Impact of Continuous Evaluation of Technology and Therapy: 30 Years of Research Reduces Stoke and Mortality from Blunt Cerebrovascular Injury

Charles P Shahan, MD, MS, Martin A Croce, MD, FACS, Timothy C Fabian, MD, FACS, Louis J Magnotti, MD, FACS

BACKGROUND: Blunt cerebrovascular injury (BCVI) was underdiagnosed until the 1990s when blunt carotid injuries were found to be more common than historically described. Technological advancements and regionalization of trauma care have resulted in increased screening and improved diagnosis of BCVI. The aim of this study was to demonstrate that systematic evaluation of the screening and diagnosis of BCVI, combined with early and aggressive treatment, have led to reductions in BCVI-related stroke and mortality.

STUDY DESIGN: Patients with BCVI from 1985 to 2015 were identified and stratified by age, sex, and Injury Severity Score. BCVI-related stroke and mortality rates were then calculated and compared. Patients were divided into 5 eras based on changes in technology, screening, or treatment algorithms at our institution.

RESULTS: Five hundred and sixty-four patients were diagnosed with BCVI: 508 carotid artery and 267 vertebral artery injuries. Sixty-five percent of patients were male, mean age was 41 years, and mean Injury Severity Score was 27. Incidence of BCVI diagnosis increased from 0.33% to approximately 2% of all blunt trauma (p < 0.001) during the study period. Ninety (14%) patients suffered BCVI-related stroke, with the incidence of stroke significantly decreasing over time from 37% to 5% (p < 0.001). Twenty-eight (5%) patients died as a direct result of BCVI, and BCVI-related mortality also decreased significantly over time from 24% to 0% (p < 0.001).

CONCLUSIONS: Although increased screening has resulted in a higher incidence of injuries over time, BCVI-related stroke and mortality have decreased significantly. Continuous critical evaluation of evolving technology and diagnostic and treatment algorithms has contributed substantially to those improved outcomes. Appraisals of technological advances, preferably through prospective multi-institutional studies, should advance our understanding of these injuries and lead to even lower stroke rates. (J Am Coll Surg 2017; –):1–5. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Originally described in the late 19th century by Verneuil, blunt cerebrovascular injuries (BCVIs) pose a relatively uncommon but potentially devastating threat to victims of blunt trauma. In the mid-20th century, these injuries were considered rare, with <100 cases reported in the literature before 1990. During the last 30 years, however, regionalization of trauma care combined with advances in digital subtraction angiography (DSA) and CT angiography (CTA), has resulted in a tremendous increase in the recognition of BCVI. In addition, recognition of the stroke potential of vertebral artery injuries (previously ignored and underdiagnosed) has resulted in focused screening protocols that attempt to identify these injuries. With increased screening, there has been a concomitant increase in the recognized incidence of BCVI. In fact, modern reports of BCVI suggest that the true incidence is 2% to 3% of all blunt trauma patients.

After BCVI, the potential for either an ischemic or embolic stroke exists. In fact, before the development of diagnostic screening criteria, most injuries were...
recognized only after symptoms developed, which, in turn, led to a workup that ultimately identified the arterial injury.\textsuperscript{2,8,9} Not surprisingly, if left untreated, our experience has been that up to 40% of patients with BCVI will go on to suffer a stroke.\textsuperscript{10} However, some reports have indicated an untreated stroke rate as high as 70%, and there is considerable variability in the stroke rate, depending on the vessel injured and the grade of the injury.\textsuperscript{11}

Both technology and treatment have advanced remarkably in step with increasing recognition of BCVI. Several studies identified the importance of early diagnosis and treatment for the prevention of stroke.\textsuperscript{10,12,13} In many institutions, technological advances have led to the adoption of CTA as the primary diagnostic modality for BCVI instead of DSA. However, we have shown that CTA remains inferior to DSA for diagnosis and continue to use it as a confirmatory test.\textsuperscript{4,5,14-16} Treatment of BCVI has also evolved from operative to nonoperative with anticoagulation and selective use of endovascular interventions representing the mainstay of therapy.\textsuperscript{2,7,8,10,17,19-21}

The aim of this study is to demonstrate our institutional experience and the use of continuous evaluation of technology and treatment strategies, and the impact of those evaluations on outcomes after BCVI. We believe that the critical evaluation of emerging technology and therapy has led to substantial decreases in both BCVI-related stroke and mortality, and balanced resource use with the risk of missed injuries and anticoagulation in multiply injured trauma patients.

