A safe and effective management strategy for blunt cerebrovascular injury: Avoiding unnecessary anticoagulation and eliminating stroke

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BACKGROUND: Few injuries have produced as much debate with respect to management as have blunt cerebrovascular injuries (BCVIs). Recent work (American Association for the Surgery of Trauma 2013) from our institution suggested that 64-channel multidetector computed tomographic angiography (CTA) could be the primary screening tool for BCVI. Consequently, our screening algorithm changed from digital subtraction angiography (DSA) to CTA, with DSA reserved for definitive diagnosis of BCVI following CTA-positive study results or unexplained neurologic findings. The current study was performed to evaluate outcomes, including the potential for missed clinically significant BCVI, since this new management algorithm was adopted.

METHODS: Patients who underwent DSA (positive CTA finding or unexplained neurologic finding) over an 18-month period subsequent to the previous study were identified. Screening and confirmatory test results, complications, and BCVI-related strokes were reviewed and compared.

RESULTS: A total of 228 patients underwent DSA: 64% were male, with mean age and Injury Severity Score (ISS) of 43 years and 22, respectively. A total of 189 patients (83%) had a positive screening CTA result. Of these, DSA confirmed injury in 104 patients (55%); the remaining 85 patients (45%) (false-positive results) were found to have no injury on DSA. Five patients (4.8%) experienced BCVI-related strokes, unchanged from the previous study (3.9%, $p = 0.756$); two were symptomatic at trauma center presentation, and three occurred while receiving appropriate therapy. No patient with a negative screening CTA result experienced a stroke.

CONCLUSION: This management scheme using 64-channel CTA for screening coupled with DSA for definitive diagnosis was proven to be safe and effective in identifying clinically significant BCVIs and maintaining a low stroke rate. Definitive diagnosis by DSA led to avoidance of potentially harmful anticoagulation in 45% of CTA-positive patients (false-positive results). No strokes resulted from injuries missed by CTA. (*J Trauma Acute Care Surg.* 2016;80: 915–922. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Diagnostic study, level III.

KEY WORDS: Blunt cerebrovascular injury; CT angiography; digital subtraction angiography; blunt carotid injury; blunt vertebral injury.

Few injuries in trauma care continue to create as much debate as blunt cerebrovascular injury (BCVI). BCVI is observed in 1% to 2% of all blunt trauma patients.[1] Left untreated, 10% to 40% of these injuries will result in a BCVI-related stroke.[2–5] While it is widely accepted that anticoagulation is the mainstay of therapy for these injuries, there is no consensus about the optimal method of diagnosis or timing of reevaluation.[6] In fact, vigilant screening for BCVI remains the mainstay for early diagnosis and treatment, leading to improved outcomes and reduced stroke rates.

Nevertheless, there are some who feel that these injuries should not be screened for at all, based on the belief that most BCVI-related strokes are not preventable.[3] Even among those institutions that have made screening for BCVI a priority, there is no uniformity in the method of diagnosis. Computed tomographic angiography (CTA) has become the diagnostic tool of choice, and there has been a movement away from using digital subtraction angiography (DSA), although it remains the criterion standard diagnostic test.[7] Recently, all but a few institutions have removed DSA completely from their BCVI diagnostic algorithm.[8]

Previous work from our institution suggested that 64-channel multidetector CTA should be the primary screening tool for BCVI.[9] In fact, subsequent to that study, our institutional BCVI screening algorithm was changed such that CTA replaced DSA as the primary screening modality (Fig. 1). DSA is still used in two situations, in those patients with a positive screening CTA result because of the low positive predictive value and in those patients with a negative screening CTA result that have an unexplained neurologic examination because of the relatively low sensitivity and concern of clinically relevant missed injuries.

This study was performed to examine outcomes following the institutional algorithm change described earlier. The purpose of the current study was to determine if there had been an increase in clinically relevant missed injuries resulting in BCVI-related stroke this new management algorithm was adopted. Based on anecdotal experience, our hypothesis was that there had not been clinically significant injuries missed by the change in our screening algorithm.

