



# KOSOVA JOURNAL OF SURGERY

- EDITORIAL: RIFAT LATIFI, LUAN JAHA, NEXHMI HYSENI: The Signing of the MOU between the Kosova College of Surgeons and the University of Prishtina - Transformative Partnership Larger than the Naked Eye Can See
- BIANCA WAHLEN, AYMAN EL-MENYAR: Management of Blunt Cardiac Injury
- AMIT KRISHNAN, ABBAS SMILEY, RIFAT LATIFI: Diaphragmatic Hernia in Adults Admitted Emergently to the Hospital: Clinical Characteristics, Risk Stratification and Outcomes
- MICHAEL PFEIFFER, SILVIA EXTERNBRINK: Comorbidity of Polyneuropathy and Lumbar Spinal Stenosis;
- ILIR VELA, IGOR DZIKOVSKI, NEXHATI JAKUPI, ET AL: BRAF (V600E) Mutation in Papillary Thyroid Carcinoma Single Center Experience
- QAIDAR ALIZAI, BELLAL JOSEPH: From Challenge to Success: Transforming Care through Brain Injury Guidelines

**Volume 8**  
**Issue 1**  
**June 2024**  
**ISSN: 3027-5008 (Online)**  
**ISSN: 3027-5016 (Print)**



# Systematic Review - From Challenge to Success: Transforming Care Through Brain Injury Guidelines

Qaidar Alizai, MD <sup>1</sup>; Bellal Joseph, MD, FACS <sup>1</sup>

<sup>1</sup>Division of Trauma, Critical Care, Emergency Surgery, and Burns, Department of Surgery, College of Medicine, University of Arizona, Tucson, Arizona, USA.

*Presentation: Invited Presentation at the Kosova College of Surgeons Third Annual Clinical Congress, October 2023, Kosova.*

## Corresponding Author:

**BELLAL JOSEPH, MD, FACS**

University of Arizona, Department of Surgery, Division of Trauma, Critical Care, And Emergency Surgery  
1501 N. Campbell Ave, Room 5411, P.O. Box 245063, Tucson, AZ 85724,  
Email: [bjoseph@surgery.arizona.edu](mailto:bjoseph@surgery.arizona.edu)

### Abstract

**Background:** Traumatic brain injury (TBI) has the highest incidence of all common neurological disorders and is associated with high morbidity and mortality. Management of TBI accounts for a large proportion of emergency surgical, neurosurgical, and critical care practice. Although a vast majority of TBIs are managed non-operatively, neurosurgical interventions are an absolute life-saving necessity when required. The Brain Injury Guidelines (BIG) were developed to guide the triage, management, and appropriate disposition of TBI patients based on patients' medical history, clinical, and radiologic findings.

**Objectives:** The aim of this review was to summarize the public health burden due to TBI, the Brain Injury Guidelines, and the role of trauma and acute care surgeons in the management of TBI.

**Findings:** The brain injury guidelines classify head injury patients into BIG 1, BIG 2, or BIG 3 groups. The proposed management for BIG 1 is a 6-hour period of

observation in the emergency department, without the need for neurosurgical consultation (NSC) or a repeat head computed tomography (RHCT) scan. For BIG 2, the plan consists of hospitalization of the injured patient, and for BIG 3, hospitalization, RHCT, and NSC are suggested. In the recently validated AAST-BIG multi-institutional trial, none of the 301 BIG 1 patients worsened clinically, 4 patients (1.3%) had progression on RHCT with no change in management, and none required neurosurgical intervention. In the BIG 2 category, 2 of 295 patients (0.7%) worsened clinically, and 21 (7.1%) had progression on RHCT. None of the BIG 1 and BIG 2 patients had post-discharge emergency department visits or 30-day readmissions. Only BIG 3 patients required neurosurgical intervention (280 of 1,437 patients [19.5%]). Implementing BIG would have reduced CT scan use and NSC by 29% overall, with a 100% reduction in BIG 1 patients and a 98% reduction in BIG 2 patients.

**Conclusions and Relevance:** The Brain Injury Guidelines have been validated at 10 Level I and Level

II trauma centers in the recently concluded AAST BIG multi-institutional trial and have been established as a safe and effective tool to guide the management of TBI by acute care surgeons while at the same time reducing hospital costs.

