Time to stroke: A Western Trauma Association multicenter study of blunt cerebrovascular injuries

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BACKGROUND: Screening for blunt cerebrovascular injuries (BCVIs) in asymptomatic high-risk patients has become routine. To date, the length of this asymptomatic period has not been defined. Determining the time to stroke could impact therapy including earlier initiation of antithrombotics in multiply injured patients. The purpose of this study was to determine the time to stroke in patients with a BCVI-related stroke. We hypothesized that the majority of patients suffer stroke between 24 hours and 72 hours after injury.

METHODS: Patients with a BCVI-related stroke from January 2007 to January 2017 from 37 trauma centers were reviewed.

RESULTS: During the 10-year study, 492 patients had a BCVI-related stroke; the majority were men (61%), with a median age of 39 years and ISS of 29. Stroke was present at admission in 182 patients (37%) and occurred during an Interventional Radiology procedure in six patients. In the remaining 304 patients, stroke was identified a median of 48 hours after admission: 53 hours in the 144 patients identified by neurologic symptoms and 42 hours in the 160 patients without a neurologic examination and an incidental stroke identified on imaging. Of those patients with neurologic symptoms, 88 (61%) had a stroke within 72 hours, whereas 56 had a stroke after 72 hours; there was a sequential decline in stroke occurrence over the first week. Of the 304 patients who had a stroke after admission, 64 patients (22%) were being treated with antithrombotics when the stroke occurred.

CONCLUSIONS: The majority of patients suffer BCVI-related stroke in the first 72 hours after injury. Time to stroke can help inform clinicians about initiation of treatment in the multiply injured patient. (*J Trauma Acute Care Surg.* 2018;85: 858–866. Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Prognostic/Epidemiologic, level III.

KEY WORDS: Blunt cerebrovascular injuries; carotid artery injury; cerebrovascular accident; stroke; vertebral artery injury.

Blunt cerebrovascular injuries (BCVIs), identified in 1% to 3% of blunt trauma patients typically following a hyperextension injury, result in devastating stroke in 20% of patients who are not treated with antithrombotic therapy.[1] Screening to identify BCVI during a patient's asymptomatic period has been pursued to identify these injuries early and institute antithrombotic treatment.[2–5] Despite interest in this injury for over three decades, the length of this asymptomatic period has not been

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defined. What percentage of patients who suffer a stroke following BCVI do so in the first hours, first days, or first week following injury? With the recognition that antithrombotic treatment markedly reduces the stroke rate,[6–8] quantification of this latent period is critical. Determining the time to stroke could impact optimal timing for initiation of antithrombotic treatment in the multiply injured patient. Understanding the timing of BCVI-related stroke might also influence the willingness to initiate antithrombotics in patients with potential or borderline contraindications such as traumatic brain injury (TBI), high-grade solid organ injuries (SOIs), or complex pelvic fractures. The purpose of the current study was to determine the time to stroke in patients with a BCVI who develop a stroke. We hypothesized the majority of patients suffer BCVI-related stroke 24 hours to 72 hours after injury.

METHODS

Data of patients with a BCVI-related stroke during their index hospitalization between January 2007 and January 2017 were compiled and retrospectively reviewed from 37 trauma centers. Patients at each site were identified via the trauma registry at the respective trauma center. Patient demographics were recorded, and additional patient variables analyzed included: time to stroke (hours after admission), method of stroke identification, time to antithrombotic treatment, type of antithrombotic treatment, and neurologic outcome following treatment. The method of stroke identification was divided into two groups: (1) neurologic symptoms identified on clinical examination that subsequently triggered confirmatory radiographic imaging using computed tomography (CT) scanning or magnetic resonance imaging or (2) radiographic imaging performed for another indication that identified a stroke in patients without a neurologic examination (e.g., those with severe TBI, intubated/sedated patients). For patients in the latter group, time to identification of stroke on imaging was recorded; this implies the admit head CT scan was negative. Appropriate antithrombotic treatment was defined as antiplatelet agents (aspirin or clopidogrel) or systemic heparin with a partial thromboplastin level of at least 40 seconds to 50 seconds. Patients who were subtherapeutic on their heparin infusion were considered to be not adequately treated. Patients' injuries were classified according to the Denver grading scale[9] (Table 1). Exclusion criteria included patients with common carotid artery injuries (CAIs) or injuries due to a penetrating mechanism. Imaging modality used to diagnose the BCVI was not recorded. Statistical analysis was performed using SAS for Windows (SAS Institute, Cary, NC); Wilcoxon two-sample test was used to test significance. This study was approved by each participating center's institutional review board.