PATIENTS AND METHODS

Identification of Patients

Approval was obtained for this retrospective study from the University of Tennessee Health Science Center's Institutional Review Board. All patients who underwent four-vessel DSA for suspected BCVI during the 18-month period from March 2013 through September 2014 were included. This cohort was chosen based on the assumption that it would capture two important groups of interest, namely, those with a positive screening CTA result and those with a negative screening CTA result who had unexplained neurologic symptoms. The patients with a negative screening CTA result and unexplained neurologic symptoms would be those at risk of a clinically relevant missed injury based on the relatively low sensitivity of CTA. The patients with a positive screening CTA result were of interest based on the low positive predictive value of the test described previously.[9]

Data Collection

Medical records and the trauma registry of the Presley Regional Trauma Center in Memphis, Tennessee, were reviewed for demographics, injuries, Glasgow Coma Scale (GCS) score,

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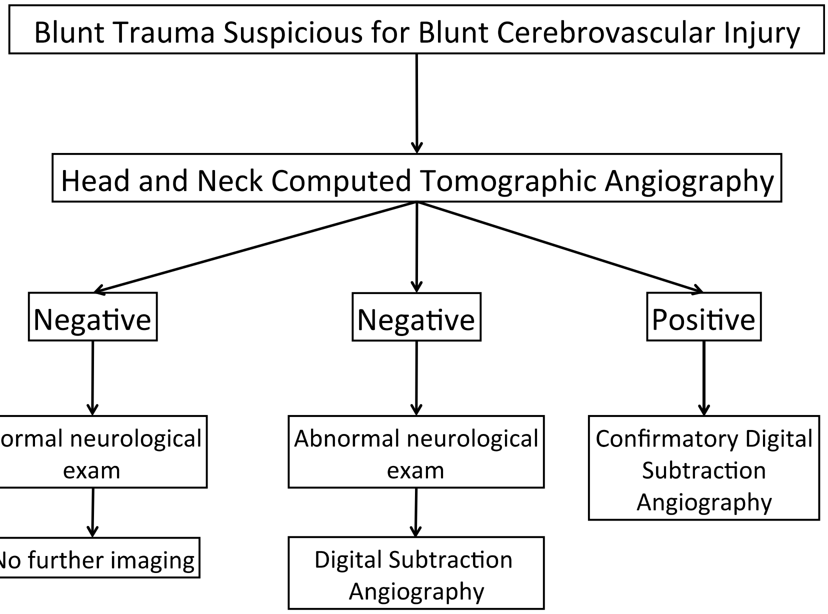

Figure 1. Current screening algorithm for all patients following blunt trauma suggestive of BCVI.

Injury Severity Score (ISS), head and neck Abbreviated Injury Scale (HNAIS) score, medications, laboratory results, and imaging results. Outcomes including angiography- and treatment-related complications, intensive care unit (ICU) days, hospital length of stay, stroke, death, and discharge disposition were also recorded. Injury grading of BCVI was based on the scale described by Biffl et al.[10]

Anticoagulation

Patients with suspected BCVI are started on systemic anticoagulation by heparin infusion with a goal partial thromboplastin time of 40 seconds to 50 seconds until DSA can be performed. Patients with confirmed BCVI are continued on either systemic anticoagulation with heparin transitioning to warfarin or antiplatelet (aspirin and/or clopidogrel) therapy based on vessel and injury grade. Most injuries are reevaluated after 7 days, the exception being Grade IV vertebral injuries, which are not typically reimaged. Anticoagulation is stopped immediately if confirmatory DSA reveals no injury.

Statistical Analysis

Data were recorded and managed using REDCap electronic data capture tools hosted at The University of Tennessee Health Science Center.[11] All data were analyzed using SAS version 9.4 (SAS Institute, Cary, NC). Normally distributed continuous variables were analyzed using the Student's t test, while nonparametric continuous variables were analyzed using the Wilcoxon rank-sum test. Categorical data were analyzed using the χ^2 or analysis of variance tests where appropriate.

RESULTS

Patient Characteristics

A total of 228 patients underwent DSA during the 18-month study period ending in September 2014. During the same period, 3,523 patients were screened for BCVI with CTA. The majority of patients were male (64%) in the fifth decade of life (median, 43 years, interquartile range [IQR], 30–55 years). These were moderate to severely injured patients with a median ISS of 22 (IQR, 13–30) and a median HNAIS score of 3.0 (IQR, 3–4). The most common mechanism of injury was motor vehicle collision (Table 1).

