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Blunt cerebrovascular injury: contribution of Timothy C Fabian MD and investigators from the University of Tennessee at Memphis to our understanding of the injury

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SUMMARY

Our understanding of blunt cerebrovascular injury (BCVI) has evolved considerably over recent decades. It was once seen as a rare injury that was difficult or impossible to predict and had no useful prevention or treatment measures available. In the late 20th century, work by physicians caring for these injuries began to show that this was not the case. There were distinct risk factors for the injury and the often seen interval between injury and stroke provided an opportunity for stroke prevention. Timothy Fabian and the investigators at Memphis have been one of the groups at the forefront of this type of inquiry for >30 years. The contributions of this group has advanced the care of BCVI immensely. This review examines some of the work done by Dr Fabian and his colleagues and its importance in the care of injured patients.

Over the last three decades, our awareness and understanding of blunt cerebrovascular injury (BCVI) has evolved from the idea that it was a rare but devastating injury to the current understanding that it is more common than once believed, is associated with specific injury patterns and early diagnosis and treatment prevents stroke. The first mention of the entity in medical literature occurred in 1872 and was described by Aristide Auguste Stanislas Verneuil, a French physician and surgeon, on autopsy of a railroad worker that had succumbed to his injuries.[1] His symptoms prior to his death had included hemiplegia. While there were reports and small series published intermittently after that first description, the injury remained somewhat of an enigma and was generally not felt to be a common entity.

Although it was not quite as far back as 1872, Timothy Fabian and his colleagues at Memphis did develop an early interest in this injury. Fabian and colleagues first published on BCVI in 1990 and they have continued, along with a select few other groups, to be at the forefront of the examination of this problem for over three decades. The group has extensively published on incidence, diagnosis, treatment, and outcome of the injury and much of what we know about this entity is due to these efforts. In his 2011 Scudder Oration on Trauma given at the 97th Annual Clinical Congress of the American College of Surgeons, Fabian discussed BCVI and demonstrated his intense interest in, passion for, and detailed knowledge of all aspects of the injury.[2] He touched on history, anatomy, risk factors, screening criteria, diagnosis, treatment, and directions for future research. Table 1 briefly summarizes the papers published by Fabian and the Memphis group on the topic from 1990 to 2018. This report will describe the contributions of Fabian and his co-investigators to our understanding of the injury and its care.

DIAGNOSIS AND SCREENING

Diagnosis and screening for these injuries has changed dramatically as we have learned more about their characteristics. Fabian first examined the issue in 1990 in what, at that time, was the largest published series of patients with BCVI (21).[3] One of the striking findings was that roughly half of these patients had an interval between presentation and development of neurological changes. This led the authors to surmise that opportunities for diagnosis of these injuries while asymptomatic may exist. Of the 21 injuries, 20 were diagnosed by angiography. Based on the concomitant injuries seen in this series as well as work by others, the idea of broadly screening based on mechanism of injury producing acute flexion or extension of the neck is discussed. The authors acknowledge that the high numbers of negative examinations likely produced by such criteria makes screening by angiography less attractive and they end with a call for more research into the utility of other screening modalities such as Duplex Doppler.

By the late 90s, greater awareness of BCVI had allowed for a better understanding of the issues surrounding the condition. Screening criteria had been developed and there was growing interest in alternative screening modalities. Published in 2001, the next paper by the Memphis group on the subject examined their intervening experience.[4] In addition to carotid artery injury (CAI), the paper closely examined their experience with vertebral artery injury (VAI). Indications for screening included neurological deficit not consistent with brain imaging, neck hematoma, Horner syndrome, basilar skull fracture through the foramen lacerum, cervical spine fracture through the transverse foramen, and severe complex facial fracture. The CAI rate in this study was 0.5 as compared with 0.33 in earlier work and the VAI rate was 0.4. Awareness of the injury and associated injury patterns led to

Table 1 Articles published on blunt cerebrovascular injury by Timothy Fabian and the Memphis investigators from 1990 to 2018