**Keywords:** BIG, Brain injury guideline, Traumatic brain injury, Brain injuries

## Manuscript

### Introduction

Traumatic brain injury (TBI) is the most common neurologic disorder and a leading cause of death in adult trauma patients (1, 2). TBI poses a huge public health burden with over 1.7 million events annually in the US alone (3). Any blunt or penetrating force to the head can result in disruption of the intracranial tissues including ischemia, vascular damage, and breaches in the integrity of the blood-brain barrier, all contributing to the deterioration of brain tissue (4). This can have both short-term and delayed consequences for the patient, often leading to persistent issues like cognitive impairments, visual challenges, pain, sleep disturbances, and even post-traumatic epilepsy (5). This makes TBI complicated and challenging to treat.

The management of TBI spans from the initial assessment and stabilization to long-term rehabilitation (6). Several classification systems have been introduced for brain injuries, but conventionally, TBIs have been classified based on the Glasgow coma scale (GCS) score into mild (GCS 13-15), moderate (GCS 9-12), and severe (GCS 3-8) TBI (7). In most of the guidelines, the management of severe TBI includes neurologic assessment, imaging, neurosurgical consultation, and sometimes, neurosurgical interventions (8). However, not all TBIs are the same. Most mild to moderate injuries self-resolve without deterioration (9). Various clinical algorithms and guidelines have been developed to ensure standardized care of these patients (10, 11, 12, 13). However, despite these efforts, many TBI patients undergo CT scans, neurosurgical consults, and repeat head computed tomography (RHCT) scans, which do not change the management in most cases and most of these patients get discharged home without any neurosurgical intervention. (6). Sometimes, when these patients have other injuries, the care of those injuries is also delayed because of unnecessary wait for neurosurgical

consultation and observation for their head injuries. Due to the above-mentioned reasons, there is a need to implement evidence-based guidelines that can help triage and manage TBI patients while improving health-care resource utilization. Brain injury guidelines (BIG) were originally developed a decade ago to address these concerns (6). The purpose of this review is to provide a concise summary of the need, application, and future of BIG.

### PICO Questions

Question 1: Do patients classified as BIG 1 and BIG 2 categories according to the BIG require routine RHCT scans and neurosurgical consultations?

Question 2: Can pediatric TBI patients classified as BIG 1 be safely managed without neurosurgical consultation?

### Search Strategy

A systematic review was performed to answer our PICO questions in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines to determine the use of BIG and the deviation in management of TBI patients from the BIG protocol (Supplemental Digital Content 1).

All studies investigating the BIG for the management of TBI patients were eligible for inclusion. We included observational trials, retrospective studies, and conference abstracts published between January 1, 2014, and July 1, 2024. Commentaries (e.g., expert opinion), case reports, case series, reviews, and studies published in non-peer-reviewed journals were excluded. The primary outcome of interest was the use of RHCT and neurosurgical consultation in TBI patients managed using BIG.

A comprehensive search of PubMed from January 1, 2014, and July 1, 2024, was performed (Q.A.). The search strategy was reviewed by Q.A and B.J. using a Peer Review of Electronic Search Strategy checklist. All bibliographies were reviewed, and additional references identified were screened and included in the analysis. The final accession of the database was performed on July 1, 2024. All study titles were screened independently by both the authors (Q.A. and B.J.) to determine relevance. The abstracts of any title included by either reviewer were further evaluated. Selected references then underwent full-text review separately by both investigators. Standardized data abstraction forms



were utilized to record variables of interest (e.g., author, study design, BIG classification, sample size, mortality, progression of ICH, repeat head CT, neurosurgical consultation, and need for neurosurgical intervention). We attempted to obtain additional data from the authors of studies that met inclusion criteria but did not report all variables of interest. When provided with these data, these studies were incorporated into our analyses.

### The Birth of BIG

Traditionally, TBI patients were managed by neurosurgeons. However, with the limited availability of neurosurgeons, the role of trauma surgeons in managing mild TBI is critical. Considering the complexities of previous guidelines, an easy and practical algorithm for the management of head injury patients, the BIG (Figure 1), was developed (6).

