Moderate Traumatic Brain Injury in Adult Population: The Latin American Brain Injury Consortium Consensus for Definition and Categorization

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Moderate traumatic brain injury (TBI) is a diagnosis that describes diverse patients with heterogeneity of primary injuries. Defined by a Glasgow Coma Scale between 9 and 12, this category includes patients who may neurologically worsen and require increasing intensive care resources and/or emergency neurosurgery. Despite the unique characteristics of these patients, there have not been specific guidelines published before this effort to support decision-making in these patients. A Delphi consensus group from the Latin American Brain Injury Consortium was established to generate recommendations related to the definition and categorization of moderate TBI. Before an in-person meeting, a systematic review of the literature was performed identifying evidence relevant to planned topics. Blinded voting assessed support for each recommendation. A priori the threshold for consensus was set at 80% agreement. Nine PICOT questions were generated by the panel, including definition, categorization, grouping, and diagnosis of moderate TBI. Here, we report the results of our work including relevant consensus statements and discussion for each question. Moderate TBI is an entity for which there is little published evidence available supporting definition, diagnosis, and management. Recommendations based on experts' opinion were informed by available evidence and aim to refine the definition and categorization of moderate TBI. Further studies evaluating the impact of these recommendations will be required.

KEY WORDS: Traumatic brain injury, Moderate, Potentially severe traumatic brain injury, Moderate head injury, Consensus, Categorization, Neuroworsening, Neurosurgery, Neurocritical care

Traumatic brain injury (TBI) is an important global public health problem. In the coming years, it is projected to be the third leading cause of death and disability.[1] TBI is a dynamic and heterogeneous entity.[2] Severity of TBI is categorized based on the Glasgow Coma Scale (GCS)[2,3] with a score of 9–12 typically considered to reflect a moderate TBI. Moderate TBI in low-income countries most commonly affect young people involved in traffic accidents or violence, often under the influence of alcohol or illicit drugs, and they tend to have concomitant extracranial injuries.[4] In developed countries, moderate TBI

ABBREVIATIONS: NW, neuroworsening; **TBI,** traumatic brain injury.

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predominates in elderly individuals because of falls or low-energy trauma.[4] Globally, 20% of all TBI admissions are categorized as moderate.[5,6] Moderate TBI is clinically significant because patients are at high risk for neurological deterioration, and nearly a quarter will require emergency neurosurgery.[4,7] In moderate TBI, the presence of comorbidities or anticoagulation increases the risk of complications and poor outcome.[8,9] Moderate TBI definition, categorization, and diagnosis present challenges.[4] Approximately 60% of patients with moderate TBI have intracranial hemorrhages and will require admission to an intensive care unit (ICU), neuromonitoring, and sometimes surgery.[10-12] The risk of neuroworsening (NW) (acute deterioration in the neurological examination, neuroimaging or other monitored variables) can be up to 30%.[13-16] The aim of this consensus was to generate answers to critical and controversial questions related to the definition and categorization of moderate TBI, with the additional aim of fostering though and discussion needed to guide and optimize future research and guidelines for moderate TBI in environment with differing resources.

In Table 1, we delineated the rationale of each question of the consensus.

METHODS

Using a structure and methods similar to the Seattle International severe TBI Consensus Conference,[69] the Latin American Brain Injury Consortium convened a group of 81 experts (neurointensivists, neurosurgeons, anesthesiologists, and emergency medicine physicians from 17 countries) with specific inclusion criteria: (1) >10 years of experience in moderate TBI management; (2) active involvement in acute care of moderate TBI; (3) representation of pertinent disciplines; (4) geographic diversity around Latin America; (5) training in systematic literature reviews; and (6) ability to commit time to the consensus development. A preconsensus systematic review of moderate TBI literature using Medline, Embase, and Google Scholar was performed as described in **Supplemental Digital Content 1** (http://links.lww.com/NEU/E183), looking for available evidence. Nine predefined PICOT questions[70] were developed after carefully identifying gaps in the literature. More specifically, we aimed to use a step-by-step approach to address gaps in definitions and categorization of moderate TBI. The Delphi method[71] was applied for virtual rounds of voting and final in-person voting was performed on September 2022 in Santiago, Chile. An anonymous electronic voting (SurveyMonkey Inc) and analysis application (Vevox, Auga Technologies Ltd) was used. The prespecified threshold for consensus was 80% or greater agreement by at least 80% of the panelists. We made "recommendations" when voting on a topic was consistent but provided "suggestions" when responses were inconsistent.[72] If consensus was not obtained, the question was classified as unresolved.

