is

also associated with the majority of ischemic stroke cases among patients with traumatic brain injury.²²

Patients admitted with blunt trauma and risk factors for TCVI routinely undergo a screening neck CT angiogram (CTA) to look for TCVI. Due to the increasing use of screening CTAs for this purpose, the estimates of TCVI incidence have been growing at a significant rate over the

ABBREVIATIONS ASA+, ASA– = with aspirin treatment, without aspirin treatment; CTA = CT angiogram; CTA+, CTA– = CTA positive for TCVI, CTA negative for TCVI; GCS = Glasgow Coma Scale; INR = international normalized ratio; ISS = Injury Severity Score; LOS = length of stay; PRBC = packed red blood cell; RERI = relative excess risk due to interaction; RR = relative risk; TCVI = traumatic cerebrovascular injury.

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last decade.¹⁸ The majority of TCVIs identified by screening CTAs are initially asymptomatic.^{16,37} Because most ischemic strokes are thromboembolic,¹⁶ prophylactic treatment with antithrombotic medications is preferred by the majority of clinicians who manage patients with TCVI.¹⁹ Although systemic anticoagulation is contraindicated in one-third of trauma patients due to other injuries,^{37,41} evidence suggests that antiplatelet agents carry a lower risk of hemorrhagic complications and are therefore used as an alternative to anticoagulation in many centers.^{9,14,41} However, the risk of hemorrhagic complications due to antiplatelet agents has not been assessed in the TCVI population. We sought to determine if treatment of TCVI patients with antiplatelet agents is associated with a higher risk of hemorrhagic complications, as reflected by the risk of blood transfusion.

Methods

Study Design

This was an institutional review board–approved retrospective cohort study at an American College of Surgeons Level 1–verified trauma center. Standard management of patients with blunt trauma at our center includes a screening neck CTA on admission to assess for TCVI; most patients with a CTA interpreted as showing evidence of injury (CTA+) to the extracranial carotid or vertebral arteries are treated with aspirin (ASA+)—325 mg orally or per rectum daily for the duration of the hospital stay. Anticoagulation for the treatment of TCVI is generally avoided.

Data Sources

An administrative database was used to generate a list of all patients admitted to our center with a diagnosis of blunt trauma and undergoing a neck CTA on admission between January 1, 2013, and December 31, 2016. Demographic data (i.e., age, race, and sex) and injury characteristics (i.e., mechanism, Injury Severity Score [ISS], and Glasgow Coma Scale [GCS] score at hospital presentation) were obtained from the hospital's trauma registry. Clinical characteristic and outcome data were collected from a query of the hospital's electronic medical record data table. Clinical characteristics included base excess, lactic acid, systolic blood pressure, and international normalized ratio (INR) on hospital admission. Clinical outcomes included data related to transfusion of packed red blood cells (PRBCs), mean hospital length of stay (LOS), ICU LOS, ventilator support days, and nosocomial occurrence of pneumonia, adult respiratory distress syndrome, and acute kidney injury. Additional data on CTA+ patients were obtained from a prospective center database on patients with TCVI.

Variable Definitions

Race was defined as white, black, and other (the latter was combined into a single category due to small sample sizes of patients in non-white and non-black racial categories). Age was categorized as 18–29 years, 30–49 years, 50–69 years, and ≥ 70 years. The INR was dichotomized as evidence of coagulopathy (i.e., $\text{INR} \geq 1.2$) and no evi-

dence of coagulopathy (i.e., $\text{INR} < 1.2$). The injury mechanism was defined as blunt or penetrating. The ISS was categorized as minor injury (i.e., 1–14), moderate injury (15–24), and severe injury (≥ 25). The GCS score was categorized as traumatic brain injury (i.e., GCS score 3–8), mild/moderate head injury (i.e., GCS score 9–12), and no head injury (i.e., GCS score 13–15). Systolic blood pressure was categorized as < 90 mm Hg and ≥ 90 mm Hg. Using methodology proposed by Quan and colleagues,³¹ the ICD diagnosis codes from billing data were used to identify comorbidities, including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, rheumatic disease, peptic ulcer disease, chronic obstructive pulmonary disease, dementia, liver disease, diabetes, hemi- or paraplegia, renal disease, malignancy, metastasis, and HIV/AIDS.

