Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting

From the American College of Emergency Physicians (ACEP)/Centers for Disease Control and Prevention (CDC) Panel to Revise the 2002 Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting:
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ABSTRACT

This clinical policy provides evidence-based recommendations on select issues in the management of adult patients with mild traumatic brain injury (TBI) in the acute setting. It is the result of joint efforts between the American College of Emergency Physicians and the Centers for Disease Control and Prevention and was developed by a multidisciplinary panel. The critical questions addressed in this

clinical policy are: (1) Which patients with mild TBI should have a noncontrast head computed tomography (CT) scan in the emergency department (ED)? (2) Is there a role for head magnetic resonance imaging over noncontrast CT in the ED evaluation of a patient with acute mild TBI? (3) In patients with mild TBI, are brain specific serum biomarkers predictive of an acute traumatic intracranial injury? (4) Can a patient with an isolated mild TBI and a normal neurologic evaluation result be safely discharged from the ED if a noncontrast head CT scan shows no evidence of intracranial injury? Inclusion criteria for application of this clinical policy's recommendations are nonpenetrating trauma to the head, presentation to the ED within 24 hours of injury, a Glasgow Coma Scale score of 14 or 15 on initial evaluation in the ED, and aged 16 years or greater. The primary outcome measure for questions 1, 2, and 3 is the presence of an acute intracranial injury on noncontrast head CT scan; the primary outcome measure for question 4 is the occurrence of neurologic deterioration.

INTRODUCTION

There are more than 1 million emergency department (ED) visits annually for traumatic brain injury (TBI) in the United States.[1,2] The majority of these visits are for "mild" injuries that are primarily the result of falls and motor vehicle crashes.[1,2] In nonpediatric patients, the highest incidence of mild TBI is seen in males between the ages of 15 and 24 years and in men and women 65 years of age and older.[3] It has been reported that up to 15% of patients with head trauma evaluated in the ED with a Glasgow Coma Scale (GCS) score of 15 will have an acute lesion on head computed tomography (CT); less than 1% of these patients will have a lesion requiring a neurosurgical intervention.[4-9] Depending on how disability is defined, 5% to 15% of patients with mild TBI may have compromised function 1 year after their injury.[10,11]

The challenge to the emergency physician is identifying which patients with a head injury have an acute traumatic intracranial injury,* and which patients can be safely sent home. The initial version of this clinical policy was published in 2002 and designed to provide the best evidence available to answer these questions.[12] Since then, several well-designed studies have been published that have added to our understanding of mild TBI and assist in clinical decisionmaking.[5,6,8,9,13] Consequently, this clinical policy provides an update of the 2002 document.

The question of how best to define a mild TBI is of great importance and has been a source of confusion.[14] A small subset of these patients will harbor a life-threatening injury; some will have neurocognitive sequelae for days to months after the injury.[15,16] In fact, it is difficult to convince a patient disabled from the postconcussive syndrome that their injury was "mild." Unfortunately, there exists no consensus regarding classification. Terms used have included "concussion," "mild TBI," "minor TBI," "minimal TBI," "grade I TBI," "class I TBI," and "low-risk TBI." Even the terms "head" and "brain" have been used interchangeably. Head injury and TBI are 2 distinct entities that are often, but not necessarily, related. A head injury is best defined as an injury that is clinically evident on physical examination and is recognized by the presence of ecchymoses, lacerations, deformities, or cerebrospinal fluid leakage. A traumatic brain injury refers specifically to an injury to the brain itself and is not always clinically evident; if unrecognized, it may result in an adverse outcome.

The American Congress of Rehabilitation Medicine delineated inclusion criteria for a diagnosis of mild TBI, of which at least 1 of the following must be met[17]:

1. Any period of loss of consciousness of less than 30 minutes and GCS score of 13 to 15 after this period of loss of consciousness;
2. Any loss of memory of the event immediately before or after the accident, with posttraumatic amnesia of less than 24 hours; or
3. Any alteration in mental state at the time of the accident (eg, feeling dazed, disoriented, or confused).

The Centers for Disease Control and Prevention has developed a similar conceptual definition for mild TBI[18]: Occurrence of injury to the head, resulting from blunt trauma or acceleration or deceleration forces, with one or more of the following conditions attributable to the head injury during the surveillance period:

- Any period of observed or self-reported transient confusion, disorientation, or impaired consciousness
- Any period of observed or self-reported dysfunction of memory (amnesia) around the time of injury
- Observed signs of other neurologic or neuropsychological dysfunction
- Any period of observed or self-reported loss of consciousness lasting 30 minutes or less.

Both definitions are broad and contribute to the difficulty of interpreting the mild TBI literature.

Historically, the system most often used for grading severity of brain injury is the GCS. The phrase "mild TBI" is usually applied to patients with a score of 13 or greater. Some authors have suggested that patients with a GCS score of 13 be excluded from the "mild" category and placed into the "moderate" risk group because of their high incidence of lesions requiring neurosurgical intervention.[19-21] Lesions requiring neurosurgical intervention may not be the only injuries that require identification. In a prospective study, patients with a GCS score of 13 or greater were grouped according to the presence or absence of acute intracranial injury.[20] Despite having GCS scores of 13 to 15, those patients with intraparenchymal lesions performed on neuropsychological testing similar to those patients categorized as having moderate TBI (GCS scores 9 to 12).

*Acute traumatic intracranial injuries include the spectrum of injuries including isolated fractures of the cranium, subarachnoid hemorrhage, subdurals, epidurals, hemorrhagic, and bland contusions.

Created by Teasdale and Jennett[22] in 1974, the GCS was developed as a standardized clinical scale to facilitate reliable interobserver neurologic assessments of comatose patients with head injury. The original studies applying the GCS score as a tool for assessing outcome required that coma be present for at least 6 hours.[22-24] The scale was not designed to diagnose patients with mild or even moderate TBI, nor was it intended to supplant a neurologic examination. Instead, the GCS was designed to provide an easy-to-use assessment tool for serial evaluations by relatively inexperienced care providers and to facilitate communication between care providers on rotating shifts.[22] This need was especially great because CT scanning was not yet available. Since its introduction, the GCS has become quite useful for diagnosing severe and moderate TBI and for prioritizing interventions in these patients. Nevertheless, for mild TBI, a single GCS score is of limited prognostic value and is insufficient to determine the degree of parenchymal injury after trauma.[22] On the other hand, serial GCS scores are quite valuable in patients with mild TBI. A low GCS score that remains low or a high GCS score that decreases predicts a poorer outcome than a high GCS score that remains high or a low GCS score that progressively improves.[24,25] From an emergency medical services' and ED perspective, the key to using the GCS in patients with mild TBI is in serial determinations. When head CT is not available, serial GCS scores clearly are the best method for detecting patients who require a neurosurgical procedure. The GCS score continues to play this role and to provide important prognostic information. However, the previous discussion makes it clear that the use of a single GCS determination cannot be used solely in diagnosing mild TBI. In one of the original multicenter studies validating the scale in the pre-CT era, approximately 13% of patients who became comatose had an initial GCS of 15.[24]

The immediate challenge in the ED lies in identifying the apparently well, neurologically intact patient who has a potentially significant intracranial injury. These patients are the focus of this clinical policy. A second challenge is to identify those patients at risk for having prolonged postconcussive symptoms and those at risk for the postconcussive syndrome in order to ensure proper discharge planning. Meeting the second challenge has proven to be elusive and remains an area in need of research.

Increased attention has been brought to bear on concussions and postconcussive issues as a result of the wars in Afghanistan and Iraq. TBI has been labeled the "signature injury" resulting from these conflicts. The proportion of military personnel presenting with a blunt TBI has increased dramatically, primarily because of an increase in survival after exposure to concussive weapons (primarily a result of lower-yield improvised explosive devices, coupled with modern body armor that reduces fatal penetrating injuries). In the Afghanistan/Iraq conflicts, approximately 20% of returning combat personnel have experienced a TBI in theater.[26]

Definitions

Since the initial 2002 clinical policy, an analysis of the literature has driven a change in the working definition of mild TBI as it applies to this document. The majority of patients classified as having mild TBI have a GCS score of 15 when they are in the ED, and consequently this group was the focus of the first clinical policy.[12] The Canadian CT Head Rule, which has a primary outcome measure of a neurosurgical lesion, includes patients with a GCS of 14 and allows for a period of 2 hours for normalization of the GCS score before deciding on imaging.[27] Since this clinical policy was first published, several studies have used the Canadian CT Head Rule criteria, and therefore the panel members decided to use a GCS of 14 or 15 as inclusion criteria.

In the 2002 edition of this clinical policy, the literature suggested that the absence of loss of consciousness or amnesia in patients with blunt head injury were negative predictors of having an intracranial injury; therefore, in the 2002 clinical policy, inclusion criteria for application required the presence of loss of consciousness or posttraumatic amnesia and implied that the absence of loss of consciousness or posttraumatic amnesia in patients with a nonfocal neurologic examination and GCS score of 15 precluded the need to obtain a head CT (if age less than 61 years and patient was not on anticoagulants).[12] Since the publication of the first edition of this clinical policy, 2 well-designed studies have demonstrated that neither loss of consciousness nor posttraumatic amnesia are sufficiently sensitive to identify all patients at risk.[8,28] After a review of these studies, the panel decided to change the inclusion criteria by eliminating these factors as criteria for this clinical policy. Because mild TBI management in the pediatric population has been presented in a clinical policy developed by the American Academy of Pediatrics and the American Academy of Family Physicians, this clinical policy specifically addresses mild TBI in patients aged 16 years or older.[29]

Inclusion criteria for application of this clinical policy's recommendations are:

- Nonpenetrating trauma to the head
- Presentation to the ED within 24 hours of injury
- A GCS score of 14 or 15 on initial evaluation in the ED and
- Age 16 years or greater

Exclusion criteria for application of this clinical policy's recommendations include:

- Penetrating trauma
- Patients with multisystem trauma
- GCS score less than 14 on initial evaluation in the ED and
- Age less than 16 years

Evidence-based practice guidelines require that a focused question be asked and that a clear outcome measure be identified. The 2002 clinical policy[12] identified 3 critical questions relevant to clinical practice:

1. Is there a role for plain film radiographs in the assessment of acute mild TBI in the ED?
2. Which patients with acute mild TBI should have a noncontrast head CT scan in the ED?