A group of recognized experts in the management of TBI were invited for monitoring all aspects of the consensus. Their contributions and criticisms were considered during discussions rounds.

RESULTS

Table 2 summarizes the voting results, recommendations, suggestions, and level of evidence of them.[73]

DISCUSSION

Question 1

> "Moderate" is an inadequate term to characterize this large and heterogeneous group of TBI patients. Patients with a GCS 13 should be categorized as moderate brain injury instead of mild"

The definition of moderate TBI as constituting a postresuscitation GCS score of 9–12 has been made arbitrarily without supportive evidence of clinical correlates. Indeed, the term moderate groups a heterogeneous population with different clinical courses and outcomes. Studies show that almost a third of the lesions present on computed tomography (CT) of patients with moderate TBI are severe enough to ultimately require surgical intervention.[11,12,19,31,61,74] The risk of NW is high, with an average prevalence of 30%. Almost half of moderate TBI victims will have long-term neurocognitive and psychological sequelae.[5,19,61,74] Moderate TBI's mortality rate of 15% is noteworthy.[19,61,74,75] A more specific term that improves characterization of this population is needed. The Committee on Neurotrauma of the World Federation of Neurosurgical Societies proposed some criteria to define, categorize, and manage individuals with mild TBI, excluding those with GCS 13 because their clinical evolutionary characteristics were like moderate TBI.[76] Stein[77] calls GCS 13 the "unlucky number," because a third of these individuals had intracranial lesions, many of which required surgery, suggesting that GCS 13 should instead be grouped in the moderate category. A predictive model of TBI demonstrated that the mortality rate of GCS 13 patients is comparable with the moderate group,[19] so the analysis of available evidence supports that patients with a postresuscitation GCS score of 13 should be included in the moderate group.[76-78]

Question 2

> "GCS alone is insufficient to categorize moderate TBI"

In the 1980s, the Traumatic Coma Data-Bank project proposed classifying "severe" as those individuals with TBI who have a GCS of less than 9.[79] Rimel et al proposed categorizing TBI as "mild" and "moderate" when the GCS was between 13 and 15 and 9 and 12, respectively.[80,81] GCS scoring requires training to maximize inter-rater and intra-rater reliability; kappa indices vary between 0.3 and 0.8.[21,82,83] The highest rate of disagreement occurs when evaluating the verbal and ocular components.[21] GCS is a clinical scale that, with the exception of posturing, fails to inform precise anatomic and pathophysiological information related to brain lesions.[2,27] In addition, multiple circumstances affect accurate GCS determination.[14,20,21,82-85] See **Supplemental Digital Content 2** (http://links.lww.com/NEU/E184).

Question 3

> "CT scan is essential to improve categorization of moderate TBI"