Figure 1. Brain Injury Guidelines

Brain Injury Guidelines			
Variables	BIG 1	BIG 2	BIG 3
LOC	Yes/No	Yes/No	Yes/No
Neurologic examination	Normal	Normal	Abnormal
Intoxication	No	No/Yes	No/Yes
CAMP	No	No	Yes
Skull Fracture	No	Non-displaced	Displaced
SDH	≤ 4mm	5 - 7 mm	≥ 8 mm
EDH	≤ 4mm	5 - 7 mm	≥ 8 mm
IPH	≤ 4mm, 1 location	5 - 7 mm, 2 locations	≥ 8 mm, multiple locations
SAH	Trace	Localized	Scattered
IVH	No	No	Yes
THERAPEUTIC PLAN			
Hospitalization	Observation (6hrs)	Yes	Yes
RHCT	No	No	Yes
NSC	No	No	Yes

Over a three-year period, a retrospective cohort analysis of 3,803 blunt traumatic brain injury (TBI) patients was conducted at a level 1 trauma center. Patients with positive findings on initial head CT were included, while those requiring emergent surgery or transferred from other institutions were excluded. BIG was structured into three categories (BIG 1, BIG 2, and BIG 3) based on patients' histories, examinations, and CT findings. Each category had a specific therapeutic plan for hospitalization, further scans, and neurosurgical intervention. Patients stratified as BIG 1 should be observed for six hours, BIG 2 patients should be hospitalized and observed without neurosurgical consultation and routine repeat head CT (RHCT), whereas neurosurgical consultation and RHCT are reserved for BIG 3 patients.

The study aimed to determine the concordance between guideline-based and actual therapeutic plans using statistical analysis. A kappa value of 0.97 was reported, implying a concordance of 97% between the assigned and the verified BIG categories, proving the accuracy and practicability of these guidelines (6).

### Clinical or radiologic progression

One major concern with the BIG was the potential progression of intracranial bleeds with clinical or radiologic deterioration. Since BIG recommends observation without neurosurgical consultation for BIG 1 and 2 patients, it would be a disaster to discharge a patient home from the observation unit with a risk of intracranial bleed progression post-discharge. Therefore, a low threshold was kept for progression to avoid any misfortunate events. In this study, only 2.6% of the BIG 2 patients and 21.6% of BIG 3 patients progressed on repeat head CT scans (6).

Figure 2: Characteristics of 9 patients that failed BIG 2 criteria

Patient Number	Age, y	CAMP	Neurologic Examination on Presentation	ICH	Reason for the RHCT	Worsening RHCT	Worsening Status	Neurosurgical Intervention
1	48	No	Normal	IPH, localized	Routine	Yes	New SAH	No
2	82	No	Normal	SDH, 5 mm	Routine	Yes	New SAH	No
3	43	No	Normal	IPH, localized	Routine	Yes	Larger IPH (15 mm)	No
4	21	No	Normal	IPH, localized	Routine	Yes	Diffuse IPH	No
5	14	No	Normal	IPH, localized; SDH, 4 mm	Neurodecline	Yes	Larger SDH (8.5 mm)	No
6	95	No	Normal	IPH, localized; SAH, 2 mm	Routine	Yes	Larger SAH (7 mm)	No
7	95	No	Normal	IPH, localized; SAH, 2 mm	Neurodecline	Yes	Larger SAH (8 mm)	No
8	75	No	Normal	IPH, localized; SDH, 5 mm	Routine	Yes	New SAH	No
9	22	No	Normal	IPH, localized	Routine	Yes	Diffuse IPH	No

\*All these 9 patients were assigned to the BIG 2 category.

CAMP, coumadin, aspirin, plavix, motrin; IPH, intraparenchymal hemorrhage; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage.

Only 4.2% of BIG 3 patients progressed on RHCT with neurologic deterioration. Based on RHCT, less than 3% of BIG 3 patients required neurosurgical intervention. The study concluded that if BIG had been followed, 342 RHCT scans, 121 inpatient hospital admissions, and 434 NSCs could have been avoided (6).