Authors	Article title	Main conclusions
Fabian TC, George SM Jr, Croce MA, Mangiante EC, Voeller GR, Kudsk KA	Carotid artery trauma: management based on mechanism of injury	► Roughly half of patients had an interval between injury and onset of neurological changes. ► Anticoagulation may be useful as treatment. ► Aggressive screening should be considered in patients with appropriate mechanism.
Miller PR, Fabian TC, Bee TK, Timmons S, Chamsuddin A, Finkle R, Croce MA	Blunt cerebrovascular injuries: diagnosis and treatment	► CAI rate was 0.5, VAI rate was 0.4. ► Awareness and aggressive screening led to 77% of injuries being diagnosed prior to neurological symptoms. ► Heparin and aspirin were associated with lower stroke rates. ► Highlighted screening criteria and the need for development of screening tools other than cerebral angiography.
Miller PR, Fabian TC, Croce MA, Cagiannos C, Williams JS, Vang M, Qaisi WG, Felker RE, Timmons SD	Prospective screening for blunt cerebrovascular injuries: analysis of diagnostic modalities and outcomes	► Found higher VAI rate (0.71 vs 0.4) than previous work with aggressive screening. ► 79% of CAI and all VAI were diagnosed prior to development of neurological changes. ► Found CTA and MRA sensitivity with technology available at the time to be only about 50% as compared with cerebral angiography. ► Antiplatelet therapy or anticoagulation remain main treatment affecting stroke rate after discovery of injury.
DiCocco JM, Emmett KP, Fabian TC, Zarzaur BL, Williams JS, Croce MA	Blunt cerebrovascular injury screening with 32-channel multidetector CT: more slices still do not cut it	► Re-examined CTA utility in screening after adoption of 32 channel scanners. ► Found sensitivity to remain poor at about 50% for both CAI and VAI. ► Found 75 false positive CTA studies which would have led to unnecessary anticoagulation.
DiCocco JM, Fabian TC, Emmett KP, Magnotti LJ, Zarzaur BL, Bate BG, Muhlbauer MS, Khan N, Kelly JM, Williams JS, Croce MA	Optimal outcomes for patients with blunt cerebrovascular injury (BCVI): tailoring treatment to the lesion	► Described lowest stroke rate reported of 4% with the addition of endovascular therapy to anticoagulation/antiplatelet therapy in treatment of more severe lesions. ► 41% of patients underwent endovascular treatment. ► Highlighted need for long-term follow-up and development of specific indications for endovascular therapy in BCVI.
DiCocco JM, Fabian TC, Emmett KP, Magnotti LJ, Zarzaur BL, Khan N, Kelly JM, Croce MA	Functional outcomes following blunt cerebrovascular injury	► Evaluated functional outcomes at up to 3 years after injury. ► Telephone contact and modified FIM/FAM questionnaire. ► No difference in long-term outcome between CAI and VAI. ► Main predictor of poor outcome was stroke. ► Further highlighted need for screening and prevention of stroke.
Fabian TC	Blunt cerebrovascular injuries: anatomic and pathological heterogeneity create management enigmas	► Scudder oration. ► Delves into anatomy, history, risk factors and screening criteria, diagnosis—especially problems with CTA. ► Discusses importance of treatment with anticoagulation or antiplatelet therapy and possible role of endovascular treatment. ► Outlines future work including BCVI registry and clinical trials network with prospective observational trials (imaging, blood flow, treatment) followed by prospective comparisons based on results.
Paulus EM, Fabian TC, Savage SA, Zarzaur BL, Botta V, Dutton W, Croce MA	Blunt cerebrovascular injury screening with 64-channel multidetector CT: more slices finally cut it	► Examined CTA performance with 64-channel scanner in nearly 600 patients. ► Found sensitivity much better than past at 68% per vessel and 84% per patient. ► Concluded that CTA was now an adequate screening tool. ► Continued to use angiography for confirmation after positive CTA due to the still low positive predictive value of 36%.
Shahan CP, Magnotti LJ, Stickley SM, Weinberg JA, Hendrick LE, Uhlmann RA, Schroeppel TJ, Hoit DA, Croce MA, Fabian TC	A safe and effective management strategy for blunt cerebrovascular injury: avoiding unnecessary anticoagulation and eliminating stroke	► Found no increase in missed injuries after 18-month period of adoption of 64-channel CTA screening for BCVI. ► Five injuries resulted in stroke, but none were missed by CTA. ► Maintained angiography as confirmatory study.
Shahan CP, Croce MA, Fabian TC, Magnotti LJ	Impact of continuous evaluation of technology and therapy: 30 years of research reduces stroke and mortality from blunt cerebrovascular injury	► Evaluated trends in incidence, diagnosis, treatment, and outcome over 30-year period. ► Incidence had increased to 1.85% of blunt trauma victims over time as understanding of injury patterns and screening programs have grown. ► Treatment with antiplatelet agents or anticoagulation has remained the mainstay of treatment. ► Endovascular treatment use peaked between 2006 and 2009 and is now used in roughly 10% of patients. ► Current stroke rate is down to 4.8% and BCVI-related mortality is 0% in the latest cohort.
Shahan CP, Gray RI, Croce MA, Fabian TC	Impact of circle of Willis anatomy in traumatic blunt cerebrovascular injury-related stroke	► Found normal anatomy—fully intact circle of Willis—is not protective of stroke. ► Persistent fetal-type enlarged posterior communicating artery is likely protective. ► Surmised that further study and identification of high-risk patients may allow for tailored treatment.