TABLE 1. Rationale for Consensus Questions

Question	Rationale
Is the term "moderate" appropriate to characterize this large and heterogeneous group? Should GCS of 13 be considered in moderate group?	Since its original description, the GCS has been the basis for classifying TBI as mild (15-13), moderate (12-9), and severe (8-3).[2] Initially GCS 13 was included in the mild category. Moderate TBI comprises a wide and heterogeneous group that may have different clinical presentations, lesional spectrum, evolutive profile, risk of deterioration,[4] and outcomes.[17] The term "moderate" may not adequately reflect the severity, the risk of neuroworsening, or the outcomes of these individuals[18,19]
Is GCS alone enough to categorize TBI as "moderate"?	GCS has been used as a consciousness level scale, and it has been validated and broadly implemented throughout the world for categorization and follow-up of TBI.[2,20] GCS has 3 components, with a minimum and maximum score of 3 and 15 points, respectively.[2,20] GCS has limitations, and various factors can generate confusion with its clinical interpretation[2,20,21]
Does neuroimaging help to categorize moderate TBI?	Neuroimaging provides information about the type of injury and its evolution, location of focal lesions, presence of mass effect, and risk of delayed complications.[22] CT is the modality of choice during the acute phase and their characterization has proposed to be correlated with the severity of injury.[22-24] Marshall et al developed a CT scale based mainly on the presence and volume of the space-occupying lesion, basal cisterns status, and the position of the midline.[25] In addition, it analyzes whether the hemorrhagic collections have been surgically evacuated or not[25]
What parameters should be used to define neuroworsening? What are the risk and consequences of neuroworsening?	There is no widely accepted and validated definition of NW in moderate TBI, and existing ones are extrapolated from severe TBI.[26-28] In general, NW has been defined as a decline in the neurological examination[29]; however, it can also reflect worsening of neuroimaging or neuromonitoring assessments[30] The available evidence allows us to point out that NW is prevalent, estimated to occur in a third of patients.[8,10-15,31,32] NW is an acute, critical event that can occur early or late after injury. Its causes and risk factors are numerous, and it is associated with higher morbidity and mortality[10,13-15]
Should moderate TBI be subcategorized?	Moderate TBI is a large and heterogeneous group. One of the key aspects for the optimal management is recognizing when more aggressive treatment is needed to avoid neuroworsening and additional brain damage.[13,14] Primary and secondary injuries are diverse.[8,10-13,33] Most of these injuries have epidemiological and pathophysiological features similar to severe TBI; however, there are certain characteristics (clinical, prognosis, outcome) that identifies them as particular group[8,10-14,33]
Should moderate TBI individuals be hospitalized? All need intensive care?	There is no clear guidance for patient admission to hospital in moderate TBI. Triage guidelines based on expert opinion suggest that individuals with GCS less than 14 should be transferred to a trauma center.[34] There is great variability in terms of hospitalization and management strategies worldwide[35]
Can noninvasive neuromonitoring provide useful information in the evaluation or follow-up of moderate TBI?	Noninvasive brain monitoring has a role in the management of neurocritical patients.[29,36-60] Most of the noninvasive methods are aimed at evaluating ICP. They are reproducible, low cost, portable, and radiation free but operator-dependent. The learning curve is less demanding than for invasive. Available methods include optic nerve sheath diameter, transcranial Doppler, ICP waveform analysis, and pupillometry[29,36-60]
Is invasive ICP monitoring needed for all patients with moderate TBI?	Current severe TBI guidelines leave ICP monitoring in moderate TBI "at the discretion of the treating physician"[22] The dynamic nature of lesions associated with moderate TBI and the high and unpredictable risk of neuroworsening make invasive ICP monitoring a necessary tool in certain situations[4,8,10,11,13,31,61-66]
What specific and neurocritical care measures should be adopted in the management of moderate TBI?	The CRASH-3 trial evaluated the effects of antifibrinolytic therapy in individuals with moderate and severe TBI.[67] General and targeted neurocritical care measures established for severe TBI can be applied according to the categorization of moderate TBI[68]

CT, computed tomography; GCS, Glasgow Coma Scale; ICP, intracranial pressure; NW, neuroworsening; TBI, traumatic brain injury.

TABLE 2. Questions, Voting, Recommendations, and Level of Evidence of the LABIC Consensus for Definition and Categorization of Moderate TBI

Question	Voting results	Recommendation or suggestion	Level of evidence[a]
1. Is the term "moderate" appropriate to characterize this large and heterogeneous group of individuals? Should patients with a GCS of 13 be considered in the moderate TBI group?	37.7% votes in favor and 62.3% votes against the "moderate" term as a comprehensive definition of these patients. 89.3% votes in favor and 10.6% votes against including patients with a postresuscitation GCS of 13 in the moderate group	The group suggests that the "moderate" categorization is not sufficient for characterization of these patients. The group strongly recommend maintaining a "high alert status" and to not underestimate the risk of neuroworsening in patients with moderate TBI. The consensus suggests including patients with GCS 13 in the moderate group	C-EO
2. Is GCS alone enough to categorize TBI as "moderate"?	5.9% in favor and 89.7% against using only GCS to categorize patients with moderate TBI. 99% were in favor of maintaining continuous training of GCS assessment to minimize the bias and variation in the initial evaluation of moderate TBI	The experts recommend not using only GCS for categorization of patients with moderate TBI. We also recommend the continuous training of providers to maintain an appropriate use of the GCS, with the aim of reducing bias and variation that affects the final score	C-EO
3. Does neuroimaging help to categorize moderate TBI?	91.2% in favor and 8.8% against the use of neuroimaging for better categorization of moderate TBI. The group voted 82.5% in favor of serial CT evaluation in the absence of advanced neuromonitoring systems	The group recommends the use of neuroimaging for better categorization of moderate TBI. The group recommends combining the GCS with information obtained about the primary injury from the CT scan. Owing to the dynamic nature of moderate TBI, as well as the risk of neurological deterioration the group recommends serial CT evaluation in patients before surgery and in absence of advanced neuromonitoring systems, in the following situations: (1) 6–12 h after the initial CT scan, depending on the initial injury and the time between the trauma and the first CT (2) 24 h Especially in areas were no neuromonitoring is available. This suggestion is based on weak evidence (3) 48 h postadmission. Especially in areas where no neuromonitoring is available. This suggestion is based on weak evidence (4) at any time in case of neuroworsening	C-EO
4. What parameters should be used to define neuroworsening in moderate TBI? What are the risk and consequences of deterioration of neurological status in moderate TBI?	97% in favor and 3% against using specific criteria to define neuroworsening in moderate TBI	The group recommends defining neuroworsening in moderate TBI as the "deterioration in 1 or more of the following baseline characteristics: clinical, imaging, or neuromonitoring status (invasive or noninvasive), sufficient to require medical or surgical therapy" (Table 3). The group recommends the development and implementation of institutional protocols for surveillance, detection, and early treatment of neuroworsening	C-EO