Screening

Of the 228 patients, 189 (83%) underwent DSA secondary to a positive screening CTA result (Fig. 2). Of these patients, 104 (55%) were confirmed to have an injury, with a total of 129 injured vessels: 74 internal carotid artery injuries and 55 vertebral artery injuries. Eighty-five (45%) of the screening studies were classified as false positives as they were found to have no injury on confirmatory testing. The summary of the findings in the patients confirmed to have BCVI is shown in Table 2.

TABLE 1. Overall Characteristics of the Study Population

	Overall (n = 228)
Male, %	63.6
Age, median (IQR)	43 (30 to 55)
Mechanism of injury, %	
Motor vehicle collision	56.6
Fall	15.4
Motorcycle collision	7.5
Assault	6.1
Pedestrian vs. auto	5.3
Other	9.1
ISS, median (IQR)	22 (30 to 55)
HNAIS score, median (IQR)	3.3 (3 to 4)
Base excess, median (IQR), mEq/L	−3.8 (−1.8 to −7.9)

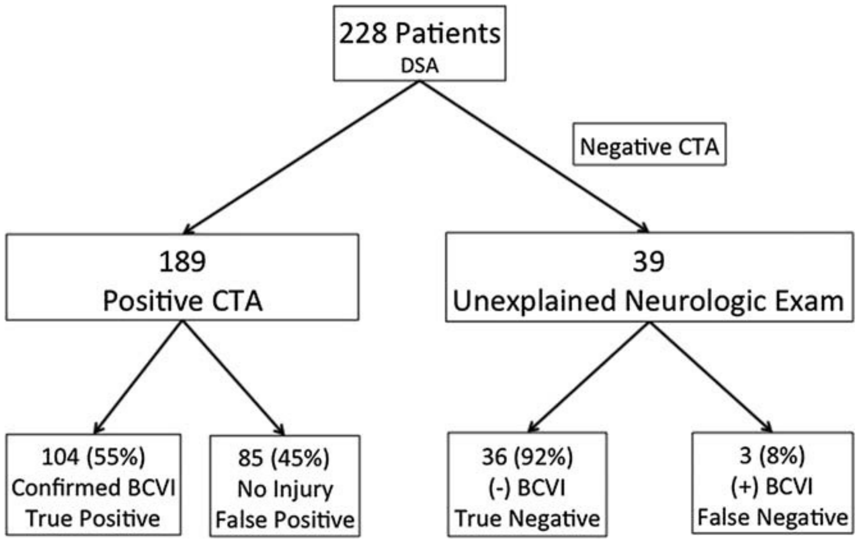

Figure 2. Graphical representation of those patients undergoing DSA for suspected BCVI following CTA.

Thirty-nine (17%) of those who underwent DSA had a negative screening examination result but had an unexplained neurologic deficit. Thirty-six (92%) of these patients were confirmed not to have an injury, while three (8%) were found to have an injury that was missed by screening CTA. The median time to DSA in the cohort was 9 hours (IQR, 5–12 hours). Table 3 lists the false-positive screening CTA results by location and grade, with 87% of these being suspected Grade I injuries.

Table 4 shows the comparison of patients who screened positive by CTA. They were similar demographically; however, the median ISS was significantly higher in the patients confirmed to have an injury. The median GCS and HNAIS scores were similar in these two groups, indicating that those with confirmed BCVI were more likely to have multiple injuries.

Treatment

Of patients with confirmed BCVI, 68% were initially treated with a heparin infusion. The remaining 32% were started on antiplatelet therapy. Heparin was stopped in the 85 patients (45%) found to have no injury on confirmatory testing, preventing unnecessary anticoagulation in almost half of the patients with a positive CTA result.

Endovascular interventions were infrequent, but the most common was placement of a stent, which was performed in 11 patients (10%). Seven of the patients treated with a stent had Grade 3 injuries, while four had Grade 2 injuries. There were three patients (2.8%) who had coil embolization performed, all of which were to treat an arteriovenous fistula.

At discharge, 26% of the patients were treated with warfarin, 40% with aspirin alone, 24% with aspirin and clopidogrel, 5% with clopidogrel alone, and 5% were prescribed therapeutic enoxaparin.