3. Can a patient with mild TBI be safely discharged from the ED if a noncontrast head CT scan shows no evidence of acute injury?

In this revision, the first question about the role of plain film radiographs was not readdressed because the panel concluded that there is no new evidence that changes the recommendation made in 2002:

> *Recommendation B: Skull film radiographs are not recommended in the evaluation of mild TBI. Although the presence of a skull fracture increases the likelihood of an intracranial lesion, its sensitivity is not sufficient to be a useful screening test. Indeed, negative findings on skull films may mislead the clinician.*

The questions addressed in this clinical policy update are:

1. Which patients with mild TBI should have a noncontrast head CT scan in the ED?
2. Is there a role for head magnetic resonance imaging (MRI) over noncontrast CT in the ED evaluation of a patient with acute mild TBI?
3. In patients with mild TBI, are brain-specific serum biomarkers predictive of an acute traumatic intracranial injury?
4. Can a patient with an isolated mild TBI and a normal neurologic evaluation result be safely discharged from the ED if a noncontrast head CT scan shows no evidence of intracranial injury?

The panel considered several outcome measures in developing this clinical policy, including presence of an acute abnormality on noncontrast CT scan, clinical deterioration, need for neurosurgical intervention, and the development of postconcussive symptoms. Presence of an acute intracranial injury on noncontrast head CT scan was chosen as the primary outcome measure; development of a lesion requiring neurosurgical intervention was the secondary outcome measure for questions 1, 2, and 3. Neurologic deterioration was the primary outcome measure for question 4.

The limitations of these outcome measures were discussed. There is a paucity of literature that discusses the natural course of acute traumatic intracranial lesions in patients who initially appear intact. The Canadian CT Head Rule suggests that there are inconsequential traumatic lesions, such as "smear" subdurals (subdurals less than 4 mm thick), for which detection is not necessary[27]; however, this is based on survey data and not on prospective studies. Unfortunately, there is insufficient evidence available to use the development of postconcussive symptoms as an outcome measure at this time.

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature. MEDLINE and the Cochrane Database were searched for articles published from January 2000 through 2007. Specific key words/phrases used in the searches are identified under each critical question. Searches were limited to English-language sources, human studies, and aged 16 years or older. References obtained on the searches were reviewed by panel members (title and abstract) for relevance before inclusion in the pool of studies to be reviewed. Additional articles were reviewed from the bibliographies of articles cited and from hand searches of published literature. Some literature from the 2002 policy[12] (1980 to 2001) is also included in this current policy.

The panel used the American College of Emergency Physicians clinical policy development process as described below. This policy is based on the existing literature; where literature was not available, consensus of panel members was used. Outside review comments were received from physicians and individuals with expertise in the topic area and practicing in the fields of emergency medicine, neurology, neuroradiology, neurosurgery, and neuropsychology. Their responses were used to further refine and enhance this policy.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for strength of evidence and classified by the subcommittee members into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the weakest evidence for therapeutic, diagnostic, and prognostic clinical reports, respectively (Appendix A). Articles were then graded on 6 dimensions thought to be most relevant to the development of a clinical guideline: blinded versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures (reliability and validity), biases (eg, selection, detection, transfer), external validity (ie, generalizability), and sufficient sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula, taking into account design and quality of study (Appendix B). Articles with fatal flaws were given an "X" grade and not used in formulating recommendations in this policy. Evidence grading was done with respect to the specific data being extracted and the specific critical question being reviewed. Thus, the level of evidence for any one study may vary according to the question, and it is possible for a single article to receive different levels of grading as different critical questions are answered. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of this policy.

Clinical findings and strength of recommendations regarding patient management were then made according to the following criteria:

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on strength of evidence Class II studies that directly

address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).

Level C recommendations. Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or in the absence of any published literature, based on panel consensus.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

It is the goal of the panel to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain enough quality information to answer a critical question, the members of the panel believe that it is equally important to alert emergency physicians to this fact.

Recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. The panel clearly recognizes the importance of the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the crucial questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in hospital-based EDs.

Inclusion Criteria. This guideline is intended for patients with blunt trauma to the head who present to the ED within 24 hours of injury, who have a GCS score of 14 or 15 on initial evaluation in the ED, and are 16 years of age or older.

Exclusion Criteria. This guideline is not intended for patients with penetrating trauma or multisystem trauma, who are younger than 16 years, or who have a GCS score of less than 14 on initial evaluation in the ED.

CRITICAL QUESTIONS

1. Which patients with mild TBI should have a noncontrast head CT scan in the ED?

Recommendations

Level A recommendations. A noncontrast head CT is indicated in head trauma patients with loss of consciousness or posttraumatic amnesia only if one or more of the following is present: headache, vomiting, age greater than 60 years, drug or alcohol intoxication, deficits in short-term memory, physical evidence of trauma above the clavicle, posttraumatic seizure, GCS score less than 15, focal neurologic deficit, or coagulopathy.

Level B recommendations. A noncontrast head CT should be considered in head trauma patients with no loss of consciousness or posttraumatic amnesia if there is a focal neurologic deficit, vomiting, severe headache, age 65 years or greater, physical signs of a basilar skull fracture, GCS score less than 15, coagulopathy, or a dangerous mechanism of injury.*

*Dangerous mechanism of injury includes ejection from a motor vehicle, a pedestrian struck, and a fall from a height of more than 3 feet or 5 stairs.

Level C recommendations. None specified.

Key words/phrases for literature searches: mild traumatic brain injury, minor traumatic brain injury, head computed tomography, diagnosis, prognosis, Coumadin, neurocognitive testing, physical examination, aspirin, clopidogrel, loss of consciousness, anticoagulation, elderly.

Some of the studies on mild TBI have focused on identifying lesions in need of neurosurgical intervention.[27,30,31] The literature does not clearly identify which patients with intracranial lesions deteriorate, nor is it clear on the relationship between acute traumatic intracranial lesions in predicting the development of postconcussive symptoms. Therefore, the panel chose the presence of an acute traumatic intracranial lesion on noncontrast head CT scan as the primary outcome measure on patients with mild TBI, and the presence of an acute lesion requiring neurosurgical intervention as a secondary outcome measure.

Early studies working from trauma registries established that up to 15% of mild TBI patients with a GCS score of 14 or 15 will have an acute intracranial injury on noncontrast head CT, of whom up to 1% will harbor a lesion requiring a neurosurgical intervention.[19,24,30-34] None of these early investigators were able to develop a statistical model that could be used to classify 95% of patients into a CT-normal or CT-abnormal group. However, Miller et al[31] prospectively studied 2,143 patients and identified nausea, vomiting, severe headache, or depressed skull fracture as having a positive predictive value of 100% for those patients requiring neurosurgical intervention. No patient without a risk factor deteriorated even if CT scan findings were positive.

Working with the predictors identified in earlier studies, 2 seminal papers published in 2000[4] and 2001[27] had significant influence on clinical decisionmaking in mild TBI; these studies stimulated a number of well-designed studies during the subsequent years that have shed some light on best practice in caring for these patients. Stiell et al,[27] in a Class II study, performed a derivation study by prospectively evaluating 3,121 patients, 2,489 of whom had a GCS score of 15, using a structured assessment tool. Only 2,078 (67%) of the 3,121 patients had a CT scan; telephone follow-up and a neuropsychiatric test were used as a surrogate for negative CT scan findings. Patients had a follow-up interview at 14 days to assess outcome. The primary outcome measure was the need for neurosurgical intervention, and the secondary outcome was a "clinically important brain injury," defined by a survey consensus. "Clinically unimportant lesions" included solitary contusions less than 5 mm in diameter, smear subdurals less than 4 mm thick, isolated pneumocephalus, and closed depressed skull fractures not through the inner table. Because the study sites were the primary neurosurgical centers for the

respective cities, the authors concluded that no patient with "clinically unimportant" CT scan findings deteriorated after discharge. The authors concluded that CT in mild TBI is indicated only in those patients with one of 5 high-risk factors, the Canadian CT Head Rule: failure to reach a GCS score of 15 within 2 hours of injury, suspected open skull fracture, sign of basal skull fracture, vomiting more than once, or age greater than 64 years.

In a Class I study, Haydel et al[4] prospectively assessed 1,429 patients who had a GCS score of 15 in the ED and a history of loss of consciousness or amnesia of the traumatic event. The study consisted of an initial phase with 520 patients in whom predictors for intracranial injury were identified, followed by a validation phase that included 909 patients. The authors reported that 93 (6.5%) of their patients had an intracranial lesion and that 6 (0.4%) required neurosurgical intervention. Seven predictors of abnormal CT scan findings were identified, ie, the New Orleans Criteria: headache (any head pain), vomiting, age greater than 60 years, intoxication, deficit in short-term memory (persistent anterograde amnesia), physical evidence of trauma above the clavicle, and seizure. Absence of all 7 findings had a negative predictive value of 100% (95% confidence interval [CI] 99% to 100%).

Two studies have compared the performance of the New Orleans Criteria and the Canadian CT Head Rule.[5,6] Smits et al,[6] in a Class I study, applied these 2 decision rules at 4 university hospitals in the Netherlands to 3,181 consecutive adult patients with a GCS score of 13 or 14 or a GCS of 15 plus one of the risk factors identified by the decision rules. The New Orleans Criteria had a sensitivity for identifying a neurosurgical lesion of 100% (95% CI 34.2% to 100%) and a specificity of 5.3% (95% CI 2.5% to 8.3%). It had a sensitivity for identifying an intracranial injury of 98.3% (95% CI 94% to 99.5%) and a specificity of 5.6% (95% CI 2.7% to 8.8%). The Canadian CT Head Rule had a sensitivity for identifying a neurosurgical lesion of 100% (95% CI 64.6% to 100%) and a specificity of 37.2% (95% CI 34.1% to 40.4%). It had a sensitivity for identifying an intracranial injury of 83.4% (95% CI 77.7% to 87.9%) and a specificity of 39.4% (95% CI 36.0% to 42.8%). The study validated the high sensitivity of both rules for identifying lesions requiring neurosurgical intervention. It demonstrated the superiority of the New Orleans Criteria over the Canadian CT Head Rule for identifying acute traumatic lesions; however, the higher sensitivity of the New Orleans Criteria was at the expense of a significantly lower specificity.