Continued

Table 1 Continued

Authors	Article title	Main conclusions
Shahan CP, Sharpe JP, Stickley SM, Manley NR, Filiberto DM, Fabian TC, Croce MA, Magnotti LJ	The changing role of endovascular stenting for blunt cerebrovascular injuries	► Evaluated outcomes with decrease in endovascular stenting use starting in 2013. ► Direct vascular surgery involvement resulted in stenting use of 8.9% as compared with 34% in earlier cohorts. ► Stroke rate did not change. ► Stent-related stroke rate decreased to 0%.
Shahan CP, Stavely TC, Croce MA, Fabian TC, Magnotti LJ	Long-term functional outcomes after blunt cerebrovascular injury: a 20-year experience	► Evaluated outcome of evaluable patients over 20-year period. ► Seventy-seven patients (19% of survivors) were contacted. ► Median follow-up was range was 3.3 years, maximum follow-up was 19.4 years. ► Advancing age, ISS, and stroke were found to be independent predictors of poor mobility on follow-up.

CAI, carotid artery injury; CTA, CT angiography; FIM/FAM, functional independence measurement and functional activity measurement; ISS, injury severity score; MRA, magnetic resonance angiography; VAI, vertebral artery injury.

77% rate of CAI diagnosis prior to development of neurological symptoms. This was much better than seen in previous work. Although virtually all of these injuries were diagnosed by angiography, the authors noted that the improving technologies of computed tomography angiography (CTA) and magnetic resonance angiography (MRA) showed promise as possible screening modalities in the future.

Moving forward, the trauma program in Memphis implemented an aggressive screening pathway for BCVI based on the previous criteria and began a prospective comparison of the screening modalities of angiography, CTA, and MRA. This experience was reported at the American Surgical Association meeting in 2002 and published that year.[5] While the CAI rate in this study was similar to previous work, the VAI rate was 0.71 vs the 0.4 noted in earlier work. This demonstrated that VAI was likely much more prevalent than once believed and, like CAI, aggressive screening led to recognition of this pattern. Unfortunately, the sensitivity of both CTA and MRA using the technology available at the time was poor at around 50%. These data seemed to indicate that aggressive screening based on sound criteria was associated with increased recognition of these types of injuries. Unfortunately, when compared with cerebral angiography as the gold standard, CTA and MRA with the technology available at the time were inadequate as a screening tool with poor sensitivity. The authors did predict that, with ongoing technological development, angiography would eventually be supplanted by less invasive screening techniques.

Over the following years, the surgeons at Memphis continued to screen aggressively for BCVI and, in 2007, obtained upgraded CTA technology in the form of 32-channel CT scanners. In an attempt to examine the improved imaging capability in the screening for BCVI, the results of screening for 684 patients undergoing both CTA and digital subtraction angiography (DSA) were examined.[6] All patients meeting the previously described screening criteria underwent screening angiography and CTA was employed widely for the evaluation of head, face, and neck injuries in general. Evidence of vascular injury on CTA also resulted in DSA. In this cohort, 90 patients were found to have 109 injured vessels: 52 CAI and 57 VAI. Despite the assumption of improved accuracy with the 32 slice scanners, the sensitivity when compared with DSA was still around 50%. Advancing technology had yet to compare favorably to the gold standard of DSA. In addition, the authors noted that there were 75 false positive injuries when CTA was compared with DSA. Fabian and his coauthors compared and contrasted other contemporaneous studies which showed better performance of CTA versus DSA. The authors noted that some publications have reported excellent sensitivity but obtain the gold standard test of DSA only on patients with a positive result on CTA rather than directly compare the two imaging techniques.