The main exposures were positive CTA and use of ASA (i.e., CTA+ and ASA+). Patients were classified according to whether the neck CTA showed evidence of a TCVI (CTA+) or no evidence of TCVI (CTA–), and whether each patient was treated with aspirin (i.e., ASA+) or was not treated with aspirin (ASA–). The outcome of interest was the need for transfusion following the initial 24-hour resuscitative period. Only transfusions > 24 hours after admission were included as the main outcome, to exclude initial transfusions given for injury-related blood loss.

Statistical Analysis

Demographic, injury, comorbidity, and clinical characteristics and outcomes were compared among the CTA/ASA groups by using an ANOVA or Pearson's chi-square test for continuous and categorical variables, respectively. A Cox proportional hazards regression assuming equal time at risk was used to estimate relative risks (RRs) and associated 95% confidence intervals for the association between CTA/ASA exposure and need for transfusion of PRBCs after 24 hours. Models were adjusted for the following: age; ISS; diagnosis of myocardial infarction, congestive heart failure, or peripheral vascular disease; number of PRBC units transfused in the first 24 hours of admission; and having an $\text{INR} \geq 1.2$ at admission. A relative excess risk due to interaction (RERI) was used to examine whether the combined exposure of CTA+/ASA+ resulted in an absolute increased risk of PRBC transfusion outside of the expected risk due to CTA+ and ASA+ separately (i.e., additive interaction). A positive RERI suggests a higher risk than expected, a negative RERI suggests a lower risk, and a RERI of 0 suggests no different risk than expected. Due to the fact that the patient population probably included individuals who were already taking aspirin or other antiplatelet agents at the time of admission, a characteristic for which we were not able to collect data due to the retrospective nature of the study design, models were stratified by age category in an effort to account for the likelihood of preinjury use of antiplatelet agents.

Results

A total of 2867 patients were included, of whom 196

TABLE 1. Comparison of demographic, injury, clinical presentation, and clinical outcome characteristics by CTA and ASA status

Characteristic	CTA+/ASA+, n = 196	CTA+/ASA-, n = 86	CTA-/ASA+, n = 295	CTA-/ASA-, n = 2290	p Value*
Demographics					
Sex (%)					
Male	119 (60.7)	50 (58.1)	194 (65.8)	1545 (67.5)	0.0829
Female	77 (39.3)	36 (41.9)	101 (34.2)	745 (32.5)	
Race (%)					
Black	43 (22.1)	23 (26.7)	57 (19.3)	578 (25.5)	0.1471
White	144 (73.8)	60 (69.8)	216 (73.2)	1548 (68.3)	
Other	8 (4.1)	3 (3.5)	22 (7.5)	142 (6.3)	
Mean age in yrs	45.0 ± 19.0	46.0 ± 19.8	51.7 ± 19.9	40.5 ± 17.8	<0.0001
18–29	56 (28.6)	24 (27.9)	49 (16.6)	791 (34.5)	<0.0001
30–49	61 (31.1)	23 (26.7)	80 (27.1)	819 (35.8)	
50–69	57 (29.1)	27 (31.3)	195 (35.6)	522 (22.8)	
≥70	22 (11.2)	12 (14.0)	61 (20.7)	158 (6.9)	
Injury					
Blunt mechanism (%)	192 (98.0)	82 (95.3)	291 (98.6)	2211 (96.6)	0.1598
Mean ISS	21.2 ± 11.4	21.4 ± 15.7	18.7 ± 12.4	11.9 ± 10.4	<0.0001
1–14	64 (32.7)	32 (37.6)	136 (46.1)	1624 (71.0)	<0.0001
15–24	67 (34.2)	23 (27.1)	95 (32.2)	402 (17.6)	
≥25	65 (33.2)	30 (35.3)	64 (21.7)	262 (11.5)	
Mean GCS score	12.2 ± 4.6	10.2 ± 5.5	12.8 ± 4.2	13.5 ± 3.6	<0.0001
3–8	40 (20.6)	34 (40.0)	50 (17.1)	257 (11.3)	<0.0001
9–12	12 (6.2)	3 (3.5)	8 (2.7)	58 (2.5)	
13–15	142 (73.2)	48 (56.5)	234 (80.1)	1966 (86.2)	
Clinical presentation					
Mean base excess	-3.0 ± 3.6	-4.6 ± 5.5	-3.2 ± 4.0	-2.2 ± 3.5	<0.0001
Mean lactic acid	2.4 ± 1.9	3.2 ± 2.8	2.5 ± 1.9	2.3 ± 2.1	0.0009
Mean systolic blood pressure	133.3 ± 27.0	132.2 ± 39.9	133.6 ± 27.2	137.0 ± 25.6	0.0367
<90 mm Hg (%)	6 (3.1)	8 (11.8)	16 (5.5)	35 (1.9)	<0.0001
Mean INR	1.11 ± 0.23	1.16 ± 0.51	1.13 ± 0.38	1.09 ± 0.76	0.5339
≥1.2 (%)	32 (16.4)	19 (22.9)	56 (19.1)	243 (10.8)	<0.0001
Clinical outcome					
Mean units PRBCs					
First 24 hrs	0.9 ± 2.1	1.2 ± 3.0	1.0 ± 2.4	0.3 ± 1.6	<0.0001
Overall	2.9 ± 4.9	1.8 ± 3.6	2.7 ± 4.6	0.8 ± 2.8	<0.0001
Mean hospital LOS, days	15.2 ± 18.0	7.6 ± 13.0	13.8 ± 13.1	5.4 ± 9.0	<0.0001
Mean ICU LOS, days	14.9 ± 15.7	11.8 ± 17.0	12.7 ± 10.8	9.2 ± 9.3	<0.0001
Mean ventilator support, days	13.8 ± 14.2	9.4 ± 14.3	11.3 ± 9.7	7.4 ± 7.9	<0.0001
Pneumonia (%)	21 (10.7)	8 (9.3)	20 (6.8)	60 (2.6)	<0.0001
Adult respiratory distress syndrome (%)	4 (2.0)	1 (1.2)	2 (0.7)	5 (0.2)	0.0010
Acute kidney injury (%)	4 (2.0)	1 (1.2)	9 (3.1)	12 (0.5)	<0.0001

