Blunt cerebrovascular injuries: Outcomes from the American Association for the Surgery of Trauma PROspective Observational Vascular Injury Treatment (PROOVIT) multicenter registry

Rachel M. Russo, MD, MAS, Anders J. Davidson, MD, MAS, Hasan B. Alam, MD, Joseph J. DuBose, MD, Joseph M. Galante, MD, Timothy C. Fabian, MD, Stephanie Savage, MD, MS, John B. Holcomb, MD, Thomas M. Scalea, MD, AAST PROOVIT Study Group *and* **Todd E. Rasmussen, MD**, *Sacramento, California*

BACKGROUND: Administering antithrombotics (AT) to the multiply injured patient with blunt cerebrovascular injury (BCVI) requires a thoughtful assessment of the risk of stroke and death associated with nontreatment. Large, multicenter analysis of outcomes stratified by injury grade and vessel injured is needed to inform future recommendations.

METHODS: Nine hundred and seventy-one BCVIs were identified from the PROspective Vascular Injury Treatment registry in this retrospective analysis. Using multivariate analysis, we identified predictors of BCVI-related stroke and death. We then stratified these risks by injury grade and vessel injured. We compared the risk of adverse outcomes in the nontreatment group with those treated with antiplatelet agents and/or anticoagulants.

RESULTS: Stroke was identified in 7% of cases. Overall mortality was 12%. Both increased with increasing BCVI grade. Treatment with ATs was associated with lower mortality and was not significantly affected by the choice of agent. Withholding ATs was associated with an increased risk of stroke and/or death across all subgroups (Grade I/II: odds ratio [OR], 4.66; 95% confidence interval [CI], 2.48–8.75; Grade III: OR, 7.0; 95% CI, 2.01–24.5; Grade IV: OR, 4.43; 95% CI, 1.76–11.1) even after controlling for covariates. Predictors of death included more severe trauma, Grade IV injury, and the occurrence of stroke. Arterial occlusion, hypotension, and endovascular intervention were significant predictors of stroke. Patients that experienced a BCVI-related stroke were at a 4.2× increased risk of death. The data set lacked the granularity necessary to evaluate AT timing or dosing regimen, which limited further analysis of stroke prevention strategies.

CONCLUSION: Stroke and death remain significant risks for all BCVI grades regardless of the vessel injured. Antithrombotics represent the only management strategy that is consistently associated with a lower incidence of stroke and death in all BCVI categories. In the multi-injured BCVI patient with a high risk of bleeding on anticoagulation, antiplatelet agents are an efficacious alternative. Given the 40% mortality rate in patients who survived their initial trauma and developed a BCVI-related stroke, nontreatment may no longer be a viable option. (*J Trauma Acute Care Surg.* 2021;90: 987–995. Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Epidemiological III; Therapeutic IV.

KEY WORDS: Blunt cerebrovascular injury; anticoagulation; stroke; antithrombotic; antiplatelet.

Submitted: September 8, 2020, Revised: February 8, 2021, Accepted: February 13, 2021, Published online: February 22, 2021.

From the University of California Davis Medical Center, Department of Surgery, Division of Trauma, Acute Care Surgery, and Surgical Critical Care (R.R., J.G.), Sacramento; David Grant Medical Center, Department of Surgery (R.R.), Travis AFB, Fairfield, California; University of Michigan, Department of Surgery, Division of Vascular Surgery (A.D.), Ann Arbor, Michigan; Northwestern University, Feinberg School of Medicine, Department of Surgery (H.A.), Chicago, Illinois; University of Maryland R Adams Cowley Shock Trauma Center (J.D., T.S.), Baltimore, Maryland; University of Tennessee Health Sciences Center, Department of Surgery (T.F.), Memphis, Tennessee; University of Wisconsin Madison Medical Center, Department of Surgery (S.S.), Madison, Wisconsin; Uniformed Services University of the Health Sciences, Department of Surgery, Division of Trauma and Acute Care Surgery (J.H., R.R.), Bethesda, Maryland; and Uniformed Services University of the Health Sciences, Department of Surgery, Division of Vascular Surgery (T.R.), Bethesda, Maryland.

Portions of this analysis were presented at the 76th Annual Meeting of the American Association for the Surgery of Trauma (AAST), September 13 to 16, 2017, in Baltimore, MD.

The AAST PROOVIT study group is: John Sharpe, MD; Tiffany Bee MD; Timothy Fabian, MD, University of Tennessee Health Sciences Center-Memphis. Jonny Morrison, MD, PhD; David Feliciano, MD; Thomas M. Scalea, MD, University of Maryland; R Adams Cowley Shock Trauma Center, Baltimore, MD. David Skarupa, MD; Jennifer A. Mull, RN, CCRC; Yohan Diaz Zuniga, MD, University of Florida-Jacksonville, Jacksonville, FL. Jeanette M Podbielski, RN, CCRP; Garrett Jost, University of Texas Health Sciences Center-Houston, Houston, TX. Richard D. Catalano, MD; Ahmed M. Abou-Zamzam Jr, MD; Xian Luo-Owen, PhD, Loma Linda University Medical Center, Loma Linda, CA. Jennie Kim, MD; Kenji Inaba, MD, Los Angeles County + University of Southern California Hospital, Los Angeles, CA. Nathaniel Poulin, MD, East Carolina Medical Center, John Myers, MD. Michael Johnson, MD; Kristin Rocchi, RN, The University of Texas Health Sciences Center at San Antonio, San Antonio, TX. John K. Bini, MD; Joshua Pringle, MD; Karen Herzing, BSN, RN; Kailey Nolan, BS, Wright State Research Institute - Miami Valley Hospital, Dayton. Ramyar Gilani, MD; Tikesha Smith; Reginva Knight, Ben Taub General Hospital/Baylor College of Medicine, Houston, TX; JBSA Fort Sam Houston, TX. Peter Hammer, MD, Indiana University School of Medicine, Indianapolis, IN. Scott.T.Trexler, MD, San Antonio Military Medical Center/US Army Institute of Surgical Research. Nicholas Namias, MD, MBA, Ryder Trauma Center, University of Miami/Jackson Memorial, Miami, FL. Juan Asensio, MD, FACS, Creighton University School of Medicine, Omaha, NE. Joseph M. Galante, MD; Misty Humphries, MD, University of California-Davis, Sacramento, CA. Ravi R. Rajani, MD, Emory University School of Medicine-Grady Memorial Hospital, Atlanta, GA. George Dulabon, MD; Riyad Karmy-Jones, Peace Health Southwest Washington Medical Center, Vancouver, WA. Andreas Larentzakis MD, George Velmahos, MD, Massachusetts General Hospital, Boston, MA. Suresh Agarwal, MD, University of Wisconsin, Madison, WI. Jayraan Badiee MPH; Michael Sise, MD, Scripps Mercy Hospital. San Diego, CA. Alan Cook, MD; Annette Taylor, RN, BSN, CCRC; John Zumbuhi, RN, MSHA, CCRC, CRCP; Antonia Greigo, CCRC, Chandler Regional Medical Center, Chandler, AZ. Fausto Y. Vinces, DO; Salvatore Docimo, DO, Lutheran Medical Center, Brooklyn, NY. Matthew M. Carrick, MD; Kathy Rodkey, RCIS, CCRC, Medical City Plano, Plano, TX. Sameer Hirji, MD; Reza Askari, MD, Brigham and Women's Hospital, Boston, MA. Forrest O. Moore, MD; Richard Butler, MD, John Peter Smith Hospital, Fort Worth, TX.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.jtrauma.com).