Complications

Anticoagulation complications were rare, with only one patient (1.4%) developing heparin-induced thrombocytopenia. No patient required cessation of antithrombotic therapy because of a complication. There were no patients who had worsening of a traumatic brain injury or solid organ injury while on therapy. Angiography-related complications were also infrequent, occurring in 1.7% of the patients. There were two femoral artery pseudoaneurysms, which required operative repair. There were two access site hematomas, which resolved spontaneously. There were no iatrogenic dissections or strokes.

TABLE 2. Distribution of DSA-Positive BCVIs by Location and Grade

	Vessel				
Grade	Right ICA, n (%)	Left ICA, n (%)	Right Vertebral, n (%)	Left Vertebral, n (%)	Total, n (%)
I	15 (39)	20 (56)	15 (52)	11 (42)	61 (47)
II	6 (16)	2 (6)	2 (7)	2 (8)	12 (9)
III	14 (37)	10 (28)	3 (10)	1 (4)	28 (22)
IV	2 (5)	1 (3)	9 (31)	12 (46)	24 (19)
V	1 (3)	3 (8)	0	0	4 (3)
Total	38 (29)	36 (28)	29 (22)	26 (20)	

ICA, internal carotid artery.

TABLE 3. Distribution of False-Positive Screening CTA Results by Location and Grade

	Vessel				
Grade	Right ICA, n (%)	Left ICA, n (%)	Right Vertebral, n (%)	Left Vertebral, n (%)	Total, n (%)
I	17 (85)	17 (85)	20 (83)	30 (91)	84 (87)
II	1 (5)	0	2 (8)	2 (6)	5 (5)
III	1 (5)	3 (15)	0	0	4 (4)
IV	1 (5)	0	2 (8)	1 (3)	4 (4)
V	0	0	0	0	
Total	20 (21)	20 (21)	24 (25)	33 (34)	

ICA, internal carotid artery.

TABLE 4. Comparison of CTA-Positive Patients Following Confirmatory DSA

	DSA Positive (n = 104)	DSA Negative (n = 85)	p
Male, %	58	63	0.567
Age, median (IQR)	39 (30 to 50)	47 (31 to 57)	0.086
ISS, median (IQR)	22 (13 to 44)	17 (10 to 26)	0.001
Base excess, median (IQR)	−5.1 (−2.7 to −7.9)	−3.6 (−1.3 to −7.6)	0.316
GCS score, median (IQR)	15 (12 to 15)	15 (14 to 15)	0.934
HNAIS score, median (IQR)	3 (3 to 4)	3 (3 to 4)	0.100
ICU days, median (IQR)	4 (0 to 10)	3 (0 to 8)	0.182
Length of stay, median (IQR)	12 (7 to 19)	6 (3 to 17)	0.0004

Stroke occurred in a total of five patients (4.7%) with BCVI. Three of these patients had symptoms present on admission, and two developed symptoms while on appropriate therapy for a known injury. None of the patients with an injury missed by screening CTA developed a stroke.

DISCUSSION

The use of any screening modality should take into consideration the potential benefits of early detection compared with the presumed risks associated with complications and costs. DSA remains the criterion standard for the diagnosis of BCVI.[7] Nevertheless, DSA is invasive, labor intensive, and costly. As a result, many institutions have abandoned the use of DSA in favor of CTA since it is less invasive, less labor intensive, and less expensive.

Previous work from our institution showed that 32-channel multidetector CTA alone is inadequate for BCVI screening, with an unacceptably low sensitivity of only 52%.[12] In a follow-up study, the only published work in which all patients underwent both CTA and DSA, comparing 64-channel multidetector CTA with DSA, we found that although the sensitivity of CTA had increased to 68%,[9] the positive predictive value remained remarkably low at 36%. Thus, with CTA alone, up to 64% of the patients diagnosed with BCVI would receive unnecessary anticoagulation. Consequently, our screening algorithm narrowed from using specific injury patterns as a trigger for DSA to using CTA as a screening modality coupled with a confirmatory DSA. In our current algorithm, any patient with a positive screening CTA result or unexplained neurologic finding undergoes a formal confirmatory DSA. With this current series of BCVI patients, we describe our experience subsequent to our BCVI screening algorithm change.