RESULTS

During the 10-year period, 492 patients suffered a BCVI-related stroke during their initial hospitalization; the majority were men (61%), with a median age of 39 years (range, 2–89 years) and an ISS of 29 (range, 4–75). The mechanisms of injury included motor vehicle collisions in 248 patients (50%), fall in 66 patients (13%), motorcycle collisions in 50 patients (10%), autopedestrian accidents in 44 patients (9%), assault in 23 patients (5%), bicycle/all-terrain vehicle in 18 patients (4%), and other mechanisms in 43 patients (9%).

Stroke at Admission

Stroke was evident at the time of initial evaluation in 182 patients (37%) (Fig. 1). Of these, 118 patients had CAIs, 61 patients had vertebral artery injuries (VAIs), and three patients had a combination of injuries. Of the patients with CAI, there were 14 Grade I, 31 Grade II, 16 Grade III, 50 Grade IV, and 6 Grade V injuries, and in 4 patients, the injury was not graded. Among the 61 patients with VAI, there were 6 Grade I, 21 Grade II, 3 Grade III, 32 Grade IV, and 2 Grade V injuries. Stroke occurred during an interventional radiology procedure for BCVI management (stent deployment, intra-arterial lytics, or embolization) in six patients. All procedure-related strokes occurred in the first 6 years of the study and included both CAI and VAI, Grades I to III.

Stroke Following Admission

In 304 patients, there was no evidence of stroke at the time of initial evaluation. In these patients the diagnosis of a stroke was made at a median of 48 hours (range, 1.3–1,046 hours) after admission. The diagnosis of a stroke was made at a median of 54 hours (range, 3.5–394 hours) in the 144 patients with new neurologic symptoms and 42 hours (range, 1.3–1,046 hours) in the 160 patients without a neurologic exam/stroke identified on imaging. Type and grade of BCVI are depicted in Table 2. Of those patients with neurologic symptoms, 88 (61%) suffered a stroke within 72 hours, whereas 56 developed a stroke after 72 hours. The time intervals to stroke are noted in Figures 2 and 3. Time interval to stroke identification based on imaging in those patients without a neurologic examination is depicted in Figure 4.

Of the 304 patients, the majority (220 [72%]) of patients who developed a stroke were not receiving antithrombotic treatment at the time of diagnosis. An additional 10 patients were on systemic heparin infusion, but were subtherapeutic, and in 10 patients, the timing of the stroke in relation to the start of their antithrombotic treatment was unclear (Fig. 1). Median time to stroke in the 220 patients not receiving antithrombotics was 38 hours. Stated contraindications to treatment included TBI (113 patients), cervical spine injuries (11 patients), TBI and SOI or pelvic injury (11 patients), pelvic injury (6 patients), SOI (5 patients), lower extremity traumatic amputation/extremity degloving injuries (5 patients), pelvic injury and SOI (2 patients), and shock (1 patient). The remaining 66 patients who were not on treatment did not have a recorded contraindication to antithrombotic treatment. In the 92 patients who had symptoms heralding

TABLE 1. Denver Grading Scale for BCVI

Grade I: irregularity of the vessel wall or a dissection/intramural hematoma with <25% luminal stenosis
Grade II: intraluminal thrombus or raised intimal flap is visualized, or dissection/intramural hematoma with 25% or more luminal narrowing
Grade III: pseudoaneurysm
Grade IV: vessel occlusion
Grade V: vessel transection/extravasation/carotid-cavernous fistula