TABLE 2. Continued.

Question	Voting results	Recommendation or suggestion	Level of evidence[a]
5. Should moderate TBI be grouped into subcategories?	96.6% in favor and 3.4% against using specific subgroups of moderate TBI based on GCS plus CT Marshall classification. 87.5% of the group was in favor for the use of a "traffic light method"[14] to categorize and guide the monitoring and management of moderate TBI	The group suggest considering the use of a "traffic light method" to categorize and guide the monitoring and management of moderate TBI. The 3 risk groups proposed can be graphically identified by the colors of the traffic light[14] (Figure): Group A: low risk for neuroworsening (green light) • GCS 12 or 13 + Marshall CT class I Group B: medium risk for neuroworsening (yellow light) • GCS 9–11 + Marshall CT class I • GCS 9–13 + intracranial hemorrhage of <25 cc + midline shift <5 mm and open basal cisterns Group C: active neuroworsening (red light) • GCS from 9 to 11 + Marshall CT class II, III, or IV • GCS 9 to 13 + Marshall CT class III or IV, or new intracranial hemorrhage, with 2 of the following criteria: (1) >25 cc; (2) midline shift >5 mm; (3) compressed or effaced basal cisterns	C-EO
6. Should moderate TBI individuals be hospitalized? Do all need intensive care?	95.6% in favor and 4.4% against hospitalizing all patients with "moderate TBI" in centers that meet the minimum conditions necessary for their management	The group recommends hospitalizing all patients with "moderate TBI" in centers that meet the minimum conditions for their management. These minimum conditions include trained staff in emergency and trauma management, availability of CT 24 h × 7 d, availability of neurosurgery 24 h × 7 d, availability of monitoring of basic physiological parameters and availability of ICU The group suggests admission to the ICU for all yellow and red patients in the traffic light scheme (Figure) (subgroup B or C) or any patient who has undergone neurosurgery. Low-risk individuals (subgroup A/green light) should be hospitalized, and they can be monitored in a low complexity unit but should still undergo strict clinical-CT surveillance if there are not noninvasive neuromonitoring systems available	C-LD
7. Can noninvasive neuromonitoring provide useful information in the initial evaluation or follow-up of moderate TBI?	91% in favor and 9% against the use of noninvasive neuromonitoring modalities	The group recommends the use of noninvasive neuromonitoring modalities as supplements to the clinical and CT examination for initial evaluation and follow-up of moderate TBI, especially in areas where there is no availability of invasive monitoring systems	C-EO

TABLE 2. Continued.

Question	Voting results	Recommendation or suggestion	Level of evidence[a]
8. Is invasive ICP monitoring needed for all patients with moderate TBI?	83.1% in favor and 16.9% against considering invasive ICP monitoring in patients with moderate TBI at high risk of neuroworsening	The group recommends considering invasive ICP monitoring in patients with moderate TBI at high risk of neuroworsening (group C/red light) The group suggest invasive ICP monitoring in individuals with GCS from 9 to 11 + Marshall CT class II, III, or IV (alone or additional to the craniectomy or craniotomy if considered) or GCS 9 to 13 + Marshall CT class III or IV, or new occupying space lesion (with 2 of the following criteria: (1) >25 cc; (2) midline shift >5 mm; (3) compressed or effaced basal cisterns) (alone or additional to the craniotomy or craniectomy if considered) In addition, the group suggests additional criteria to consider invasive monitoring: • Postoperative evacuation of multiple cerebral contusions or acute subdural hematoma • GCS 9–11 with cerebral contusions located in the temporal or frontal lobes • Moderate TBI associated severe chest trauma and acute respiratory distress syndrome requiring lung-protective ventilation, high PEEP levels and/or prone ventilation • Moderate TBI with severe abdominal trauma with abdominal compartment syndrome • Moderate TBI with prolonged traumatic shock	C-LD
9. What specific and neurocritical care measures should be adopted in the management of moderate TBI?	95.16% votes in favor and 4.84% votes against the implementation of general care measures to reduce the prevalence of secondary injuries. 81.8% of the group was in favor of the administration of tranexamic acid	The group recommends high-quality supportive care to reduce the prevalence of secondary injuries in patients with moderate TBI. The group additionally suggests the administration of tranexamic acid (according to the CRASH III protocol) in this same population of patients. Specific terapeutics measures such as intracranial hypertension management, correction of coagulopathy, blood pressure management; or the use of other neuromonitoring parameters such as cerebral metabolic monitoring should follow the management guidelines for severe TBI when appropriate	A (tranexamic acid) C-LD (general and specific neurocritical care measures)