The mean values are expressed ± SD; otherwise the values represent number of patients (%).

* Estimated from chi-square and ANOVA for categorical and continuous variables, respectively.

(6.8%) were CTA+/ASA+, 86 (3.0%) were CTA+/ASA-, 295 (10.3%) were CTA-/ASA+, and 2290 (79.9%) were CTA-/ASA-. There was no difference in sex or race among the exposure groups; however, the CTA-/ASA- group was younger than the other exposure groups ($p < 0.0001$) (Table 1). In addition, the CTA-/ASA- group had the lowest ISS ($p < 0.0001$) and higher GCS ($p < 0.0001$)

than the other exposure groups. Examining clinical presentation characteristics, base excess was lowest for the CTA-/ASA- group ($p < 0.0001$), whereas the CTA+/ASA- group had higher lactic acid levels ($p = 0.0009$) and was more likely to have a systolic blood pressure < 90 mm Hg ($p < 0.0001$) and to be coagulopathic ($p < 0.0001$). Those who were CTA-/ASA- had a lower likelihood of

TABLE 2. Comparison of comorbidities by CTA and ASA status

Comorbidities	CTA+/ASA+, n = 196	CTA+/ASA-, n = 86	CTA-/ASA+, n = 295	CTA-/ASA-, n = 2290	p Value*
Myocardial infarction	6.1	1.3	13.2	1.8	<0.0001
Congestive heart failure	2.6	3.8	12.2	1.3	<0.0001
Peripheral vascular disease	7.1	6.4	12.5	4.1	<0.0001
Cerebrovascular disease	24.5	23.4	23.7	8.0	<0.0001
Rheumatic disease	0.5	0.0	2.0	0.8	0.1421
Peptic ulcer disease	0.5	1.3	0.7	0.1	0.0858
Chronic obstructive pulmonary disease	8.7	5.1	15.9	8.4	0.0002
Dementia	2.6	1.3	2.7	1.1	0.0557
Mild liver disease	2.0	6.4	4.7	5.6	0.1846
Diabetes					
w/o chronic complications	16.8	12.8	26.8	9.3	<0.0001
w/ chronic complications	0.5	0.0	1.7	0.1	<0.0001
Hemiplegia or paraplegia	7.1	7.7	5.1	1.9	<0.0001
Renal disease	4.6	3.8	4.1	1.3	0.0001
Malignancy	0.0	0.0	1.7	0.9	0.1906
Moderate or severe liver disease	0.0	0.0	0.0	0.3	0.6505
Metastasis	0.0	0.0	0.0	0.4	0.4822
HIV/AIDS	0.0	0.0	0.0	0.1	0.8450

The list of comorbidities is from Quan H, Sundararajan V, Halfon P, et al: Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 43:1130–1139, 2005. Values are expressed as percentages.

