CE 2.0 ANCC Contact Hours

Traumatic Injury May Be a Predisposing Factor for Cerebrovascular Accident

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ABSTRACT

The purpose of the study was to assess whether trauma may be an independent risk factor for stroke. Evidence has shown that trauma patients experience a hypercoagulable state postinjury, increasing the risk of thrombotic events. A case-controlled, retrospective analysis was performed on admitted trauma patients over a 2-year period. Results revealed that trauma patients are 1.6 times more likely to have a cerebrovascular accident (CVA) during their hospital admission, when compared with nontrauma patients with similar CVA risk factors. Several statistically significant differences between the groups were identified. On the basis of these results, trauma appears to be an independent, nonmodifiable risk factor for CVA.

Key Words

Cerebrovascular accident, Hypercoagulable state, Trauma

Stroke is the third leading cause of death in America today, with 795,000 strokes per year and 610,000 of these being new strokes. Each year, approximately 137,000 deaths occur and 266,000 persons suffer permanent disabilities due to new or recurrent stroke.[1] The average health care expenditure after stroke is $140,000, with average initial hospitalization charges of $33,600. Total cost to the American health care system ranges from 40 billion to 70 billion dollars per year.[1] These numbers indicate that stroke is a significant burden on our health care system. Despite advances in the treatment of acute stroke as well as rehabilitation of survivors of stroke, proper preventative strategies of the modifiable risk factors provide the ultimate patient and public health benefit.

Patients suffering from acute traumatic injury have been shown to experience a prothrombotic state.[2-4] It is well described in the literature that these patients are disproportionally at risk for venous thromboembolic events, such as deep venous thrombosis (DVT) and pulmonary embolism (PE).[5,6,7] The timing and incidence of the hypercoagulable state is ill defined, especially when considering a large and diverse group of patients, such as the trauma population. The prothrombotic state is only diagnosed after an event such as a DVT or a PE has occurred. Emerging literature focuses on better identifying at-risk patients, as well as screening and treatment of these patients. What role the prothrombotic state plays in causing acute cerebrovascular accidents (CVAs) in the trauma population is poorly defined. Well-described risk factors for stroke in the general medical population exist; these modifiable risk factors include hypertension (HTN), diabetes mellitus, atrial fibrillation (Afib), tobacco use, cerebrovascular disease, dyslipidemia, physical activity, and obesity. Nonmodifiable risk factors include age, race/ethnicity, and predisposing genetic factors. Other, less well-described risk factors for stroke also include illness, infection, and inflammatory states.[1,8]

Stroke-specific risk factors for traumatic injury include cerebrovascular injury, maxillofacial injuries, cervical spinal injuries, and traumatic brain injury.[9-15] Whether traumatic injury is in itself a risk factor for stroke and whether that risk is modifiable through therapeutic methods after trauma are unknown. This study was designed to evaluate whether trauma is, within itself, an independent risk factor for stroke.

METHODS

A case-controlled, retrospective analysis of all trauma admissions from 2008 to 2010 was performed using the University of Louisville Hospital's trauma registry. A total of 7633 patients were evaluated, with 64 patients having suffered a CVA. These patients were identified, using various mechanisms. A combination of initial and subsequently changing neurologic examinations, brain

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TABLE 1 Demographics of Trauma Patients With CVA Versus Matched Trauma Control Group[a]

	n	ISS	Age, y	HTN	Afib	DM	Tobacco Use	Mortality Rate	SNF Placement
CVA	41	18 ± 10	51 ± 24	21 (51)	3 (7)	11 (27)	24 (58)	9 (22)	26 (81)
No CVA	120	18 ± 4	32 ± 26	27 (23)	2 (2)	11 (9)	44 (37)	8 (7)	34 (28)
P		NS	<.001	<.002	<.1	<.007	<.02	<.009	<.0001

Abbreviations: Afib, atrial fibrillation; CVA, cerebrovascular accident; DM, diabetes mellitus; HTN, hypertension; ISS, injury severity score; NS, not significant; SD, standard deviation; SNF, skilled nursing facility.

[a]*Values are given as mean ± SD or n (%).*

computed tomographic findings, brain magnetic resonance imaging findings, and subsequent cerebral angiography or computed tomography angiography was used. Injury-related CVAs (eg, CVA in the presence of significant brain injury of blunt cerebrovascular injury) were excluded. A control group of 120 trauma patients, matched for injury severity score and mechanism of injury, was used for comparison. Known modifiable risk factors such as history of HTN, Afib, diabetes, and tobacco use were assessed. Nonmodifiable risk factors, including age, mechanism of injury, presence of associated injuries, presence of vascular injury, and presence of patent foramen ovale, or other cardiac defect, were noted. All patients in this study were started on thromboembolic prophylaxis with either subcutaneous enoxaparin (30 mg twice daily or 40 mg twice daily for those weighing >100 kg) or subcutaneous low-molecular-weight heparin when associated injuries allowed. It must be taken into account that prophylaxis was occasionally held for periods not exceeding 24 hours because of operative interventions. Prophylaxis was continued for the duration of the patient hospital stay. Timing of chemoprophylaxis from admission to CVA was not evaluated because of wide variability. Prophylaxis was started as soon as injury would allow; if there was no contraindication, it was started on postinjury day 1. Univariate and multivariate analyses were performed on these populations.