In a Canadian prospective comparative study involving 1,822 patients with a GCS score of 15, Stiell et al[5] reported results similar to that of Smits et al.[6] Both the Canadian CT Head Rule and the New Orleans Criteria had sensitivities of 100% for identifying *neurosurgical lesions* (95% CI 63% to 100% for both rules) but a specificity of 76.3% (95% CI 74% to 78%) versus 12.1% (95% CI 11% to 14%), respectively. In this study, the 2 rules performed equally well in identifying *clinically important brain injuries*, with a sensitivity of 100% (95% CI 96% to 100%) but with the Canadian CT Head Rule demonstrating a specificity of 50.6% (95% CI 48% to 53%) versus the New Orleans Criteria with a specificity of 12.7% (95% CI 11% to 14%). The improved performance of this study over that of Smits et al[6] in identifying nonsurgical traumatic lesions is most likely explained by its stricter definition of what constitutes a "clinically significant" lesion. In addition, not all patients received imaging and outcome in these patients was based on telephone follow-up within 14 days. A third study from Australia, a retrospective chart review of 240 head trauma patients with a GCS score of 15, in essence reported the same findings as above.[35] Both the New Orleans Criteria and Canadian CT Head Rule identified all patients with neurosurgical lesions, but the New Orleans Criteria outperformed the Canadian CT Head Rule in identifying an intracranial injury.

Studies that provided external validation of the New Orleans Criteria and Canadian CT Head Rule identified several limitations. Both decision rules use loss of consciousness or amnesia as entry criteria, and neither applies to patients on anticoagulants. Thus, neither rule could be reliably applied to all patients with head trauma. In addition, if the primary outcome measure of acute intracranial injury is used (without subcategorizing into significant and nonsignificant, as done in the Canadian CT Head Rule), it becomes clear that specificity is sacrificed for sensitivity. Indeed, the Smits et al[6] study cited above reported that the New Orleans Criteria would reduce CT scans by only 3%, whereas the Canadian CT Head Rule would reduce scans by 37%. Consequently, clinicians are faced with the dilemma of choosing the outcome measure they are most interested in and deciding the risk they are willing to take in missing an acute, nonsurgical lesion.

Using the New Orleans Criteria and the Canadian CT Head Rule as a framework, several groups have tried to develop improved decision rules for all patients with mild TBI regardless of loss of consciousness or posttraumatic amnesia. In the United Kingdom, the National Institute for Health and Clinical Excellence (NICE) published guidelines for CT imaging that included GCS score of 14, signs of basal skull fracture, neurologic deficit, vomiting, amnesia before impact greater than 30 minutes, posttraumatic seizures, coagulopathy, dangerous mechanism, age greater than 64 years.[36] The Neurotraumatology Committee of the World Federation of Neurosurgical Societies (NCWFNS) proposed guidelines that included GCS score of 14, suspected skull fracture, neurologic deficits, vomiting, amnesia, loss of consciousness, headache, coagulopathy, previous neurosurgery, history of epilepsy, alcohol or drug abuse.[37] In a Class III study, Fabbri et al[9] applied the NICE and NCWFNS criteria to a 7,955-patient trauma database. The NICE guidelines were less sensitive than the NCWFNS guidelines but more specific for identifying intracranial lesions; they were also more specific in identifying neurosurgical lesions.

In a Class II study, Smits et al[38] applied the NICE criteria, as well as the NCWFNS, New Orleans Criteria, Canadian CT Head Rule, and European Federation of Neurological Societies

to the Dutch database of 3,181 mild TBI patients. In this external validation study, the European Neurological Societies criteria demonstrated 100% sensitivity for clinically relevant traumatic CT findings, as well as for neurosurgical lesions; however, the specificity was so low that all patients would need a CT. The NICE criteria identified 94% (95% CI 93% to 99%) of neurosurgical lesions and 82% (95% CI 77% to 86%) of neurocranial injuries. The NICE criteria specificity was the best of the guideline tests, at 37% to 57%.

In a Class II study, Ibanez et al[8] prospectively studied 1,101 mild TBI patients older than 14 years who had a GCS score of 14 or 15. A comprehensive clinical variable data collection sheet was used and all patients had a head CT regardless of loss of consciousness or amnesia. On univariate analysis, the following independent variables were found to predict intracranial lesions: GCS score of 14, loss of consciousness, vomiting, headache, signs of basilar skull fracture, neurologic deficit, coagulopathy, hydrocephalus treated with shunt, associated extracranial lesions, and patient age 65 years or greater. The authors attempted to build a prediction model but were unable to achieve 100% sensitivity for intracranial lesions with acceptable specificity. Of the 491 patients in this study who did not have loss of consciousness, 1.8% had an intracranial injury and 0.6% required neurosurgery. This study's results thus challenged the commonly held premise that loss of consciousness was a reliable discriminator for deciding who with mild TBI requires neuroimaging.

Smits et al,[28] in a Class II study, analyzed a prospectively collected database of mild TBI patients older than 15 years with a GCS score of 15. Of 2,462 patients, 754 had neither loss of consciousness nor posttraumatic amnesia. There was an 8.7% occurrence of an intracranial injury in those patients with loss of consciousness or posttraumatic amnesia versus 4.9% in those without; the need for a neurosurgical intervention was 0.4% versus 0.5% in patients with no loss of consciousness or posttraumatic amnesia. Odds ratios were performed for independent risk factors of mild TBI, including those from the New Orleans Criteria and Canadian CT Head Rule, and were found to be independent of whether the patient had loss of consciousness or posttraumatic amnesia. Loss of consciousness was found to have an odds ratio of 1.9 (95% CI 1.3 to 2.6) for intracranial injury; posttraumatic amnesia had an odds ratio of 1.7 (95% CI 1.3 to 2.3). In a Class III study from Japan, Ono et al[39] studied 1,145 patients and reported that in those patients with no loss of consciousness or amnesia, 3.5% had an intracranial lesion and 0.3% required neurosurgery.

Using the mild TBI database of 3,181 patients from 4 Dutch university medical centers that was used in several of the above referenced studies, Smits et al[13] performed a logistic regression analysis to develop a prediction rule that would apply to mild TBI patients regardless of whether they had experienced loss of consciousness or posttraumatic amnesia. The database incorporated the variables from the New Orleans Criteria and the Canadian CT Head Rule plus variables from other guidelines. Internal validation was performed using bootstrapping. Ten major and 8 minor criteria were identified that allowed for a sensitivity of 94% to 96% and a specificity of 25% to 32% for identifying intracranial lesions. The rule awaits external validation.

The large databases from Spain,[8] Italy,[9] and Holland,[13] allow for a look at individual variables and their associated odds ratio for identifying acute intracranial lesions in heterogenous mild TBI patients, with or without loss of consciousness or amnesia (Table).

Although both the New Orleans Criteria and the Canadian CT Head Rule have been validated, they must be applied within the limits of their inclusion criteria, and the clinician should understand their sensitivity and specificity for both neurosurgical lesions and for intracranial injury. Specifically, these rules are valid when applied to patients who have had a loss of consciousness or amnesia and who are not on anticoagulants. Data from the studies presented in the Table bring attention to the variables that should be considered when deciding on whether the mild TBI patient should undergo imaging. These variables include a GCS score less than 15, a dangerous mechanism of injury, a neurologic deficit, or use of anticoagulants. Two retrospective studies suggest that antiplatelet agents may increase risk of intracranial injury after closed head injury, but further study is needed.[40,41] Although identified in the New Orleans Criteria, neither seizure nor mild or moderate headache emerge as univariate predictors of intracranial injury. Alcohol does not emerge as a univariate predictor in the 2 Class II studies.[8,13] On the other hand, a dangerous mechanism of injury, ie, pedestrian versus vehicle or fall from a height, does emerge as an important factor in deciding who to image.

There are no good studies that have demonstrated the value of a cognitive assessment in predicting an intracranial injury. Vilke et al[42] specifically studied the value of a detailed neurologic examination, including a careful mental status assessment, in predicting the presence of an acute intracranial lesion on CT scan. The study's well-defined methodology was undermined by its small sample size of only 58 patients. Three patients (5%) were found to have positive CT scan findings, 2 of whom had a normal neurologic examination result, of whom 1 required a craniotomy. The United States military currently uses a structured assessment tool for patients with mild TBI, the Military Acute Concussion Evaluation (MACE).[43] The sections in this tool include history, neurologic examination, orientation, memory, and concentration. The ability of the MACE to predict intracranial injury has not been studied.

Future Directions

Future research must begin with a collaborative effort in the neuroscience community on how to define mild TBI and how to measure its related outcomes. The true incidence of mild TBI is unknown. Epidemiologic studies have focused on those patients treated in trauma centers and admitted; they therefore have selection bias. Many patients sustain mild TBI but do not seek medical care and are thus not included in estimates, which

Table. Predictor variables for intracranial lesions.