CT, computed tomography; EO, expert opinion; GCS, Glasgow Coma Scale; ICP, intracranial pressure; ICU, intensive care unit; LABIC, Latin American Brain Injury Consortium; LD, limited data; TBI, traumatic brain injury.
[a]Level of evidence following Guidelines of American Heart Association/American Stroke Association.[73]

Despite some limitations, the Marshall CT scale has been widely validated and has good predictive performance for intracranial hypertension and functional outcome in brain injured patients.[3,25,86-88] It is commonly used both in daily clinical practice and for research purposes[1] and has additionally played a role in in stratifying patients within TBI management protocols in low-resource areas.[28]

Subsequently, Maas et al[89] developed a predictive model based on CT scan parameters obtained from logistic regression analysis. This "Rotterdam Scale" is an ordinal model that may be more

TABLE 3. Proposed Criteria for Neuroworsening Definition

1. Clinical	
Decrease in total GCS of 2 or more points	Classical criteria[a]
Any deterioration in neurological status	
New loss of pupil reactivity	
Pupil asymmetry of ≥2 mm or bilateral mydriasis	Current criteria[b]
Decrease in motor GCS of 1 or more points	
New focal motor deficit	
Seizures	
Worsening headache	Proposal criteria to add
Vomiting increase (frequency, intensity)	In nonintubated moderate TBI
2. Imaging	
New space occupying lesion	
Increase in volume of previous lesion	
New onset or increase in volume of cerebral edema	
Basal cisterns compressed or absent (new onset or worsening of previous 1)	
Midline shift increase	
3. Noninvasive neuromonitoring	
Transcranial Doppler (PI > 1.4)	
Optic nerve sheath diameter (>5 mm)	
Pupillometry (NPI <3)	
Change ICP waveform (P2 > o = P1)	
Epileptic discharges	
4. Invasive neuromonitoring	
ICP >22 mm Hg	
Change ICP waveform (P2 > o = P1)	
PbtO2 <20 mm Hg	
SjVO2 <50%	

GCS, Glasgow Coma Scale; ICP, intracranial pressure; NPI, neurologic pupillary index; TBI, traumatic brain injury.
[a]According to Selfotel trial[26]
[b]According to CREVICE and SIBBIC consensus[27,28]

discriminative and have better predictive power for outcome when compared with the Marshall score.[90,91] Other CT-based classification models have been proposed as well.[92,93]

Question 4

"Neuroworsening must be recognized and treated aggressively"

There is not an accepted and validated definition of NW specific for moderate TBI. Current definitions come from severe TBI or stroke.[26-28,94,95] In a study of epidural hematomas, (most of them moderately severe TBI) and other series, patients initially presenting with 3 or more points in the verbal component of the GCS but who subsequently deteriorated and died were described to "talk and die."[96-102]

The classic criteria to define NW are based on clinical parameters[29]; however, NW can manifest in different ways depending on what is evaluated (Table 3).

We propose to define "neuroworsening (in moderate TBI) as the acute deterioration of 1 or more of the following baseline characteristics: clinical, imaging, or neuromonitoring (invasive or noninvasive) sufficient to required medical or surgical therapy."

The causes of NW can be intracranial (intracranial hypertension, tissue hypoxia, cerebral edema, new hemorrhage or progression of existing ones, seizures, vasospasm) or systemic (hypotension, hypoxemia, intrathoracic or intra-abdominal compartment syndrome, hypoglycemia, hypocapnia, hyperthermia).[26,28,32] NW can be "early or late" (before or after 72 hours postinjury).[13,26,32] Prevention and early detection of NW has a central role in the management of moderate TBI.[8,10-15,31] NW incidence ranges from 15% to 40%.[8,10-15,31,32] NW is strongly associated with poor outcomes.[10-13,15] Some of the risk factors that predict NW in moderate TBI are lower GCS, Marshall CT types III and IV, subdural hematoma, temporal or frontal-basal contusions, presence of extracranial lesions, higher injury severity score, arterial hypertension, high D-dimer levels, and low platelet count.[13,15]

