Diagnostic accuracy of computed tomography angiography (CTA) for diagnosing blunt cerebrovascular injury in trauma patients: a systematic review and meta-analysis

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Abstract

Objectives Previous literature showed that the diagnostic accuracy of computed tomographic angiography (CTA) is not equally comparable with that of the rarely used golden standard of digital subtraction angiography (DSA) for detecting blunt cerebrovascular injuries (BCVI) in trauma patients. However, advances in CTA technology may prove CTA to become equally accurate. This study investigated the diagnostic accuracy of CTA in detecting BCVI in comparison with DSA in trauma patients.

Methods An electronic database search was performed in PubMed, EMBASE, and Cochrane Library. Summary estimates of sensitivity, specificity, positive and negative likelihood, diagnostic odds ratio, and 95% confidence intervals were determined using a bivariate random-effects model.

Results Of the 3293 studies identified, 9 met the inclusion criteria. Pooled sensitivity was 64% (95% CI, 53–74%) and specificity 95% (95% CI, 87–99%). The estimated positive likelihood ratio was 11.8 (95%, 5.6–24.9), with a negative likelihood ratio of 0.38 (95%, 0.30–0.49) and a diagnostic odds ratio of 31 (95%, 17–56).

Conclusion CTA has reasonable specificity but low sensitivity when compared to DSA in diagnosing any BCVI. An increase in channels to 64 slices did not yield higher sensitivity. There is a risk for underdiagnosis of BCVI when only using DSA to confirm CTA-positive cases, especially in those patients with low-grade injuries.

Key Points

• Low sensitivity and high specificity were seen in identifying BCVI with CTA as compared to DSA.
• Increased CTA detector channels (≤ 64) did not lead to higher sensitivity when detecting BCVI.
• The use of CTA instead of DSA may lead to underdiagnosis and, consequently, undertreatment of BCVI.

Keywords Cerebrovascular trauma · Wounds, nonpenetrating · Angiography, digital subtraction · Computed tomography angiography

Abbreviations

BCVI Blunt cerebrovascular injury
CTA Computed tomography angiography
DSA Digital subtraction angiography

Introduction

Blunt cerebrovascular injuries (BCVI) collectively describe all non-penetrating traumatic injuries to the extra- or intracranial carotid and vertebral arteries. The mechanism of injury is either high-energy flexion, extension, or rotation of the neck, or a direct blow to or laceration of the blood vessels. At the level of the vessel wall, there is a risk of tear formation of the tunica intima because of the increased
arterial strain. Expedited by a trauma-induced state of hypercoagulability caused by the initial trauma, the exposed subendothelial collagen activates the coagulation cascade, leading to an intraluminal thrombus formation at the site of the tear or a complete vessel occlusion. The arterial defect can also be a gateway for blood to enter the underlying layers of the vessel wall and can cause the formation of a traumatic (pseudo) aneurysm. As a result, patients with a BCVI are at risk of a secondary brain injury caused either by thromboembolism or occlusion of the artery [1–4].

Previously, BCVI was considered a rare cause of cerebral ischemia and ischemic stroke. Due to improved diagnostic imaging modalities, awareness, and the introduction of standard screening protocols, such as the Memphis and (modified) Denver criteria, the reported incidence of BCVI among blunt trauma patients has increased over recent years [5–9]. The prevalence ranges from 1–2% in patients with blunt trauma to 9% in patients with a severe head injury [3, 10, 11]. When comparing BCVI to non-traumatic brain injuries such as stroke, BCVI is associated with poorer cognitive outcomes, although long-term outcomes following BCVI are missing [12].

There is a 72-h window after injury to provide anti-aggregation and anticoagulation therapy to reduce the risk of secondary brain injury [4]. Screening of patients suspected of BCVI remains pivotal as up to 80% of these patients do not display neurological symptoms at presentation [13, 14]. The golden standard for diagnosing BCVI is digital subtraction angiography (DSA). However, non-invasive and fast screening modalities such as computed tomography angiography (CTA) are increasingly utilized in the acute phase [15–18]. A previously published meta-analysis showed great variability in the sensitivity of BCVI detection using CTA when compared to DSA [19]. Although DSA is the golden standard to date, recent data suggest that CTA with 64 channels has comparable sensitivity rates in diagnosing BCVI and could potentially replace DSA [19, 20]. Therefore, we performed a systematic review and meta-analysis to evaluate the contribution of new data on CTA sensitivity in diagnosing BCVI [19]. We hypothesized that CTA would result in similar accuracy for diagnosing BCVI compared to the golden standard DSA.