METHODS

Patients with BCVI during a 30-year period starting in 1985 were identified from hospital records and the trauma registry at the Elvis Presley Regional Trauma Center in Memphis, TN. Demographics, injuries, and outcomes, including BCVI-related stroke and mortality were recorded.

Patients were then placed into 1 of 5 groups based on the era in which they were injured. These eras were based on changes in institutional screening and treatment algorithms or technological advances (Table 1). The first era (1985 to 1995) consisted of patients who had a BCVI diagnosed by angiography, which was typically performed only after neurologic symptoms had developed. During this time period, there was no defined screening criteria for BCVI.\textsuperscript{10} From 1996 to 2005, a specific set of injuries (Table 2) that had been shown to correlate with the presence of BCVI was used as a trigger for screening angiography.\textsuperscript{22} During the next era (2006 to 2009), any patient with an indication (mechanism of injury, loss of consciousness, physical examination findings) for either a head and/or cervical spine CT also underwent screening CTA using 32-channel multi-detector technology. It was during this time period that any abnormality identified on CTA was added to the list of specific injuries to trigger a screening angiogram.\textsuperscript{7} In mid-2009, the CT technology was upgraded to 64-channel multi-detector machines, which led to a significant increase in sensitivity (68%) and negative predictive value (97.5%).\textsuperscript{4} The study during the fourth era (2010 to 2012) led to a substantial institutional screening algorithm change, where CTA became the primary screening test for BCVI, with DSA was reserved for those patients with a positive screening CTA or a negative screening CTA, but an unexplained neurologic deficit. The patients studied in the fifth era (2013 to 2015) were all diagnosed with the most recent screening algorithm, and monitoring of outcomes in these patients allowed us to validate the earlier change in our algorithm and ensure there were no strokes resulting from missed injuries.

Statistical analysis was performed using SAS software, version 9.4 (SAS Institute). Analysis of variance and chi-square tests were used to determine demographic differences between the patients in each era. A Cochran-Armitage test for trend was used to determine the significance of the changes in mortality and stroke over time.

### Table 1. Eras of Research

<table>
<thead>
<tr>
<th>Era</th>
<th>Years</th>
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<tbody>
<tr>
<td>I</td>
<td>1985 to 1995</td>
</tr>
<tr>
<td>II</td>
<td>1996 to 2005</td>
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<tr>
<td>III</td>
<td>2006 to 2009</td>
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<tr>
<td>IV</td>
<td>2010 to 2012</td>
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<tr>
<td>V</td>
<td>2013 to 2015</td>
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</tbody>
</table>

### Table 2. Triggers for Digital Subtraction Angiography

<table>
<thead>
<tr>
<th>Trigger</th>
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<tr>
<td>Le Fort II and III fractures</td>
</tr>
<tr>
<td>Skull base fracture</td>
</tr>
<tr>
<td>Cervical spine fracture</td>
</tr>
<tr>
<td>Seatbelt mark</td>
</tr>
<tr>
<td>Horner’s syndrome</td>
</tr>
<tr>
<td>Unexplained neurologic deficit</td>
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</table>
RESULTS

Five hundred and sixty-four patients were diagnosed with BCVI over 30 years. There were 508 carotid artery and 267 vertebral artery injuries. The patients were predominantly male (65%), with a mean age of 41 years and mean Injury Severity Score of 27. There were no demographic differences between the eras with respect to sex (chi-square, \( p = 0.8373 \)) or Injury Severity Score (ANOVA, \( p = 0.4346 \)). Interestingly, the proportion of all blunt trauma patients who were male during the same time period was 68%, indicating a possible predisposition for these injuries in females. However, females were also significantly more likely to be victims of a motor vehicle accident, which is by far the most common cause of BCVI (chi-square, \( p < 0.0001 \)). There was a significant difference in the mean age between the eras (ANOVA, \( p = 0.0107 \)) with an increase from 34 years to 43 years. Detailed demographic characteristics are displayed in Table 3.