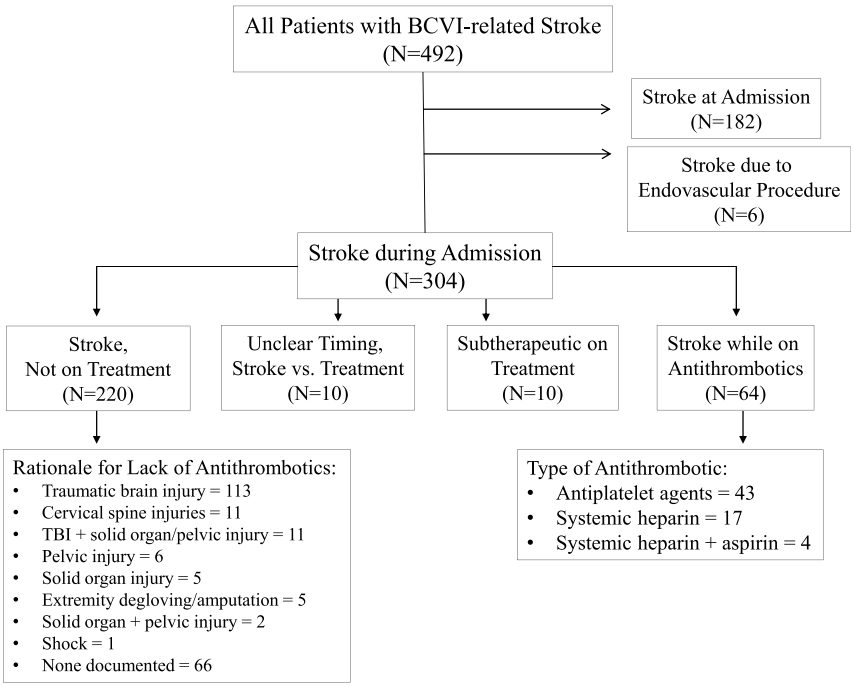

Figure 1. Delineation of patients with BCVI-related stroke.

their BCVI-related stroke and were not being treated for their BCVI, median time to stroke was 96 hours for Grade I injuries (16 patients), 31 hours for Grade II injuries (20 patients), 38 hours for Grade III injuries (15 patients), 38 hours for Grade IV injuries (41 patients).

Of the 304 patients who had a stroke after admission, 64 patients (22%) were being treated with antithrombotics when the stroke occurred. Of these, 17 patients (27%) were on systemic heparin with a wide variety of injury types (12 CAIs: Grade I in 7 patients, Grade II in 3 patients, Grade III in 1 patient, and Grade IV in 1 patient; 5 VAIs: Grade I in 1 patient, Grade II in 2 patients, Grade IV in 1 patient, and unclear in 1 patient), 4 patients (6%) were on systemic heparin and antiplatelet agents (all CAIs, equally divided between Grades I and IV injuries), and 43 patients (67%) were on antiplatelet agents (20 CAIs: Grade I in 3 patients, Grade II in 6 patients, Grade III in 8 patients, and Grade IV in 3 patients; 23 VAIs: no Grade I injuries, Grade II in 8 patients, Grade III in 2 patients, and Grade IV in 13 patients). The 43 patients on antiplatelet agents included aspirin 325 mg (23 patients), aspirin 81 mg (12 patients), aspirin 300 mg (3 patients), clopidogrel 75 mg (2 patients), aspirin/clopidogrel (2 patients), and aspirin 100 mg (1 patient). The median time to stroke for all patients on antithrombotics was 81 hours. Time to stroke for patients on antithrombotic treatment was significantly longer than that for those patients not on treatment (81 vs. 38 hours; $p < 0.0001$). Comparing only those patients with neurologic symptoms signaling their stroke, median

TABLE 2. Type and Grade of BCVI in Patients Who Developed a Stroke Following Admission

Vessel Injured	Grade of Injury	Stroke Identified by Neurologic Symptoms (n = 144)	Stroke Identified by Imaging (n = 160)
CAI	I	16 (11%)	21 (13%)
	II	20 (14%)	35 (22%)
	III	23 (16%)	19 (12%)
	IV	26 (18%)	21 (13%)
	V	1	3 (2%)
	Unknown	0	1
VAI	I	8 (5%)	10 (6%)
	II	16 (11%)	19 (12%)
	III	5 (3%)	4 (3%)
	IV	28 (19%)	26 (16%)
	V	1	0
	Unknown	0	1