Address for reprints: Rachel M. Russo, MD, MAS, NHDP-BC, Department of Surgery, University of California Davis Medical Center, Room OP512, 2315 Stockton Blvd., Sacramento, CA 95817; email: rmrusso@ucdavis.edu, rachelmrusso@gmail.com.

DOI: 10.1097/TA.0000000000003127

Blunt cerebrovascular injuries (BCVIs) affect 1% to 3% of blunt trauma patients.[1] These rare injuries result in significant morbidity and mortality, particularly if left untreated.[2–4] Blunt cerebrovascular injury–related stroke has been associated with a stroke-related mortality exceeding 50%.[5,6] Despite the importance of treatment, 25% to 40% of patients with BCVIs go untreated because of perceived contraindications (such as traumatic brain injury, solid organ injury, and pelvic trauma) to antithrombotic (AT) agents.[6] Further confounding the decision to initiate AT therapy is disagreement on the risks of nontreatment. Existing single-center studies have reported a wide variation in stroke risk, leading some to question whether treatment is necessary for all BCVIs.[2–4] Ideal management of the multiply injured patient requires thoughtful evaluation, weighing the risk of hemorrhagic complications from ATs against the possibility of stroke and stroke-related death without them.[7] Large, multicenter analysis of BCVI outcomes stratified by injury pattern and treatment rendered is needed to inform future recommendations.[8]

We have performed a large multicenter retrospective analysis of BCVIs, using data gathered through the American Association for the Surgery of Trauma's (AAST) multicenter PROspective Vascular Injury Treatment (PROOVIT) registry. In this report, we aim to identify risk factors for BCVI-related stroke and death, stratify these risks by injury grade and vessel injured, and evaluate the risks associated with nontreatment. In so doing, we strive to inform the management of the multiply injured patient by identifying the BCVIs that may benefit the most from initiation of AT therapy. We hypothesize that nontreatment will significantly increase the risk of stroke and death for all BCVIs, regardless of the injury pattern.

METHODS

Data Collection

The PROOVIT study was approved by the AAST Multicenter Trials Committee. Collaborating centers were enrolled through an open invitation letter or through the AAST multicenter trials website. Collaborating centers obtained local institutional review board approval before participating. Data were collected prospectively and entered by registrars designated by individual centers into the online data collection portal.

Patients with injury to named cerebrovascular vessels incurred between February 2013 and December 2019 were enrolled. Captured data included patient demographics and admission physiology. Modalities used to establish diagnosis and subsequent treatment were recorded prospectively, as were the complications and outcomes.

Inclusion Criteria

Patients above the age of 2 years with a radiographic, duplex, angiographic or clinical/operative diagnosis of blunt traumatic injury to the internal carotid artery (ICA), common carotid artery (CCA) or vertebral artery (VA) were included for analysis if the initial management occurred at the enrolling center (i.e., patient arrived from point of injury and not prior medical center or facility).

Exclusion Criteria

Patients were excluded if they were under the age of 2 years, did not have a diagnosed injury to the carotid or vertebral artery, or were initially managed at another medical center facility prior to transfer to an enrolling center. Injuries with incomplete data were excluded.

Data Analysis

Injury severity was classified according to the Biffl et al. grading scale for BCVIs (see appendix 1), as described in the Eastern Association for the Surgery of Trauma (EAST) BCVI management guidelines.[8] The database does not specify degree of occlusion resulting from flow limiting lesions. We therefore lacked the granularity to distinguish between Grade I and II injuries; which were subsequently combined for analysis. Initial comparisons were made from these four categories of injury severity (Grade I/II, Grade III, Grade IV, and Grade V). Normally distributed continuous variables were analyzed using parametric tests with results reported as mean ± standard deviation. Skewed continuous variables were analyzed using nonparametric tests with results reported as median (interquartile range). χ^2 Testing was done to compare proportions between groups. Kruskal-Wallis test on ranks or one-way analysis of variance was used for analysis of continuous variables. On our first analysis of the demographic differences between grades of injury it was clear that the small number of Grade V injuries were driving significant p values because of severe injury characteristics (Table 1A). Therefore, a second analysis was conducted excluding Grade V injuries. Variables that maintained a significant difference between groups are marked with an asterisk on Table 1A. Table 1B presents demographic variables by treatment group. The any AT category includes patients that received any antiplatelet or anticoagulant for the treatment of BCVI at any time. Antiplatelet use was defined as any type of antiplatelet medication (e.g., clopidogrel, aspirin, or ticagrelor) initiated in the hospital, exclusive of preinjury use. Anticoagulation was defined as any type of anticoagulant used to treat BCVI and included heparin, low-molecular weight heparin, other heparinoids, warfarin, or rivaroxaban. Anticoagulants administered solely for prophylaxis against deep venous thrombosis were not included as treatment for BCVI in this analysis.

Univariate and multivariate logistic regression were conducted individually for death and stroke (Tables 2 and 3). Any variable found to be significant in the univariate analysis ($p < 0.1$) was included in a multivariate analysis. Using the hierarchical agglomerative clustering technique, outcomes were clustered by their unique study ID to adjust for the effect of multiple injuries in a single patient. Additionally, outcomes were clustered by facility with interfacility correlation calculated. To account for these clusterings, the multivariate model was created using the clustered regression trees approach.[9] All models were repeated excluding patients with multiple injuries to determine if there was any change in significance or evidence of confounding. Variables were excluded from the multivariate model if they demonstrated multicolinearity with other variables (e.g., head Abbreviated Injury Scale [AIS] score and Injury Severity Score [ISS]). Variables were considered significant in the final multivariate model if alpha is less than 0.05. Odds ratios (OR) are presented with a 95% confidence interval (CI).

A subgroup analysis was performed to compare the effect of VA or carotid artery injury on the risk of stroke or death by injury grade. Grade V injuries were dropped from this analysis

given the small number of patients and notable poor outcomes. Because of the low number of CCA injuries, CCA and ICA injuries were combined into a single group of carotid artery (CA) injuries for these analyses. Excluding CCA injuries did not significantly change the results (data not shown). An initial χ^2 analysis was used to compare the incidence of stroke and death by vessel injured within each grade of injury (Fig. 1). This analysis was followed by a multivariate logistic regression controlling for age, sex, ISS, Glasgow Coma Scale (GCS) score, and treatment received (Table 4).