### Material and methods

#### Literature search

Studies containing CTA as diagnostic imaging for BCVI that were published until February 24, 2021, were screened independently by two investigators (C.C.K., W.B.S.). An electronic database search was performed in both PubMed, EMBASE, and Cochrane Library using the following keywords: carotid, carotid artery, vertebral artery, intracranial, extracranial, neck, vertebral and vascular system, combined with blunt wound, or blunt trauma, or nonpenetrating injury/wound using the Boolean operator AND for the population. The index and reference test were defined using the keywords: computed tomography angiography, CTA, angiography, and angiotomography, digital subtraction angiography, digital subtraction arteriography, DSA, cerebral angiography, and diagnosis. Additional publications were identified through citation chaining of the bibliography of reviews and other potentially relevant studies.

#### Study selection and data extraction

Both investigators (C.C.K., W.B.S.) reviewed titles and abstracts for relevance and identified potentially relevant citations for full-text review using the online reviewing tool Rayyan (http://rayyan.qcri.org) [21]. The complete inclusion and exclusion criteria are shown in Table 1.

Investigators extracted the subsequent data: study design; date of patient screening; study location; inclusion and exclusion criteria; number of patients included; number of patients excluded; number of patients included in the final analysis; reference and index test; mean age and gender of participants; primary unit of analysis; who reviewed the reference and index test and whether this was done blinded; the arteries examined for BCVI; the type of CT scanner and DSA equipment; the number of slices; slice thickness; size interval; level of reconstruction; injection rate; type of contrast used in CTA and DSA; typical contrast volume used in CTA and DSA; true positives, negatives, false positives, and negatives.

| Table 1 | Inclusion and exclusion criteria |
| --- | --- |
| **Inclusion criteria** | **Exclusion criteria** |
| Population: Age ≥ 16 with blunt trauma suspected of BCVI identified by the Denver or modified Memphis criteria. | Case reports, editorials, and opinions |
| Intervention: multidetector CT angiography | Case studies with less than five patients |
| Study design: primary studies on diagnostic accuracy | Unoriginal and unpublished studies. |
| Data: presented allowing two-by-two contingency table construction. | Studies with missing data / full text irretrievable: |
| | In case of protocol and publication: at least 1 try for contact to gain the article. |
| | In case the article was not available: at least 1 try with the department’s secretary for gaining the article. |
Assessment of methodological quality

Methodological quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies, second version (QUADAS-2), which investigates both risks of bias as well as applicability concerns [22]. QUADAS-2 uses 7 questions to assess study selection and setting, conduct, and interpretation of the reference and index test, and flow and timing using three levels of bias (high, low, and unclear). Patient selection was considered at low risk of bias when a consecutive or random sample of patients was enrolled, when the case-control design was avoided, and when a study avoided inappropriate exclusions. A low-risk setting was one in which all patients underwent both CTA and DSA. Additionally, there was a low risk of bias in the interpretation of the index and/or reference test if the reviewers had no prior knowledge of the results of the reference test or the index test. A maximum of 48-h interval between CTA and DSA is presumed to be appropriate [19].

Data synthesis

Some studies reported data on blunt carotid artery injury (BCVI\textsubscript{carotid}) or blunt vertebral artery injury (BCVI\textsubscript{vertebral}) separately but did not include data on BCVI per patient [6, 19, 23–25]. Patients diagnosed with BCVI could potentially have multiple injuries to either or both the carotid and vertebral arteries. Therefore, studies that only reported results for BCVI\textsubscript{carotid} and BCVI\textsubscript{vertebral} did not allow for calculation of diagnostic accuracy per patient. Instead, all data were combined in one larger overall group called “any BCVI.” In this group, true and false positives and negatives were either assessed per patient and/or from the combined results of BCVI\textsubscript{carotid} and BCVI\textsubscript{vertebral} if no per-patient data was given. Separate analyses on diagnostic accuracy were also performed for BCVI\textsubscript{carotid} and BCVI\textsubscript{vertebral}.