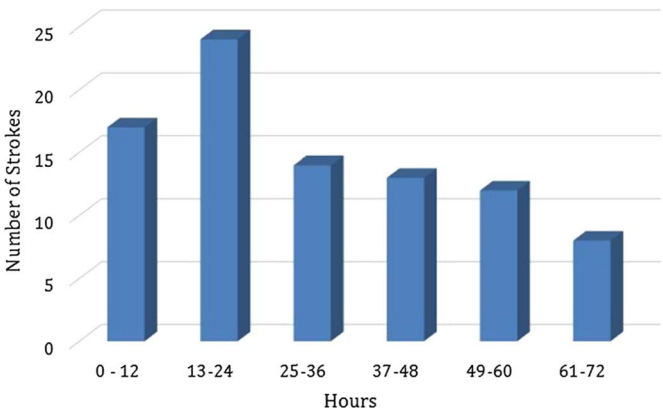

Figure 2. Time to stroke in patients with BCVI-related ischemia identified with neurologic symptoms within 72 hours (n = 88), categorized in 12-hour intervals following admission.

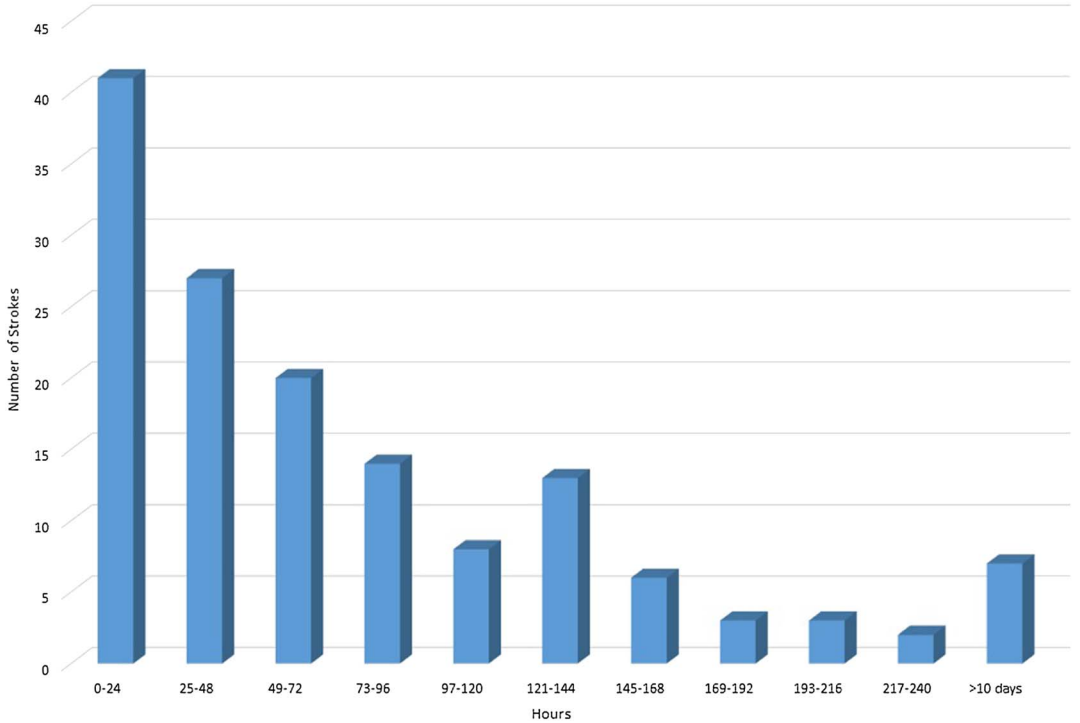

Figure 3. Time to stroke in all patients with BCVI-related ischemia identified with neurologic symptoms within 72 hours (n = 144), categorized in 24-hour intervals following admission.

time to stroke was significantly longer for those on treatment versus those not on treatment (84 vs. 42 hours; $p = 0.0004$).

Once a stroke was identified, the majority of patients were treated with antithrombotics as an inpatient (Table 3), with only 13 patients not receiving treatment and 30 patients not documented. Most patients receiving antithrombotic treatment have a reported improvement in their neurologic outcome. The mortality in the study population was high, with 155 patients (32%) dying. In 86 patients (55%), death was attributed to the BCVI-related stroke; in 8 patients (5%), it was a combination of the