Clearly, the first concern with any algorithm change, especially a screening algorithm, was the possibility of an increase in clinically relevant missed injuries. In the previous study, the majority of injuries missed by CTA were low grade and thus less likely to result in BCVI-related stroke. In addition, none of the BCVI-related strokes in that study were missed by CTA. While we understood that a number of clinically insignificant injuries would be missed, it would not be acceptable to have an increase in BCVI-related stroke secondary to screening failures. As none of the patients with a negative CTA result developed a BCVI-related stroke, this study has shown that the change in our screening algorithm resulted in no clinically relevant missed injuries.

The low positive predictive value (36%) demonstrated in the previous study[9] is an important reason why DSA remains in the current algorithm. While there have been numerous evaluations of CTA diagnosis of BCVI as it has improved,[13–17] the study by Paulus et al.[9] remains the only large series comparing CTA with DSA in every patient. While most institutions have completely abandoned DSA except in the case of endovascular interventions, it is our contention that anticoagulation in a large number of patients with multiple injuries without an indication is potentially harmful.[8] It has been argued that the risk of complications from anticoagulation is low, while the cost, resources used, and rate of complications associated with DSA are too high to justify its use.[18] While complications related to anticoagulation were infrequent in this study, it seems prudent to anticoagulate patients with multiple injuries only when necessary. Thus, we feel that the findings of this study support the continued use of DSA to confirm BCVI identified on screening CTA.

In this study, 45% of the screening CTA results were false positive, making the positive predictive value of CTA equal to 55%. This is increased from the previous study's positive predictive value of 36%.[9] We believe this increase from the previous study is most likely related to increasing experience among the interpreting radiologists. Despite this improvement, the use of CTA alone for BCVI diagnosis would have resulted in an additional 85 patients receiving anticoagulation without a true indication. Given that the average length of anticoagulation before reevaluation is 7 days, an additional 595 heparin infusion days were avoided by the use of DSA for confirmation of suspected BCVI. While the medication alone is inexpensive, the cost of therapeutic monitoring and keeping the patient at a higher level of care for an additional week must be considered. In addition, the use of heparin in a patient with multiple injuries is not without its own inherent consequences.

At our institution, DSA is routinely performed by a dedicated neurovascular service, composed of vascular surgeons, neurosurgeons, and interventional neurologists. The procedure-related complication rate was comparable with that of other studies. Notably, there were no iatrogenic strokes or dissections in this cohort. Only two of the patients with a complication required an intervention, both of which were operative repair of a femoral pseudoaneurysm.

Despite similar ICU lengths of stay, patients with confirmed BCVI were found to have longer overall stay compared with those patients without BCVI. However, it must also be noted that the ISS for this group of patients was also significantly increased when compared with those patients without BCVI, confounding the contribution of BCVI in this population multiple injuries.

From the Denver group, Cothren et al.[6] have demonstrated that anticoagulation remains critical in the prevention of BCVI-related stroke. Our work has confirmed these findings by maintaining a low stroke rate with appropriate use of anticoagulation. Biffl et al.[5] described the importance of follow-up imaging for BCVI, which is routinely performed at our institution considering the impact on management it can have as it often guides long-term treatment decisions. In fact, the BCVI-related stroke rate of this cohort was just less than 5%, which is unchanged from that of our previous study.[9] More importantly, there were no missed injuries that resulted in a stroke. Thus, the algorithm change did not result in any *clinically significant* missed injuries, confirming its overall utility.

This study has several limitations, including the retrospective approach taken. The generalizability of the study may be limited by both the fact that the patients were all treated at a high-volume Level I trauma center that aggressively screens for BCVI and that a dedicated neurovascular service performs all DSA and assists with the management of patients with BCVI.

When looking forward, it is important to account for continued technological advancement in this field, especially with regard to CTA. As our record has demonstrated, each incremental change in technology needs to be carefully vetted to determine how it should best be used. Our institution will undergo an upgrade to 128-channel multidetector CT machinery in the near future, at which point further study will be needed to reevaluate the role that both CTA and DSA have in the diagnosis of BCVI.