	Smits et al,[13] OR (95% CI)	Ibanez et al,[8] OR (95% CI)	Fabbri et al,[9] OR (95% CI)
Class of evidence	II	II	III
Variable			
GCS 14	2 (1-3)	7 (4-14)	19 (14-26)
Neurologic deficit	2 (1-3)	7 (2-25)	19 (13-28)
Signs of basilar skull fracture	14 (8-22)	11 (6-23)	10 (6-16)
Loss of consciousness	2 (1-3)	7 (4-11)	2 (2-3)
Posttraumatic amnesia	1.7 (1-2)	3 (2-5)	8 (6-12)
Headache	1.4 (1-2)	1 (0.8-2)	–
Headache, severe	–	3 (2-6)	–
Vomiting	3 (2-4)	4 (2-7)	5 (3-8)
Posttraumatic seizure	3 (1-10)	2 (0.25-17)	3 (2-5)
Alcohol or drug intoxication	1 (0.6-2)	1 (0.3-3)	–
Anticoagulation	2 (1-4)	4 (3-7)	8 (3-9)
Age ≥65 years	–	2 (1-3)	2 (1-3)
Dangerous mechanism	2 (1-4)	–	3 (2-4)

underestimates the true incidence of mild TBI. More thorough and accurate epidemiologic evaluation of mild TBI is needed to define the enormity of the problem and to direct both public education and prevention strategies.

An improved elucidation of the pathophysiologic characteristics of mild TBI is critical for the research and development of therapeutic measures. Pharmacologic therapy used to prevent or reduce neuronal injury after mild TBI remains a formidable yet crucial goal. More conclusive evidence is needed to help identify in a timely manner the small but important number of patients who develop intracranial lesions despite initially normal CT scan findings and normal neurologic examination results.

2. Is there a role for head MRI over noncontrast CT in the ED evaluation of a patient with acute mild TBI?

Recommendations

Level A recommendations. None specified.
Level B recommendations. None specified.
Level C recommendations. None specified.

Key words/phrases for literature searches: mild traumatic brain injury, minor traumatic brain injury, head computed tomography, magnetic resonance imaging, neuroimaging, neuroradiography.

Using standard 1.5-T MRI imaging sequences, MRI is up to 30% more sensitive than CT scanning in detecting acute traumatic intracranial injury in patients with mild TBI.[44] Most studies comparing CT results with MRI results in patients with TBI do not distinguish between mild TBI and more severe TBI. Four studies were identified in which concussion patients with mild TBI can be isolated; the prevalence of abnormal MRI results in these 4 studies ranged from 10% to 57%.[45-48]

Doezema et al[45] performed a prospective blinded cohort study of 58 patients with minor head injury. The patients underwent MRI within 24 hours of discharge from the ED; 10% of the discharged patients had abnormal MRI scan results including cortical contusions and small subdural hematomas. CT was performed in the ED on 2 of the 3 patients exhibiting small subdurals on follow-up MRI, although no abnormality was detected on CT. The remaining 3 patients with an abnormal follow-up MRI scan result did not receive a CT scan in the ED. This study found no significant difference in symptoms between patients with abnormal and those with normal MRI scan results.

In a study by Hofman et al,[46] 21 patients with mild TBI received an MRI examination within 5 days of injury. Twelve (57%) of these patients had abnormal MR findings, including small extra-axial hematomas, both hemorrhagic and nonhemorrhagic contusions, and diffuse axonal injury. Hughes et al[47] studied patients who were diagnosed with mild TBI and subsequently underwent MRI and neurocognitive examinations between 24 and 72 hours postinjury. The initial MRI demonstrated abnormalities that could be attributed to TBI in 6% (5/80) of patients. Voller et al[48] reported that 25% (3/12) of patients with mild TBI had MRI abnormalities, including contusions, diffuse axonal injury lesions, and an epidural hematoma. None of these studies demonstrated clear clinical relevance of these abnormal MRI scan results in patients with mild TBI, and none were conducted within a time frame relevant for ED disposition of patients.

Unfortunately, there are no well-designed studies that specifically examine the use of MRI within 24 hours of injury in mild TBI patients. Therefore, at this time no evidence-based recommendations can be made about the use of MRI compared with CT in the ED setting.

Potentially limiting factors for using MRI to diagnose mild TBI include cost constraints, availability, and accessibility issues. Challenges to patient care include safety issues such as patients with pacemakers and certain ferromagnetic foreign bodies. Compatibility with life-support and traction/stabilization devices is also somewhat problematic. Further, patient motion

artifacts are less of an issue with CT than with MRI, and acute "neurosurgically relevant" hemorrhage is still reliably diagnosed with CT.

Nevertheless, recent improvements in MRI technology cannot be ignored. Scan times have decreased and specialized pulse sequences have improved our sensitivity for the detection of both *structural* and *functional* traumatic brain abnormalities associated with mild TBI. These MR techniques include magnetization transfer MRI, fluid-attenuated inversion recovery, fast field echo T2-weighted imaging, gradient-echo imaging, susceptibility-weighted imaging, diffusion-weighted imaging, diffusion tensor imaging, magnetic resonance spectroscopy, functional MRI, and magnetic source imaging.[46,49-53] One very recent study using diffusion tensor imaging in 10 patients aged 14 to 19 years, with a normal CT result and presenting with a GCS score of 15, demonstrated a correlation between the severity of postconcussion symptoms and diffusion tensor imaging abnormalities.[54] Although many of these techniques are not yet widely available and are currently largely research tools, they are likely to become incorporated into the routine imaging assessment as improvements in technology facilitate their acquisition and interpretation.

Unfortunately, the intrinsic heterogeneity of TBI (eg, male versus female, young versus old, associated comorbidities, multiple mechanisms of injury), coupled with the numerous potential variables of MRI (eg, low field versus high field, imaging parameters, choice of pulse sequence, time of imaging relative to time of injury), make generalization of study results difficult. TBI is a dynamic process and imaging is a static process; the conclusion of any imaging study should take into consideration the timing of the injury relative to the timing of the scan. Although the lesions that are detected on MRI as opposed to CT are not likely to change neurosurgical decisionmaking, they may nevertheless provide clinically meaningful data that could refine mild TBI diagnosis, prognosis, and medical management.

Future Directions

As MRI technology continues to evolve and becomes more uniformly available, there could be a role for its use in the ED. Studies examining the role of MRI at early time points (less than 24 hours) and the relationship of pathologic changes to outcome (postconcussive symptoms and postconcussive syndrome) are needed. Moreover, standardized protocols and normative time-dependent databases are needed to more accurately interpret the findings.

3. In patients with mild TBI, are brain-specific serum biomarkers predictive of an acute traumatic intracranial injury?

Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. In mild TBI patients without significant extracranial injuries and a serum S-100B level less than 0.1 μg/L measured within *4 hours of injury*, consideration can be given to not performing a CT.*

*This test has not yet received Food and Drug Administration approval for clinical use in the United States.

Key words/phrases for literature searches: mild traumatic brain injury, minor traumatic brain injury, head computed tomography, diagnosis, biomarkers, glucose, international normalized ratio, partial thromboplastin time, prothrombin time.

Several brain-specific serum proteins have been examined for their ability to predict traumatic abnormalities on head CT scan after mild TBI. Rapid deceleration forces to the head can result in excessive axonal shear and traumatic injury to the neuronal axon and supporting cells such as astrocytes. The proteins released during this process diffuse into the cerebrospinal fluid, cross the blood-brain barrier, and reach the peripheral circulation where they can be detected.

Neuronal proteins studied include neuron-specific enolase and tau. Astrocyte proteins studied include S-100B, creatine kinase BB isoenzyme, and glial fibrillary acidic protein. Glucose, norepinephrine, epinephrine, and dopamine have also been studied as markers for injury.

Of these serum markers, S-100B is perhaps the best studied. S-100B increases and decreases rapidly after head injury, making early measurement crucial. Although S-100B has been found in cell culture models to be released within 15 seconds of injury, the earliest it has been detected in human serum is 30 minutes after injury; the half-life of S-100B in serum after mild TBI is approximately 97 minutes.[55]

Eight studies were reviewed that reported on the relationship between serum S-100B and head CT scan after mild TBI.[56-63] In general, this protein is a sensitive but not specific predictor of CT abnormalities. At low serum cutoff levels the sensitivities range from 90% to 100%, with specificities ranging from 4% to 65%.

In a Class II study of 226 adults admitted to the hospital with isolated mild head injury and a GCS score of 13 to 15, Muller et al[61] found the sensitivity of S100-B measured within 12 hours of injury to be 0.95 (95% CI 0.76 to 1.0) and the specificity 0.31 (95% CI 0.25 to 0.38). When the 16 subjects with a GCS score of 13 were removed from analysis, the sensitivity decreased slightly to 0.94 (95% CI 0.91 to 0.97), without significantly changing the specificity of 0.31 (95% CI 0.25 to 0.37). This study reveals the increase in sensitivity that occurs when the overall severity of the cohort is increased by including those with a GCS score of 13, as most of the subsequent S-100B studies do. However, when the proportion of the cohort with a GCS score of 13 is relatively small, as is the case in the Muller et al[61] study, the impact of this severity bias on the test characteristics of S-100B is minimal.

Similar results have been found by other investigators using the 0.1 μg/L cutoff. In a Class II study, Biberthaler et al[57] measured serum S100-B levels within 3 hours of injury in 1,309 patients with isolated mild TBI and correlated these to CT scan. Approximately 3% of subjects had a GCS score of 13; 7% of subjects had an acute

intracranial injury on head CT scan. The sensitivity of S-100B was found to be 0.99 (95% CI 0.96 to 1.0) and the specificity 0.30 (95% CI 0.29 to 0.31). In a Class II study, Poli-de-Figueiredo et al[63] studied S-100B in 50 consecutive patients with mild TBI (2 had a GCS score of 13). Six patients had a positive CT result, and they reported a sensitivity of serum S-100B measured within 3 hours of injury to be 1.0 (95% CI 0.8 to 1.0) and the specificity 0.20 (95% CI 0.11 to 0.35).

In a Class III study using a slightly higher cutoff level of 0.12 μg/L, Biberthaler et al[58] found the sensitivity of serum S100-B measured within 2 hours of injury to be 1.0 (95% CI 0.86 to 1.0) and the specificity 0.46 (95% CI 0.36 to 0.57) among 104 patients with isolated mild TBI. Twenty-three percent of the group had an intracranial injury on head CT and 3 subjects (2.9%) had a GCS score of 13.