In this study, all patients categorized as BIG 1 and BIG 3 were consistent with the BIG. However, management of 9 patients categorized as BIG 2 were not in concordance with the established BIG 2. The details of 9 patients who failed the BIG 2 criteria are provided in **Figure 2**. Seven patients did not have any decline in neurologic examination but failed because of the progression of hemorrhage on RHCT. The remaining two patients had worsening neurologic examination, resulting in an upgrade of the patient to BIG 3 classification. However, none of these 9 patients initially classified as BIG 2 required any neurosurgical interventions. This proves the safety and efficacy of the BIG guidelines.

### **Role of Trauma and Acute Care Surgeons**

BIG places acute care surgeons at the forefront of TBI management. Their expertise is pivotal in accurately classifying patients into the appropriate BIG categories, ensuring timely interventions, and optimizing patient outcomes. This highlights the evolving role of trauma and acute care surgeons in the modern healthcare landscape, where multidisciplinary collaboration is paramount.

### **BIG For Small**

While the BIG were verified and validated as safe and practical, these could not be applied to pediatric patients as the original study was performed on adult patients only. The non-guided management of pediatric head injury patients was even more concerning because of the excessive unnecessary radiation exposure of these patients with RHCT in addition to unnecessary neurosurgical consults and hospitalization (18). Radiation exposure in children has been shown to be associated with a significantly high risk of developing life-threatening malignancies later in life (19). Although some recommendations had been proposed for severe head injuries, there were no solid guidelines for mild traumatic brain injuries in children till this point. Therefore, another study was conducted on the application of BIG in pediatric and adolescent patients (20). About 405 BIG 1 patients aged 21 or less were enrolled prospectively. Patients were stratified based on neurosurgical consultation into

the neurosurgical consultation (NC) group and the no-NC group. Overall, 32% of patients received RHCT with only 3.7% showing progression of the ICH and none of them requiring neurosurgical intervention. After the BIG 1 implementation, the no-NC group was found to have no difference in the progression of intracranial bleed and neurosurgical intervention with a significant reduction in repeat head CT scans. This concluded the safety and efficacy of BIG in pediatric trauma patients. Since the patients were followed for 30 days after injury, this study also provided evidence for the long-term safety of the guidelines in these patients. This was the first of its kind study that suggested that pediatric patients without skull fractures with a small intracranial bleed (4mm or less) and a GCS of 13-15 can be safely observed without any neurosurgical consultation or intervention. With this observation, this study successfully concluded that BIG was safe and effective in both adults and pediatric patients in level 1 trauma centers.

### **BIG for transfer recommendations**

One major issue with head injury patients is the unnecessary transfer of these patients to level 1 trauma centers for neurosurgical assessment (21). Interfacility transfers affect trauma patient care of the receiving centers as well as the financial burden for the patients. Capron and colleagues in 2017 noted that 8.5% of BIG 2 and 19% of BIG 3 patients were transferred by helicopter (22). These transfers were costly, with an average rate of \$2,300 for ground transfer and \$35,000 for air transfer for approximately 50 miles, and it was potentially unsafe in extreme weather. This study used BIG in patients transferred from other facilities to their level 1 trauma center and showed that none of the transferred TBI patients, categorized as BIG 1, deteriorated and only one BIG 2 patient was admitted with worsening (22). They also showed that overall, only 8% of the patients transferred for intracranial injury and only 12% of the BIG 3 patients expectedly required neurosurgical procedures. These proved the efficacy of BIG in preventing unnecessary transfers in TBI patients and the safety of these guidelines in recommending transfer and neurosurgical consult in the BIG 3 patients. Like the concerns raised in our previous studies, this study also noted the controversial nature of BIG 2 categorization. Of 59 BIG 2 patients, there was no mortality, however, one required a lumbar-peritoneal shunt for persistent CSF leak and another one was readmitted (without neurosurgical interventions) for clinical

deterioration. This study rightfully concluded that due to their potential for deterioration, the decision to transfer BIG 2 patients should be individualized.

