Cost-Effectiveness of Universal Screening for Blunt Cerebrovascular Injury: A Markov Analysis

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BACKGROUND: Blunt cerebrovascular injury (BCVI) is a significant cause of morbidity and mortality after blunt trauma. Numerous screening strategies exist, although which is used is institution- and physician-dependent. We sought to identify the most cost-effective screening strategy for BCVI, hypothesizing that universal screening would be optimal among the screening strategies studied.

STUDY DESIGN: A Markov decision analysis model was used to compare the following screening strategies for identification of BCVI: (1) no screening; (2) Denver criteria; (3) extended Denver criteria; (4) Memphis criteria; and (5) universal screening. The base-case scenario modeled 50-year-old patients with blunt traumatic injury excluding isolated extremity injures. Patients with BCVI detected on imaging were assumed to be treated with antithrombotic therapy, subsequently decreasing risk of stroke and mortality. One-way sensitivity analyses were performed on key model inputs. A single-year horizon was used with an incremental cost-effectiveness ratio threshold of $100,000 per quality-adjusted life-year.

RESULTS: The most cost-effective screening strategy for patients with blunt trauma among the strategies analyzed was universal screening. This method resulted in the lowest stroke rate, mortality, and cost, and highest quality-adjusted life-year. An estimated 3,506 strokes would be prevented annually as compared with extended Denver criteria (incremental cost-effectiveness ratio of $71,949 for universal screening vs incremental cost-effectiveness ratio of $12,736 for extended Denver criteria per quality-adjusted life-year gained) if universal screening were implemented in the US. In 1-way sensitivity analyses, universal screening was the optimal strategy when the incidence of BCVI was greater than 6%.

CONCLUSIONS: This model suggests universal screening may be the cost-effective strategy for BCVI screening in blunt trauma for certain trauma centers. Trauma centers should develop institutional protocols that take into account individual BCVI rates. (J Am Coll Surg 2023;236:468–475. © 2022 by the American College of Surgeons. Published by Wolters Kluwer Health, Inc. All rights reserved.)

In patients with blunt trauma, blunt cerebrovascular injury (BCVI) is a significant cause of morbidity and mortality. In contrast with nontraumatic vascular dissection, most BCVI is asymptomatic in the initial hours after injury.[1,2] Ischemic stroke can occur in up to 30% of BCVI, typically within 72 hours after injury, but BCVI-related stroke has been reported days to months later.[3-6] There is a large burden associated with stroke when measured by

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose. Ronald J Weigel, CME Editor, has nothing to disclose.

Presented virtually at the 93rd Annual Meeting of the Pacific Coast Surgical Association, Maui, HI, February 2022.

Received August 21, 2022; Revised November 5, 2022; Accepted November 8, 2022.

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https://doi.org/10.1097/XCS.0000000000000490
ISSN 1879-1190/22

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Abbreviations and Acronyms

BCVI	=	blunt cerebrovascular injury
CA-AKI	=	contrast-induced acute kidney injury
CTA	=	CT angiography
DC	=	Denver criteria
eDC	=	expanded Denver criteria
MS	=	Memphis criteria
NS	=	no screening
QALY	=	quality-adjusted life-year
WTP	=	willingness-to-pay

both quality-adjusted life-years (QALYs) lost and cost.[7-9] A recent Western Trauma Association multicenter study showed that most patients with BCVI-related stroke were young, with a median age of 39 years, in contrast with ischemic stroke in the general population, where the median age is around 69 years.[4,10] Therefore, prevention of stroke or reduction in its risk of occurrence is critical in the blunt trauma patient, because the downstream impact is substantial.

Stroke is the leading cause of death and disability worldwide, causing enormous economic costs to individuals and the healthcare system.[11] Direct medical costs for stroke range from $1,593 to $34,138, with insurance status and hospital length of stay potentially playing key roles in variability.[11] However, after a stroke, up to 50% of survivors remain critically disabled, leading to high costs for poststroke care. The average lifetime per person cost for inpatient care, rehabilitation, and follow-up after stroke is estimated at $140,048 in the US.[7] Therefore, prevention, reduction, and early identification of BCVI-related strokes after blunt trauma may play a critical role in reducing costs.