At a still higher cutoff of 0.2 μg/L, S100-B performed similarly well. In a Class II study of 182 adolescents and adults admitted to the hospital with mild TBI, Ingebrigtsen et al[60] found the sensitivity of S100-B to be 0.90 (95% CI 0.59 to 0.98) and the specificity 0.65 (95% CI 0.58 to 0.72) when measured within 12 hours of injury. Ten (5.5%) subjects had a GCS score of 13 and 5.5% had an intracranial injury on head CT.

Concomitant alcohol intoxication does not appear to affect the test characteristics of S100-B. In a Class II study of 139 adults with isolated mild TBI, Mussack et al[62] found the sensitivity of S100-B to be 1.0 (95% CI 0.83 to 1.0) and the specificity to be 0.50 (95% CI 0.41 to 0.59) when measured within 3 hours of injury. The mean blood alcohol concentration for the group was 182 mg/dL; 14% had an intracranial injury on head CT. Three (2.2%) subjects had a GCS score of 13. In a Class III study of 29 sober and 20 intoxicated adults with isolated mild TBI, Biberthaler et al[59] found serum S100-B levels measured within 3 hours of injury to be significantly higher among those with an abnormal CT scan result, both among the sober patients (0.94 μg/L versus 0.12 μg/L) and intoxicated patients (0.89 μg/L versus 0.15 μg/L). The mean blood alcohol concentration for the intoxicated group was 143 mg/dL. Overall, 31% had an intracranial injury on head CT; 5 (10%) subjects had a GCS score of 13.

Among mild TBI patients with significant extracranial injuries, S100-B may not perform as well. Because S-100B is found in small amounts in adipose, skin, and cartilage, this finding is not surprising.[64] In a study of 96 adolescents and adults with a GCS score of 13 to 15 in addition to other injuries, Bazarian et al[56] found the sensitivity of S100-B at a cutoff of 0.08 μg/L to be 0.8 (95% CI 0.36 to 0.96) and the specificity to be 0.04 (95% CI 0.01 to 0.09). In this study, 3 (3%) subjects had a GCS score of 13, and 5% had an intracranial injury on head CT scan.

Brain-specific serum markers aside from S-100B have received considerably less attention. Levitt et al[65] measured serum levels of dopamine and epinephrine within approximately 3 hours of injury in 107 intoxicated patients with mild TBI. Unfortunately, because half of the cohort had a GCS score less than 14, this study was not considered generalizable to the milder forms of TBI being analyzed in this clinical policy. Serum levels of neuron-specific enolase,[62] tau,[66] glucose,[62] creatine kinase-BB,[65] and norepinephrine[65] have not been found to be reliably predictive of intracranial injury. The relationship between glial fibrillary acidic protein and head CT has not been studied in mild TBI cohorts.

Serum markers have the potential to eliminate the need for head CT scans in mild TBI patients. Unlike the clinical variables used in head CT decision rules (eg, headache, amnesia), serum marker measurements are more objective and less prone to interrater variability. Of the markers studied to date, S100-B appears to have the most promise as a pre–head CT screening test. From a population standpoint, this could result in a 30% reduction in unnecessary CT scans.[57] S100-B may not perform as well in patients with significant trauma outside of the head, so caution should be used when applying these results to patients with multiple trauma.

Future Directions

Despite the great potential of serum markers to predict abnormal head CT scan results after mild TBI, several unaddressed issues remain. Although S100-B appears best suited to the role of pre–head CT screening, its cost-effectiveness has not been demonstrated. Identification of a serum protein with high specificity would increase the number of patients who could safely avoid CT scanning. In addition, identification of a marker that accurately predicts abnormal head CT scan results in the presence of extracranial injuries would expand the use of these markers to multiple trauma patients, a group in whom mild TBI is frequently overlooked.[67,68]

Combining the results of S-100B with clinical variables or with other serum markers such as nonspecific enolase or tau into a clinical prediction rule could potentially improve detection of an abnormal CT scan result. Finally, glial fibrillary acidic protein, a protein studied extensively in patients with severe TBI, has not been examined in human mild TBI cohorts. These areas would be fruitful avenues for future research.

4. Can a patient with an isolated mild TBI and a normal neurologic evaluation result be safely discharged from the ED if a noncontrast head CT scan shows no evidence of intracranial injury?

Recommendations

Level A recommendations. None specified.

Level B recommendations. Patients with an isolated mild TBI who have a negative head CT scan result are at minimal risk for developing an intracranial lesion and therefore may be safely discharged from the ED.*

*There are inadequate data to include patients with a bleeding disorder; who are receiving anticoagulation therapy or antiplatelet therapy; or who have had a previous neurosurgical procedure in this population.

Level C recommendations. Mild TBI patients discharged from the ED should be informed about postconcussive symptoms.

Key words/phrases for literature searches: mild traumatic brain injury, minor traumatic brain injury, head computed tomography, outcome, prognosis, postconcussive syndrome, concussion, brain CT, discharge.

Although much research effort has been expended in attempting to determine criteria for which mild TBI patients require a head CT scan, less effort has been expended in determining the true prognostic value of a head CT scan that is read as negative for an acute intracranial lesion. Nagy et al,[69] in a Class III prospective study of 1,170 mild TBI patients with a GCS score of 15 and who underwent CT and admission for 24 hours, found that none of the patients with a negative scan result later deteriorated. The authors' recommendation was to discharge mild TBI patients from the ED after a negative head CT scan result. Livingston et al,[70] in a small prospective study of 79 mild TBI patients with an initial GCS score of 15 and a negative head CT scan result who were discharged from the ED, found that none had deteriorated at 48 hours after discharge. This study was limited because of sample size and the fact that 22 of the 79 patients were lost to follow-up. Dunham et al,[71] in a retrospective Class III study of 2,252 trauma center admissions who had a head CT scan, found that none of the patients with an initial negative head CT scan result required subsequent neurosurgical operative intervention.

Livingston et al[72] attempted to address the issue of ED discharge of mild TBI patients after a negative head CT scan result in a prospective study of 2,152 patients. Of the 1,788 patients with a negative CT scan result, 33 (0.02%) ultimately required neurosurgical or critical care. Unfortunately, the study's methodology precludes drawing any conclusions because the clinical characteristics of the "miss" group were not well described.

In an attempt to quantify the magnitude of the problem of delayed complications in mild TBI patients with a negative head CT scan result, af Geijerstam and Britton[73] undertook a comprehensive literature review involving 2,187 abstracts and 410 full-text articles that altogether represented more than 62,000 mild TBI patients who presented with a GCS score of 15. In only 3 cases could a definite early (<2 days) adverse outcome be identified. Eight additional patients with possible early adverse outcomes were also observed. The authors' conclusion, based on their review, is that the scientific evidence supports that a CT strategy is a safe way to triage mild TBI patients for admission (and hence, discharge).

A major step forward towards answering the question of the safety of discharging mild TBI patients who have a negative head CT scan result was made by af Geijerstam et al[74] with a Class I prospective study involving 39 hospitals in Sweden. Mild TBI patients with a GCS score of 15 were randomized to immediate head CT or hospital admission for observation. Of the 1,292 mild TBI patients in the immediate CT arm, 82 (6.3%) had a positive reading. Of those with a negative interpretation (and who were discharged from the ED unless other factors required admission), none later developed a complication that required admission to the hospital or surgery (3-month follow-up).

To date, there have not been any studies that have had sufficient power to address specific subpopulations of patients with mild TBI who may be at additional risk for delayed complications and for whom immediate ED discharge after a negative head CT scan result may not be appropriate. These subpopulations could include patients with bleeding disorders, patients on anticoagulant therapy, patients with previous neurosurgical procedures (such as a ventriculoperitoneal shunt), and those with significant previous neurologic disease.

The decision to discharge a mild TBI patient from the ED must be coupled with appropriate discharge instructions. Appendix C provides fundamentals of discharge instructions. One study evaluated abstracted records from the National Hospital Ambulatory Medical Care Survey for 306 patients with isolated mild TBI.[75] Of these patients, 9% were discharged without any recommendations for follow-up, and 28% had only "return to the ED as needed" for a follow-up recommendation. Fung et al[76] reviewed mild TBI discharge instruction sheets from 15 institutions for the presence of 6 factors that were deemed significant for postdischarge patient monitoring based upon a literature review: GCS score less than 15, amnesia, headache, vomiting, neurologic deficit, and seizure. Only a single institution's discharge instruction sheet contained all 6 factors, with only 2 of the 6 factors present on the forms from all institutions. They also found that most of the discharge instructions sheets were at an inappropriately high-grade reading level. In a related issue, Saunders et al,[77] in a small prospective study, found that mild TBI patients rarely remember their discharge instructions, which implies that it is best to provide post-mild TBI discharge instructions in a written form. An additional issue in discharge planning that has not been adequately studied is the practice of home observation and frequent waking.

A glaring omission from most mild TBI discharge instruction sheets is the lack of any mention of the possibility of the patient developing postconcussive symptoms. These are defined as somatic, cognitive, and affective symptoms that include headache, sleep disturbances, dizziness/vertigo, nausea, fatigue, oversensitivity to noise/light, attention/concentration problems, memory problems, irritability, anxiety, depression, and emotional lability.[78] The incidence of postconcussive symptoms varies widely in studies and is found to usually diminish over time. Bazarian and Atabaki,[79] in a relatively small study, found that 58% of mild TBI patients had persistent symptoms 1 month postinjury, whereas de Kruijk et al[80] found that 28% had symptoms at 6 months postinjury. They also found that evaluating patients for headache, nausea, and dizziness in the ED can identify those patients at greater risk for postconcussive syndrome: those with all 3 symptoms have a 50% chance of

having postconcussive syndrome at 6 months; those with none, a 28% chance. Carroll et al,[15] in an extensive review of 428 studies, concluded that most adults with postconcussive symptoms recover within 3 to 12 months of their injury. Sheedy et al[81] have developed an algorithm based on delayed memory, pain score, occupation, and years of education that, in a small sample, was able to accurately forecast those patients at high risk for moderate/severe postconcussive syndrome symptoms at 1 month postinjury. Holm et al,[16] after a systematic review of 743 studies, concluded that the provision of educational information about postconcussive syndrome symptoms can reduce long-term complaints. However, 2 reports cast doubt on the effectiveness of early treatment of postconcussive symptoms.[82,83]

Future Directions

Patients with a GCS score of 15 and normal head CT scan findings remain at risk for the development of cognitive, psychosocial, and neurobehavioral abnormalities related to mild TBI. These postconcussive symptoms may adversely affect the patient's personal, financial, and social life.[16] Thus, future research must address mechanisms for identifying patients at risk and interventions that may minimize or prevent disability.