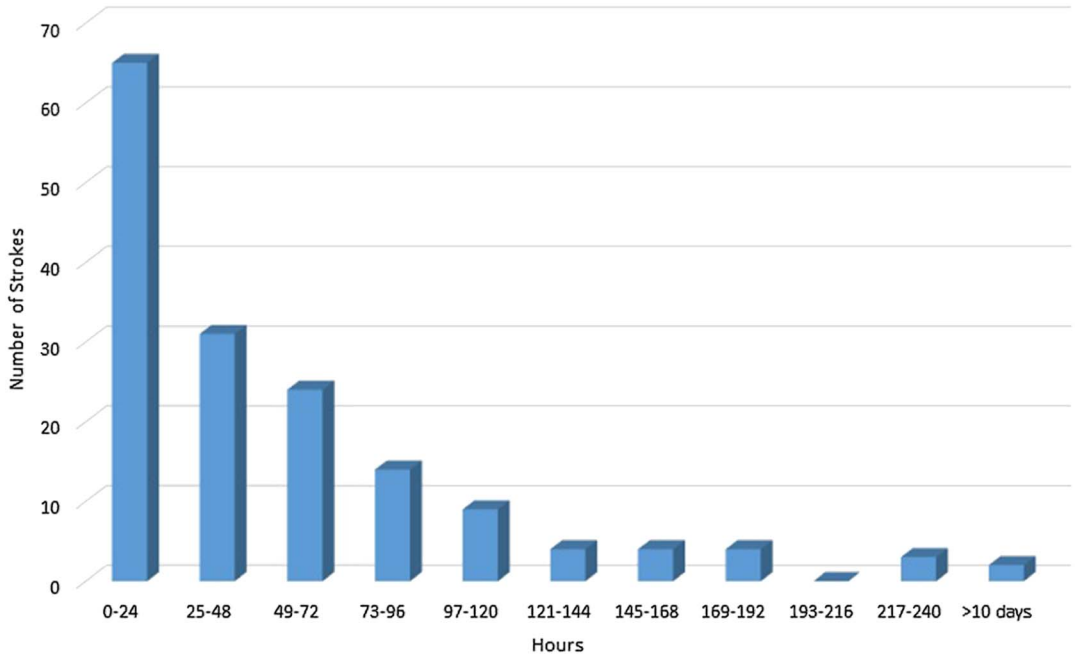

Figure 4. Time to identification of stroke on imaging in patients who were unevaluable (n = 160).

TABLE 3. Treatment Modalities Following BCVI-Related Stroke

Inpatient Treatment	Neurologic Improvement	No Neurologic Improvement	Neurologic Outcome Not Recorded
Systemic heparin (n = 108)	58	35	15
Aspirin (n = 89)	40	44	5
Aspirin/clopidogrel (n = 38)	23	14	1
Systemic heparin + aspirin (n = 22)	19	1	2
Lovenox (enoxaparin sodium) (n = 7)	4	3	0
Heparin + aspirin + clopidogrel (n = 5)	2	2	1
Heparin to Coumadin (warfarin) (n = 4)	3	0	1
Heparin to Lovenox (n = 4)	3	1	0
Aspirin + Coumadin (n = 4)	3	0	1
Aspirin + Lovenox (n = 3)	3	0	0
Heparin to aspirin (n = 2)	0	1	1
Clopidogrel (n = 2)	0	1	1
Heparin + Eliquis (apixaban) (n = 2)	2	0	0
Coumadin (n = 2)	0	2	0
Aspirin to Coumadin (n = 1)	0	1	0
Heparin + aspirin + argatroban (n = 1)	0	1	0
None (n = 13)	5	2	6
Total (n = 307)	165 (54%)	108 (35%)	34 (11%)

BCVI-related stroke and TBI; and in the remaining 61 patients (40%), death was from other causes.

DISCUSSION

For patients with BCVI who do not have neurologic symptoms at presentation, stroke occurs at a median of 48 hours following admission. Patients who suffer a BCVI-related stroke can be identified in 1 of 2 ways. Either they develop a neurologic symptom concerning for stroke that prompts CT imaging, or they are unevaluable (intubated, sedated, TBI, shock, etc.) and a stroke is identified on imaging, often in an incidental manner. While the latter group can have the time to imaging identification of stroke calculated (in this study, 42 hours for those 160 patients), this is not truly representative of the actual time to stroke for the patient, merely the identification of ischemia on CT or magnetic resonance imaging. These patients may have had a stroke present at admission but simply not identified on early imaging, as ischemia may not be evident on early CT imaging. Hence, using this group of BCVI-related stroke patients to determine timing of stroke is unreliable. An analysis of those patients with neurologic symptoms heralding their BCVI-related stroke is the best source of time-to-stroke determination. In this study, that subgroup was 144 patients, and they had a median time to stroke of 54 hours. The majority (61%) developed their strokes within 72 hours, consistent with our hypothesis. More interesting, however, is the trend in time to stroke for the patients in this subgroup who manifested neurologic symptoms; the peak incidence of stroke occurs within the first 24 hours, specifically between 13 hours and 24 hours, and then serially decreases out to day 5. There was a small spike in the incidence of stroke on day 6, but then the serial decrease extends out to day 10.