The optimal method of BCVI screening has been difficult to ascertain because screening criteria across trauma centers are not uniform.[12] In addition, the most optimal treatment when BCVI is detected has not been standardized.[13] Imaging quality and interpretation expertise is varied across trauma centers. Before the first implemented screening strategies in the late 1990s, BCVI incidence was reported to be approximately 0.1%, an order of magnitude lower than most estimates today.[2,14] Multiple clinical screening strategies have been developed since then to identify patients who may benefit from screening CT angiography (CTA) or other screening modalities. The most used criteria are the Memphis criteria (MC), Denver criteria (DC), and expanded DC (eDC).[2] The diagnostic performance of BCVI clinical screening criteria is poor. With a sensitivity of 74%, eDC outperforms other BCVI screening algorithms. Up to 20% of Grade 3 BCVI and higher are missed with sensitive screening algorithms, and many now argue for universal BCVI screening.[15-17] However, the most cost-effective strategy for BCVI screening is unknown, and recent literature has demonstrated that universal screening may be an appropriate strategy in select patient populations.[15] We aimed to compare universal screening, MC, DC, eDC, and no screening (NS) and identify the optimal strategy with cost-effectiveness analysis. We hypothesized that universal screening would be the most cost-effective method of BCVI screening.

METHODS

Overview

A Markov decision model was constructed and used to compare various screening strategies for BCVI. BCVI was defined and graded using the Biffl Scale with presence of injury on CTA.[18] Five screening strategies were compared: universal screening, MC, DC, eDC, and NS. NS was included in the model because most cost-effectiveness models include a baseline that mimics the natural history of the disease.[19] In general, NS is not used in the US, and it is important to note that inclusion of NS does not impact the results of the model and that ultimately the 2 optimal strategies are compared with each other via their incremental cost-effectiveness ratio. Patients were modeled for an acute blunt trauma and assigned a true BCVI state, which was further categorized as detected or missed based on the modeled screening strategy. Each cohort then was able to transition into 3 distinct states each model cycle:

death, stroke, and a general posttrauma state (Figure 1). Transition probabilities between each state were conditional on the presence and detection of BCVI. The model was implemented using Python (Python Software Foundation, Python Language Reference, version 3.9.5; available at http://www.python.org). All code is available on request.

Patient population and model inputs

All model input variables used in the analysis are provided in Table 1. A recent study by Black and colleagues describes performance characteristics of each screening strategy based on retrospective review at an institution that had implemented universal screening, with BCVI defined as presence on CTA.[15] Because performance characteristics are related to the underlying population in which they are measured, model estimates of underlying probability of BCVI were also informed by this study, as well as average age and injury severity scores.[15] In modeling of the acute event, a recent meta-analysis by Kim and colleagues was used to provide estimates of stroke risk and mortality in patients with BCVI, with and without use of antithrombotic therapy.[2] We assumed that only patients with BCVI found on imaging would be treated with antithrombotic therapy. For patients without BCVI, initial probability of mortality was estimated using an average mortality of all blunt trauma patients.[24] For follow-up greater than 1 month, patients were assumed to have comparable mortality rates to the general, age-matched population, except those with previous stroke, who had an elevated relative risk of mortality. In our base-case scenario, patients were followed for a single-year time horizon. A single-year horizon was chosen secondary to limited information about long-term follow-up of patients with blunt trauma, and scarce literature specific to patients with BCVI. In addition, a single year was used because the majority of stroke related to BCVI is believed to occur within 72 hours of injury and is not a recurrent event.[4,29]

Utility, costs, and outcomes

In this model, costs included imaging, initial stroke events, and the monthly/chronic cost of stroke. Patients experienced decrements in QALY based on utilities for stroke and posttrauma states. Costs and utilities were discounted at an annual rate of 3% as standard.[30] Costs were based on a healthcare payer perspective and are adjusted for inflation to 2018.