A second subgroup analysis was performed to determine the effect of treatment strategy on the risk of stroke or death stratified by injury grade (Table 5). The CA and VA injuries were combined within each grade category for this analysis, as the individual vessel injured had not shown a significant effect on outcomes (Table 4). To account for the influence of survivor bias on outcomes, stroke and death were combined into a single dichotomous categorical outcome. The final analysis then represents the pooled odds ratio for nontreatment to be associated with an "adverse outcome" within each grade. Early deaths (<24 hours) were excluded from this analysis as we felt this timeframe may not represent a potential therapeutic window. Covariates in these multivariate models included age, sex, ISS, and GCS score.

Data were analyzed using Stata version 14 (Stata Corp LLC., College Station, TX).

RESULTS

Epidemiology

The PROOVIT registry contained 1051 BCVIs. Records with missing data were discarded, leaving 971 injuries in 920 patients included in our analysis (Supplemental Figure 1, http://links.lww.com/TA/B923). There were 606 Grade I/II, 134 Grade III, 214 Grade IV, and 17 Grade V injuries in the data set. Table 1A includes demographics, diagnostic modalities, management strategies, and outcomes stratified by injury grade. Prior antiplatelet therapy and anticoagulation therapy were rare in this cohort (less than 6% in all grades). Injury Severity Score, presenting SBP, and GCS were similar across the grades. Hard

TABLE 1A. Characteristics by Grade of Injury

Variables	Grade I–II	Grade III	Grade IV	Grade V	*p*
Total injuries	606	134	214	17	
Demographics					
ICA	263 (44%)	99 (74%)	57 (27%)	7 (41%)	<0.001*
CCA	27 (4.5%)	6 (4.5%)	2 (1%)	1 (6%)	0.111
VA	316 (52%)	29 (22%)	155 (73%)	9 (53%)	<0.001*
Previous anticoagulant	16 (3%)	3 (2%)	3 (1.5%)	1 (6%)	0.577
Previous antiplatelet	18 (3%)	4 (3%)	6 (3%)	0 (0%)	0.912
ISS, med (IQR)	22 (13–30)	19 (13–34)	22 (16–29)	38 (16–75)	0.096
Presenting SBP (mean ± SD)	127 ± 30	128 ± 29	126 ± 30	118 ± 31	0.606
GCS, med (IQR)	14 (6–15)	14 (6–15)	14 (7–15)	7 (3–14)	0.088
AIS head, med (IQR)	3 (2–4)	3 (2–3)	3 (2–4)	3 (2–5)	0.005*
Hard signs present	17 (3%)	5 (4%)	5 (2%)	8 (47%)	0.001
Soft signs present	209 (35%)	35 (26%)	72 (34%)	11 (65%)	0.012
Diagnosis					
Diagnosis by CTA	568 (94%)	111 (83%)	195 (91%)	15 (88%)	0.001*
Diagnosis by Angio	35 (6%)	22 (16%)	18 (8%)	2 (12%)	0.001*
Diagnosis in operating room	3 (0.5%)	1 (1%)	1 (0.5%)	0 (0%)	0.075
Initial management					
Observation	591 (97.5%)	121 (90%)	197 (92%)	13 (76%)	<0.001*
Endovascular	7 (1%)	8 (6%)	11 (5%)	3 (18%)	<0.001*
Open	2 (0.3%)	0 (0%)	1 (0.4%)	1 (6%)	0.004
Treatment					
Antihypertensive	83 (14%)	13 (10%)	19 (9%)	0 (0%)	0.083
Antiplatelet	411 (68%)	73 (54%)	139 (65%)	7 (41%)	0.005*
Therapeutic anticoagulation	279 (46%)	74 (55%)	92 (43%)	3 (18%)	0.013
Antiplatelet and anticoagulation	191 (31.5%)	43 (32%)	71 (33%)	2 (12%)	0.34
No antiplatelet or anticoagulation	107 (17.6%)	30 (22.4%)	54 (25%)	9 (52.9%)	0.001*
Repeat imaging prior to discharge	321 (53%)	87 (65%)	107 (50%)	7 (41%)	0.027
Outcomes					
Stroke	30 (5%)	11 (8%)	26 (12%)	2 (12%)	0.004*
Early death (<24 h)	13 (2%)	6 (4.5%)	8 (4%)	4 (23.5%)	<0.001
In hospital death	57 (9.4%)	15 (11%)	37 (17%)	9 (53%)	<0.001*

*$p < 0.05$ after exclusion of Grade 5 injuries.
med, median; IQR, interquartile range; Angio, angiography.

TABLE 1B. Characteristics by Treatment Group

Variables	No Treatment	Any AT	*p*
Total injuries	200 (20.6%)	771 (79.4%)	
Demographics			
Previous anticoagulant	10 (5.0%)	13 (1.7%)	0.006
Previous antiplatelet	3 (1.5%)	25 (3.2%)	0.198
ISS, med (IQR)	26 (17–41)	21 (13–29)	0.001
Presenting SBP (mean ± SD)	121 ± 36	128 ± 28	0.003
GCS, med (IQR)	8 (3–15)	14 (8–15)	0.001
AIS head, med (IQR)	3 (3–5)	3 (2–4)	0.001
Hard signs present	18 (9.0%)	17 (2.2%)	0.001
Soft signs present	66 (33.0%)	261 (33.8%)	0.820
Diagnosis			
Diagnosis by CTA	187 (93.5%)	702 (91.0%)	
Diagnosis by Angio	11 (5.5%)	67 (8.7%)	
Diagnosis in operating room	4 (2.0%)	4 (0.5%)	
Injury characteristics			
Grade I/II	107 (53.5%)	499 (64.7%)	
Grade III	30 (15.0%)	104 (13.5%)	
Grade IV	54 (27.0%)	160 (20.7%)	
Grade V	9 (4.5%)	8 (1.0%)	
ICA	108 (54.0%)	318 (41.2%)	
CCA	6 (3.0%)	30 (3.9%)	
VA	86 (43.0%)	423 (54.9%)	
Additional management			
Endovascular	29 (14.5%)	0	
Open	4 (2.0%)	0	
Repeat imaging prior to discharge	73 (36.5%)	449	0.001
Outcomes			
Stroke	28 (14.0%)	41 (5.3%)	0.001
Early death (<24 h)	31 (15.5%)	0	0.001
In hospital death	78 (39%)	40 (5.2%)	0.001

and soft signs of vascular trauma were more prevalent in Grade V injuries but were not statistically different between Grades I/II, III, and IV. Computed tomography angiography (CTA) was the most prevalent means of diagnosis (92%). Conventional angiography was more commonly used to identify Grade III injuries (16%) compared with other injury grades. Diagnosis in the operating room was uncommon throughout the cohort (<1%). Observation or medical management was the predominant initial management strategy throughout all grades (95%). Endovascular management occurred uncommonly (3%), and initial operative intervention was rare (0.4%).