It is possible that the scanning resolution of a head CT limits the diagnosis of clinically significant neuronal lesions that may be responsible for the postconcussive symptoms. In these situations, MRI and other neuroimaging modalities in the acute evaluation of mild TBI may be of prognostic value, but this is as yet unproven. The implication on the management and follow-up of the nonoperative lesions found on CT scanning or other neuroimaging studies is also an area in need of elucidation.

Because we, as care providers, make a potentially irrevocable decision in terms of discharging a mild TBI patient based upon a negative head CT scan result, one issue that may directly impact the validity of this decision is the reliability of the initial negative reading of the head CT scan. This topic is rarely addressed in any studies, but is alluded to in the study by Livingston et al.[72] In their study, of the initial 1,664 negative head CT scan readings (by a radiology resident or trauma surgeon), 19 (1.1%) were read as positive by the staff radiologist at a later time. This represents an important issue that requires attention at an institutional level.

Additional areas for future research include the determination of the optimal time postinjury to perform a head CT and further delineation of the subpopulations of mild TBI patients who, despite a negative head CT scan result, are at increased risk for developing untoward sequelae and thus may not be appropriate for immediate discharge despite a normal head CT scan result.

Relevant industry relationships of panel members: There were no relevant industry relationships disclosed by panel members.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical question.

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Evidentiary Table.