The primary objective was to determine the most cost-effective strategy for screening, which was calculated using an incremental cost-effectiveness ratio approach with a willingness-to-pay (WTP) threshold of $100,000 per QALY gained, as in previous studies.[31,32] For each strategy, the total CT scan use, number of strokes, mortalities, cost, and QALY were calculated per 1,000 patients. Estimates provided for implementation of screening strategies across the US were adjusted for exclusion of isolated extremity injuries, using the same percentage (6.8%) as reported in the study by Black and colleagues, and are based on estimates of blunt trauma annually.[15,20,21]

Sensitivity analysis

Deterministic sensitivity analyses were conducted with each input variable to identify inputs that most directed model results. In deterministic sensitivity analyses, each input variable is varied between wide ranges while holding

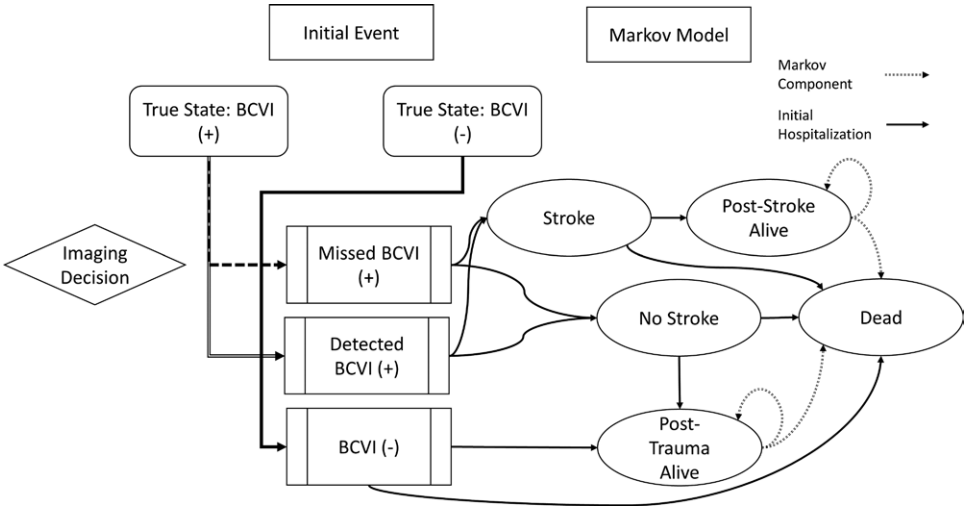

Figure 1. Conditions for the model states are shown with input variables listed in Table 1. BCVI, blunt cerebrovascular injury.

