Imaging Evidence and Recommendations for Traumatic Brain Injury: Conventional Neuroimaging Techniques

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Abstract

Imaging plays an essential role in identifying intracranial injury in patients with traumatic brain injury (TBI). The goals of imaging include (1) detecting injuries that may require immediate surgical or procedural intervention, (2) detecting injuries that may benefit from early medical therapy or vigilant neurologic supervision, and (3) determining the prognosis of patients to tailor rehabilitative therapy or help with family counseling and discharge planning. In this article, the authors perform a review of the evidence on the utility of various imaging techniques in patients presenting with TBI to provide guidance for evidence-based, clinical imaging protocols. The intent of this article is to suggest practical imaging recommendations for patients presenting with TBI across different practice settings and to simultaneously provide the rationale and background evidence supporting their use. These recommendations should ultimately assist referring physicians faced with the task of ordering appropriate imaging tests in particular patients with TBI for whom they are providing care. These recommendations should also help radiologists advise their clinical colleagues on appropriate imaging utilization for patients with TBI.

Key Words: Traumatic brain injury, brain imaging, CT, MRI

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INTRODUCTION

Traumatic brain injury (TBI) is one of the most common neurologic disorders, currently affecting 1.7 million Americans each year [1,2]. The incidence of TBI, especially mild TBI, is underestimated [3], as patients frequently dismiss their symptoms and never present to the emergency department (ED), or they believe that the admission of symptoms may compromise their work situation (eg, athletes, military personnel [4]). Although the majority of patients (nearly 80%) with diagnosed TBI are treated and released from EDs [5], the remaining 20% have more severe injuries, resulting in approximately 275,000 hospitalizations and 52,000 deaths each year. Furthermore, TBI contributes to one-third of all injury-related deaths in the United States. The economic cost of TBI was an estimated at $76.5 billion in 2010 ($11.5 billion in direct medical costs and $64.8 billion in indirect costs such as lost wages, lost productivity, and nonmedical expenditures) [6]. Moreover, affected military veterans generate an annual cost of $11,700 in medical treatment per patient, compared with $2,400 in TBI-free veterans [7]. Leading causes of TBI in the general population include falls, motor vehicle accidents, assaults, and sports-related injuries.

Imaging plays an essential role in identifying TBI patients with intracranial injury. The goals of imaging include (1) detecting injuries that may require immediate surgical or procedural intervention, (2) detecting injuries that may benefit

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from early medical therapy or vigilant neurologic supervision, and (3) determining the prognosis of patients to tailor rehabilitative therapy or help with family counseling and discharge planning. A wide variety of imaging techniques have become available to assess patients presenting with TBI. This, coupled with the inconsistent use of clinical decision rules [8], has led to increased utilization and variations in numerous imaging practices. Among hospitals reporting to the National Hospital Ambulatory Medical Care Survey, CT utilization for head trauma in the pediatric population increased from 12.8% in 1995 to 28.6% in 2000 despite stable hospitalization rates for head trauma [9]. The practical challenge for physicians is to understand the multiple facets of these imaging techniques, including which imaging techniques to implement and how to use them optimally for specific patients.

Since 2009, multiple health care agencies involving experts from the international TBI community have worked on developing and refining common data elements (CDEs) in TBI to promote the use of consistent terminology and definitions in characterizing intracranial injuries across all imaging studies, as well as all clinical aspects of TBI [10,11]. These CDEs can be used in a consistent manner for clinical practice, research, and treatment trials across multiple institutions and research studies. The CDEs include a list of the injuries that can be identified, with definitions of terms used to describe these injuries on the images, and recommended protocols and descriptors for image acquisition methods. The goal of the CDEs is to promote consistency across the field in future investigations aimed at evaluating TBI imaging.

In an effort parallel to, but distinct from, the CDEs, we performed a review of the evidence on the utility of various imaging techniques in patients presenting with TBI to provide guidance for evidence-based, clinical imaging protocols. We indicated the quality of publications for diagnostic test and interventions by assigning stratified and preferential levels of evidence (Table 1) and classes of recommendations (Table 2). These levels of evidence are based on the National Institute for Health and Care Excellence (http://www.nice.org.uk), adapted from the Oxford Centre for Evidence-Based Medicine (http://www.cebm.net) levels of evidence (2001). The intent of this article is to suggest practical imaging recommendations for patients presenting with TBI across different practice settings and to simultaneously provide the rationale and background evidence supporting their use. These recommendations should ultimately assist referring physicians faced with the task of ordering appropriate imaging tests in particular patients with TBI for whom they are providing care. These recommendations should also help radiologists advise their clinical colleagues on appropriate imaging utilization for patients with TBI. For practical purposes, recommendations are presented separately for TBI severity and apply to the differentiation of acute, subacute, and chronic TBI, as defined by Defense and Veterans Brain Injury Center recommendations (http://www.traumaticbraininjuryatoz.org/Resource-Center/The-Defense-and-Veterans-Brain-Injury-Center).