### **Validation and Impact**

After the successful development and verification, BIG were prospectively implemented in a level 1 trauma center to analyze the need for neurosurgical intervention and 30-day readmission rates in these patients (23). 254 BIG 1 patients were included in the study with a comparison of pre- and post-implementation of BIG. Although there was significant non-compliance with the guidelines during the training phase, compliance increased to 100% after implementation. 148 BIG-1 patients admitted after the guideline's implementation were successfully discharged home after a short observation in the emergency department without any deterioration and neurosurgical intervention. This validated the BIG for this cohort of patients and recommended against RHCT in examinable patients with a small ICH (<4mm).

BIG were externally validated by multiple studies (24, 25, 26) including a recent American Association for the Surgery of Trauma (AAST) multi-institutional trial, involving 10 Level I and Level II trauma centers (27). However, the most useful application of these guidelines will be their implementation in lower-level centers and non-trauma centers. Level I and II trauma centers are the receiving hospitals for transferred patients while level III and non-trauma centers are the transferring facility. To control unnecessary transfers, it's only reasonable to standardize the care at lower-level centers. The BIG was also recently validated in a level III trauma center (28). Through an analysis of three years of data from a level III trauma center, this study confirmed applicability of the BIG criteria in these centers. This underscores the credibility and practicability of these guidelines in diverse clinical settings. Notably, the guidelines' endorsement translates into tangible benefits, including their potential economic implications (29, 30).

The primary aim of this review article is to provide a background on the need for the development of brain injury guidelines that can help to reduce the use of healthcare resources, existing data on validation of BIG from various single- and multi-institutional studies, evaluating

the use of BIG in pediatric patients, and to study the role of BIG to determine transfer decisions. However, apart from BIG, various guidelines are currently in use for the management of TBI patients. Some of them include Brain Trauma Foundation guidelines, guidelines from the Association of Anaesthetists, and the Neuro Anaesthesia and Critical Care Society, and clinical guidelines from the National Institute for Health and Care Excellence for assessment and early management of head injury (31, 32, 33). The BIG differ from the above-mentioned guidelines in that BIG is primarily to triage the patients according to the injury severity and to reduce the use of RHCT and neurosurgical consultations in BIG 1 and BIG 2 patients. However, for BIG 3 patients, collaboration with neurosurgeons and the application of the above treatment pathways and clinical guidelines may be necessary.

### **Conclusion and Relevance:**

The trajectory of TBI management has evolved significantly with the introduction of BIG. Their validation through rigorous trials solidifies their relevance and effectiveness, while also shedding light on their potential economic advantages. BIG 1 and BIG 2 patients can be managed safely without NSC and RHCT. Amidst changing paradigms and increasing demands, these guidelines not only transform the way TBI is managed but also emphasize the integral role played by trauma and acute care surgeons in shaping patient outcomes.

### **Conflicts of Interest and Source of Funding:**

No funding was received for this manuscript and the authors have no conflict of interest to disclose.

**Authors Contributions:** Q.A. and B.J. designed this study, searched the literature, and participated equally in data interpretation and manuscript preparation.

**Funding:** No funding was received for this manuscript

**Data availability:** This study was a review of published articles, and the sources of included information can be found in the cited studies.

**Consent:** This is a review of published articles and does not require any consent.

**Ethical Approval:** This review study does not require approval from IRB.



# PRISMA 2020 Checklist



Section and Topic	Item #	Checklist item	Location where item is reported
<b>TITLE</b>			
Title	1	Identify the report as a systematic review.	Title Page
<b>ABSTRACT</b>			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	1,2
<b>METHODS</b>			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	2,3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	2,3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	2,3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report; whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	2,3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	2,3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	2,3
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	2,3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	2,3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	2,3
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	2,3
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	2,3
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	2,3
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	2,3
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	2,3
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	2,3
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	2,3



Section and Topic	Item #	Checklist item	Location where item is reported
<b>RESULTS</b>			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	2,3
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	3-8
Study characteristics	17	Cite each included study and present its characteristics.	3-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	3-8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	3-8
	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	3-8
Results of syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	3-8
Reporting biases	20c	Present results of all investigations of possible causes of heterogeneity among study results.	3-8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	3-8
Certainty of evidence	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	3-8
	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	3-8
<b>DISCUSSION</b>			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	3-8
	23b	Discuss any limitations of the evidence included in the review.	9
	23c	Discuss any limitations of the review processes used.	9
	23d	Discuss implications of the results for practice, policy, and future research.	8-9
<b>OTHER INFORMATION</b>			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	10
	26	Declare any competing interests of review authors.	10
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>