Antiplatelet agents were the most common medical treatment (65%), followed by therapeutic anticoagulation (46%). Both agents were used in approximately a third of the cohort (32%), whereas no AT agents were administered in 20% of patients. Antithrombotics were discontinued after subsequent imaging in 12.5% (40/321) of patients with low-grade injuries. Of patients with higher-grade injuries that were initially treated with ATs in the hospital, 12.5% (11/87), 19% (20/107), and 28% (2/7) of Grade III to V injuries, respectively, were discharged without ATs following additional imaging. Repeat imaging prior to discharge was obtained in 60% of patients. The complete breakdown of treatment rendered by grade of injury can be found in Table 1A.

Those patients that did not receive treatment were more likely to have more severe trauma as evidenced by a higher ISS score, lower presenting SBP, lower GCS, and higher AIS head score. A detailed comparison of demographic variables broken down by treatment group can be found in Table 1B.

Outcomes

The incidence of stroke for the entire cohort was 7% and increased with worsening injury grade (5%, 8%, 12%, 12%, for Grades I/II, III, IV and V, respectively). The incidence of death for the entire cohort was 12% and also increased with worsening injury grade (9.4%, 11%, 17%, 53%, for Grades I/II, III, IV, and V, respectively). Twenty-six percent of the patients that died did so in the first 24 hours. Early death (≤24 hours) was most common in those with Grade V injury (44% of all Grade V deaths). A stroke was diagnosed prior to death in 6% (2/31) of patients that died early and in 29% (25/87) of deaths after 24 hours. Of those that survived the first 24 hours postinjury, 90.7% survived until discharge. Patients with a diagnosed BCVI-related stroke had a 40% in-hospital mortality rate.

TABLE 2. Univariate and Multivariate Regression Analysis for Death

Variables	Univariate Model	Multivariate Model
Demographics		
ICA	2.03 (1.47–2.80)*	1.15 (0.22–6.06)
CCA	0.64 (0.20–2.12)	
VA	0.52 (0.37–0.72)*	1.55 (0.32–7.54)
Previous anticoagulant	2.05 (1.13–3.72)*	1.58 (0.93–2.67)
Previous antiplatelet	0.55 (0.13–2.38)	
Sex (male)	1.44 (0.97–2.14)	
Age	1.01 (0.99–1.02)	
ISS	1.05 (1.05–1.06)*	1.03 (1.02–1.03)*
Presenting SBP	0.98 (0.98–0.99)*	0.99 (0.98–1.01)
GCS	0.76 (0.73–0.79)*	0.79 (0.76–0.81)*
AIS head	1.96 (1.69–2.27)*	N/A
Hard signs present	4.67 (1.56–14.04)*	1.62 (0.42–6.28)
Soft signs present	0.77 (0.56–1.06)	
BCVI Grade 5**	10.83 (2.85–41.2)*	2.21 (0.54–9.08)
BCVI Grade 4**	2.01 (1.41–2.86)*	1.75 (1.07–2.85)*
BCVI Grade 3**	1.21 (0.88–1.68)	
Initial management		
Endovascular	1.52 (0.67–3.51)	
Open	2.43 (1.05–5.61)*	6.98 (2.42–20.1)*
Treatment		
Antihypertensive	0.74 (0.26–2.11)	
Antiplatelet	0.16 (0.10–0.26)*	0.25 (0.15–0.44)*
Therapeutic anticoagulation	0.16 (0.09–0.29)*	0.15 (0.07–0.34)*
Outcome		
Stroke	5.72 2.98–11.01)*	4.17 (1.40–12.42)*

Significance for inclusion into the multivariate model was set at $p < 0.1$, and $p < 0.05$ for the multivariate model.

C-Statistic for final multivariate model = 0.919.

*indicates predictor met significance threshold for the model.

**Compared with Grade I/II BCVI.

TABLE 3. Univariate and Multivariate Regression Analysis for Stroke

Variables	Univariate Model	Multivariate Model
Demographics		
ICA	2.94 (1.50–5.77)*	2.80 (0.40–19.98)
	0.36 (0.05–2.58)	
VA	0.37 (0.20–0.70)*	1.16 (0.23–5.86)
Previous anticoagulant	1	
Previous antiplatelet	1	
Sex (male)	1.01 (0.61–1.66)	
Age	1.00 (0.98–1.02)	
ISS	1.02 (1.01–1.04)*	1.01 (0.99–1.02)
Presenting SBP	0.99 (0.98–0.99)*	0.99 (0.98–0.99)*
GCS score	0.91 (0.86–0.97)*	0.96 (0.92–1.01)
AIS head	1.17 (0.88–1.56)	
Hard signs present	1.24 (0.50–3.03)	
Soft signs present	0.68 (0.43–1.07)	
BCVI Grade 5**	2.56 (1.12–5.83)*	1.26 (0.52–3.06)
BCVI Grade 4**	2.66 (1.45–4.84)*	2.56 (1.31–4.98)*
BCVI Grade 3**	1.71 (1.02–2.89)*	1.26 (0.75–2.14)
Initial management		
Endovascular	6.61 (3.80–11.50)*	3.41 (2.23–5.21)
Open	1	
Treatment		
Antihypertensive	0.56 (0.22–1.44)	
Antiplatelet	0.47 (0.23–0.94)*	0.73 (0.33–1.60)
Therapeutic anticoagulation	0.69 (0.31–1.54)	

Significance for inclusion into the multivariate model was set at $p < 0.1$, and $p < 0.05$ for the multivariate model.

C-Statistic for final multivariate model = 0.736.

*Predictor met significance threshold for the model.

**Compared with Grade I/II BCVI.

Patients who did not receive AT treatment were at a significantly higher risk of stroke and/or death than those that were treated, regardless of the grade of injury (Fig. 1). Of those patients that did not receive ATs, 15.5% (31/200) died within 24 hours. Within the BCVI cohort without arterial transections that survived long enough to be treated but did not receive ATs, 94 had low-grade (I/II) lesions, 24 had pseudoaneurysms and 46 had arterial occlusions. Fourteen percent (23/164) of these patients developed a stroke and 51% (84/164) died prior to hospital discharge. In all 15% (122/853) of patients that survived to hospital discharge never received AT therapy. There were 13 strokes identified among these patients.

Risk Factors Associated With Death

All demographic variables underwent univariate logistic regression to determine risk factors associated with death. Significant variables are listed on Table 2. On univariate analysis.

ICA injury, ISS, systolic blood pressure (SBP), GCS score, head AIS score, hard signs of vascular injury, injury Grades IV and V, initial open repair, and stroke were all independent predictors of death. Antiplatelet use and anticoagulation use were associated with a decreased risk of death. Death was less likely in patients with VA injury compared to those with CA injuries. These variables were placed into a multivariate model which demonstrated that ISS, GCS, initial open repair, stroke, antiplatelet use, and anticoagulation use remained significant. Patients that experienced a BCVI-related stroke were at a 4.2× increased risk of death in our multivariate analysis. The c-statistic for this regression model was 0.931 suggesting an excellent fit, and intraclass correlation between facilities was negligible (0.00; $R^2 = 0.01$).