When true and false positive and negative findings were separately reported by different radiologists, the average of each observation was calculated for that study population. Additionally, and if reported separately, the sum of the common, cervical, or intracranial carotid artery was calculated to determine BCVI\textsubscript{carotid}. Likewise, the sum of the cervical or intradural vertebral artery was calculated to determine BCVI\textsubscript{vertebral}.

Statistical analysis

True and false positives and negatives were used to individually calculate the sensitivity and specificity of CTA for each study. The 95% confidence interval was calculated using the Clopper-Pearson interval method [26]. Summary estimates of sensitivity, specificity, positive and negative likelihood, and diagnostic odds ratio and their 95% confidence intervals were determined for CTA in BCVI\textsubscript{carotid}, BCVI\textsubscript{vertebral}, and any BCVI using a bivariate random-effects model. This allowed the heterogeneity beyond chance between studies to be considered. The percentage of total variation across studies was evaluated using forest plots, chi-square, Cochrane Q, and $I^2$, which measures the impact of unobserved heterogeneity [27]. We considered $I^2$ values between 0 and 50% as medium heterogeneity, while values > 50% were considered high heterogeneity, and $p$ values < 0.05 significant.

Hierarchical summary receiver operating characteristic (SROC) plots were created for visual assessment of the threshold effect by calculating the squared correlation coefficient estimate from the between-study covariance parameter [28]. Within the SROC plot, observed data points, a summary operating point of sensitivity and specificity, and 95% confidence interval contour were displayed.

Cook’s distance was determined to analyze the influence of each study [29]. Outliers were evaluated using scatter plots using standardized predicted random effects and bivariate box plots [30]. Publication bias was assessed using Deek’s funnel plot asymmetry ($p < 0.10$ indicating significant asymmetry) [31]. To explore sources of heterogeneity, subgroup analyses, and univariate meta-regression were used. All analyses, except subgroup analyses and univariate meta-regression, were performed using STATA 16.0 (StataCorp. 2019. Statistical Software: Release 16: StataCorp LLC.) in combination with the MIDAS command [32]. Subgroup analyses and meta-regression were performed using Open Meta Analyst [33].

Results

Study selection and inclusion

Our electronic database search of PubMed, EMBASE, and the Cochrane Library yielded 3293 studies, of which 92 studies were identified as duplicates. Of the 3204 studies screened for title and abstract, 102 articles were found eligible for full-text assessment. Subsequently, 93 articles were excluded for various reasons, including not having DSA as a reference test for any and/or all patients (29 studies), not reporting the outcome or population of interest (21 studies), no CTA as an index test for any and/or all patients (8 studies), non-original studies (14 review studies), wrong study design (14 studies), and no full-text availability (7 studies). Finally, 9 studies were included for quality assessment (Fig. 1) [6, 20, 23–25, 34–37].
Quality assessment

The risk of bias and applicability were assessed using QUADAS-2 tool questions for all included (Fig. 2). Two studies reported no or unclear data on whether patients were consecutively enrolled or randomly selected, or whether a case-control design was avoided [25, 34]. One study systematically applied CTA in patients suspected of BCVI and used DSA in a minority of those patients [23]. They, therefore, anticipated a higher rate of positives in their study population. We also anticipated high risk of bias in patient selection for this study. Three studies clearly stated whether the results of the index test were interpreted without prior knowledge of the results of the reference test [20, 24, 25]. This was also the case for four studies regarding the reference test [20, 24, 25, 35]. In two studies, it was unclear whether all patients were included in the analysis [35, 37]. Overall, there were no concerns for applicability with either of the studies included. The risk of bias was not considered great enough to exclude any study from further analysis.

Study characteristics

All study and patient characteristics are summarized in Table 2. Of the 9 included studies, 3 were conducted retrospectively, 5 prospectively, and one both retrospectively and prospectively. A total of 1918 patients were screened for BCVI with both DSA and CTA, 67% male with an overall mean age of 40.5 years (range 1–94).