## References

1. Maas AI, Menon DK, Manley GT, Abrams M, Åkerlund C, Andelic N, et al. Traumatic brain injury: progress and challenges in prevention, clinical care, and research. *The Lancet Neurology*. 2022;21(11):1004-60.
2. Bhogadi SK, Alizai Q, Colosimo C, Spencer AL, Stewart C, Nelson A, et al. Not all traumatic brain injury patients on preinjury anticoagulation are the same. *The American Journal of Surgery*. 2023;226(6):5.
3. Sulhan S, Lyon KA, Shapiro LA, Huang JH. Neuroinflammation and blood-brain barrier disruption following traumatic brain injury: pathophysiology and potential therapeutic targets. *Journal of neuroscience research*. 2020;98(1):19-28.
4. Ng SY, Lee AYW. Traumatic brain injuries: pathophysiology and potential therapeutic targets. *Frontiers in cellular neuroscience*. 2019;13:528.
5. Ruet A, Bayen E, Jourdan C, Ghout I, Meaude L, Lalanne A, et al. A detailed overview of long-term outcomes in severe traumatic brain injury eight years post-injury. *Frontiers in neurology*. 2019;10:120.
6. Joseph B, Friese RS, Sadoun M, Aziz H, Kulvatunyou N, Pandit V, et al. The BIG (brain injury guidelines) project: defining the management of traumatic brain injury by acute care surgeons. *Journal of Trauma and Acute Care Surgery*. 2014;76(4):965-9.
7. Abdelmalik PA, Draghic N, Ling GS. Management of moderate and severe traumatic brain injury. *Transfusion*. 2019;59(S2):1529-38.
8. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Guidelines for the management of severe traumatic brain injury. *Neurosurgery*. 2017;80(1):6-15.
9. Levin HS, Diaz-Arrastia RR. Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *The Lancet Neurology*. 2015;14(5):506-17.
10. Marshall S, Bayley M, McCullagh S, Velikonja D, Berrigan L. Clinical practice guidelines for mild traumatic brain injury and persistent symptoms. *Canadian Family Physician*. 2012;58(3):257-67.
11. Kochanek PM, Carney N, Adelson PD. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents-(*Pediatric Critical Care Medicine* (2012) 13, 1 SUPPL,(S1-S82)). *Pediatric Critical Care Medicine*. 2012;13(2).
12. Lee JC, Rittenhouse K, Bupp K, Gross B, Rogers A, Rogers FB, et al. An analysis of Brain Trauma Foundation traumatic brain injury guideline compliance and patient outcome. *Injury*. 2015;46(5):854-8.
13. Hawryluk GW, Rubiano AM, Totten AM, O'Reilly C, Ullman JS, Bratton SL, et al. Guidelines for the management of severe traumatic brain injury: 2020 update of the decompressive craniectomy recommendations. *Neurosurgery*. 2020;87(3):427.
14. Park KB, Johnson WD, Dempsey RJ. Global neurosurgery: the unmet need. *World neurosurgery*. 2016;88:32-5.
15. Singh R, Parikh PP, Nicole M, Bhandarkar AR, Doan MK, Patel NP, et al. Trends in the neurosurgical workforce and implications in providing for an aging population. *World neurosurgery*. 2022;160:e261-e6.
16. Nico E, Grada M, Xhumari A, Seferi A, Rosseau G, Petrela M. The History and Current State of Neurosurgery in Albania. *Neurosurgery Practice*. 2023;4(2):e00037.
17. Lester A, Leach P, Zaben M. The impact of the COVID-19 pandemic on traumatic brain injury management: lessons learned over the first year. *World Neurosurgery*. 2021;156:28-32.
18. Howe J, Fitzpatrick CM, LaKam DR, Gleisner A, Vane DW. Routine repeat brain computed tomography in all children with mild traumatic brain injury may result in unnecessary radiation exposure. *Journal of Trauma and Acute Care Surgery*. 2014;76(2):292-6.
19. Meulepas JM, Ronckers CM, Smets AM, Nievelstein RA, Gradowska P, Lee C, et al. Radiation exposure from pediatric CT scans and subsequent cancer risk in the Netherlands. *JNCI: Journal of the National Cancer Institute*. 2019;111(3):256-63.
20. Azim A, Jehan FS, Rhee P, O'Keeffe T, Tang A, Vercruyse G, et al. Big for small: Validating brain injury guidelines in pediatric traumatic brain injury. *Journal of trauma and acute care surgery*. 2017;83(6):1200-4.
21. Carlson AP, Ramirez P, Kennedy G, McLean AR, Murray-Krezan C, Stippler M. Low rate of delayed deterioration requiring surgical treatment in patients transferred to a tertiary care center for mild traumatic brain injury. *Neurosurgical focus*. 2010;29(5):E3.
22. Capron GK, Voights MB, Moore III HR, Wall DB. Not every trauma patient with a radiographic head injury requires transfer for neurosurgical evaluation: Application of the brain injury guidelines to patients transferred to a level I trauma center. *The American Journal of Surgery*. 2017;214(6):1182-5.
23. Joseph B, Aziz H, Pandit V, Kulvatunyou N, Sadoun M, Tang A, et al. Prospective validation of the brain injury guidelines: managing traumatic brain injury without neurosurgical consultation. *Journal of Trauma and Acute Care Surgery*. 2014;77(6):984-8.
24. Tourigny J-N, Boucher V, Paquet V, Fortier É, Malo C, Mercier É, et al. External validation of the updated Brain Injury Guidelines for complicated mild traumatic brain injuries: a retrospective cohort study. *Journal of Neurosurgery*. 2022;137(3):782-8.
25. Wasfie T, Korbitz H, Odowd B, Hille JL, Hella J, Barber K, et al. Validation of brain injury guidelines in the elderly trauma patient presenting at a level two trauma center. *The American Surgeon*. 2023:00031348231161676.
26. Ross M, Pang PS, Raslan AM, Selden NR, Cetas JS. External