Table 1. Model Input Variables

Variable	Base-case	Distribution	Source
General demographic			
Starting age, y, median	50	Uniform (40, 60)	[15]
Median Injury Severity Score	17	Gamma (17, 1)	[15]
Annual cases of blunt trauma, US, n	2,405,000	Constant	[20,21]
Isolated extremity injury, blunt trauma, %	6.8%	Constant	[15]
Incidence of BCVI	0.076*	Uniform (0.005, 0.10)	[15]
Relative risk of mortality in stroke patients	1.75	Lognormal (1.75, 0.35)	[22]
Transition probabilities: patients with blunt cerebrovascular injury			
Stroke without therapy	0.336	Beta (79, 156)	[2]
Odds ratio of stroke with therapy†	0.20	Lognormal (0.20, 0.60)	[2]
Mortality without therapy	0.403	Beta (31, 46)	[2]
Mortality with therapy	0.166	Beta (42, 211)	[2]
Transition probabilities: patients without blunt cerebrovascular injury			
Stroke	0.011	Beta (833, 74,861)	[23]
Mortality	0.055	Beta (40,429, 694,044)	[24]
Cost‡			
CT angiography	708	Normal (708, 141.6)	[21]
Stroke (initial)	19,248	Normal (19,248, 3,850)	[25]
Cost of stroke (chronic/monthly)	2,924	Normal (2,924, 585)	[26]
Aspirin (monthly)	4	Constant	—
Utility§			
Acute stroke	0.5	Beta (49.50, 49.50)	Model assumption
Chronic stroke¶	0.64	Beta (62.13, 34.95)	[27]
Acute trauma	0.5	Beta (49.50, 49.50)	Model assumption
Chronic trauma	0.77	Beta (1.25, 0.37)	[28]
Test characteristics: sensitivity			
Denver Criteria	0.575	Beta (271, 200)	[15]
Expanded Denver Criteria	0.747	Beta (352, 119)	[15]
Memphis Criteria	0.473	Beta (223, 248)	[15]
CT	1	Constant	—
Test characteristics: specificity			
Denver Criteria	0.791	Beta (4,600, 1,216)	[15]
Expanded Denver Criteria	0.615	Beta (3,577, 2,239)	[15]
Memphis Criteria	0.839	Beta (4,880, 936)	[15]
CT	0	Constant	—

Distributions key: Uniform (a, b); Beta (α, β); Gamma (k, θ); Lognormal (μ, σ^2); Normal (μ, σ^2).
*Corresponding to 7.6% in the overall population.
†In relation to the risk of stroke in patients with BCVI.
‡Cost is modeled with SD equal to 20% of the mean value.
§Utility distributions are estimated with a variance equal to 10% of the mean value.
¶The long-term utility of a stroke is estimated using long-term utility after minor stroke.
BCVI, blunt cerebrovascular injury.

all other variables constant; for example, the incidence of BCVI was studied between 0.005 and 0.10. Additionally, a probabilistic sensitivity analysis was conducted with 10,000 iterations of randomly sampled values from estimated distributions of each input variable (Table 1). In a probabilistic sensitivity analysis, no input variable is constant (unless stated in Table 1), and all inputs for each iteration are randomly selected from the distributions provided in Table 1.

RESULTS

In our base-case scenario, we found that universal screening was the most cost-effective screening strategy, with

an incremental cost-effectiveness ratio of $71,949 per QALY gained when compared with the next most effective strategy. The other cost-effective strategies on the efficiency frontier were the DC and eDC. Both NS and the MC were dominated, as they resulted in higher costs and lower benefits than the DC, eDC, and universal screening strategies[33] (Table 2). Per 1,000 patients with blunt trauma, our model estimated approximately 21 strokes per 1,000 without any screening, compared with 15 per 1,000 with universal screening, ie a decrease in stroke of 29%. This translates to approximately 13,859 strokes averted annually in the US with universal screening compared with NS, and 10,353 fewer strokes when using the next most cost-effective strategy, the eDC, compared with NS. Annually, implementation of universal screening would require approximately 2,240,000 CT scans, compared with 925,000 with the eDC.

Deterministic sensitivity analyses indicated that results were most sensitive to the estimated true incidence of BCVI (Figure 2A). Above 6% prevalence, universal screening was the optimal strategy, but eDC screening was optimal for BCVI prevalence between 2.6% and 6.0%. The DC was optimal for prevalence between 1.26% and 2.6%, and MC between 0.88% and 1.26%. Below a prevalence of 0.88%, NS was optimal. The model was also sensitive to the odds ratio of stroke in BCVI patients who received therapy vs in those with no therapy (Figure 2B). The base-case odds ratio value in our model was 0.20, and for odds ratios between 0.01 and 0.35, the optimal screening strategy was universal screening. However, when the odds ratio of stroke in BCVI patients who receive therapy is greater than 0.35, the optimal screening strategy is the eDC.