Six studies used CTA with 16 slices or more [20, 24, 25, 35–37]. One study reported both data for 16 and 64 slices CTA [36]. We chose to consider these as two separate data sets in our analyses. Most studies used CTA with Omnipaque (Amersham Health Inc.), with varying concentrations between 300 and 350 mg/mL [35–37]. DSA was used as a reference test in all studies, with descriptions on model and contrast type being noted in almost all except for two studies [6, 34]. A complete summary of the geographical information for all commercial products is shown in Appendix 1.

All diagnostic accuracy estimates are listed in Table 3. Overall, three studies reported both outcomes for BCVI per-patient and per-artery [20, 35, 37]. The per-patient data were used to calculate true and false positives and negatives in the category “any BCVI.” If unavailable, the sum of both carotid and vertebral injuries was used.

Outlier detection, influence analysis, and publication bias

Using standardized predicted random effects and bivariate box plots, outliers were identified for all four categories (per-patient, BCVI_carotid, BCVI_vertebral, and any BCVI). In one study, outliers were detected in the category “any BCVI” [35]. Additionally, Cook’s distance depicted the same study as an outlier.
Publication bias was assessed using Deek’s funnel plot asymmetry test and visual funnel plot analysis. There was no significant asymmetry between studies in the four different categories, with $p$ values ranging between 0.187 for BCVI\textsubscript{carotid} and 0.914 for any BCVI (Table 6). No concern for publication bias was found.

**Pooled diagnostic accuracy estimates for CTA versus DSA for any form of BCVI**

After outlier removal, 8 studies were included in the analysis for diagnostic accuracy estimates of CTA versus DSA for any BCVI [6, 20, 23–25, 34, 36, 37]. Figure 3 shows the SROC plot for the detection of any BCVI with CTA vs DSA and the covariation in sensitivity and specificity of the studies included. Pooled sensitivity was 64% (95% CI, 53–74%) and specificity 95% (95% CI, 87–99%) (Figs. 4 and 5). There was a high degree of heterogeneity between studies, with an $I^2$ for sensitivity of 76.07 ($p < 0.01$) and specificity of 95.20 ($p < 0.01$) (Fig. 4). Forest plots for the pooled diagnostic odds ratio and positive and negative likelihood ratio are provided in Appendix 2.

**Pooled diagnostic accuracy estimates for CTA versus DSA in BCVI\textsubscript{carotid} and BCVI\textsubscript{vertebral}**

To determine diagnostic accuracy for CTA vs DSA in BCVI\textsubscript{carotid} and BCVI\textsubscript{vertebral}, data were combined from 7 studies [6, 20, 23–25, 35, 37]. Pooled sensitivity was 70% (95% CI, 52–84%) and specificity 98% (95% CI, 94–99%) in BCVI\textsubscript{carotid} (Table 3). Pooled sensitivity was 70% (95% CI, 55–82%) and specificity 99% (95% CI, 94–100%) in BCVI\textsubscript{vertebral} (Table 3).