retrospective validation of Brain Injury Guidelines criteria and modified guidelines for improved care value in the management of patients with low-risk neurotrauma. *Journal of neurosurgery*. 2019;133(6):1880-5.

27. Joseph B, Obaid O, Dultz L, Black G, Campbell M, Berndtson AE, et al. Validating the Brain Injury Guidelines: Results of an American Association for the Surgery of Trauma prospective multi-institutional trial. *Journal of trauma and acute care surgery*. 2022;93(2):157-65.

28. Martin GE, Carroll CP, Plummer ZJ, Millar DA, Pritts TA, Makley AT, et al. Safety and efficacy of brain injury guidelines at a Level III trauma center. *Journal of trauma and acute care surgery*. 2018;84(3):483-9.

29. Joseph B, Pandit V, Haider AA, Kulvatunyou N, Zangbar B, Tang A, et al. Improving hospital quality and costs in nonoperative traumatic brain injury: the role of acute care surgeons. *JAMA surgery*. 2015;150(9):866-72.

30. Joseph B, Haider AA, Pandit V, Tang A, Kulvatunyou N, O'Keeffe T, et al. Changing paradigms in the management of 2184 patients with traumatic brain injury. *Annals of surgery*. 2015;262(3):440-8.

31. Brain Trauma Foundation. Guidelines for the Management of Severe TBI, 4th Edition. <https://braintrauma.org/coma/guidelines/guidelines-for-the-management-of-severe-tbi-4th-ed>. Accessed March 2024.

32. Nathanson MH, Andrzejowski J, Dinsmore J, Eynon CA, Ferguson K, Hooper T, Kashyap A, Kendall J, McCormack V, Shinde S, Smith A. Guidelines for safe transfer of the brain-injured patient: trauma and stroke, 2019: Guidelines from the Association of Anaesthetists and the Neuro Anaesthesia and Critical Care Society. *Anaesthesia*. 2020 Feb;75(2):234-46.

33. National Institute for Health and Care Excellence. Head injury: assessment and early management clinical guideline. <https://www.nice.org.uk/guidance/cg176>. Accessed March 2024.