In our probabilistic sensitivity analysis, the single-year horizon model showed that universal screening was the most cost-effective strategy (Figure 3) for WTP threshold greater than $99,000. For WTP thresholds greater than $16,000 and less than $99,000, the eDC was optimal.

Table 2. Base-Case Analysis, Results of a Simulation Analysis per 1,000 Blunt Trauma Patients

Strategy	QALY per 1,000 patients	Cost per 1,000 patients, $	ICER ($/QALY)	CT scan per 1,000 patients	Stroke per 1,000 patients
NS	609	1,287,401	Dominated	0	21
MC	617	1,169,777	Dominated	185	18
DC	618	1,153,101	N/A	237	17
eDC	621	1,187,166	12,736	413	16
Universal screening	625	1,470,243	71,949	1,000	15

ICERs are calculated as (Cost A – Cost B)/(QALY A – QALY B) for 2 strategies, A and B. Table QALY and cost per 1,000 patients are rounded to the nearest whole number, but ICERs were computed using exact model outputs.

DC, Denver criteria; eDC, expanded Denver criteria; ICER, incremental cost-effectiveness ratio; MC, Memphis criteria; N/A, not applicable; NS, no screening; QALY, quality-adjusted life-year.

DISCUSSION

In this study, we found that universal screening was the most cost-effective strategy for screening of BCVI when the prevalence of BCVI is more than 6.0%. For our base-case rate of BCVI, we used a single-institution study that provided sensitivities and specificities of each screening protocol tested.[15] After implementation of a universal screening protocol, the underlying rate of BCVI in this article was 7.6%, which is significantly higher than previous estimates of 1% to 2%.[15,34] In our cost-effectiveness model, NS was dominated by other strategies, costing more than (apart from universal screening) and resulting in fewer QALYs than any other screening protocol. Although universal screening was the optimal strategy in our analysis, we found the model to be sensitive to the underlying rate of BCVI as well as to the effectiveness of antithrombotic therapy for BCVI patients. However, to account for the uncertainty in model inputs and their

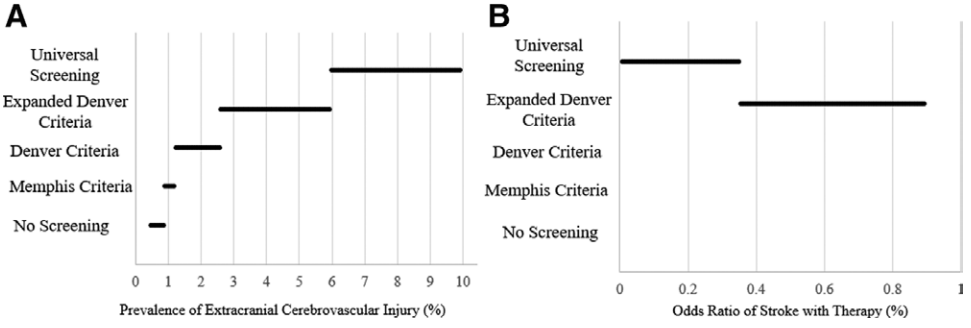

Figure 2. Optimal screening strategy based on the prevalence of extracranial cerebrovascular injury (A) and on the odds ratio of stroke with therapy vs no therapy (B). Modeled with 1-year horizon. Based on odds ratio of stroke with therapy, only the 2 optimal strategies, universal screening and extended Denver criteria, are shown in the graph.