There was a high degree of heterogeneity between studies, with an $I^2$ for sensitivity of 86.87 ($p < 0.01$) and specificity of 97.64 ($p < 0.01$) for BCVI\textsubscript{carotid} and an $I^2$ for sensitivity of 76.07 ($p < 0.01$) and specificity of 95.20 ($p < 0.01$) in BCVI\textsubscript{vertebral}.
| Study                  | Location                          | Study period From | Until   | Temporality | Index test (slices) | Reference test | No. patients screened with CTA and DSA | Gender | Mean age (years) | Scans reviewed by                                      |
|-----------------------|-----------------------------------|-------------------|---------|-------------|--------------------|----------------|----------------------------------------|--------|-----------------|--------------------------------------------------------|
| Paulus et al [20]     | Memphis, Tennessee, USA           | May 2011          | May 2012| Retrospective | CTA (64)           | DSA            | 594                                    | 373    | 221             | 43 Attending neuroradiologist                           |
| Dicocco et al [24]    | Memphis, Tennessee, USA           | January 2007      | May 2009| Retrospective | CTA (32)           | DSA            | 684                                    | 474    | 210             | 39 NA                                                   |
| Goodwin et al [36]    | Columbus, Ohio, USA               | June 2007         | February 2008 | Prospective | Cervical CTA (16) | DSA           | 158                                    | 117    | 41              | 42 (interventional) Radiologist                        |
| Sliker et al [25]     | Baltimore, Maryland, USA          | May 2004          | November 2004 | Mixed       | Cervical CTA (16 and 64) | DSA | 48                      | NA NA NA |                              | Trauma radiologist                                     |
| Malhotra et al [37]   | Richmond, Virginia, USA           | December 2003     | March 2007 | Prospective | Cervical CTA (16) | DSA           | 89                                     | 54     | 40              | 38 Attending radiologist and senior radiology resident | |
| Eastman et al [35]    | Dallas, Texas, USA                | April 2004        | February 2005 | Prospective | Helical CTA (16) | DSA          | 124                                    | NA NA NA | NA              | Attending neuroradiologist                              |
| Bub et al [23]        | Seattle, Washington, USA          | January 2001      | March 2002 | Retrospective | Cervical CTA (1, 4, and 8) | DSA | 32                      | NA NA NA | NA              | Two neuroradiologists, one third-year radiology resident. |
| Miller et al [6]      | Memphis, Tennessee, USA           | January 2000      | March 2002 | Prospective | Helical CTA (1)   | DSA            | 143                                    | NA NA 37.6 | 37.6           | Staff neuroradiologists                                |
| Biffl et al [34]      | Denver, Colorado, USA             | April 1996        | June 2001 | Prospective | Helical CTA (4)   | DSA            | 46                                     | NA NA NA | NA              | Radiologists experienced in neurovascular imaging     |
Exploration of the sources of heterogeneity found there was no significant difference between studies based on publication year and the number of CT detector rows when calculating combined pooled sensitivity and specificity of CTA for the detection of any BCVI (Table 4). There was a significant difference, however, when comparing per-artery and per-patient studies. Sensitivity was reported at 70.3% (95% CI, 41.3–88.9) in ≥ 16-slice CTA.

### Table 3 Pooled sensitivity, specificity, positive and negative likelihood ratio’s, diagnostic odds ratio’s and funnel plot’s asymmetry for CTA vs DSA per category

| Category               | No. of studies | Sensitivity (%) | Specificity (%) | Positive LRϕ (%) | Negative LRϕ (%) | DOR* | Funnel plot asymmetry (p value) |
|------------------------|----------------|-----------------|-----------------|------------------|------------------|------|---------------------------------|
| Any BCI [6, 20, 23–25, 34, 36, 37] | 8              | 64 [0.53–0.74]  | 0.95 [0.87–0.98] | 11.8 [5.6–24.9]  | 0.38 [0.30–0.49] | 31 [17–56] | 0.914                           |
| BCVI_cervical [6, 20, 23–25, 35, 37] | 7              | 70 [52–84]      | 98 [94–99]      | 35.4 [10.3–121.3] | 0.31 [0.17–0.53] | 116 [23–583] | 0.187                           |
| BCVI_vertebral [6, 20, 23–25, 35, 37] | 7              | 70 [55–82]      | 99 [0.94 –1.00] | 47.8 [10.3–221.8] | 0.30 [0.19–0.48] | 158 [26–962] | 0.474                           |

*Diagnostic odds ratio, ϕLikelihood ratio, BCVI blunt cerebrovascular injury

### Subgroup analyses and meta-regression

Fig. 3 Summary Operating Characteristic (SROC) plot for sensitivity and specificity of CTA vs DSA in diagnosing BCVI
**Table 4** The exploration of heterogeneity via subgroup analysis and meta-regression by identifying covariates in the estimated combined pooled sensitivity and specificity of CTA for detection of any BCVI

| Covariate                        | No. | Mean value (95% CI) | Meta-regression joint p |
|----------------------------------|-----|---------------------|-------------------------|
| **Temporality**                  |     |                     |                         |
| Prospective [6, 34–37]           | 5   | 610                 |                         |
| Retrospective [20, 23–25]        | 4   | 1363                |                         |
| **Number of CTA slices**         |     |                     |                         |
| <16 [6, 23, 34]                  | 3   | 226                 |                         |
| 16 [25, 35–37]                   | 4   | 385                 |                         |
| >16 [20, 24, 36]                 | 3   | 1362                |                         |
| **Primary unit of analysis**     |     |                     |                         |
| Per-artery [6, 23–25]            | 4   | 912                 |                         |
| Per-patient [34, 36]             | 2   | 202                 |                         |
| Per-artery and per-patient [20, 35, 37] | 3 | 859 | 65.9 [36.3–86.8] | 93.0 [59.8–99.2] | < 0.001$ |