The group presented a follow-up experience at the American Association for the Surgery of Trauma meeting in 2013 which demonstrated that advancing CTA technology had finally caught up with DSA in diagnostic accuracy for BCVI.[7] One hundred twenty-eight patients with 163 injured vessels were found in 595 screened patients for a positive screening rate of 22%. While the DSA technique was generally unchanged, 64-channel CT scanners were used for screening CTA. Screening criteria remained similar to previous work and included cervical spine fracture, neck soft tissue injury, basilar skull fracture, Le Fort II or III facial fracture, Horner syndrome, an unexplained neurological deficit, or CTA abnormality. In contrast to the poor sensitivity of previous technologies, CTA with 64 slice scanning showed a sensitivity of 68% per vessel and 84% per patient. Based on these data, the investigators concluded that CTA was an adequate screening test based on current technology. They continued to use DSA as a confirmatory test if CTA was positive as the positive predictive value for CTA was low at 36%.

In 2015, Fabian and colleagues reported their subsequent experience based on the insertion of CTA as a screening tool.[8] Patients at risk for BCVI based on the previously mentioned criteria underwent CTA. Those with positive studies and those with negative studies but with abnormal neurological exam suggestive of cerebral ischemia underwent DSA. They found excellent results using this algorithm. Of 3523 patients screened for BCVI during the 18-month period, 189 underwent DSA due to abnormal CTA. One hundred four (55%) were found to have at least one BCVI. Of these abnormal CTAs, 85 (45%) were found to be false positive with no injury found on DSA. Of all false positives, 87% were called as grade I injuries on CTA. Five (4.7%) of injuries developed stroke and none of these injuries were missed by CTA. If one accepts the assumption that no injuries were missed by CTA given that no strokes occurred in the negative CTA population, sensitivity for this screening modality approaches 100%. While this estimate of sensitivity may be high, it does seem that CTA is quite unlikely to miss important BCVIs using this technology. The authors also comment on the utility of maintaining DSA as a confirmatory study given that the positive predictive value of CTA was only 55%.

TREATMENT AND OUTCOME

In addition to longitudinal evaluation of optimal screening and diagnosis for BCVI, the Memphis group has been among investigators at the forefront of understanding treatment and outcomes of these potentially devastating injuries. When they first

Table 2 Blunt cerebrovascular injury grading scale

Injury grade	Description
I	Luminal irregularity or dissection with <25% luminal narrowing
II	Dissection or intraluminal hematoma with ≥25% luminal narrowing, intraluminal thrombus, or raised flap
III	Pseudoaneurysm
IV	Occlusion
V	Transection with free extravasation

published on the injury in 1990, no data were available about effective treatment.[3] Approximately half of injured patients had developed neurological symptoms at the time of diagnosis. A logical assumption that anticoagulation with heparin may be useful in this injury which promoted thrombosis was made by Fabian and others. There was some thought that this may have improved outcome but the data were few and not very clear.

This had changed by 2001 and the next published series by the group showed that treatment with either heparin or aspirin was associated with lower stroke rates than in those left untreated.[4] This was true in both CAI with a stroke rate of 6.8% in treated vessels as compared with 64% in untreated vessels and VAI with a similar reduction of stroke rate to 2.6% in treated vessels vs 54% in untreated vessels. Heparin was also associated with better overall neurological outcome than no treatment. While aspirin appeared to prevent stroke, it was not associated with better discharge neurological outcome. These data strengthened the overall idea that therapy with either antiplatelet therapy or anticoagulation prior to development of neurological symptoms served to prevent stroke. There was indication, however, that heparin may be superior in overall neurological outcome.

Outcome after BCVI was further examined in a 2010 publication after the addition to selective endovascular therapy to the treatment armamentarium.[9] Injuries were separated according to injury grade (table 2).[10]

Grade II, III, and IV BCVIs were initially treated with anticoagulation and underwent follow-up DSA on 7–10 days. Those who showed no improvement underwent stenting of the injury. Patients were loaded with aspirin and clopidogrel prior to follow-up DSA and this was continued postprocedure if stenting was performed. Of 222 patients studied, 91 (41%) underwent endovascular therapy in addition to antiplatelet therapy or anticoagulation. Two patients, both with carotid injuries, developed stroke after endovascular therapy. Overall, stroke occurred in 22 patients prior to diagnosis and in only 4%[7] of patients after BCVI diagnosis. The authors noted that this combination of therapy had resulted in the lowest BCVI stroke rate reported to date. They challenged the trauma community to continue to examine and refine the indications and techniques for endovascular therapy in BCVI moving forward.