Risk Factors Associated With Stroke

Univariate analysis was repeated for stroke (Table 3). Internal carotid artery, ISS, presenting SBP, GCS, Grades III, IV, or V injury, initial endovascular management were all independent risk factors for stroke. Stroke was less likely in patients with VA injury compared with those with CA injuries. However, nontreatment of low-grade VA injuries was associated with an 8.6-fold increase in the risk of stroke compared with similarly injured patients that received ATs. In the multivariate regression model BCVI Grade IV, hypotension on presentation, and endovascular repair remained significant. The c-statistic for this model was 0.738 suggesting a good fit, and intraclass correlation between facilities was negligible (0.02; $R^2 = 0.03$).

Risk of Adverse Outcomes by Injury Pattern and Treatment

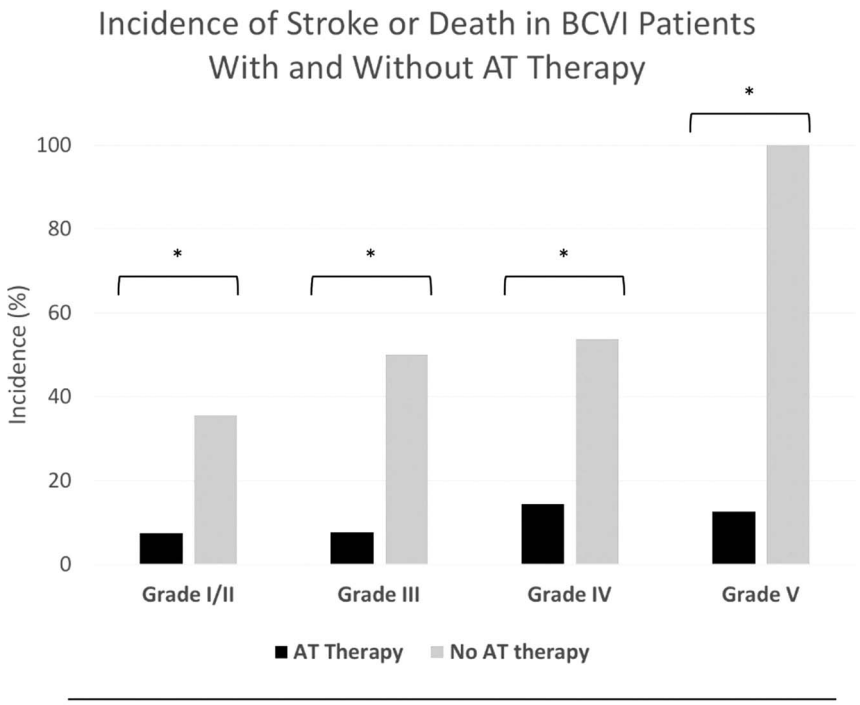
To evaluate the influence of injury pattern on outcomes, we performed a subgroup analysis of stroke and death stratified by grade of injury (I/II, III, and IV) and artery injured (carotid or vertebral). The incidence of stroke and death was significantly greater in carotid artery injuries compared to vertebral artery injuries in the Grade I/II and Grade IV subgroups ($p < 0.05$; Supplemental Figure 2, http://links.lww.com/TA/B924). However, in the more robust multivariate regression models only the Grade IV stroke subgroup remained statistically significant (OR, 7.04; 95% CI, 2.1–21.3) (Table 4).

To evaluate the influence of nontreatment on the occurrence of adverse outcomes, we compared the incidence of stroke and/or death by BCVI grade in treated and untreated patients. Nontreatment was associated with a significantly higher occurrence of adverse outcomes across all injury grades (Fig. 1). We then compared the influence of treatment strategy on the pooled risk of stroke and/or death in patients surviving long enough to be treated (>24 hours). Use of no AT therapy was associated with an increased risk of stroke or death across all subgroups (Grade I/II: OR, 4.66; 95% CI, 2.48–8.75; Grade III: OR, 7.0; 95% CI, 2.01–24.5; Grade IV: OR, 4.43; 95% CI, 1.76–11.1) even after controlling for covariates (Table 5). Antiplatelet therapy was associated with a decreased odds of stroke or death for Grades I/II, III, and IV (OR, 0.32; 95% CI, 0.18–0.57; OR, 0.26; 95% CI, 0.08–0.85; OR, 0.30; 95% CI, 0.13–0.72, respectively). Anticoagulation was associated with decreased odds of stroke or death for Grades I/II and IV (OR, 0.27; 95% CI, 0.14–0.52; OR, 0.35; 95% CI, 0.35–0.83, respectively). Combination therapy did not alter risk compared with a single agent.

DISCUSSION

Overview

Treating the multiply injured BCVI patient requires thoughtful evaluation, weighing the risk of stroke and stroke-related death against the risk of hemorrhagic complications from AT administration. The first component of this risk-benefit analysis requires an accurate evaluation of the risks of nontreatment for



	Grade I/II	Grade III	Grade IV	Grade V
Stroke, n(%)				
AT Therapy	21/499 (4.2)*	5/104 (4.8)*	15/160 (9.4)*	0/8 (0)*
No AT therapy	9/107 (8.4)	6/30 (20)	11/54 (20.4)	2/9 (22.2)
Death, n(%)				
AT Therapy	21/499 (4.2)*	4/104 (3.8)*	14/160 (8.7)*	1/8 (12.5)*
No AT therapy	36/107 (33.6)	11/30 (36.7)	23/54 (42.6)	8/9 (88.9)
Either Stroke or Death, n(%)				
AT Therapy	37/499 (7.4)*	8/104 (7.7)*	23/160 (14.4)*	1/8 (12.5)*
No AT therapy	38/107 (35.5)	15/30 (50)	29/54 (53.7)	9/9 (100)

Figure 1. The Incidence of Stroke and Death in BCVI Patients with and without AT Therapy. The incidence of stroke and/or death was significantly increased in BCVI patients that did not receive AT therapy in each grade of injury. * denotes $p < 0.05$.

TABLE 4. Comparison and Regression Analysis of Relative Rates of Stroke and Death Between Vertebral and Carotid Injuries by Grade

	Grade I/II		Grade III		Grade IV	
	Stroke*	Death*	Stroke	Death	Stroke*	Death*
VA	10/316	22/316	3/29	4/29	8/155	15/155
Carotid Artery	20/290	35/290	8/105	11/105	18/59	22/59
OR (95% CI)	1.97 (0.85–4.9)	0.96 (0.47–2.0)	0.61 (0.14–2.7)	0.32 (0.05–2.1)	7.04 (2.1–21.3)*	1.43 (0.47–4.3)

Multivariate model: controlling for age, sex, ISS, GCS, treatment.
OR presented as carotid artery against the vertebral artery as the reference value.
* $p < 0.05$.