CONCLUSION

A management scheme using 64-channel multidetector CTA coupled with the use of confirmatory DSA for suspected injuries with experienced radiology staff at a high-volume Level I trauma center has proven to be safe and effective in the diagnosis of clinically significant BCVI. Continued use of DSA for injury confirmation remains critical to avoid potentially harmful and unnecessary anticoagulation. In the current study, 45% of CTA-positive patients did not have an injury (false-positive results) and would have received anticoagulation unnecessarily. Most importantly, no BCVI-related strokes occurred because of an injury missed by CTA. Thus, by using CTA as the primary screening tool with DSA confirmation of BCVI, unnecessary anticoagulation can be avoided, and an acceptably low stroke rate can be achieved.

AUTHORSHIP

C.P.S., L.J.M., and S.M.S. contributed to the study concept and design. C.P.S., L.E.H., and R.A.U. acquired the data. C.P.S., L.J.M., S.M.S., D.A.H., M.A.C., and T.C.F. performed the data analysis and interpretation. C.P.S. and L.J.M. drafted the manuscript. L.J.M., T.J.S., J.A.W., M.A.C., and T.C.F. participated in critical revision.

DISCLOSURE

The authors declare no conflicts of interest.

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DISCUSSION

Dr. Clay Cothren Burlew (Denver, Colorado): Dr. Shahan and his co-authors are to be commended for continuing to question the validity of CTA as our primary diagnostic modality for blunt cerebrovascular injuries.

I think the vast majority of us have quickly adopted CTA as the only imaging modality used for BCVI, likely performing the rare angiogram for those patients with unexplained neurologic findings. This study's primary purpose and most important finding was that no patient with a negative CTA developed a BCVI-related stroke. The use of 64-slice CTA resulted in no clinically-relevant missed injuries.

The interesting secondary question that they pose is the importance of confirmatory angiography for CTA identified injuries. And on this point I say kudos to the Memphis group. Reading your manuscript made me stop to think—should we all be doing confirmatory angiography? Are those of us only using CTA really treating almost double the number of patients that we need to? Are CTAs actually overcalling 45% of the injuries that we identify?

So my first and perhaps most obvious question, why do you think you have so many false positive CTAs? With an average of seven CTAs per day to evaluate for BCVI at your institution, are you simply overwhelming your radiologists? Or perhaps your radiologists are biased – they recognize that a confirmatory angiogram is quickly following, so does this encourage them to perhaps overcall any questionable finding on CTA, hence allowing the CTA to be an excellent screening tool? Do you have a quality review process in your radiology group to assess this discordance between CTA and angiography?

My second question, what grade of injury were the false positives? And what was the time to angiography? We recognize that 50% of Grade I and 20% of Grade II injuries resolve or heal between the time of injury and repeat imaging performed arbitrarily on Day 7. Perhaps you are merely catching this early healing phenomenon with the timing of your angiography.

And, finally, with your study group consisting of all patients undergoing angiography, how are you sure that you have captured all patients with a positive CTA? Do any patients refuse or get discharged prior to performing that confirmatory angiogram?

I think this evaluation should be a model for others. Each institution should critically review their individual rates and methods of BCVI diagnosis. For those centers with a marked increase in the identification of BCVI following institution of CTA as their screening tool, consideration of confirmatory angiography might be recommended due to the potential false positive rate of up to 45%. However, for those centers with similar screening yields and no missed injuries, perhaps confirmatory angiography is not warranted.

All programs should evaluate their injuries, appropriateness of diagnosis, and impact of subsequent treatment. Only then will we have optimal outcomes.

I'd like to thank the Association for the privilege of discussing this paper.

Dr. Frederic Pieracci (Denver, Colorado): Two quick questions, the first one Dr. Burlew alluded to already but, did you have any high-grade injuries on CTA that ended up being false positives or were all of the false positives low-grade injuries?

And the second question is, because it is bad to put someone on heparin or aspirin if they don't need to be on it, did you specifically look at bleeding complications and VTE events in the patients who were on the heparin but presumably didn't need to be because their DSA did not show an injury? Thank you.

Dr. Jeffrey Claridge (Cleveland, Ohio): My question is quick. In the false positives, did you break down which were carotid and which were vertebral?

Dr. Matthew Martin (Tacoma, Washington): It seems like your protocol didn't distinguish between carotid and vertebral and also didn't distinguish based on grade for treatment. So if I understood it correctly, a patient with a potential Grade I injury on CT angiogram would be anticoagulated and then get a formal angiography. Is that correct? If not, can you break it down?