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Haydel et al[4]	2000	Prospective	Phase 1: 520 patients >2 y of age; Phase 2: 909 patients: validation; Inclusion: GCS score 15; +LOC/amnesia; recursive partitioning analysis	Abnormal CT scan	6.5% positive CT 0.4% neurosurgical lesion; 7 predictors of abnormal CT: headache, vomiting, age over 60, drug or ETOH intoxication, deficits in short-term memory, physical evidence of trauma above the clavicle, seizure; absence of all 7 had 100% negative predictive value 100% sensitivity (95% CI 95-100); 25% specificity	No follow-up after discharge; wide CI for the measured sensitivity, questionable adequate sample size; questionable interrater reliability	I
Stiell et al[5]	2005	Prospective cohort study evaluating a convenience sample	Compared NOC and CCHR in 1,822 adults with GCS score 15	NS; secondary outcome: positive CT scan	8 patients required NS (0.4%); both rules had 100% sensitivity; CCHR was 76% specific vs 13% for the NOC; for clinically important ICI CCHR was 100% sensitive and 51% specific vs the NOC, which was 100% sensitive but only 12% specific; predicted use of CT using the rules: 52% with the CCHR; 88% with the NOC; only 3 of the NOC criteria were found to be predictors of ICI: vomiting, age >60 y, and persistent anterograde amnesia	Only 70% of patients had a CT; however, telephone follow-up was used as surrogate of no neurosurgical lesion	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Smits et al[6]	2005	Prospective cohort	3,181 consecutive adult patients with GCS score 13-15	Primary outcome: any acute intracranial finding on CT; secondary outcome: NS	3,181 patients — 92.5% with GCS score of 15; compared the sensitivity and specificity of the CCHR and NOC; 9.8% of patients had a positive CT; 0.5% needed NS; both rules had 100% sensitivity for NS; NOC had higher sensitivity for positive CT (97.7%–99.4%) than the CCHR (83.4%–87.2%); specificity for NOC was 3%-5.6% vs CCHR of 37.2%-39.7%; 5 of the 17 patients with NS had no LOC; 10 of the 17 had a GCS score of 15	Modified the rules by not using LOC as an inclusion criteria; did not use the GCS of 14 at 2 h as described in the CCHR, instead used 1 h	I
Mack et al[7]	2003	Retrospective chart review over 1 y	Patients 65 y or older; GCS score 13-15	Positive CT scan result	133 patients; 19 (14.3%) with positive CT; 4 required surgery; 4 of the 19 (21%) had a GCS of 15, no neurologic finding, alcohol use, or anticoagulation but did have external signs of trauma; no single predictor of positive CT identified	Incomplete data set; small number	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Ibanez et al[8]	2004	Prospective; age >14 y; GCS score 14/15 with or without LOC	1,101 consecutive patients; median time from injury to seen=3.5 h	Positive CT scan result; NS	83 (7.5%) ICI; 70 admitted to hospital; 12 sent home from ED after observation and a second CT; 11 patients (1%) had NS; 9 (1.8%) patients without LOC and GCS score 15 had ICI; 3 (0.6%) NS; none of guidelines reached 100% sensitivity for ICI but did for NS; 95% CI with adjusted OR performed and authors recommend that a CT be done for: GCS score <15, GCS score 15 plus: LOC, vomiting, severe headache, signs of basilar fracture, seizure, focal neurologic deficit, age >65 y plus headache, coagulation disorder, hydrocephalus with shunt, signs of significant extracranial injury; PTA, alcohol were not independently significant		II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Fabbri et al[9]	2005	Retrospective analysis of clinical performance	7,955 patients ≥10 y with GCS score 14-15; presenting within 24 h of injury; NICE vs NCWFNS	Positive CT scan result; NS; death	7,955 patients; 92% had CT; 6.8% with ICI; 9 patients had ICI diagnosed on return visit after discharge; NS in 1.3%; GCS score 14 had an OR of 19.2 for ICI (95% CI 14-26); NICE was less sensitive but more specific than NCWFNS: (93.5% vs 98%; 70% vs 46%); adding coagulopathy in NICE identified 10 ICI that would have been missed with NCWFNS	Unclear whether this database is the same as the one used in the previous article and thus if the CT order rate was as high as stated	III
Smits et al[13]	2007	The CHIP Prediction rule; prospective observational	Consecutive patients >15 y with GCS score 13 or 14 or GCS score 15 plus 1 risk factor; logistic regression analysis using variables from existing rules and guidelines with internal validation by using bootstrapping	Positive CT scan result; NS	3,181 patients; 243 (7.6%) with ICI; 5.5, 13.6, 20.5% for GCS score 15, 14, 13; 17 (0.5%) required NS; 112 patients had a second CT — no outcome change	Needs to be externally validated; complex with major and minor predictors; headache not included	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Stein and Ross[19]	1990	Retrospective	658 patients; GCS score >12, trauma center within 6 h of injury	Positive CT scan result; deterioration	658 patients >3 y (454 with GCS score 15); none of 542 patients with normal CT result deteriorated; none needed surgery; GCS score/abnormal CT result 15/13, 14/23, 13/40; 3.3% GCS score 15 with abnormal CT result	No set protocol; selection toward sicker patients	III
Williams et al[20]	1990	Retrospective	215 patients; 78 closed head injury with normal CT result; 77 closed head injury with positive CT result or depressed skull fracture; 60 with GCS score 9-12	Neuropsychological testing: verbal fluency, verbal memory, information processing speed, and recognition memory	Patients with complicated MTBI had longer period of impaired consciousness, longer PTA, impaired verbal fluency and verbal memory compared with MTBI patients; surgery did not have an effect on outcome measures; depressed skull fracture had no effect on outcome; study concludes that presence of a lesion on CT predicts more complicated course and has implications for follow-up	Unclear how patients were selected	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Shackford et al[25]	1992	Retrospective; multicenter	2,166 patients: GCS score >12; management at discretion of the trauma center; sample size calculation 2,300	Positive CT scan result; deterioration	2,166 (78%) had CT; 468 (22%) CT positive result; 933 patients had a normal neurologic examination and normal CT result: no deterioration; 1,170 had a normal CT result; and none required craniotomy; 2,112 had a normal neurologic examination result; and 59 required craniotomy; 15% GCS score 15 with positive CT result; 3.2% with craniotomy; sensitivity of CT was 100%; PPV 10%; NPV 100%; sensitivity 51%; 1 patient discharged from ED with normal examination result and no CT; returned with subdural uncomplicated; abnormal neurologic examination result associated with positive CT scan result; "Patients with MTBI and abnormal results on neurologic examination should be admitted because 1 in 4 will require treatment"; "Admission to the hospital does not guarantee skilled neurologic observation"	Not all centers followed same protocol; GCS score not correlated with CT result; only 76% of patients with GCS score 15 had a CT; limited follow-up	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Stiell et al[27]	2001	Prospective cohort; derivation study; logistic regression and recursive partitioning analysis	3,121 patients (>15 y); 80% with a GCS score of 15; all had LOC, amnesia, or disorientation; structured, standardized data sheet used	Clinically significant brain injury, ie, neurosurgical lesion, need for ICP monitoring, intubation	8% had a positive CT result; 1% neurosurgical intervention; derived CT head rule with 5 high-risk predictors: failure to reach GCS score 15 within 2 h, suspected open skull fracture, sign of basal skull fracture, vomiting more than once, age >64 y; high-risk factors were 100% sensitive for predicting need for NS and would decrease head CT by 68%; 69% specific for NS and 50% specific for ICI	67% of patients were scanned; 33% had a structured assessment survey for clinically important lesion at 14 days postdischarge; only 172 patients who did not have a CT were followed (172 randomly selected patients); solitary contusions <5 mm, localized SAH <1 mm, smear subdural <4 mm thick, isolated pneumocephaly, closed depressed skull fracture not through the inner table were not considered clinically important (based on survey consensus); no patients with a CT were followed based on the assumption from a survey and 1 abstract that their lesions were unimportant; needs validation; did not address the outcome measure used in this policy	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Smits et al[28]	2007	Prospective; multicenter	2,462 consecutive MTBI patients >15 y with GCS score 15 and at least 1 of the following: LOC, short-term memory deficit, amnesia, posttraumatic seizure, vomiting, headache, intoxication, anticoagulant use, external evidence of injury; purpose to evaluate if LOC/PTA had the same predictive value for positive CT result and for neurosurgical lesion	Positive CT scan result; neurosurgical lesion	1,708 with LOC or PTA; 75 without; positive CT result in 7.5%; 8.7% in the LOC/PTA group, 4.9% without; NS the same in both groups, 0.4%; compared with patients without LOC/PTA, LOC had OR of 1.9 and PTA of 1.7; absence of LOC or PTA does not exclude ICI and these patients need to be assessed with same clinical factors as those without; propose using LOC/PTA as risk factors that increase risk for injury	Study did not include those patients with LOC/PTA without other risk factors	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Miller et al[31]	1997	Prospective	2,143 consecutive patients; GCS score 15 with history of LOC; ETOH included; injury must be <24 h prior to ED; all had CT within 8 h; severe headache distinguished from mild to moderate headache; compared predictive value of severe headache, nausea, vomiting, depressed skull fracture to patients with no complaints; all patients monitored for at least 3 h in ED	Abnormal CT scan	1,302 (61%) no risk factors vs 841 (39%) with risk factors; 138 (6.4%) positive CT result: 48 (4%) with no risk factors vs 90 (11%) with risk factors; use of predictors had a sensitivity of 65%; PPV of someone needing NS 100% (95% CI); 5 patients (0.2%) required NS: all had risk factors; 41 patients with no risk factors but positive CT result (48 minus 7 who had only skull fracture) were hospitalized for average 2 days; none deteriorated; recommendation: use predictors to stratify need for CT	No follow-up in patients without lesion; discussion states those with lesions admitted but not stated in methodology	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Borczuk[32]	1995	Retrospective	1,448 patients; GCS score 13-15; 1,211 GCS score 15	Abnormal CT scan result; NS	8.2% abnormalities (5.9% GCS score 15); 0.72% NS (0.08% GCS score 15); cranial soft tissue injury/focal neurologic deficit/signs of basilar skull fracture/age >60 y identified all patients with neurosurgical lesion; 91.6% sensitivity for identifying any injury; focal neurologic deficit seen in 192 (13.3%) patients; 4.29 OR (2.84–6.68) of positive CT result; anticoagulant therapy in 51 (3.5%), with a 2.16 OR (0.99–4.7) of positive CT result	Retrospective; no long-term outcome	III
Jeret et al[33]	1993	Prospective; consecutive patients	712 patients; GCS score 15; age >17 y; examination by neurologist	Abnormal CT scan result	67 (9.4%) abnormal CT result; 2 (.3%) required NS; neurologic examination, digit span, object recall did not predict abnormality; no combination of physical or subjective findings predicted all patients with positive CT result; 1 deterioration in serial examination in 49 y with assault; no ETOH; totally normal initial neurologic examination result	No follow-up; lack of validation	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Nagurney et al[34]	1998	Retrospective	1,649 patients age >16 y; CT follow Masters criteria for moderate risk; elder defined ≥60 y; nonelder defined as aged 16-59 y	Positive CT scan result; need for NS	318 elder; 1,331 nonelder; male:female 3:1 in younger group, approximately equal in elder group; 20% elder, 13% younger had positive CT result; 11 (3%) elder, 33 (2%) younger needed NS; focally abnormal neurologic examination result imparted a risk ratio for an abnormal CT result of 4.4 in the elders and 7.75 in the younger group	GCS score not provided; selection bias; abnormal neurologic examination result included old lesions; no follow-up; conclude that elderly at higher risk based on age alone but does not break down correlation of age with GCS score, ie, the elderly group may have had lower GCS score	III
Rosengren et al[35]	2004	Retrospective, chart review	All patients with a GCS score of 15	Positive CT scan result; NS	240 patients; 10 ICI with 1 requiring NS; NOC would have resulted in a 3.8% reduction in CT scan with 100% sensitivity for both ICI and NS; CCHR would have resulted in a 47% reduction of CT scans with 100% sensitivity for NS but would have missed 2 patients with clinically significant CT abnormalities	Small sample; retrospective	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Smits et al[38]	2007	Prospective observational study	3,181 adult patients with a GCS score 13-15; isolated head injury; GCS score of 13 or 14, or GCS score 15 with one of the following: LOC, short-term memory deficit, amnesia, seizure, vomiting, headache, intoxication, anticoagulant, external evidence of injury above the clavicles, neurologic deficit	Primary outcome: positive CT scan result; secondary outcome: neurosurgical lesion	Positive CT result in 312 (9.8%); 25% of patients with a GCS score of 13 had a positive CT result; neurosurgical intervention on 0.5%; compared the Dutch Guidelines, the NICE guidelines, and the EFNS guidelines; EFNS guidelines were 100% sensitive for both positive CT and for NS lesions	The database was not constructed specifically to address the criteria of some of the guidelines being studied	II
Ono et al[39]	2007	Prospective	1,360 patients presenting within 6 h of injury; 1,145 enrolled	Positive CT scan result	50 positive CT results (4.7%); 7 patients (0.66%) had lesion enlargement over several h requiring surgery; in patients with GCS score 15 and no LOC/PTA positive CT result=3.5% with 0.3% needing surgery; multivariate analysis revealed significant correlation between CT and age >60, male sex, alcohol, headache, nausea, LOC/amnesia, and a JCS >0; these findings had a specificity of 100% and sensitivity of 30%; JCS O=completely awake; JCS 1=almost completely conscious; answers appropriately (this would be a GCS score 15)	Unclear if consecutive patients or if IRB approved; uses the JCS that has not been validated in head injury; pseudo validation in 168 patients	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Vilke et al[42]	2000	Prospective	Convenience sample; 58 patients with GCS score 15, age >13 y; clinically sober with LOC/amnesia; standardized neurologic examination including mental status followed by CT	Positive CT scan result	71% presented within 3 h of trauma; 82% within 24 h; 55/58 had a normal CT result; 23/58 had focal finding; 3 (5%) had a positive CT result; 2 had a normal neurologic examination result including 1 (1.7%) who required NS (patient had temporal parietal hematoma and left facial swelling); 23 patients had abnormal neurologic examination result (10 abnormal 3-object recall, 8 abnormal cerebellar); conclude that significant brain injury cannot be excluded despite normal neurologic examination result	Small n; strength is a structured neurologic examination and all patients had a CT	III
Bazarian et al[56]	2006	Nested cohort	Serum S-100B (LIA, Sangtec 100, DiaSorin, Dietzenbach, Germany) in 96 MTBI adolescent/adult subjects (8-79 y) within 6 h of injury	Positive CT scan result	AUC 0.49; at cutoff of 0.08ug/L, sensitivity=0.8, specificity=0.04; at cutoff of 1.46 ug/L, sensitivity=0.13 specificity=0.90	96 subjects came from larger pool of 792 patients with MTBI— suggests selection bias	II
Biberthaler et al[57]	2006	Prospective	Serum S-100B (ECL, Elecsys S100, Roche Diagnostics, Mannheim, Germany) in 1,309 isolated MTBI adults within 3 h of injury	Positive CT scan result	AUC=0.80 (0.75-0.84); at cutoff of 0.10 µg/L, sensitivity=0.99 (0.96-1) specificity=0.30 (0.29-0.31)	Selection bias	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Biberthaler et al[58]	2002	Prospective	Serum S-100B (LIA, LIASON, Byk Sangtec Diagnostica, Dietzenbach, Germany) in 104 patients with isolated MTBI within 2 h of injury	Positive CT scan result	AUC=0.79 (95% CI 0.7-0.89); at a cutoff of 0.12 ng/mL: sensitivity=1.0 specificity=0.46	23% with ICI, suggesting selection bias	III
Biberthaler et al[59]	2001	Prospective	Serum S-100B (LIA, LIA-mat, Byk-Sangtec Diagnostics, Dietzenbach, Germany) in 29 sober and 20 intoxicated adults with isolated MTBI within 3 h of injury	Positive CT scan result	Serum S-100B levels were higher with abnormal CT scan result in both sober (0.94 µg/L vs 0.12 µg/L) and intoxicated (0.89 µg/L vs 0.15 µg/L) patients with isolated MTBI	Multiple-trauma patients excluded; head trauma does not require LOC or amnesia; thus, may be less severe than MTBI	III
Ingebrigtsen et al[60]	2000	Prospective	Serum S-100B in 182 adolescent/adults (15-80 y of age) admitted to hospital with MTBI, within 12 h of injury (LIA, Sangtec 100, Sangtec Medical AB, Bromma, Sweden)	Positive CT scan result	At cutoff of 0.2 µg/L: sensitivity=0.90 specificity=0.65	Selection bias	II
Muller et al[61]	2007	Prospective	Serum S-100B levels (LIA, LIASON, DiaSorin AB, Bromma, Sweden) in 226 adults admitted to hospital with MTBI, within 12 h of injury	Positive CT scan result	AUC 0.73 (0.62-0.84); at cutoff of 0.1 µg/L: sensitivity=0.95 specificity=0.31	Selection bias	II
Mussack et al[62]	2002	Prospective	Serum NSE, serum glucose, and S-100B (LIA, LIASON, Byk-Sangtec Diagnostica, Dietzenbach, Germany) levels in 139 adults with MTBI within 3 h of injury	Positive CT scan result	S-100B AUC 0.86 (0.79-0.94); at a cutoff of 0.2 ng/mL: sensitivity=1.0 specificity=0.5 (0.41-0.59); NSE and glucose=NS	Selection bias	II
Poli-de-Figueiredo et al[63]	2006	Prospective	Serum S-100B level (HI, Elecsys 2010, Roche Diagnostics, Mannheim, Germany) in 55 patients with MTBI within 3 h of injury	Positive CT scan result	AUC 0.82 (0.69-0.96); at cutoff of 0.1 µg/L: sensitivity=1.0 specificity=0.2	Small number and patient ages not given	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Bulut et al[66]	2006	Prospective	Serum tau (ELISA) in 60 adults with MTBI within 10 h of injury	Positive CT scan result	No significant difference in levels in patients with negative CT result and positive CT result (150 vs 201 pg/mL, *P*=0.47)		I
Nagy et al[69]	1999	Prospective cohort	1,170 consecutive patients with GCS score 15; all patients had CT and were admitted for observation for minimum of 24 h	CT abnormality; neurologic deterioration	1,131 patients with negative CT result: none had neurologic deterioration	23-h follow-up only	III
Livingston et al[70]	1991	Prospective	Assess safe discharge in patients with normal CT findings and normal neurologic examination results; GCS score of 14-15; no focal neurologic findings	Deterioration after discharge	111 patients; 15 (14%) had abnormal CT findings; 5 patients with normal CT findings admitted because of lethargy; of patients with normal neurologic examination results and normal CT findings who were discharged, 79 had GCS score of 15 and 11 had GCS score of 14; 66 (59%) patients were positive for ETOH	Small number of patients; 57 (63%) patients contacted by telephone in 48-h follow-up; none had deterioration	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Dunham et al[71]	1996	Retrospective analysis of a prospective database	2,587 consecutive patients aged >13 y with head injury, LOC, or PTA; 2,252 direct transports used for analysis	Positive CT scan result	163 (7.2%) of 2,252 direct transports with positive CT scan findings; 1,481 patients with GCS score of 15 and amnesia; 45 (3.0%) with positive CT findings; 54 (12.4%) of 435 patients with GCS score of 14 had positive CT findings; 29 (25.0%) of 116 patients with GCS score of 13 had positive CT findings; 15 (10.0%) of 150 patients ages >60 y with GCS score of 15 had positive CT findings; positive CT findings were independently related to cranial soft tissue injury, age, and GCS score; 35 (42.1%) of 83 patients with skull fracture had positive CT findings; no patient required craniotomy for hematoma when the CT scan performed on day of injury revealed negative findings; all patients who deteriorated did so within 4 h of arrival	Trauma center admissions (selection bias toward the more severe); no standard protocol; 196 (8.7%) of 2,252 patients did not have a CT scan performed; unknown follow-up; skull fracture data related to fractures seen on CT were not on plain radiographs	III
Livingston et al[72]	2000	Prospective cohort	2,152 consecutive "minimal head injury" patients >16 y; (GCS score 14/15); all patients had CT and were admitted for observation	Clinical deterioration, need for craniotomy or death at 20 h and at discharge	"NPV of negative CT: 99.70"; change for "preliminary" to "final" CT reading: 19/1,664 from negative to positive; 13/93 from nondiagnostic to positive	417 patients excluded from original data set of 2,569, mainly because of early discharge; confusing, incomplete data analysis	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
af Geijerstam and Britton[73]	2005	Formal review	2,187 abstracts reviewed and 410 full text articles reviewed covering 62,000 patients with MTBI (GCS score 15)	Adverse outcomes after initial evaluation in <2 days	3 definite; 8 possible		III
af Geijerstam et al[74]	2006	Randomized trial	2,602 patients with MTBI (GCS score 15); 39 hospitals (Sweden) >6 y; CT vs admission for observation	Dichotomized extended Glascow Outcome Scale; mortality; severe loss of function	No significant difference between groups; 23% overall not completely recovered in 3 mo; no patients with normal immediate CT had complications later	3-mo follow-up on 2,590 of 2,602 patients	I
Bazarian et al[75]	2005	Retrospective observational	306 isolated MTBI patients; evaluated for type of care and discharge recommendations from ED	Patient evaluated (physical examination, CT); patient disposition; discharge instructions	9% discharged without any recommendation for follow-up; 28% had "return prn" instructions; 44% had CT	Secondary analysis of NHAMCS survey data	III
Fung et al[76]	2006	Survey	Review of MTBI discharge forms from 15 hospitals	Inclusion of 6 items on discharge instructions deemed to be important by literature review; reading level of form	Only 1 form had all 6; only 2 of 6 items present on every form; mean reading level of 8.2; proposed MTBI discharge instruction sheet	No validation of importance of items; PCS not included on proposed discharge form; abuse of the term "evidence-based"	III
Saunders et al[77]	1986	Prospective	47 consecutive patients; inclusion/exclusion not specified	Remembering discharge instructions; deterioration	1 patient was discharged with normal examination results and skull radiographs; developed subdural hematoma; neurosurgery was performed; patient left with a deficit	Small number of patients; no CT scans performed	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Bazarian and Atabaki[79]	2001	Prospective observational	83 MTBI patients (GCS score 15) >16 y of age; intoxicated patients excluded	Presence of postconcussive symptoms by validated telephone questionnaire	Follow-up on 69 patients; 58% had PCS at 1 mo	342 of 425 patients excluded because of drug/alcohol use	III
de Kruijk et al[80]	2002	Prospective cohort	107 patients >15 y of age with GCS score 14/15; LOC <15 min; posttraumatic amnesia <1 h and no focal neurologic signs	Presence of headache, nausea, vomiting in ED vs posttraumatic complaints at 6 mo	Presence of more symptoms in ED correlated with lower rate of recovery; overall, 28% had symptoms at 6 mo	Only 79 patients followed at 6 mo; intoxicated patients excluded	III
Sheedy et al[81]	2006	Prospective cohort	Patients with closed head trauma >18 y, English-speaking, GCS score 13-15 in the ED, negative head CT result or no indication for a CT with any of the following: loss of balance, LOC or altered consciousness, retro- or antegrade amnesia, confusion, vomiting, nausea, blurred vision, headache; 29 patients in the prospective cohort	Multiple test for cognition, amnesia, balance, pain, postconcussive symptoms	Delayed memory, pain score, occupation and years of education could forecast moderate/severe postconcussive symptoms with sensitivity/specificity of 92/92 at 1 mo	Convenience sample; single observer; not all patients had CT	III
Andersson et al[82]	2007	Randomized controlled trial	131 controls; 264 with tailored treatment (information, counseling, encouragement, drug treatment)	Change in rate of postconcussive symptoms and life satisfaction at 1 y	No significant improvement in treatment group	Ages 16-60 y; unclear treatment protocol	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Ghaffar et al[83]	2006	Randomized control trial	Consecutive MTBI patients 16-60 y of age with no major medical illness; 97 treatment: customized treatment (drugs, psychotherapy, physiotherapy, occupational therapy); 94 control	Testing for postconcussive symptoms, psychosocial functioning, psychological stress, and cognition	No significant differences between groups	No predefined treatment protocol	II