*Test of comparison between <16 and 16 slices
ϕTest of comparison between <16 and >16 slices
§Test of comparison between per-artery and per-patient
¥Test of comparison between per-artery and per-artery and per-patient

Fig. 4 Forest plot for pooled sensitivity and specificity for CTA vs DSA in diagnosing BCVI

Fig. 5 Forest plot for pooled sensitivity, specificity, positive and negative likelihood ratios, diagnostic scores and diagnostic odds ratios for CTA vs DSA in diagnosing BCVI
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In diagnosing BCVI as defined by DSA (Table 6). This is slices) and DSA as a reference test [38–40]. This could studies including both higher channel CTA (i.e., > 64 accuracy in detecting BCVI. A possible explanation for the observed low sensitivity is the absence of recent studies including both higher channel CTA (i.e., > 64 slices) and DSA as a reference test [38–40]. This could be attributed to the invasiveness of DSA and the possible complications associated with the technique, higher cost, and its availability in both equipment and expertise. Although one might expect a higher diagnostic accuracy with high-channel CTA, its intra- and interobserver reliability and the expected better yield of detection of BCVI are not established.

Due to its widespread availability, lower invasiveness, and cost-effectiveness, CTA is already widely used in clinical practice to detect BCVI. The complex hemodynamic nature of BCVI, the applied protocols, and guidelines have mainly focused to rule out any patients with a false negative finding for BCVI with CTA, thus eliminating the need for anticoagulation treatment. Although DSA is still presumed to be the golden standard, it is selectively and mostly used to confirm the presence of BCVI in either clinically suspected cerebrovascular injury with negative CTA or to better visualize a highly suspected BCVI on DSA. Therefore, the possibility and desirability of replacing DSA for CTA as the golden standard in diagnosing BCVI is still a subject of discussion.

The use of DSA to only confirm the presence of BCVI on CTA raises other concerns. Studies have shown that neurological symptoms in patients with BCVI might be delayed [12, 13]. Due to the low sensitivity of CTA shown in this study, a substantial number of patients with a false-negative outcome for BCVI are missed, which would leave them untreated. Hence, the pivot question seems to be how harmful undertreatment is in undiagnosed BCVI patients. Assuming that high-grade BCVIs are detected on both DSA and CTA imaging, patients with low-grade BCVI (such as intimal irregularity or intramural hematoma) would be most at risk for undertreatment. However, despite the available recommendations to treat this patient category either with aspirin or heparin for secondary prevention of thrombus formation [39, 41, 42], there is no established evidence that this has a beneficial effect in preventing cerebrovascular events.

This study has some important limitations. First, due to the heterogenic nature of the population in different studies and the difference in sample size, it is difficult to extrapolate the finding to the general trauma population. The use of different equipment with different settings and contrasts limits the applicability of the results to all kinds of equipment used in the field, especially when outdated CT scanners are increasingly being replaced by scanners with 256-detector rows, low-kVp imaging, multi-energy reconstruction, and all kinds of post-processing 3D reconstruction technology. Also, nontrivial settings such as the velocity of injection of the contrast might have influenced the diagnosis of BCVI. Future studies should therefore focus on more modern scanners and standardized protocols.

Second, the human factor is even more important in visualizing subtle changes in imaging. There is no evidence on how accurate radiologists or other specialists are in diagnosing (mild) BCVI in CTA. Subsequently, factors such as special interest, experience, exposure, and central referral might influence the accuracy to visualize even small and subtle changes in imaging [43]. This should be the focus of future studies to rule out the bias introduced by human inconsistency and establish minimum requirements in caregivers to establish a reliable and reproducible statement.

Third, there is a risk of selection bias when including only patients diagnosed with both CTA and DSA. It is possible that, due to time restrictions, patients with polytrauma suspected for BCVI were not included for both CTA and DSA screening. This could lead to an underrepresentation of patients with high-grade BCVI or even those with low-grade dissections that are only screened when severe and/or delayed neurological symptoms occur.