To our knowledge, this is the first study to determine the precise time frame for stroke due to BCVI. The general timing of stroke following these injuries has been postulated in the literature. Early in the investigation and identification of these injuries, some argued that BCVI-related strokes were unavoidable because of their early onset after traumatic injury.[10,11] Subsequently, several groups recognized that although the asymptomatic period of BCVI could range from hours to years, the majority of patients appeared to become symptomatic between 10 hours and 72 hours.[2,12–15] The present study confirms the gestalt of these prior publications and expands on the precise time frame of BCVI-related stroke.

With approximately 60% of BCVI-related strokes occurring within 72 hours of admission, and greater than 85% by day 7, the initiation of treatment is critical as antithrombotics almost universally prevent stroke.[2,8] However, most patients with BCVI are multiply injured, and historically 25% to 40% of such patients were considered to have a contraindication to treatment.[16] In this study, more than 75% of patients who had a stroke were not being treated with antithrombotics. There is an ongoing concern that antithrombotic treatment for BCVI may increase the risk of bleeding in patients with TBI, cervical spine injuries, SOIs, or complex pelvic fractures. Patients with severe TBI, a very high-risk population for BCVI,[17] are particularly problematic.

The question of early antithrombotic treatment in some of these high-risk individuals has been addressed by several groups.[7,18,19] Although all suggest early initiation of antithrombotics is reasonable in patients with TBI, SOI, and cervical spine injuries, specifics regarding treatment and outcome are understandably difficult to discern in these retrospective studies. The most recent publication from the Memphis group states early antithrombotic treatment in patients with concomitant TBI or SOI does not worsen these injuries.[18] However, the specific time to initiation of treatment is not reported, stating antithrombotics were "instituted in all patients as early as possible" and "SOI has not been considered a contraindication" to treatment. McNutt et al.[19] report a significantly longer time to treatment in multisystem trauma patients compared with those with isolated BCVI (62 vs. 30 hours). This underscores that there are some inherent management differences in these groups with regard to the initiation of antithrombotics. With equivalent stroke rates between the multiply injured group and the isolated BCVI group, and no recorded bleeding complications, however, the authors suggest early antithrombotics are safe. Finally, Callcut et al.[7] suggested the benefit of early antithrombotic treatment, and the significant reduction in stroke, outweighed the risks in patients with TBI and cervical spine injuries. In that study, only 62% of patients with TBI or cervical spine injuries received antithrombotic treatment at any point in their hospitalization; early treatment appears to correlate with treatment initiation on median hospital day 3, with 84% of patients started on treatment by day 7.

These three reports center on the essential question of the risk/benefit of antithrombotic therapy in BCVI patients. With the majority of patients in these three studies not started on antithrombotic treatment in the first 24 hours, or perhaps even in the first 3 days, these studies emphasize and reflect the tiered decision-making process in these multiply injured patients.

And although they provide evidence that antithrombotic treatment may be instituted in patients who are multiply injured with high-risk injuries, they also underscore the importance of individualized determination in these complex trauma patients. These decisions should be based on repeat CT scan imaging, need for operative intervention, and complexity of the TBI or spine injury. Individual factors such as recent craniotomy, early worsening of a hemorrhagic contusion on repeat CT scan at 6 hours, or placement of an external ventricular drain may justifiably delay antithrombotic treatment in a TBI patient. Similarly, ongoing damage control resuscitation for the patient in hemorrhagic shock will impact such decisions in patients with SOI or pelvic fractures. One of the purposes of the present study was to help inform this shared decision-making process between the neurosurgery, spine, and trauma teams regarding antithrombotic treatment for BCVI. By understanding the time-to-stroke risk in these patients, thoughtful management plans can be constructed and information shared with patients and family members.