TABLE 5. Multivariate Regression for Stroke or Death by Treatment Received

	Grade I/II	Grade III	Grade IV
Antiplatelet	0.32 (0.18–0.57)*	0.26 (0.08–0.85)*	0.30 (0.13–0.72)*
Anticoagulation	0.27 (0.14–0.52)*	0.36 (0.11–1.19)	0.35 (0.15–0.83)*
Both	0.22 (0.10–0.47)*	0.42 (0.12–1.54)	0.31 (0.12–0.83)*
None	4.66 (2.48–8.75)*	7.0 (2.01–24.5)*	4.43 (1.76–11.1)*

Analysis excludes early deaths within 24 hours.
*Denotes a statistically significant difference.
Multivariate model: controlling for age, sex, ISS, GCS.

the patient at hand. Wide variation in stroke and mortality reported in single-center studies makes estimating an individual's risk of adverse outcomes challenging. Our analysis includes a large collection of BCVIs obtained from the AAST's multicenter PROOVIT registry. We identified multiple predictors of BCVI-related stroke and death and stratified these risks of adverse outcomes by injury grade and vessel injured. Overall, the incidence of stroke and death increased with increasing BCVI grade. Nontreatment universally increased the odds of stroke and/or death across all grades of injury. This relationship was maintained even when controlling for the severity of initial trauma. Treatment with AT therapy was associated with a lower incidence of stroke and/or death in all BCVI categories except transection (Grade V). Choice of agent (antiplatelet vs. anticoagulant) did not have a significant effect on outcomes. Patients that experienced a BCVI-related stroke were at a 4.2× increased risk of death in our multivariate analysis. The sum of the analyses in this article suggests that the decision to withhold AT treatment is detrimental and must be carefully considered.

Epidemiology

The current study includes 971 BCVIs, mostly involving the VA (52%) and ICA (45%) with only a small number of injuries to the CCA (3%). In comparison, the largest study out of Europe encompassed 786 BCVIs of which 45% were injuries to the VA and 55% were injuries to the CA (ICA and CCA were not differentiated in this study).[10] Our analysis includes the largest collection of high-grade injuries, totaling 214 occlusions and 17 transections, respectively. We found flow-limiting dissections (Grades I/II), pseudoaneurysms (Grade III), occlusions (Grade IV), and transections (Grade V) of the CA and VA to be associated with a 5%, 8%, 12%, and 12% incidence of stroke, respectively. These numbers represent a significant reduction in the incidence of stroke compared with similar studies from decades past. Biffl et al. reported a 3%, 11%, 33%, and 44% incidence of stroke in Grade I, Grade II, Grade III, and Grade IV BCVI, respectively.[11,12] Our findings support a trend toward decreasing stroke rates over time, which may represent the influence of wider screening protocols and improved management strategies.[13]

Overall mortality in this analysis was 12.2% in comparison to other reports that range from 13% to 24%.[7,10,13] Most BCVI patients survived long enough to potentially be treated, as death within 24 hours was uncommon except in Grade V injuries. Of those patients that survived the first 24 hours postinjury, 90.7% survived until discharge. Patients that initially survived their injuries but died in the hospital were more likely to have suffered from more severe trauma (higher ISS, lower GCS) or to have developed a post-BCVI stroke. Stroke was more likely in those with carotid occlusions and when trauma was more severe (higher ISS, lower GCS, lower SBP). These factors were independent predictors of death on our multivariate analysis. After correcting for injury severity, stroke increased the risk of death 4.2-fold, resulting in a 40% in-hospital mortality rate in this cohort. This finding is similar to prior literature indicating a 50% mortality rate for patients with BCVI-related stroke.[5] Nontreatment was universally associated with an increased risk of stroke and death in all injury grades. Patients that did not receive AT therapy had nearly triple the incidence of stroke (14% verses 5%) and an almost 8× higher mortality (39% verses 5%) compared to patients that were treated. While the protective effects of AT remained after correcting for differences in age, sex, GCS, and injury severity score, a causal relationship between reduction in stroke and reduction in death could not be established from this dataset. In contrast to AT therapy, endovascular repair was associated with a greater risk of stroke, consistent with previous studies.[14,15]

Flow-Limiting Lesions (Grades I/II)

The clinical significance of low-grade (Grade I/II) BCVIs has been called into question following several single-institutional studies finding the incidence of stroke in this cohort to be quite low (in some cases, <1%).[3,7,16,17] The low incidence of stroke in this group has been attributed in part to a high false-positive rate of CTA when used as the sole diagnostic modality.[18] The potential for misdiagnosis has raised concerns that patients without BCVI may be exposed to unnecessary ATs and their associated risks without any benefit. For this reason, some institutions have instituted confirmatory testing with angiography or short-interval repeat imaging when low-grade BCVI is suspected. Nonetheless, our study found that CTA is by far the most common imaging modality used to diagnose Grade I/II injuries. Despite the potential inclusion of patients without BCVI in this low-grade cohort, we identified a clinically significant risk of stroke in this group. When treatment was withheld from patients with low-grade BCVI 8.4% experienced a stroke, which conferred an associated mortality of 33.6%. This relationship also held true when examining the stroke risk of flow-limited lesions isolated to the VA. Though smaller analyses have suggested low-grade VA injuries are not clinically significant,[16] our study found that nontreatment of low-grade VA injuries was associated with an 8.7-fold increase in the risk of stroke or death (95% CI 3.85–19.9; $p < 0.001$). The incidence of stroke in low-grade CA injures was more than double that of low-grade VA injuries (3.2% vs. 6.9%, respectively), but was similarly influenced by treatment or the lack thereof. After controlling for differences in injury and demographic characteristics, the odds of stroke was not statistically different between low-grade vertebral and carotid artery injuries. Given the likely inclusion of patients with false-positive identification of low-grade BCVIs, the true risk of stroke and stroke-related death in untreated Grade I/II injuries may be even higher.

Pseudoaneurysms (Grade III)

While there is much debate regarding the management of Grade III BCVIs, we found AT treatment predominated with endovascular repair reserved for a select few (3%). Enlarging pseudoaneurysm was the most frequent indication for carotid stenting and vertebral artery embolization. Nontreatment of

pseudoaneurysms conferred a 7.0× increased risk of poor outcome. The incidence of stroke from Grade III injuries quadrupled (20% vs. 4.8%) and mortality increased nearly ten times (36.7% vs. 3.8%) when AT therapy was withheld. The overall incidence of stroke following pseudoaneurysm was 8.2% in this series, which is similar to modern series (10.0%)[7] and in contrast to older reports with rates of stroke as high as 32.5% in Grade III BCVIs.[3] Endovascular repair was an independent predictor of stroke in this analysis, associated with a 3.4-fold increased odds of stroke. The infrequent use of endovascular interventions in our study reflects a trend of substantially decreasing use of these treatments for BCVIs. Early reports from experts in Memphis and Baltimore reported a stent rate of 34–36% for BCVIs.[5] However, now the general opinion about the natural history of dissections and pseudoaneurysm is that the overwhelming majority will heal over time. Additionally, procedural complications and the risk of poststent stroke has led to a reduction in the use of endovascular stents.[14,15,19] Detailed study of Grade III BCVIs with a different dataset is needed to further elucidate the injury characteristics that may influence who may benefit from endovascular therapy.