A second case-matched control group of 14 121 medical and surgical patients without traumatic injury and diagnosed with a CVA during admission were obtained from the hospital database over the same period of time. Patients who were admitted with a primary diagnosis of CVA were excluded. This group was controlled for known risk factors of CVA identified in the prior comparison (age, HTN, diabetes mellitus, Afib, and tobacco use) and compared with the study population to assess the risk of trauma as an independent risk factor for CVA. Univariate and multivariate analysis were performed.

RESULTS

After admission for trauma, a total of 64 CVAs were identified in the patient population studied, making the overall rate of CVA 0.8%. Of this group of trauma patients, 23 injury-related CVAs were found, leaving 41 patients with noninjury-related CVA. Compared with a control group of 120 trauma patients matched for injury severity score and mechanism of injury, several significant differences were found (Table 1). The 41 trauma patients with CVA were older (standard deviation of age, 51 ± 24 vs 32 ± 26; $P \leq .001$) than the matched trauma control group of 120 patients. Chronic medical illnesses were more common in the trauma-related CVA group as well. A preexisting diagnosis of HTN in the trauma-related CVA group occurred in 21 (51%), compared to 27 (23%), $P \leq .002$, in the trauma control group. Diabetes was also more common in the CVA group, 11 (27%) versus 11 (9%), $P \leq .007$. Tobacco abuse was more common in the trauma-related CVA group (58% vs 37%, $P \leq .02$), and mortality rate was higher as well (22% vs 7%, $P \leq .009$). No difference was found in presence of Afib (7% vs 2%, $P < .1$). A higher rate of extended care facility placement was required in the trauma-related CVA group (81% vs 28%, $P \leq .0001$).

When compared with a second control group of 14,121 medical and surgical patients, obtained from a hospital database over the same period of time, trauma patients were 1.6 times more likely to develop CVA during admission than medical/surgical patients, given the same number of previously identified CVA risk factors ($P = .024$) (Table 2). Furthermore, on logistical regression, trauma was the only significant risk factor for CVA between the 2 groups. The trauma patients tended to be younger and, on follow-up, had higher 6-month post-CVA functional assessment than medical/surgical patients who suffered nontrauma-related CVA.

DISCUSSION

A stroke is a serious, life-threatening, and often fatal event in a patient's life. Survivors of stroke may have severe functional impairment for the remainder of their lives. Risk factors after trauma for CVA have been previously described and include blunt carotid artery injury (intimal dissection, pseudoaneurysm, thrombosis, cavernous fistula, and transection), cervical spine injury, traumatic brain injury, and vertebral artery injury. Much has been

TABLE 2 Rate of CVA in Trauma Patients Versus Medical/Surgical Patients From 2008 to 2010

Patient Population	n	No. of Noninjury CVA	Odds Ratio	*P*
Trauma	7633	41	1:1.6	.024
Medical/Surgical	14,121	46		

Abbreviation: CVA, cerebrovascular accident.

written over the past 30 years concerning the role these injuries play in creating thromboses in the arterial supply to the brain, resulting in cerebral anoxia. The purpose of this study was to determine whether there is another population of trauma patients without injury-related CVA who subsequently developed CVA. This study did identify 23 patients who suffered CVA, with previously described injury patterns, for an incidence of 0.3%, which compares to reported rates from Biffl et al[9] in Colorado and Fabian et al[10] in Memphis, as well as reported rates from Cincinnati[16] and Miami.[15] However, 41 CVA events occurred in patients without these reported injury patterns, with an overall incidence of 0.5%, making them more common than injury-related CVA in this study.

This subset of 41 patients, in whom CVA developed after admission, differed from both comparison groups (matched trauma patients and medical/surgical patients) in several significant ways. A higher incidence of tobacco use, HTN, and diabetes was present, when comparing the noninjury-related CVA group with matched trauma controls. These patients were also significantly older than the trauma control group. This comparison validates previously published studies assessing the impact of these risk factors on the general population's CVA risk. Furthermore, it identifies a subgroup of patients that perhaps should have more prophylaxis at baseline than the typical trauma patient.

Another concerning finding is that patients suffering CVA after trauma were younger than medical/surgical patients admitted over the same period of time and required placement at extended care facilities more often than those medical/surgical patients with similar injuries and no CVA. This subpopulation represents a potential burden to society in terms of both economic impact as well as loss of productive years of work. The trauma patients suffering CVA lost more productive years than the medical/surgical group. They also tended to be more debilitated after traumatic injury than injury severity score– and mechanism of injury–matched trauma peers. A glimmer of hope is identified in the finding that trauma patients had a better functional recovery at 6 months than the medical/surgical group; however, the reason for this is unclear, as is the extent of return to preinjury function. It could be postulated that their outcome after rehabilitation was better because of their younger age at the time of CVA, as multiple trauma-related studies as well as CVA-related studies have shown this to be the case. Further research into this area might help shed light on these factors.