Question 5

"Moderate TBI requires subgrouping which can be facilitated with a traffic light model"

Multiple series have shown that individuals with GCS of 9 or 10 have a higher risk of NW, clinical and radiological features (ie, poorer Marshall CT score) that require intensive neuromonitoring and often more aggressive treatment, in consonance with severe TBI.[8,10-15,33] In addition, GCS 9–10 has been consistently associated with higher mortality and worse functional outcomes.[8,11-13] Compagnone et al,[13] proposed subcategorizing moderate TBI as "mild moderate" (GCS 11-13) and "severe moderate" (GCS 9-10). The traffic light method (GCS + Marshall CT) provides a simple, practical, and easy way to categorize risk groups (Figure).[14] The term "potentially severe" was proposed for individuals with GCS 9–10.[14]

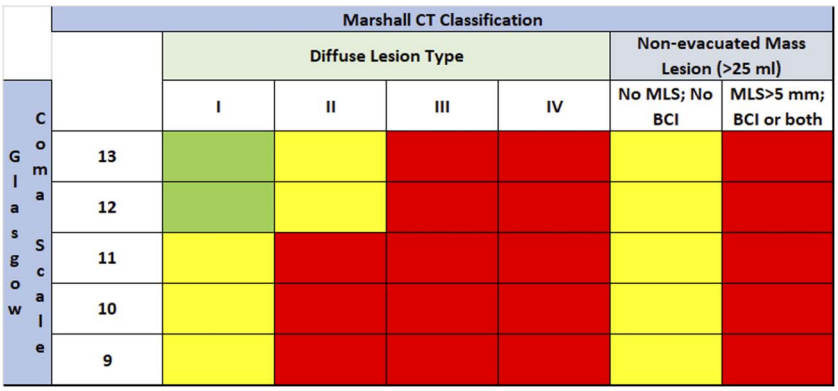

FIGURE. *Traffic Light Method to categorize patients with moderate traumatic brain injury according to the risk of neuroworsening based on Glasgow Coma Scale and Marshall CT classification. Modified from reference 14. BCI, basal cistern impairment (compressed or absent); CT, computed tomography; MLS, midline shift.*

Question 6

"All moderate TBI should be hospitalized, high risk groups should go to the ICU"

A European survey showed that patients with moderate TBI with abnormal CT scans were admitted to ICU in 63% of cases.[35] Akerlund showed that moderate TBI victims with markers of systemic metabolic stress had worse prognosis and poorer outcome than patients with severe TBI with a normal metabolic profile.[103] In addition, patients with moderate TBI and metabolic stress required endotracheal intubation, intracranial pressure (ICP) monitoring, and decompressive craniectomy in a similar proportion to severe TBI, reflecting the high risk of deterioration and mortality in the moderate group.[103]

In the largest cohort of moderate TBI, 66% of patients were admitted to the ICU with a proportion of unfavorable functional outcomes of 33% and a mortality rate of 7.2%.[8]

A recent cohort of patients with TBI admitted to the ICU in Nigeria showed a mortality of 52% (5.5% of them moderate TBI), suggesting limited availability of resources reserved for more severe patients.[104] In Iceland, a mortality of 9% was reported in moderate TBI admitted to the ICU.[105] A recent study in patients with GCS 13–15 and lesions on CT scan found better outcomes when patients were admitted to the ICU.[106]

Question 7

"Noninvasive neuromonitoring can assist assessment and stratification of moderate TBI patients"

Noninvasive neuromonitoring could help to initial evaluation and better discrimination of moderate TBI.[29,39-60] In addition, it can help one to anticipate NW and to predict the outcome.[36,54,58-60] These methods provide different and potentially complementary information.[29,39-60,107,108] The benefits and limitations of each technique are discussed in **Supplemental Digital Content 3** (http://links.lww.com/NEU/E185).