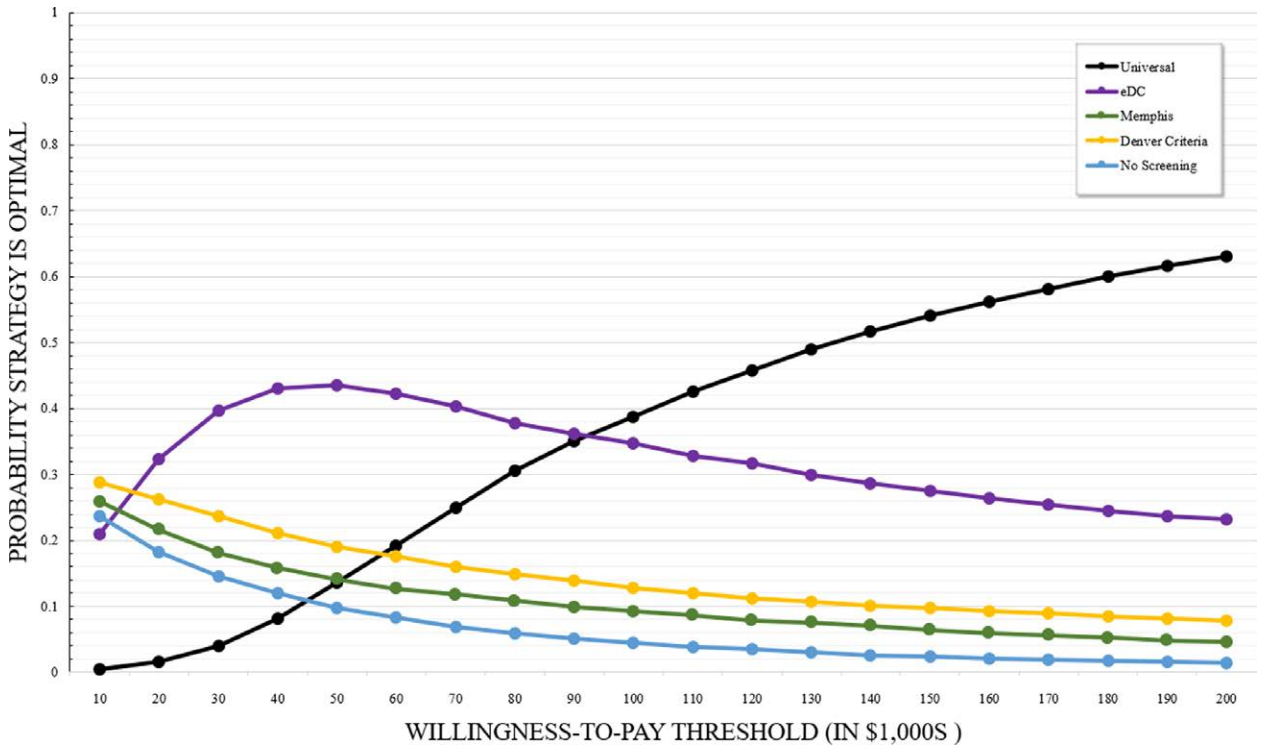

Figure 3. Optimal screening strategy for cerebrovascular injury in patients of blunt trauma: probabilistic sensitivity analysis, modeled with 1-year horizon. eDC, extended Denver criteria.

underlying distributions, we used a probabilistic sensitivity with 10,000 iterations of unique input variable sets. This also demonstrated universal screening to be the most cost-effective strategy for WTP thresholds greater than $99,000 per QALY gained, consistent with the findings of our base-case analysis.

Estimates of the reduction in risk of stroke from antithrombotic therapy were based on a recent meta-analysis by Kim and colleagues that includes 10 studies, 5 of which did not find significant difference in stroke compared with no therapy.[2] Although the synthesized data demonstrated an odds ratio of 0.20 (95% CI 0.06 to 0.65, $p < 0.0001$), the quality of certainty of evidence was graded to be very low, secondary to serious bias, inconsistencies, and indirectness.[2] In our analysis, we found that eDC was the optimal strategy as the effectiveness of antithrombotic therapy diminished, and in 1-way sensitivity analyses, this threshold was an odds ratio of 0.35 vs no therapy. In other words, if the odds ratio of stroke in patients that receive antithrombotic therapy vs no therapy is greater than 0.35, universal screening is no longer the most cost-effective strategy. However, given the existing data on the incidence of stroke after BCVI, universal screening appears to be the most effective strategy for preventing stroke in trauma patients. Further studies are needed to better define the incidence of stroke that occurs after BCVI.