There has been a significant increase in the observed incidence of BCVI over time. Initially the incidence of BCVI was 0.67% of all blunt trauma, which increased to 1.85% of blunt trauma patients after 2013 (Cochran-Armitage trend test, \( p < 0.0001 \)). Anticoagulation was the primary therapy throughout the study period, but there was a significant difference in the use of endovascular stents between the eras. There was a peak in the use of stents in the third era (2006 to 2009), with 43% of patients having a stent placed. The use of stents has decreased significantly. In fact, in the fifth era (2013 to 2014), stents were only used in 10% of patients (chi-square, \( p < 0.001 \)).

In the first era (1985 to 1995), 37% of patients with BCVI experienced a stroke, and in the fifth era (2013 to 2014) only 4.8% of those with BCVI experienced a stroke (Cochran-Armitage trend test, \( p < 0.0001 \)). Finally, the incidence of BCVI-related death decreased significantly over time. In the first study, 24% of patients diagnosed with BCVI died, and in the 2 most recent studies, no mortalities were attributed to BCVI (Cochran-Armitage trend test, \( p < 0.0001 \)).

Figure 1 shows the incidence of stroke and mortality from each era over time.

DISCUSSION

Continuing study and evaluation of BCVI has resulted in dramatic decreases in both stroke and mortality, despite the increased incidence. The observed increased incidence of BCVI seems to be primarily the result of creation and expansion of screening criteria for these injuries, coupled with enhanced technology detecting subtle injuries that might have been missed previously. We have shown that new technology requires thorough vetting to determine appropriate use. This study also demonstrates that

Table 3. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1985 to 1995 (n = 67)</th>
<th>1996 to 2005 (n = 110)</th>
<th>2006 to 2009 (n = 222)</th>
<th>2010 to 2012 (n = 128)</th>
<th>2013 to 2015 (n = 228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>64</td>
<td>61</td>
<td>66</td>
<td>60</td>
<td>63</td>
</tr>
<tr>
<td>Age, y, mean ± SD</td>
<td>34 ± 14</td>
<td>37 ± 16</td>
<td>40 ± 14</td>
<td>43 ± 15</td>
<td>43 ± 17</td>
</tr>
<tr>
<td>Injury Severity Score, mean ± SD</td>
<td>26 ± 15</td>
<td>30 ± 14</td>
<td>28 ± 14</td>
<td>26 ± 13</td>
<td>22 ± 16</td>
</tr>
<tr>
<td>Incidence of blunt cerebrovascular injury, %</td>
<td>0.67</td>
<td>0.38</td>
<td>1.42</td>
<td>3.75</td>
<td>1.85</td>
</tr>
<tr>
<td>Patients treated with stent, %</td>
<td>—</td>
<td>16</td>
<td>41</td>
<td>34</td>
<td>10</td>
</tr>
</tbody>
</table>

Figure 1. Incidence of blunt cerebrovascular injury-related stroke and mortality by era.
incremental changes in diagnostic and treatment modalities can result in large gains in outcomes over time, even for relatively uncommon injuries.