In conclusion, this systematic review and meta-analysis showed moderate to good specificity for CTA (Table 5) in diagnosing BCVI as defined by DSA (Table 6). This is in line with previously published results on the diagnostic accuracy between CTA and DSA for low-channel CTA. However, contrary to our hypothesis and previous results by Paules et al, this study did not find that an increase of CTA channels beyond 16 slices showed higher diagnostic accuracy in detecting BCVI. A possible explanation for the observed low sensitivity is the absence of recent studies including both higher channel CTA (i.e., > 64 slices) and DSA as a reference test [38–40]. This could be attributed to the invasiveness of DSA and the possible complications associated with the technique, higher cost, and its availability in both equipment and expertise. Although one might expect a higher diagnostic accuracy with high-channel CTA, its intra- and interobserver reliability and the expected better yield of detection of BCVI are not established.

Due to its widespread availability, lower invasiveness, and cost-effectiveness, CTA is already widely used in clinical practice to detect BCVI. The complex hemodynamic nature of BCVI, the applied protocols, and guidelines have mainly focused to rule out any patients with a false negative finding for BCVI with CTA, thus eliminating the need for anticoagulation treatment. Although DSA is still presumed to be the golden standard, it is selectively and mostly used to confirm the presence of BCVI in either clinically suspected cerebrovascular injury with negative CTA or to better visualize a highly suspected BCVI on DSA. Therefore, the possibility and desirability of replacing DSA for CTA as the golden standard in diagnosing BCVI is still a subject of discussion.

The use of DSA to only confirm the presence of BCVI on CTA raises other concerns. Studies have shown that neurological symptoms in patients with BCVI might be delayed [12, 13]. Due to the low sensitivity of CTA shown in this study, a substantial number of patients with a false-negative outcome for BCVI are missed, which would leave them untreated. Hence, the pivot question seems to be how harmful undertreatment is in undiagnosed BCVI patients. Assuming that high-grade BCVIs are detected on both DSA and CTA imaging, patients with low-grade BCVI (such as intimal irregularity or intramural hematoma) would be most at risk for undertreatment. However, despite the available recommendations to treat this patient category either with aspirin or heparin for secondary prevention of thrombus formation [39, 41, 42], there is no established evidence that this has a beneficial effect in preventing cerebrovascular events.

This study has some important limitations. First, due to the heterogenic nature of the population in different studies and the difference in sample size, it is difficult to extrapolate the finding to the general trauma population. The use of different equipment with different settings and contrasts limits the applicability of the results to all kinds of equipment used in the field, especially when outdated CT scanners are increasingly being replaced by scanners with 256-detector rows, low-kVp imaging, multi-energy reconstruction, and all kinds of post-processing 3D reconstruction technology. Also, nontrivial settings such as the velocity of injection of the contrast might have influenced the diagnosis of BCVI. Future studies should therefore focus on more modern scanners and standardized protocols.

Second, the human factor is even more important in visualizing subtle changes in imaging. There is no evidence on how accurate radiologists or other specialists are in diagnosing (mild) BCVI in CTA. Subsequently, factors such as special interest, experience, exposure, and central referral might influence the accuracy to visualize even small and subtle changes in imaging [43]. This should be the focus of future studies to rule out the bias introduced by human inconsistency and establish minimum requirements in caregivers to establish a reliable and reproducible statement.

Third, there is a risk of selection bias when including only patients diagnosed with both CTA and DSA. It is possible that, due to time restrictions, patients with polytrauma suspected for BCVI were not included for both CTA and DSA screening. This could lead to an underrepresentation of patients with high-grade BCVI or even those with low-grade dissections that are only screened when severe and/or delayed neurological symptoms occur.

In conclusion, this systematic review and meta-analysis showed moderate to good specificity but low sensitivity of CTA in diagnosing BCVI compared to DSA. Furthermore, CTA with higher channels (16-64) did not increase the diagnostic accuracy of CTA compared to lower channels (<16). This might lead to a risk of undertreatment of BCVI in false-negative cases, especially in those with low-grade injuries. It is unclear whether this is associated with an increased risk of cerebrovascular events. Future studies should focus on a, the diagnostic accuracy of nowadays widely available 256-channel CTA, the inter- and intra-observer reliability, and on the harmfulness of undertreatment of BCVI patients.
Table 5  The characteristics of computed tomography angiography (CTA) per study