AUC, area under the curve; *CCHR*, Canadian CT Head Rule; *CHIP*, CT in Head Injury Patients; *CI*, confidence interval; *CT*, computed tomography; *ECL*, electrochemiluminescence immunoassay; *ED*, emergency department; *EFNS*, European Federation of Neurological Societies; *ELISA*, Enzyme-Linked Immunosorbent Assay; *ETOH*, alcohol; *GCS*, Glascow Coma Scale; *h*, hour; *HI*, heterogeneous immunoassay; *ICI*, acute traumatic intracranial injuries; *ICP*, intracranial pressure; *IRB*, Institutional Review Board; *JCS*, Japanese Coma Scale; *LIA*, luminoimmunometric assay; *LOC*, loss of consciousness; *mo*, month; *MTBI*, mild traumatic brain injury; *NCWFNS*, Neurotraumatology Committee of the World Federation of Neurosurgical Societies; *NHAMCS*, National Hospital Ambulatory Medical Care Survey; *NICE*, National Institute for Clinical Excellence; *NOC*, New Orleans Criteria; *NPV*, negative predictive value; *NS*, neurosurgery; *NSE*, neuron-specific enolase; *OR*, odds ratio; *PCS*, postconcussive syndrome; *PPV*, positive predictive value; *prn*, as needed; *PTA*, posttraumatic amnesia; *SAH*, subarachnoid hemorrhage; *vs*, versus; *y*, year.

Appendix A. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing ≥2 interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix C. Fundamentals of discharge planning/discharge instructions for patients with mild traumatic brain injury.

Discharge instructions design considerations: Instructions to patients and their families should:

- Be written at approximately a sixth- to seventh-grade level
- Given to the patient and immediate caregiver in both print and verbal form
- Layout and type fonts appropriate for low literacy materials (ie, no type font under 12 points, wide margins, left justified)

Building blocks for discharge instructions: Patients who have been assessed in the emergency department (ED) using recommendations in this mild traumatic brain injury clinical policy have a very low rate of developing delayed intracranial pathology. For patients who have a negative head computed tomography (CT) result or have been deemed too low risk for neuroimaging, home observation, including frequent waking or assessment of pupils, is not supported by the literature and thus is not recommended.

Patients who develop the following symptoms should be instructed to return to the ED for re-evaluation:

Repeated vomiting
Worsening headache
Problems remembering
Confusion
Focal neurologic deficit
Abnormal behavior
Increased sleepiness or passing out
Seizures

Postconcussive symptom education: Postconcusssive symptoms should be identified at the time of assessment. A list of these symptoms should be provided to the patient in written and verbal form and be used as a prompt for the patient to seek referral to a specialist in traumatic brain injury. These symptoms should either have lasted for greater than 3 weeks or less time if planning to return to sports.

Postconcussive Symptoms

Chronic headaches
Dizziness, balance problems
Nausea
Vision problems
Increased sensitivity to noise and/or light
Depression or mood swings
Anxiety
Irritability
Memory problems
Difficulty concentrating or paying attention
Sleep difficulties
Feeling tired all the time

Patients who are experiencing postconcussive symptoms should refrain from strenuous mental or physical activity until they are symptom free. They may require 2 to 3 days off work or school.

Proper patient referral is recommended, ideally to a specialist in traumatic brain injury.

Injury prevention information about seatbelt, alcohol, and helmet safety should be provided.

More information about TBI and discharge planning can be found at http://www.cdc.gov/ncipc/tbi/.