The algorithm for diagnosis of BCVI at our institution has changed significantly over time as a result of these studies. Evaluating CTA and, most importantly, comparing it with DSA, which remains the gold standard for diagnosis, has been critical to limiting overtreatment. Computed tomography angiography has demonstrated excellent sensitivity and negative predictive values, making it a very good screening tool. However, even the most recent technology (64-channel multi-detector machines with 3-dimensional reconstruction) has yielded only a 55% positive predictive value. We recognize that almost every other institution has abandoned DSA in favor of CTA, and that resource use has been a large component of this shift in diagnostic strategy.\textsuperscript{14,15,17,22} We also recognize that studies from our institution have simultaneously argued that although anticoagulation poses little additional risk to patients with hemorrhagic injuries, DSA should continue to be used to limit unnecessary anticoagulation.\textsuperscript{5,24} It is our position that considering the alarmingly low positive predictive value of CTA, an unacceptable number of patients would be exposed to anticoagulation without any potential benefit if DSA were to be abandoned as a confirmatory test.\textsuperscript{5} In fact, if we were to use CTA as our sole diagnostic modality, we would effectively double the number of patients placed on anticoagulation, potentially increasing the rate of complications from anticoagulation.

Treatment for BCVI has been based primarily on anticoagulants or antiplatelet medications since the first era (1985 to 1995). These agents remain the mainstay of therapy.\textsuperscript{10,25} Anticoagulation consists of a low-intensity heparin infusion (aPTT 40 to 60 seconds). Antiplatelet therapy is accomplished with either aspirin or clopidogrel, alone or in combination. Advancing endovascular technology led to initial enthusiasm for the use of stents to treat these injuries. During the third era (2006 to 2009), there was a peak in the use of stents, however, given the added cost and potential for complications, we have become more conservative in their use and have found no difference in outcomes. Cothren and colleagues\textsuperscript{25} showed that despite the early interest in their use, stents are rarely needed and have very limited indications for use, and our outcomes have reaffirmed that anticoagulation alone is adequate therapy for the majority of BCVI. We believe there is still a role for the use of stents based on specific injuries and they are still used in the treatment of our patients (10% of injuries). In fact, there are currently 2 predominant indications for stenting: enlarging carotid pseudoaneurysms (grade 3 injuries) and dissections with narrowing of approximately 70%. Ultimately, a multi-institutional prospective study to evaluate injury-specific outcomes coupled with long-term follow-up would be required to determine which injuries are best managed by stent placement.

There are limitations to this study. This is a retrospective study of data collected from a single institution for 30 years, and although we have attempted to incorporate evidence from other institutions, there is an inherent bias to our approach to BCVI. There are also inherent limitations to looking at outcomes during such a prolonged time period, as there have been significant changes in personnel, technology, and resources at our institution that are not easily quantifiable. Nonetheless, our recent stroke and mortality rates are among the best reported.

The next frontier for BCVI we believe lies in the following areas: determining which patients need more aggressive intervention to prevent stroke, and the treatment of those who present with symptoms. Determining which patients can benefit from the use of stents is an important step. Those patients who present with symptoms and are determined to have a BCVI-related stroke have been somewhat neglected by the study of this disease, as there has been no effort to study measures that can mitigate the effects of a stroke once it has occurred. Many patients who suffer BCVI-related stroke present with symptoms, and most of those who have delayed strokes do so early in their hospital course.\textsuperscript{5,7,26,27} There might be opportunities for revascularization that are being missed, and we believe that this can be a way to substantially reduce the remaining morbidity of BCVI. Clearly, there are hurdles to evaluating this, and these patients pose challenges not seen in nontrauma patients with ischemic strokes who have been shown to benefit from aggressive interventions. If we are to reduce morbidity from BCVI, specifically the incidence of BCVI-related stroke, prospective, multi-institutional studies to address these issues are necessary.

**CONCLUSIONS**

Continuous evaluation of technology and therapy has resulted in drastic reductions in both stroke and mortality in the last 3 decades. Critical evaluation should be applied to all emerging technology to find the appropriate incorporation into diagnostic algorithms. Future improvements in reducing BCVI-related stroke will require multi-institutional studies, likely in combination with highly selective interventions in those patients who present with symptoms.
Author Contributions
Study conception and design: Shahan, Croce, Fabian, Magnotti
Acquisition of data: Shahan
Analysis and interpretation of data: Shahan, Magnotti
Drafting of manuscript: Shahan, Magnotti
Critical revision: Croce, Fabian

REFERENCES