| Study | Scanner | Slices | Thickness (mm) | Contrast | Injection rate (mL/s) | Typical volume (mL) | Area scanned |
|-------|---------|--------|----------------|----------|-----------------------|---------------------|--------------|
|       |         | No.    | Thickness interval (mm) | Type | | | |
| Toshiba Aquilion 64-channel computed tomographic scanners | 64-neck 64-body | 1.0 | 0.5 | Optiray 320 (Guerbet LLC) | 5 | 60-75 (neck), 120 (full body) | From the clavicles to the apex of the calvarium |
| Toshiba Aquilion 32-channel computed tomography scanners | 32 | 1 | 0.5 | Optiray 320 (Guerbet LLC) | 4 | 120 | From the clavicles to the apex of the calvarium |
| Toshiba Aquillion 64 detector scanner | 64 | 1.0 | 0.5 | Omniprope 350 (GE Healthcare) | 4 | 75–100 | From the aortic arch to the circle of Willis |
| General Electric (GE), Advantage Lightspeed 16-slice CT scanner | 16 | 1.25 | 0.5 | Omniprope 350 (GE Healthcare) | 4 | 85–125 | From the aortic arch to the circle of Willis |
| Philips Medical Systems, MX8000 IDT, Brilliance 16 Power, or Brilliance Big Bore | 16-neck 16-body | NA | NA | Omniprope 300 (GE Healthcare) | 4 | 100 | From the aortic arch to the circle of Willis |
| Siemens Somatom Sensation-16 multidetector scanner | 16 | 2 | NA | Omniprope 300 (Amersham Health Inc) | 4 | 80 | From the aortic arch to the circle of Willis |
| General Electric (GE) Advantage Lightspeed 16-channel CT scanner GE Medical Systems | 16 | 1.25 | 0.55 | Omniprope 300 (Amersham Health Inc) | 3.5 | 125 | From the aortic arch to the vertex of the head |
| General Electric (GE) Lightspeed four-slice and eight-slice helical multidetector CT scanners and GE HighSpeed single-slice helical CT scanner. | 1, 4, 8 | 1 to 3, mean 1.5 | NA | NA | 4 | 80–110 | From the aortic arch to the circle of Willis |
| Siemens Somatom 4 helical scanner | 4 | 1 | NA | NA | NA | 125 | Including both the aortic arch and the skull base |
| General Electric(GE) Hilite scanner | 1 | NA | NA | Optiray 320, (Mallinckrodt Pharmaceuticals) | 2.5 for 20 s 1.75 for 60s | 155 | From the bottom of C3 to the sella turcica |

NA not available, CTA computed tomography angiography
Table 6  The characteristics of digital subtraction angiography (DSA) per study

| Study                     | Scanner                                      | Contrast Type                          | Typical volume (mL) |
|---------------------------|----------------------------------------------|----------------------------------------|---------------------|
| Paulus et al [20]         | Siemens AXIOM Artis biplane system           | Optiray 320 (Guerbet LLC)              | 50–100              |
| DiCocco et al [24]        | Siemens AXIOM Artis biplane system           | Optiray 320 (Guerbet LLC)              | 50–100              |
| Goodwin et al (64 slices) | Multistar Plus angiographic unit             | Omnipaque 350 (GE Healthcare) and Visipaque 320 (GE Healthcare) | 100–150              |
| Goodwin et al (16 slices)| Multistar Plus angiographic unit             | Omnipaque 350 (GE Healthcare) and Visipaque 320 (GE Healthcare) | 100–150              |
| Sliker et al [25]         | NA                                           | NA                                     | NA                  |
| Malhotra et al [37]       | GE Advantix Biplane Angiography System       | Omnipaque 300 (Amersham Health Inc.)   | 100–150              |
| Eastman et al [35]        | Siemens Artis BA biplane neuroangiographic unit | Omnipaque 300 (Amersham Health Inc.) | NA                  |
| Bub et al [23]            | Philips biplane fluoroscopy tables with 12-inch image intensifier | NA | NA |
| Miller et al [6]          | NA                                           | NA                                     | NA                  |
| Biffl et al [34]          | NA                                           | NA                                     | NA                  |

NA not available, DSA digital subtraction angiography

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Methodology

- retrospective
- diagnostic or prognostic study

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