Occlusion (Grade IV)

Grade IV BCVI posed the highest risk of stroke and stroke-related death in this cohort. More than half the patients with Grade IV injuries that did not receive AT therapy experienced an adverse outcome. Nontreatment of Grade IV injuries was associated with more than twice the incidence of strokes (20.5% vs. 9.4%) and nearly five times the incidence of death (42.6% vs. 8.7%). We found CA occlusion to carry the highest risk of stroke of all the injury patterns, with an incidence of 30.5%. The early onset and high rate of stroke following CA occlusion has led some to questions whether stroke in this cohort is truly preventable.[5,20] While this stroke rate is substantial, it is lower than what has been reported in other series (50–70%).[3,5,20,21] Those CA occlusions that went untreated further increased the odds of stroke and death 6-fold. The odds of adverse outcomes were significantly decreased when ATs were used. Occlusion was the only BCVI grade in which the odds of stroke was significantly higher in injuries to the CA compared with the VA after adjusting for confounding variables. Nonetheless, there remained a clinically significant incidence of stroke (5.0%) and mortality (9.7%) in Grade IV injuries to the VA in this study. The odds of stroke and death following VA occlusion was significantly reduced by the use of ATs and increased 7-fold by withholding them. On multivariate analysis, lack of AT therapy for Grade IV injuries conferred a 4.4× increased risk of poor outcomes. In contrast to the conclusions of other studies,[21,22] our analysis would indicate that all Grade IV injuries pose a clinically significant risk of stroke and death and should warrant treatment.

Treatment Strategy

All of our analyses underscored the benefit of treating BCVIs while highlighting the risks of nontreatment. Withholding ATs was associated with a substantially higher pooled odds ratio of stroke and death in all BCVI grades even after adjusting for differences in patient age, demographics, and comorbid injuries. Our study encompassed patients from multiple centers with no standardized treatment protocol between them and likely included patients that were treated with AT *after* the diagnosis of stroke was made; nonetheless this relationship held true. The risks of nontreatment were equally severe regardless of the chosen AT strategy in the comparison group (antiplatelet agent vs. anticoagulant). This finding is consistent with a recent Cochrane review that failed to identify a difference in stroke-risk-reduction between anticoagulation and antiplatelet agents for the treatment of carotid artery dissections; noting, however that antiplatelet agents may pose less risk of hemorrhage.[23]

Establishing the risks of nontreatment represents only half of the equation factoring into the decision to start or withhold ATs from the multiply injured BCVI patient. The dataset does not have the granularity to compare potential complications of AT use. Fortunately, several other studies have evaluated the use of ATs in this cohort. Multiple studies have reported strategies to safely administer ATs early after injury without any demonstrated worsening of TBI in patients with BCVI and comorbid brain injury.[7,18,24,25] Other groups have evaluated the use of antiplatelet agents in BCVI patients with concurrent TBI, solid organ injuries, or major orthopedic injuries have found no clinically significant hemorrhagic complications attributed to aspirin use.[7,18,24,25] Only one study has reported an increase in blood transfusion in multi-injured BCVI patients treated with aspirin.[26] However, the total transfusion volume in aspirin-treated patients was only 0.9 units of packed red blood cells (PRBCs) (compared to 0.3 units PRBCs) over the entire hospitalization. The morbidity of a BCVI-related stroke would seem to outweigh the risk of an additional unit of blood transfusion or even the hypothetical risk of a delayed laparotomy for solid organ injury.

Limitations

This study has a number of limitations. Our dataset does not contain information regarding the timing of BCVI diagnosis, the timing of stroke, neurologic sequela, or means of stroke diagnosis; nor does it contain information regarding the timing of AT treatment relative to the diagnosis of stroke. Therefore, our analysis may include patients that received ATs after the development of stroke in the treatment group. As a result, the protective benefits of ATs and the risks of nontreatment may be underestimated in our analysis. Additionally, our data set does not contain specifics regarding AT dosing or monitoring protocol. We considered any patient who received AT for BCVI to be "treated." Since we do not have the means to determine whether those on anticoagulation reached the targeted PTT goal of the treating physician, some patients on "treatment" may not have received the full benefits of anticoagulation. Because of these limitations in the dataset, we chose to analyze the outcomes of patients with adverse outcomes by comparing those who received any AT treatment at any point during hospitalization to those that did not receive treatment at any time. Additionally, the incidence of stroke-related death may be higher than we reported in the nontreatment group as the diagnosis of stroke at presentation is challenging for patients who died early after injury and present no opportunity for intervention. Nonetheless, while stroke and death may not have been preventable for a fraction of patients, we demonstrated that treatment was associated with significantly better outcomes in survivors even after adjusting for injury severity.

We have no data to elucidate complications that may have arisen secondary to AT exposure or to ascertain the rationale for nontreatment, which limits our ability to achieve our broader goal

of identifying those patients in whom treatment is most beneficial. While it is generally accepted that antiplatelet agents carry less risk of bleeding complications than anticoagulant agents, we have no data to evaluate this claim from within our dataset. However, our findings that antiplatelet therapy yielded equivalent outcomes compared with anticoagulants may support further research into aspirin-based BCVI treatment regimens. Research to elucidate the optimal agent, timing of initiation, dose, and monitoring protocol for the treatment of BCVI is desperately needed.

Conclusion

In summary, stroke and death remain significant risks for all BCVI grades regardless of vessel injured. Antithrombotics represent the only management strategy that is consistently associated with a lower incidence of stroke and death in all BCVI categories. Antiplatelet agents are an efficacious alternative to anticoagulation and warrant further investigation as a therapy for the multiply-injured BCVI patient. Given the 40% mortality rate in patients who survived their initial trauma and developed a BCVI related stroke, nontreatment may no longer be a viable option.

AUTHORSHIP

AAST PROOVIT Study Group, J.D., J.G., T.F., S.S., J.H., T.S., and T.E.R. participated in the data collection. R.R., A.D., H.A., J.D. participated in the data analysis and interpretation. R.R., A.D. participated in the article preparation. H.A., J.D., J.G., T.F., S.S., J.H., T.E.R. participated in the critical revision.

DISCLOSURE

The authors declare no conflicts of interest.

The project described was supported by the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH), through grant UL1 TR001860. This work was funded by the National Trauma Institute, Award NTI-NTRR15–05, and supported by the Office of the Assistant Secretary of Defense for Health Affairs through the Defense Medical Research and Development Program under the prime award W81XWH-15-2-0089. The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702–5014 is the awarding and administering acquisition office. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense or the National Trauma Institute.