Is there a difference between carotid and vertebral artery injuries, both in management and in prognosis? And finally, does your treatment algorithm distinguish anything based on grade of injury?

Dr. Pamela Garcia (Phoenix, Arizona): From what cohort have you derived those that went into the diagnostic testing for BCVI? So how did you identify those? Of the 282, were they all head, face and neck injuries? Or were they only those that were selectively included in your study because they underwent that particular testing? Because that underlying bias will certainly influence your positive predictive value.

Dr. Michel Aboutanos (Richmond, Virginia): So my question goes toward the quality improvement. Did you look at who is reading your CTA? Was it the same radiographer? What time were they being read—more at night versus the day?

Did you have any purpose in comparing one radiologist versus another to see if that's really the issue and not the fact that you have a lot more positive because the test is over-diagnosing versus being over-read? Thank you.

Dr. Charles P. Shahan (Memphis, Tennessee): Thank you, Dr. Burlew and others for your questions.

The first question of why we have so many false positive CTAs in regards to the radiologists' potentially overcalling, I think that's absolutely the case. I'm not entirely sure that the fact that they know that the patient or that the patients are going to get a confirmatory test plays into that.

But they, admittedly, overcall injuries, especially if there is any sort of issue with the quality of the imaging or the contrast bolus timing and things like that. You know, in speaking with them they absolutely overcall injuries, which is why we have so many false positives.

As far as the grade of the false positives, we have looked at that and actually the study that Dr. Paulus published a couple of years ago really broke that down in detail. And we haven't been able to find any correlation with low to high grade.

There are certainly very few Grade Vs that are overcalled. And most of them tend to be I to II. But we haven't been able to correlate a grade with overcalling.

And how are we sure that we captured all of our patients? Well, we're not. So by the methodology that we used for this study because we don't perform DSA in all of our patients any more this is the only way that we could potentially capture any patient who had an injury.

As far as the timing to digital subtraction angiography and whether patients may refuse or just leave before they can get it, we actually have a very cooperative group of neurovascular folks who typically perform the exam within 12 hours and often much sooner, day or night, as far as, or weekends, to confirm their tests so I don't think there are many patients that we have a suspected injury. And I don't know of any patients who had a suspected injury that checked out or just refused confirmatory testing.

To address the question about missing high-grade injuries, that is typically not the case. You know, in the previous study that resulted in this algorithm, 60% of the injuries that were missed on CTA were Grade I and then the majority of the remainder were Grade II. There were very few Grade III and there were almost no Grade IV and V that were missed.

Looking at bleeding complications, that's certainly something to consider. And we are actively looking at it at this time but we don't have numbers that I can give you.

And as far as the issues of VTE, the decision to put people on heparin or not specifically refers to systemic, low-intensity heparin infusions and does not have anything to do with normal heparin or enoxaparin prophylaxis in terms of VTE so we have not looked at VTE specifically in these patients.

We did not specifically break down the carotids versus vertebrals in terms of our false positives, again, because that was previously looked at in the last study that compared DSA and CTA in all of the patients.

So we hesitate to try and break down the numbers that much when we don't have the gold standard test on all of these patients.

Looking at carotid versus vertebral treatment, especially early-on in patients, we don't differentiate necessarily between patients who have a suspected carotid versus vertebral injury in terms of our initial treatment. We typically tailor that once the confirmatory DSA has been performed.

Regarding who gets screened, we perform, as Dr. Burlew mentioned, approximately seven screening CTAs per day. And that can certainly vary with the season.

But we don't use these pre-defined injuries any more necessarily because the screening CTAs are performed during other indicated workup, we do a lot more screening CTAs than we ever did screening previously. So there could certainly be bias there in terms of who does get screened and that's another possibility where we could potentially be missing injuries.

But that's why the arm of our algorithm where those who have an unexplained neurological deficit, whether or not they have a screening CTA, will get a digital subtraction angiogram.

And someone, again, asked about time to DSA. As I mentioned, we have a very cooperative group of neurovascular team that will typically do these very rapidly and in the middle of the night, even on the weekends, as long as they are available.

Thank you.