In 2017, the role of and outcomes from the integration of endovascular therapy was examined again.[11] The investigators in Memphis observed that the role of stenting in local BCVI management appeared to have changed with the integration of vascular surgeons into the treatment team in 2013. Thus, moving forward, endovascular therapy was spearheaded by vascular surgeons rather than interventional radiologists. Stent utilization was restricted to selected grade II and III injuries after review by the treatment team. The stent utilization was only used in 8.9% of BCVIs as compared with 30%–40% prior to this change in management. Stroke rate remained low at 3.9% while stent-related stroke rate was 0% in the later study group. Other investigators during this time, most notably, the Denver group, had also recognized the need for further examination of the role of stenting for BCVI after early enthusiasm.[12] While there appeared to be an important role for the addition of endovascular therapy, more study with the development of specific guidelines were needed.

Fabian and colleagues studied long-term outcomes after BCVI in 2013.[13] They evaluated available data on outcomes in 68 patients with a mean follow-up interval of 35 months. Telephone interviews were conducted using a modified functional independence measurement and functional activity measurement (FIM/FAM) questionnaire. This demonstrated that CAI and VAI have similar long-term outcomes. Unsurprisingly, the development of stroke after either injury was the major predictor of functional outcome. This work further highlighted the importance of screening and preventative treatment in patients with BCVI.

In 2017, the investigators in Memphis, led by Dr Fabian, published a study summarizing the lessons learned from 30 years of careful examination of BCVI screening, diagnosis, and treatment.[14] Their experience was divided into five time periods from 1985 through 2015 and changes over time were examined. Interestingly, the mean age of those with BCVI increased from 34 years to 43 years over the time of examination. Overall observed incidence steadily grew to a peak of 1.85% of all blunt trauma patients in the later era. This is certainly a product of more aggressive screening over time. Some type of anticoagulation was the mainstay of therapy throughout the 30 years, but the use of endovascular stenting peaked between 2006 and 2009 and has decreased to roughly 10% in 2013–2014. Stroke rate has decreased significantly and was only 4.8% in the most recent era, and BCVI-related death has gone from 24% in the initial examination to 0% in the most recent experience.

SUMMARY AND FUTURE DIRECTIONS

Fabian and the Memphis group have approached the problem of BCVI with typical intellectual zeal and doggedness. The rigorous nature of the work that has resulted has contributed to the trauma community's knowledge of all aspects of the injury and patients are better off due to this. Due to their work as well as excellent work by other authors, BCVI has transformed from a rare but potentially devastating injury that little could be done about to an injury that should be screened for aggressively with well-understood tools and that should be treated to avoid poor outcomes. With each advance in understanding of the spectrum of BCVI, these investigators have attempted to acknowledge the limitations of their recommendations and outline directions for future investigation. In fact Dr Fabian, in his 2011 Scudder oration, outlined his vision for future advancement of the understanding of the problem.[2] This included establishment of a BCVI registry and clinical trials network with subsequent studies on imaging, cerebral blood flow, and therapy. These observational trials would serve as the basis for randomized controlled trials with the development of appropriate funding resources. Fabian and colleagues have moved on to begin early investigation into the relationship of cerebrovascular anatomy on stroke rate in BCVI, finding that normal anatomy is not protective, but the increased collateral flow provided by a persistent fetal-type enlarged posterior communicating artery is likely protective.[15] Multi-institutional observational studies have been conducted looking at treatment and randomized trials are in the offing to further evaluate treatment paradigms.[16] Screening has become a topic of intense study in recent years. This is largely due to the persistent problem of 8%–20% patients with BCVI developing stroke from after admission who did not fall under established

screening algorithms. Proposed solutions being studied include universal screening of all blunt trauma victims or screening of all blunt trauma patients with any injury above the clavicles.[17 18]

Tim Fabian and the investigators in Memphis, along with many other exceptional physician-scientists have done the groundwork and set the stage for the rest of us to move forward in further understanding the spectrum of BCVI. I have heard it said that we stand on the shoulders of giants in such endeavors which is clearly true. In North Carolina, we have a less grand way of describing the importance of recognizing the work and support that may come from previous work in a particular field. Those that come later might be called post turtles. If you see a turtle on top of a fence post, you know it had some help getting there. In addition to his clinical expertise and research acumen, Tim Fabian has helped put a lot of turtles on a lot of posts, and the world of surgery is better for it.

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