To our knowledge, this is the first decision analysis that compares cost-effectiveness strategies for screening using recent data. The associated costs and quality-of-life burden with BCVI-associated stroke and neurological complications are significant.[35] One previous decision analysis has demonstrated the most cost-effective modality for screening of BCVI to be CTA, although this study compared modalities rather than screening criteria.[36] A recent study by Malhotra and colleagues[37] showed selective CTA in high-risk patients to be the optimal strategy, rather than universal screening. However, these results are previous to recent data about universal screening test performance characteristics that have been shown to miss BCVI in almost 20% of patients.[16,17,37] As imaging modalities have improved, it stands to reason that the reported incidence of BCVI is higher than originally known.[14-17] Our analysis indicates that universal screening may be the best method to reduce the catastrophic and costly consequences of missed BCVI.

An important finding of our study is that the cost-effectiveness method of BCVI screening is dependent on the incidence of BCVI as well as the effectiveness of antithrombotic therapy. This suggests that there is room for institutional protocols to be developed that determine

the most effective screening strategy locally. In centers with a high volume of BCVI, universal screening may be the most effective method for screening. In centers with a lower number of BCVIs, eDC may be the most effective method of screening. Further studies are needed to better elucidate when one strategy may be better than the other. The adoption of universal screening may eventually lead to more nuanced selection criteria. For example, a ground-level fall likely has a different rate of BCVI than a high mechanism rollover motor vehicle crash or pedestrian struck by a high-speed automobile. Future research is needed to elucidate if all patients or a subset of high-risk mechanisms benefit from universal screening. In the meantime, this study and the work by previous authors demonstrate that the current selection criteria do not adequately capture BCVI, and universal screening may be the most cost-effective strategy.

Our model is subject to multiple limitations, particularly with respect to the paucity of data available about outcomes of patients with BCVI. There are limited long-term follow-up data of trauma patients, and the impact of early detection of BCVI on long-term outcomes is unknown. There is limited certainty in the evidence about therapy for BCVI, and the strength of the effect may significantly impact model results. Our model assumes that the effect of antithrombotic therapy is immediate, and that the only strokes attributable to undetected BCVI occur during the initial month. However, it is likely that later strokes do occur in undiagnosed BCVI, which would further strengthen our finding that universal screening is the most cost-effective method. However, 1 additional limitation is that our estimates of the efficacy of antithrombotic therapy are based on patients in whom BCVI was detected in institutions that did not have universal screening. Therefore, many of our injuries may be low-grade and unaffected by treatment, which may result in overtreatment. The choice of antithrombotic therapy cannot be determined in our analysis, because our data are based on an aggregate estimate that does not distinguish between types of therapy.[2] An additional limitation is use of a single-center study to determine test performance characteristics, and whether their results generalize to other populations is unknown. In addition, the model did not account for potential harmful effects of increased CTA use, namely contrast-induced acute kidney injury (CA-AKI). Data about CA-AKI are limited to a single study, which showed no difference in CA-AKI rates pre- and postimplementation of universal screening for BCVI.[16] Additionally, consensus guidelines from the American College of Radiology and National Kidney Foundation reported that historic risks of CI-AKI were overstated.[38] More recent studies have suggested that contrast nephropathy may not exist, and that IV contrast is not nephrotoxic.[39,40] Although planned initially, a 5-year time horizon could not be performed due to limitations on data about long-term outcomes after BCVI.

CONCLUSIONS

In conclusion, our model suggests universal screening for blunt cerebrovascular injury using CTA is beneficial for blunt trauma patients if the rate of BCVI is 6.0% or greater. However, these results are sensitive to the underlying incidence of BCVI as well as the effectiveness of antithrombotic therapy, suggesting that institutional practices and guidelines should be developed. Future studies should focus on defining BCVI incidence with universal screening and determining long-term morbidity and mortality after BCVI.

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