When weighing individual factors in the risk/benefit analysis for treatment, the number of injured vessels and the grade of injury should be considered. For example, a patient with a Grade IV liver injury and an anterior posterior compression II pelvic fracture who has a right Grade III carotid injury, left Grade I vertebral injury, and a right Grade IV vertebral injury might have a different urgency for antithrombotic administration compared with the severe TBI with hemorrhagic contusions with a single Grade I CAI. Although the numbers in this study are relatively small, when stratifying patients by grade of injury, it appears that higher-grade injuries result in stroke sooner. As one progresses from a Grade I injury through to Grade IV injury, the median time to stroke drops from Grade I injuries to Grades II to IV injuries (96 vs. 38 hours). Early repeat imaging may play a role in antithrombotic treatment decisions in the multiply injured patient. With the recognition of early resolution/healing of Grade I injuries,[6] repeat CT angiogram at 24 hours to 72 hours may be warranted to determine if the injury persists and requires treatment if the patient has other injuries that increase the risk of bleeding with BCVI treatment. Conversely, high-grade injuries rarely resolve[6,20]; early repeat imaging is not warranted, and initiation of antithrombotics should incorporate the known risk of stroke by injury grade[1,9,15] and the patient's risk of bleeding from associated injuries. This, however, should not be construed as a suggestion not to treat Grade I injuries. As noted in this population, 37 patients with Grade I CAIs and 18 patients with Grade I VAIs suffered stroke.

The optimal choice of antithrombotic treatment remains controversial. Several reports have suggested that antiplatelet agents and systemic heparin have similar efficacy to prevent stroke following BCVI.[1,19,21] In this study, in patients who sustained stroke while hospitalized and on treatment, twice as many patients were on antiplatelet agents (17 vs. 43 patients). It is difficult to know how to interpret these findings. This study did not collect information on all patients with BCVI, so the actual percentage of patients treated with antiplatelet agents versus systemic heparin is unknown. However, there are multiple reports that detail the mechanisms and clinical implications of aspirin resistance.[22–24] Aside from noncompliance, issues attributed to aspirin resistance include low aspirin dosing (81 mg),[25] increased platelet turnover,[26] and drug interactions from nonsteroidal anti-inflammatory drugs.[27] Perhaps more concerning, however, is that patients may have dual-antiplatelet resistance, with clopidogrel resistance occurring in up to 40% of patients.[28] Identified high-risk groups for aspirin resistance include female sex, obesity, and diabetes.[22] Dose escalation (up to 500 mg) and increased frequency (twice rather than once daily) followed by point-of-care platelet assay have demonstrated tailored antiplatelet therapy may play a role in high-risk patients.[29] The majority of research on this topic is in the cardiology literature, specifically acute coronary syndromes and percutaneous coronary interventions; there have been no studies to date in the trauma population, so extrapolation to the injured patient may not be universal. However, these results should be further investigated and may offer a cautionary note. Conversely, 10 patients suffered a stroke while subtherapeutic on their heparin infusion, and 17 patients sustained a stroke while on therapeutic heparin, defined as a partial thromboplastin time of more than 40 seconds. Hence, a conundrum exists: should one utilize antiplatelet agents, which are arguably more "immediate" in their efficacy but may potentially have a higher failure rate, versus initiating systemic heparin, which may be more effective but only if therapeutic levels are reached rapidly? If aspirin is utilized for treatment of a BCVI, however, a dose of 325 mg is likely warranted.

Treatment of patients following their BCVI-related stroke also remains an area of investigation, with no fewer than 16 different inpatient treatments utilized in the current report. Although neurologic improvement was not, per se, a specific outcome variable in this study, there appears to be an association in neurologic improvement with poststroke treatment. Although the neurologic outcome was only grossly defined as "improved" or "not improved" without specific qualification, these findings echo the original reports from the 1990s, which support treatment for BCVI-related stroke.[12,30] Additionally, the impact of any associated TBI on neurologic recovery was not incorporated into the analysis. Future multicenter prospective studies are needed to assess the optimal treatment following stroke to achieve the best functional outcomes. Finally, this study underscores that mortality due to BCVI-related stroke remains significant. Overall mortality rate in this study population was 32%, with more than half of the deaths due to BCVI-related stroke.