Question 8

"Invasive ICP monitoring should be considered in high risk group"

Meta-analysis in moderate TBI showed that despite a 44% prevalence of intracranial hypertension, ICP monitoring rates do not exceed 20%.[109] The indications for ICP monitoring in patients with moderate TBI could not be established because of heterogeneity and high risk of bias of the included studies, although there was a trend toward higher likelihood of ICP monitoring among patients with GCS 9–10.[62,109,110] Recommendations for invasive ICP monitoring are based on the clinical picture supported by neuroimaging findings.[11-13,15,30,62,109,110] The available series indicate that the group with GCS 9–10 have clinical and pathophysiological features similar to severe TBI and greater risk of NW, especially when CT features associated with intracranial hypertension are present.[11-13,15,30,62,109,110] Supported by this, ICP monitoring should be considered in patients categorized as "red" with the traffic light method either in the period before or after neurosurgery.[14] On the other hand, certain clinical situations in which a neurological examination cannot be performed (general anesthesia for extracranial surgery) or there are concomitant systemic situations that can trigger or aggravate intracranial hypertension (thoracic trauma, acute respiratory distress syndrome, abdominal hypertension, or prolonged arterial hypotension) should prompt consideration of invasive ICP monitoring.[4,110]

Question 9

"Supportive care and targeted treatments are essential to avoid secondary insults"

TABLE 4. Proposed Future Research

Consensus recommendation/ suggestion	Knowledge gaps and future research
"Moderate" term is inadequate to characterize this large and heterogeneous group	Beyond a "semantic" issue, the term moderate is ambiguous and underestimates the risk, severity, and poor outcomes of this large and heterogeneous group. We therefore propose replacing the term "moderate" with the term "potentially severe" to highlight the need for careful evaluation and monitoring in these cases. Discussions around the world by specialists, societies, and foundations dedicated to neurotrauma are necessary to justify a change in terminology
"GCS alone is insufficient to categorize moderate TBI"	Owing to limitations of the GCS, alternative scales such as the Four Score (Full Outline of Unresponsiveness Score) or the pupillary-GCS (GCS-P) should be tested in the moderate TBI group. Research assessing the validity of the traffic light method (GCS + Marshall CT classification) is urgently needed
"CT scan is essential for better categorization of moderate TBI"	There are no established protocols for serial neuroimaging follow-up in patients with moderate TBI. Studies assessing imaging protocols could improve detection of early complications and decrease secondary injuries. In addition, other scales (Rotterdam, Helsinki) should be evaluated, validated, and compared with Marshall classification in the moderate TBI group. Research assessing the validity of the traffic light method (GCS + Marshall's CT classification) is urgently necessary
"Neuroworsening should be recognized and avoided"	An accepted and validated definition of neuroworsening in patients with moderate TBI will increase the ability of the clinician to identify patients with high risk of early deterioration, make decisions and management plans, and improve outcomes. Research endpoints should include validation of our proposed definition, and protocol development for identification of neuroworsening as a key target in the management of moderate TBI
"Moderate TBI needs to be subgrouped. The traffic light method is a simple way"	Prospective studies are needed to validate the utility of this proposed risk stratification model in guiding triage and the use of noninvasive and invasive monitoring and particularly for optimizing timely recognition of treatable complications Research on blood levels of biomarkers indicative of inflammation or neuronal or glial damage may become a useful tool to follow-up and to refine identification of high-risk patients
"Hospitalization is needed for all moderate TBI. ICU admission is needed for high-risk groups"	There are no clear directions for patient admission to specific hospital facilities or trauma centers with minimum standards for the safe and appropriate care of patients with moderate TBI The minimum criteria that a center should meet to manage a patient with moderate TBI should be evaluated and validated in clinical studies with the aim to improve outcomes. Prospective studies aimed at evaluating whether the traffic light method helps to discern where in the hospital a patient should be admitted according to their categorization are essential
"Noninvasive neuromonitoring could supplement patient assessment"	Studies are necessary to validate noninvasive monitoring methods in the categorization and follow-up of individuals with moderate TBI, as well as the development of protocols for serial assessments
"Invasive ICP monitoring should be considered in the high-risk group"	Prospective clinical research to establish indications for invasive ICP monitoring in moderate TBI is urgently needed
"General care is essential to avoid secondary insults"	General and targeted neurocritical care therapies and relevant neuromonitoring and therapeutic protocols should be evaluated in prospective clinical studies assessing patient outcomes

CT, computed tomography; GCS, Glasgow Coma Scale; ICP, intracranial pressure; ICU, intensive care unit; TBI, traumatic brain injury.