REFERENCES

1. Paulus EM, Fabian TC, Savage SA, Zarzaur BL, Botta V, Dutton W, Croce MA. Blunt cerebrovascular injury screening with 64-channel multidetector computed tomography: more slices finally cut it. *J Trauma Acute Care Surg*. 2014;76(2):279–283; discussion 84-5.
2. Emmett KP, Fabian TC, DiCocco JM, Zarzaur BL, Croce MA. Improving the screening criteria for blunt cerebrovascular injury: the appropriate role for computed tomography angiography. *J Trauma*. 2011;70(5):1058–1063; discussion 63-5.
3. Biffl WL, Ray CEJr., Moore EE, Franciose RJ, Aly S, Heyrosa MG, Johnson JL, Burch JM. Treatment-related outcomes from blunt cerebrovascular injuries: importance of routine follow-up arteriography. *Ann Surg*. 2002;235(5):699–706; discussion −7.
4. Cothren CC, Biffl WL, Moore EE, Kashuk JL, Johnson JL. Treatment for blunt cerebrovascular injuries: equivalence of anticoagulation and antiplatelet agents. *Arch Surg*. 2009;144(7):685–690.
5. Stein DM, Boswell S, Sliker CW, Lui FY, Scalea TM. Blunt cerebrovascular injuries: does treatment always matter? *J Trauma*. 2009;66(1):132–143; discussion 43-4.
6. Burlew CC, Sumislawski JJ, Behnfield CD, et al. Time to stroke: a Western trauma association multicenter study of blunt cerebrovascular injuries. *J Trauma Acute Care Surg*. 2018;85(5):858–866.
7. McNutt MK, Kale AC, Kitagawa RS, et al. Management of blunt cerebrovascular injury (BCVI) in the multisystem injury patient with contraindications to immediate anti-thrombotic therapy. *Injury*. 2018;49(1):67–74.
8. Bromberg WJ, Collier BC, Diebel LN, Dwyer KM, Holevar MR, Jacobs DG, Kurek SJ, Schreiber MA, Shapiro ML, Vogel TR. Blunt cerebrovascular injury practice management guidelines: the eastern Association for the Surgery of trauma. *J Trauma*. 2010;68(2):471–477.
9. Torgo L, da Costa JP. Clustered multiple regression. In: Kiers HAL, Rasson JP, Groenen PJF, Schader M, eds. *Data analysis, classification, and related methods. Studies in classification, data analysis, and knowledge organization*. Berlin, Heidelberg: Springer; 2000. https://doi.org/10.1007/978-3-642-59789-3_35.
10. Weber C, Lefering R, Kobbe P, Horst K, Pishnamaz M, Sellei R, Hildebrand F, Pape HC. Blunt cerebrovascular artery injury and stroke in severely injured patients: an international Multicenter analysis: reply. *World J Surg*. 2018;42(10):3452–3453.
11. Biffl WL, Moore EE, Offner PJ, Brega KE, Franciose RJ, Burch JM. Blunt carotid arterial injuries: implications of a new grading scale. *J Trauma*. 1999;47(5):845–853.
12. Biffl WL, Moore EE, Elliott JP, Ray C, Offner PJ, Franciose RJ, Brega KE, Burch JM. The devastating potential of blunt vertebral arterial injuries. *Ann Surg*. 2000;231(5):672–681.
13. Shahan CP, Croce MA, Fabian TC, Magnotti LJ. Impact of continuous evaluation of technology and therapy: 30 years of research reduces stroke and mortality from blunt cerebrovascular injury. *J Am Coll Surg*. 2017;224(4):595–599.
14. Burlew CC, Biffl WL, Moore EE, Pieracci FM, Beauchamp KM, Stovall R, Wagenaar AE, Jurkovich GJ. Endovascular stenting is rarely necessary for the management of blunt cerebrovascular injuries. *J Am Coll Surg*. 2014;218(5):1012–1017.
15. Cothren CC, Moore EE, Ray CEJr., Ciesla DJ, Johnson JL, Moore JB, Burch JM. Carotid artery stents for blunt cerebrovascular injury: risks exceed benefits. *Arch Surg*. 2005;140(5):480–485.
16. Scott WW, Sharp S, Figueroa SA, Madden CJ, Rickert KL. Clinical and radiological outcomes following traumatic grade 1 and 2 vertebral artery injuries: a 10-year retrospective analysis from a level 1 trauma center. *J Neurosurg*. 2014;121(2):450–456.
17. Griessenauer CJ, Fleming JB, Richards BF, et al. Timing and mechanism of ischemic stroke due to extracranial blunt traumatic cerebrovascular injury. *J Neurosurg*. 2013;118(2):397–404.
18. Shahan CP, Magnotti LJ, Stickley SM, Weinberg JA, Hendrick LE, Uhlmann RA, Schroeppel TJ, Hoit DA, Croce MA, Fabian TC. A safe and effective management strategy for blunt cerebrovascular injury: avoiding unnecessary anticoagulation and eliminating stroke. *J Trauma Acute Care Surg*. 2016;80(6):915–922.
19. Shahan CP, Sharpe JP, Stickley SM, Manley NR, Filiberto DM, Fabian TC, Croce MA, Magnotti LJ. The changing role of endovascular stenting for blunt cerebrovascular injuries. *J Trauma Acute Care Surg*. 2018;84(2):308–311.
20. Cothren CC, Moore EE, Ray CEJr., Ciesla DJ, Johnson JL, Moore JB, Burch JM. Screening for blunt cerebrovascular injuries is cost-effective. *Am J Surg*. 2005;190(6):845–849.
21. Lauerman MH, Feeney T, Sliker CW, Saksobhavivat N, Bruns BR, Laser A, Tesoriero R, Brenner M, Scalea TM, Stein DM. Lethal now or lethal later: the natural history of grade 4 blunt cerebrovascular injury. *J Trauma Acute Care Surg*. 2015;78(6):1071–1074; discussion 4-5.
22. Lytle ME, West J, Burkes JN, Beteck B, Fisher T, Daoud Y, Gable DR, Shutze WP. Limited clinical relevance of vertebral artery injury in blunt trauma. *Ann Vasc Surg*. 2018;53:53–62.
23. Beletsky V, Nadareishvili Z, Lynch J, Shuaib A, Woolfenden A, Norris JW, Canadian Stroke Consortium. Cervical arterial dissection: time for a therapeutic trial? *Stroke*. 2003;34(12):2856–2860.
24. Callcut RA, Hanseman DJ, Solan PD, Kadon KS, Ingalls NK, Fortuna GR, Tsuei BJ, Robinson BR. Early treatment of blunt cerebrovascular injury with concomitant hemorrhagic neurologic injury is safe and effective. *J Trauma Acute Care Surg*. 2012;72(2):338–345; discussion 45-6.
25. Shahan CP, Magnotti LJ, McBeth PB, Weinberg JA, Croce MA, Fabian TC. Early antithrombotic therapy is safe and effective in patients with blunt cerebrovascular injury and solid organ injury or traumatic brain injury. *J Trauma Acute Care Surg*. 2016;81(1):173–177.
26. Griffin RL, Falatko SR, Aslibekyan S, Strickland V, Harrigan MR. Aspirin for primary prevention of stroke in traumatic cerebrovascular injury: association with increased risk of transfusion. *J Neurosurg*. 2018;1–8.