This study has several limitations. Each center identified patients with BCVI-related stroke; this could have missed some BCVI-related strokes that either were attributed to the associated TBI or were not appropriately coded in the trauma registry. Screening criteria for BCVI and associated treatment were at the discretion of each trauma center. The total number of patients with BCVI and type and timing of treatment were not recorded; hence, efficacy of treatment cannot be fully evaluated. Carotid artery injuries and VAIs have different stroke risks and different clinical presentations when stroke occurs; we evaluated all patients with BCVI, focusing on time to stroke rather than stroke incidence or symptoms. For the 66 patients who did not have a recorded rationale for the contraindication to antithrombotic treatment, this may not have been well documented and is difficult to obtain in a retrospective data collection. This analysis focused on in-hospital stroke due to BCVI, and there is a finite percentage of strokes that develop following hospital discharge,[31] who would not have been captured in the current analysis. Although newer technologies such as transcranial Doppler monitoring for microemboli have been suggested in the role of

BCVI management,[32] this technique was not incorporated in our review; BCVI-related stroke was defined as neurologic symptoms and/or imaging-confirmed ischemia due to a BCVI. Finally, as is true of all retrospective studies, data collection may be limited by medical record and trauma registry resources.

In summary, this study delineates a clearer time frame to stroke for patients with BCVI. Utilizing this information along with the number, location, and grade of injuries permits a more complete evaluation of the risks and benefits of initiating antithrombotic treatment in the multiply injured patient. Additionally, with the majority of patients developing neurologic symptoms of ischemia from their BCVI within 72 hours, aggressive screening protocols and early antithrombotic treatment are supported.

AUTHORSHIP

C.C.B. was involved in study design, data collection/analysis/interpretation, and writing. J.J.S., C.D.B., M.K.M., J.M., J.P.S., M.A.C., M.B., J.K., M.B., J.K., M.C.S., P.R.B., S.J., D.J.H., L.H., D.M.S., R.C., C.W., J.S., V.A., J.D., J.P.V., C.V.R.B., A.C., T.L.Z., R.C., A.E.B., T.Z.M., A.K.M., J.P.H., K.L., M.W., H.B.A., A.M.W., J.K., K.I., S.M., Y.M.C., H.L.W., B.C., C.G.D., S.S., J.L.H., D.C.C., M.D.Z., M.D.R.-Z., B.C.M., E.J.R., P.U., C.R., E.T., S.G., T.J., J.M.H., K.L.L., N.K., B.C., A.F.K., S.R.T., B.Z., C.J.W., K.J.K., T.N., S.B.Z.E., K.A.P., C.E.D., K.K., F.B., T.S.D., J.M.G., and M.J.C. were involved in data collection and critical revision of the manuscript.

DISCLOSURE

The author declares no conflict of interest.

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EDITORIAL CRITIQUE

Screening for blunt cerebrovascular injuries has become widespread practice, based on the premise that the devastating sequelae of ischemic neurologic insult might be avoided by timely interventions prior to the onset of symptoms. There are no prospective randomized trials demonstrating a clear benefit of treatment in the asymptomatic patient, and there likely never will be given the ethical issues associated with randomized assignment to a placebo arm when the stakes are so high.Consequently, the uncertainty of benefit results in the need for individualized risk:benefit analysis- repeated as each parameter evolves. What is the grade of injury, and its attendant stroke risk? What are the associated injuries, and the risk of antithrombotic therapy? With each passing day, anticoagulation generally becomes safer- but stroke risk may become higher.In analyzing the time to stroke after BCVI, the WTA multicenter trials group has sought to bring more specificity to duration of the "window of opportunity" for preventive treatment. Previous studies reported x% of strokes within y hours of injury; now we have data broken down into 12-hour increments. In addition, this paper reinforces that as injury grade goes up, not only does stroke risk increase, but time to stroke goes down. Finally, this paper demonstrates again that grade I injuries have a real- albeit low- stroke risk. What can we do with this information? Patients with BCVI should be treated with antithrombotic therapy to prevent stroke. Most of the events are going to happen within 72 hours of presentation, so the usual contraindications to antithrombotics become relative. Discussions at the time of diagnosis should focus on when it will be safe to treat- and these discussions should be repeated at least every 24 hours.

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