Trauma appeared to be an independent risk factor for CVA in this study. No blunt cerebrovascular injury was seen in this group, none had concomitant traumatic brain injury, and none suffered cervical spinal injuries, all which can be associated with stroke after trauma. Despite these findings, this group had a significant increase in risk of stroke, given the same known risk factors. The reason for this increase is still unknown, but certainly changes in the coagulation and inflammatory system could be the reason. Coagulopathy has long been a major area of interest in trauma, with both increased and decreased clotting ability having the potential to cause increased morbidity and mortality rates.[17,18] Despite our assumption of trauma patients typically suffering a decrease in clotting ability because of consumptive coagulopathy, trauma patients have been shown to experience a hypercoagulable state after injury as well. The complex interrelationships within the hemostatic mechanism are disrupted early after injury, and widely used laboratory measures such as the standard prothrombin time, partial thromboplastin time, and international normalization ratio may not give an accurate account of this hypercoagulable state at the cellular level.[19] These tests also do not assess platelet function. Some institutions[3,4,20] have begun using thromboelastography to determine clot strength and loss of clot integrity and assess the balance between clot formation and clot lysis. Thromboelastography is not a new technology but has been gaining broader application in the trauma population, as the test is inexpensive, rapid, and can be tracked over time.[20,21] All patients are continually clotting and lysing clots, a process critically important after traumatic injury. However, early detection and subsequent intervention when this process becomes pathologic, before the development of CVA, DVT, PE, etc, continues to be in question.[22]

The assumption that DVT prophylaxis will protect patients from CVA appears to be flawed, particularly in these patients.[23] All 41 patients in the trauma group received both mechanical and chemoprophylaxis for prevention of venous thromboembolism. Sequential compression devices were used on all patients, and enoxaparin injections were used twice daily as prophylaxis, starting as soon as

associated injuries would allow. Dosing adjustment for enoxaparin or change to low-molecular-weight heparin was used for patients either in renal failure or morbid obesity. These practices are standard measures for patients admitted after trauma,[24,25] and the 41 patients with noninjury-related CVA did not differ from controls in that regard. These measures have been shown to decrease the rate of DVT and subsequent PE in trauma patients.[26] But this standardized regimen of thromboembolic prophylaxis may not adequately address patients in a hypercoagulable state,[27] especially those in whom known risk factors for stroke are present.

It is not difficult to hypothesize a rationale for these findings, given the 2 aforementioned scenarios. For example, a middle-aged man with a history of HTN and diabetes mellitus, as well as a significant smoking history, already has endothelial damage and atherosclerosis putting him at increased risk for CVA at baseline. He was injured then in a motor vehicle collision and now has multiple small areas of endothelial damage from the impact, activation of the coagulation and inflammatory cascades, leading to microthrombi formation. The patient is placed on standard DVT prophylaxis, but platelet activation and clot strength remain unaffected, so the patient has increased risk of stroke despite standard DVT prophylaxis. This "two-hit" hypothesis of trauma-related CVA is conjecture and not totally modifiable to the treating physician. However, it should give pause to ask whether the patient is an appropriate candidate for antiplatelet agents if these risk factors are present.

Definitive causality of the CVA observed in the trauma-related population cannot be determined from the available data and is a limitation of this retrospective study. The patients in this study were not evaluated for the presence of either acquired or inherited coagulation pathology. Select patients did have thromboembolic prophylaxis withheld on occasion, either because of risk of bleeding from their other injuries or planned surgical procedures. Again, this was not different from those in the control group. However, the effects of this treatment decision cannot be assessed and might have had an impact on the incidence of CVA. It is possible that the technique of the radiologic workup could play a factor in missing small injuries on admission. The protocol at the University of Louisville Hospital includes a noncontrast computed tomographic scan of the head and cervical spine, followed by intravenous contrast administration and computed tomographic scanning of the chest, abdomen, and pelvis. Small carotid or vertebral artery dissections or other vascular injury could be missed without the use of contrast. However, none of the patients in the noninjury-related stroke group were found to have identifiable injuries on computed tomography angiography or 4-vessel arteriography of the neck after suffering a CVA. Furthermore, none of the 41 patients demonstrated injuries consistent with possible cerebrovascular injury, making missed injuries in this population much less likely.

CONCLUSION

Trauma appears to be an independent, nonmodifiable risk factor for CVA. The incidence of noninjury-related stroke was higher in this study than injury-related stroke. The patients who suffered strokes after noninjury-related trauma did have a significantly higher rate of modifiable risk factors. They also had a higher mortality rate than a matched trauma control group and required placement in skilled nursing facilities at a higher rate. Trauma patients also had almost twice the incidence of CVA than medical/surgical patients hospitalized at the same time. Better and more widespread screening methods for coagulation abnormalities should be considered, including thromboelastography, in determining hypercoagulability after trauma. Finally, better risk stratification of patients with known risk factors and reevaluation of the efficacy of current antithrombotic regimens are necessary.

This is a prognostic study with level-2 evidence based on a retrospective case-control cohort.

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