In the CRASH-3 trial, moderate and severe TBI victims with intracranial bleeding on CT scan and no major extracranial hemorrhage admitted within 3 hours of injury were included.[67] IV tranexamic acid was administered (1 g loading dose over 10 minutes, followed by an additional 1 g over 8 hours as a maintenance dose). The primary outcome was death at 28 days. Tranexamic acid was judged safe, and it was associated with decreased mortality in the moderate TBI group (P = .005; risk ratio 0.78 [95% CI 0.64-0.95]).[67]

Supportive care is important for avoiding secondary insults and to improve the chance of functional recovery.[3,4,28,111-116] Specific terapeutics measures such as intracranial hypertension management (hyperosmolar or hypertonic therapies, targeted temperature management), correction of coagulopathy, blood pressure management; or the use of other neuromonitoring parameters such as cerebral metabolic monitoring, they should follow the management guidelines for severe TBI when appropriate, according to the categorization of moderate TBI.[4,14,22,27,69]

It is essential to establish protocols and specific prevention measures to standardize optimal care for moderate TBI.[68,117]

Future Perspectives

In Table 4 we summarize our knowledge gaps and research priorities for the future.

CONCLUSION

Moderate TBI is a prevalent and heterogeneous subgroup of patients associated with high mortality rates and poor functional outcomes. Evidence assisting the care, subcategorization, and risk stratification of patients with moderate TBI is scare. This evidence-informed expert consensus aims to promote debate and future studies which will evaluate and validate the diagnosis, categorization, and improved management strategies for this specific population of patients.

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Supplemental Digital Content 1. PICO-TS questions, search strategy (mesh terms), and a diagram of results of literature search.

Supplemental Digital Content 2. Factors that influence the correct GCS determination

Supplemental Digital Content 3. Details of the discussion of question 7 and benefits and limitations of most relevant noninvasive surrogate techniques for ICP monitoring. ICP: intracranial pressure; IHT: intracranial hypertension; ONSD: optic nerve sheath diameter ultrasound; TCD: transcranial Doppler; PI: pulsatility index; NPI: neurologic pupillary index; ICU: intensive care unit; EEG: electroencephalogram.

COMMENTS

In "Moderate Traumatic Brain Injury in Adult Population: The LABIC Consensus for Definition and Categorization," the authors create best practice recommendations for the definition and categorization of moderate traumatic brain injury (TBI). Moderate TBI is an important entity to study due to its global prevalence and the heterogeneity of this injury. The authors assembled a panel of experts and applied a Delphi consensus method. The panel identified 9 "questions" highlighting gaps in the literature pertaining to moderate TBI care which generated the recommendations. Highlights of their consensus recommendations include the suggestion to consider GCS 13 patients in the moderate TBI category, and the development of a "traffic light method" in which the authors subcategorize moderate TBI based on Glasgow Coma Scale (GCS) and Marshall Classification and use this schema to stratify "risk of neuroworsening."

Additional recommendations provided by the authors may be intuitive to specialists who routinely treat moderate TBI, such as the use of neuroimaging and noninvasive neuromonitoring. Although the authors' best practice recommendations provide some suggestions to guide the care of moderate TBI patients, given the nature of development of these guidelines and lack of supportive prospective research, clinical judgment tailored to each individual case clearly remains paramount. For example, although the authors recommend ICU admission for certain moderate TBI patients according to their traffic light method of categorization, this does not take into consideration hospital-level factors such as individual unit vs ICU care capabilities. Importantly, the authors draw attention to knowledge gaps and areas for future research based on the recommendations and suggestions they developed.

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I commend the authors and the Latin American Brain Injury Consortium (LABIC) for their efforts on tackling and finding some consensus on an expansive, challenging and very relevant topic. The authors recognize that little consensus exists regarding the definition of what constitutes a moderate traumatic brain injury. They accurately suggest that standardizing this definition will allow for better study of this subset of trauma patients, allowing for the development of treatment algorithms, study of outcomes data and a general consistency in regards to communication about these patients. This is a noble but difficult cause; as moderate traumatic brain injury is a heterogeneous group that is undoubtedly difficult to stratify as a single entity. This begs the question: Do we need to have a single term to encompass this patient subset? The authors suggest, alternatively, labeling them as "potentially severe." While this captures the high risk nature of their disease, I wonder if we should be moving away from the "mild," "moderate" and "severe" nomenclature entirely and instead consider divisions such as "progressive" vs

"nonprogressive" or "surgical" vs "nonsurgical" or "reversible" vs "irreversible," as these capture the questions that are at the heart of the matter: what, if any, monitoring or interventions is the patient currently requiring or likely to require and what is their long-term prognosis? If we are to stay with the mild, moderate and severe classification, I agree that it would be most prudent to further stratify the moderate group into subgroups, as it is certainly clear that this patient population is too diverse for a singular approach to their management and prognostication. This is a worthwhile cause and I hope that this consensus statement will serve as a framework from which LABIC can build more specific recommendations and guidelines to improve the management of these challenging patients.

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