* Estimated from chi-square test.

transfusion, both within the first 24 hours ($p < 0.0001$) and after 24 hours ($p < 0.0001$). Regarding clinical outcomes, the CTA+/ASA+ group had longer ICU stays ($p < 0.0001$), ventilator support days ($p < 0.0001$), and overall hospital LOS ($p < 0.0001$). None of the patients in the CTA+/ASA+ group had any hemorrhagic complications that were directly attributable to treatment with aspirin.

The likelihood of having an ICD diagnosis code, whether present on admission or not, for myocardial infarction ($p < 0.0001$), congestive heart failure ($p < 0.0001$), peripheral vascular disease ($p < 0.0001$), diabetes ($p < 0.0001$), and chronic obstructive pulmonary disease ($p = 0.0002$) was highest for those who were CTA-/ASA+ (Table 2). Hemiplegia/paraplegia was highest for CTA+ patients ($p < 0.0001$), and renal disease was lowest for those who were CTA-/ASA- ($p = 0.0001$).

In overall crude models with the CTA-/ASA- groups as the referent, use of aspirin was associated with increased risk of transfusion, with significantly increased RRs for both the CTA+/ASA+ (RR 2.75, 95% CI 2.14–3.53) and CTA-/ASA+ (RR 3.36, 95% CI 2.75–4.10) exposure groups (Table 3). In adjusted models the associations remained, although they were attenuated in strength for both the CTA+/ASA+ (RR 1.70, 95% CI 1.32–2.20) and CTA-/ASA+ (RR 2.02, 95% CI 1.64–2.51) groups. The RERI for the trauma population overall was -0.20 with a 95% CI of -0.88 to 0.47 , suggesting that the risk of transfusion after 24 hours for the combined CTA+/ASA+ group was no different than expected. In other words, the increased RR for the CTA+/ASA+ was due to the individual effects of cerebrovascular injury and the aspirin, not because of the combination of the two. By age groups, a similar pat-

tern of associations was observed for all age groups. That is, we observed increased RRs for the CTA+/ASA+ and CTA-/ASA+ and a nonsignificant RERI.

Discussion

Our study found that use of aspirin in patients who suffered blunt trauma with or without evidence of TCVI on the screening neck CTA upon admission is associated with a significantly higher risk of transfusion compared to patients with blunt trauma who had CTA- and ASA- status. However, specific to CTA+ patients, the use of aspirin confers no more risk than was expected from TCVI alone (i.e., without accounting for use of aspirin) and use of aspirin alone (i.e., without accounting for presence of TCVI). This pattern of results was consistent across all age groups.

Our finding of no hemorrhagic complications directly attributable to aspirin is consistent with other studies of aspirin in the treatment of TCVI.^{16,38} Considering that no obvious hemorrhagic events due to aspirin occurred in CTA+ patients, it is likely that the greater transfusion risk in these patients was the result of more subtle effects on blood loss during trauma-related orthopedic and other surgical procedures, and other causes of bleeding due to the trauma > 24 hours after injury.

Traumatic cerebrovascular injury is significantly different from spontaneous carotid and vertebral artery dissection, and from dissections occurring after low-energy trauma. Spontaneous arterial dissections, and dissections that occur after coughing fits, rapid head turning, or rapid neck extension, have been studied extensively. The risk of stroke with spontaneous and low-energy dissections was

TABLE 3. RRs and associated 95% CIs for the association between interactions of CTA and ASA status and need for transfusion after 24 hours, with additional measures of RERI

Patient Groups	No. Needing Transfusion After 24 Hrs (%)	Crude RR (95% CI)*	Adjusted RR (95% CI)†	RERI (95% CI)‡
Overall				
CTA+/ASA+	75 (38.3)	2.75 (2.14–3.53)	1.70 (1.32–2.20)	–0.20 (–0.88, 0.47)
CTA+/ASA–	19 (22.1)	1.59 (0.99–2.52)	0.88 (0.55–1.41)	
CTA–/ASA+	138 (46.8)	3.36 (2.75–4.10)	2.02 (1.64–2.51)	
CTA–/ASA–	319 (13.9)	Reference	Reference	
Age 18–29 yrs				
CTA+/ASA+	22 (39.3)	2.88 (1.82–4.55)	1.50 (0.92–2.45)	–0.38 (–1.73, 0.97)
CTA+/ASA–	8 (33.3)	2.44 (1.19–5.01)	1.23 (0.59–2.55)	
CTA–/ASA+	21 (42.9)	3.14 (1.97–5.01)	1.66 (1.03–2.69)	
CTA–/ASA–	108 (13.7)	Reference	Reference	
Age 30–49 yrs				
CTA+/ASA+	18 (29.5)	2.37 (1.44–3.91)	1.49 (0.89–2.49)	–1.01 (–2.44, 0.42)
CTA+/ASA–	6 (21.7)	1.75 (0.71–4.28)	0.96 (0.39–2.38)	
CTA–/ASA+	41 (51.3)	4.12 (2.86–5.91)	2.55 (1.74–3.72)	
CTA–/ASA–	102 (12.5)	Reference	Reference	
Age 50–69 yrs				
CTA+/ASA+	26 (45.6)	2.87 (1.85–4.46)	1.71 (1.08–2.72)	0.68 (–0.30, 1.66)
CTA+/ASA–	3 (11.1)	0.70 (0.22–2.21)	0.42 (0.13–1.38)	
CTA–/ASA+	47 (44.8)	2.82 (1.97–4.03)	1.60 (1.06–2.43)	
CTA–/ASA–	83 (15.9)	Reference	Reference	
Age ≥70 yrs				
CTA+/ASA+	9 (40.9)	2.49 (1.17–5.31)	2.02 (0.93–4.35)	–0.46 (–2.56, 1.64)
CTA+/ASA–	3 (25.0)	1.52 (0.46–5.02)	1.08 (0.31–3.70)	
CTA–/ASA+	29 (47.5)	2.89 (1.70–4.91)	2.40 (1.40–4.20)	
CTA–/ASA–	26 (16.5)	Reference	Reference	

* Estimated from Cox regression assuming equal time at risk.

† Overall model adjusted for age; ISS; diagnosis of myocardial infarction, congestive heart failure, or peripheral vascular disease; PRBC units transfused within the first 24 hours of admission; and INR ≥ 1.2 at admission.

‡ Based on adjusted models.

assessed in the Cervical Artery Dissection in Stroke Study (CADISS).²⁴ However, TCVI differs from spontaneous dissection in several ways: 1) most TCVI lesions are initially asymptomatic and discovered by screening imaging; 2) high-energy TCVI is likely to be biologically distinct from spontaneous dissections, which are frequently related to underlying connective tissue abnormalities;^{3,39} 3) the majority of patients with blunt trauma experience a hypercoagulable state^{10,20,29} soon after injury³⁴ that coincides with the time course of ischemic stroke with TCVI; and 4) patients with TCVI often have other traumatic injuries, making their management more complex than in patients with spontaneous dissection. Therefore, TCVI should be considered to be a distinct clinical setting for evaluating potential hemorrhagic risks of antiplatelet therapy.

The mechanism of most ischemic strokes due to TCVI is thromboembolic.^{16,28,36} Although a survey of clinicians found that their preferences are divided between anticoagulation and antiplatelet agents,¹⁹ and the most widely reported antithrombotic strategy is systemic anticoagulation,¹⁴ hemorrhagic complication rates of 8%–16% have been reported with anticoagulation in patients with blunt

trauma,^{8,11,26,27} and approximately one-third of patients with TCVI are not candidates for systemic anticoagulation due to concomitant injuries.^{37,41} Antiplatelet agents are a popular alternative to anticoagulation in this setting. Two retrospective studies found lower rates of bleeding complications with antiplatelet agents when compared to anticoagulation.^{9,41} Furthermore, antiplatelet agents carry a theoretical advantage in that the mechanism of stroke in TCVI is usually artery-to-artery embolism, and antiplatelet agents may be more appropriate in the high-flow, platelet-rich arterial environment. Indeed, platelets are the dominant contributors to hypercoagulability after trauma,¹⁷ and a significant percentage of patients with trauma develop thrombocytosis during the hospitalization,^{33,40} so antiplatelet therapy seems to be a logical choice for antithrombotic therapy.

Our findings are consistent with studies of the use of antiplatelet agents for the primary prevention of stroke in other clinical settings. For example, treatment with aspirin for the primary prevention of stroke in the general population is associated with an increased risk of hemorrhagic complications, such as gastrointestinal bleeding and hem-

orrhagic stroke.^{2,6,32} In fact, the use of aspirin for primary stroke prevention in the general population does not appear to have a net benefit in terms of stroke risk reduction because of hemorrhagic complications.²⁵ Primary stroke prevention with aspirin does appear to provide net benefit in specific subgroups, such as women with diabetes and elevated cardiovascular risk and some patients with chronic kidney disease.²⁵

The full antiplatelet effect of aspirin occurs within 30 minutes of ingestion, persists for the platelet lifespan,²³ and is dose dependent. Lower doses of aspirin (e.g., 81 mg) inhibit prostaglandin H-synthase 1 (COX-1), whereas higher doses (e.g., 325 mg) inhibit both COX-1 and prostaglandin H-synthase 2 (COX-2).³⁰ Low-dose aspirin seems to be effective for the primary prevention of stroke in some populations, such as women with diabetes,²⁵ but is insufficient in other populations, such as patients with atrial fibrillation without anticoagulation.¹ It has been the practice at our center to treat all patients with evidence of asymptomatic TCVI with 325 mg aspirin daily; this dose is within the American Heart Association (AHA) guidelines for dosing of aspirin for secondary prevention of stroke (50–325 mg daily).²¹ However, an analysis of bleeding complications in 31 randomized trials comparing different doses of aspirin found a higher total risk of bleeding with high-dose (> 200 mg) compared to low-dose (< 100 mg) aspirin.³⁵ Thus, it is possible that low-dose aspirin may carry a lower risk of transfusion in patients with TCVI, although it is not clear whether low-dose aspirin would also offer equivalent protection against thromboembolic stroke.

Our analysis was limited to transfusions > 24 hours after admission. The majority of transfusions in trauma patients are given within 24 hours,^{4,12,42} and any effect of a daily regimen of aspirin, which is begun in most patients with CT angiographic evidence of TCVI within the first day of admission, is likely to be apparent after this initial period.

Differing risks of transfusion with different age groups are likely due to a complex combination of factors. Patterns of injury vary between age groups, even when controlling for ISS; whereas motor vehicle crashes are more common among younger patients (with a higher chance of multiple injuries), falls are more common among older patients (with a relatively lower chance of multiple injuries).^{7,13} In addition, the clinical threshold for transfusion is also likely to differ between age groups; for instance, older patients with trauma are more likely to have preexisting cardiopulmonary disease and may be less able to tolerate blood loss.

Limitations of the Study

This study is based on a large single-center database of patients who present with trauma and on hospital radiology records. As with any large database, it is possible that some data were erroneous (e.g., some patients recorded as receiving aspirin may not have received it). In addition, comorbidity data were based on ICD codes found within billing data. A main limitation to the use of data in the billing system is the lack of information regarding whether the diagnosis was present on admission; thus, it is possible that some diagnoses occurred during the patient's stay. Moreover, the definition of some of the comorbidities

included codes for the injuries the patient sustained (e.g., cerebrovascular disease includes codes for subarachnoid and intracerebral hemorrhage and infarctions due to occlusions); without knowledge of “present on admission” status, though, it is impossible to determine which codes represent the history of these conditions or a condition associated with the patient's injury-related hospital encounter. However, there is no reason to believe the misclassification to be related to the CTA/ASA study group, and thus any bias will be nondifferential and will result in attenuation of associations toward the null (i.e., resulting in a more conservative estimate).

Another limitation of note—treatment with aspirin may not have been uniform among all patients classified as receiving aspirin. In addition, 2%–5% of the patients in each of the 4 categories in Table 1 were not listed as having a blunt trauma mechanism even though these patients were classified as having blunt trauma on admission. Thus, it is possible that some of the patients in this study actually had penetrating trauma, which would be expected to carry a higher risk of bleeding complications; however, with a similar proportion across the exposure groups, we expect any bias to be nondifferential and to cause reported associations to be underestimates of the true association. Finally, it is possible that patients had been exposed to aspirin or other antiplatelet agents prior to the occurrence of the injury and subsequent hospital admission. Although we were not able to collect data on prehospital exposure to antiplatelet agents, by stratifying by age we were able to minimize any bias resulting from lack of prehospital data.

Conclusions

Treatment with aspirin for the prevention of stroke in patients with initially asymptomatic TCVI carries a significantly increased risk of PRBC transfusion; however, this increased risk is no more than expected from the summed excess risks due to TCVI alone and aspirin use alone. Future studies are needed to determine if this risk is offset by a reduced risk of ischemic stroke.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: all authors. Acquisition of data: Griffin, Falatko, Strickland. Analysis and interpretation of data: all authors. Drafting the article: Griffin, Falatko, Aslibekyan. Critically revising the article: Harrigan, Aslibekyan. Reviewed submitted version of manuscript: Griffin, Falatko, Strickland. Approved the final version of the manuscript on behalf of all authors: Harrigan. Statistical analysis: Griffin, Aslibekyan. Administrative/technical/material support: Harrigan, Falatko. Study supervision: Harrigan.

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Supplemental Information

Previous Presentations

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