Table 1. Levels of evidence for studies of the accuracy of diagnostic tests

Level of Evidence	Type of Evidence
Ia	Systematic review (with homogeneity)* of level 1 studies†
Ib	Level 1 studies†
II	Level 2 studies‡
	Systematic reviews of level 2 studies
III	Level 3 studies§
	Systematic reviews of level 3 studies
IV	Consensus, expert committee reports or opinions, and/or clinical experience without explicit critical appraisal, or based on physiology, bench research, or "first principles"

Note: Adapted from The Oxford Centre for Evidence-Based Medicine Levels of Evidence (2001) and Centre for Reviews and Dissemination Report Number 4 (2001).

*Homogeneity means that there are no or minor variations in the directions and degrees of results among individual studies that are included in the systematic review.

†Level 1 studies are studies: (1) that use blind comparisons of the test with a validated reference standard (2) in samples of patients that reflect the population to whom the test would apply.

‡Level 2 studies are studies that have only one of the following: (1) narrow populations (the samples do not reflect the population to whom the test would apply), (2) poor reference standards (defined as that for which the "test" is included in the "reference," or for which the "testing" affects the "reference"), (3) nonblinded comparisons between the test and reference standard, and (4) case-control designs.

§Level 3 studies are studies that have at least two or three of the features listed above.

Table 2. Classification of recommendations

Class I: Conditions for which there is evidence for or general agreement that a procedure or treatment is beneficial, useful, and effective

Class II: Conditions for which there is conflicting evidence or a divergence of opinion about the usefulness or efficacy of a procedure or treatment

Class IIa: Weight of evidence or opinion is in favor of usefulness or efficacy

Class IIb: Usefulness or efficacy is less well established

Class III: Conditions for which there is evidence or general agreement that a procedure or treatment is not useful or effective and in some cases may be harmful

Note: From the American Heart Association.

Acute injuries refer to those from the time of injury to 7 days, subacute injuries refer to those between 8 and 89 days after injury, and chronic injuries refer to those injuries ≥90 days after injury. These recommendations are also concordant with the ACR Appropriateness Criteria® for head trauma [12]. We recognize that TBI imaging is a rapidly evolving field and that several recommendations presented are topics of continued investigation. Therefore, we expect that there will be an ongoing need to update this document to reflect the advances in medical knowledge.

EVIDENCE AND RECOMMENDATIONS FOR IMAGING IN ACUTE MODERATE TO SEVERE TBI

The severity of TBI is usually classified by the Glasgow Coma Scale (GCS) score as mild, moderate, or severe. Mild TBI is generally defined as GCS scores of 13 to 15, moderate TBI as GCS scores of 9 to 12, and severe TBI as GCS scores of 3 to 8 [13-15]. Overall, serial GCS scores are more valuable in predicting survival than a single GCS score [16-19]. Currently, the main goal of imaging in TBI is to determine the presence or absence of clinically addressable brain injury to triage patients to surgery, admission with close observation, or discharge home.

CT

There is strong consensus and evidence that noncontrast CT (NCCT) is the initial triaging diagnostic imaging test of choice for patients with acute moderate to severe TBI [14,20-22] (class I recommendation). NCCT is sensitive for the detection of clinically important TBI, which is defined as a severe intracranial injury potentially resulting in death, neurologic intervention, intubation for >24 hours, or admission for >2 days [23]. NCCT is sensitive and specific for the presence of intracranial hemorrhage, extra-axial fluid collections, skull fractures, and radiopaque foreign bodies such as shrapnel. NCCT also detects cerebral edema, swelling and signs of herniation (evidence level Ib). NCCT has many advantages, including its widespread availability and rapid acquisition time, with few contraindications beyond the concern of radiation exposure. Unlike MRI, it does not require screening of patients for ferromagnetic substances such as metal or cardiac pacemakers and other contraindicated implantable devices and materials before scanning.

Various NCCT classifications have been proposed to predict clinical outcomes among patients with moderate to severe TBI. Many of the outcome prediction rules incorporate NCCT findings as a major variable and use 6-month mortality or the Glasgow Outcome Scale—Extended as the outcome measure of interest. The Marshall [24] and Rotterdam [25] scores for NCCT findings are two of the major prediction tools for clinical outcomes. The Marshall score has a limitation in classifying patients with multiple injury types; another limitation in practice is that the Marshall score is not truly linear, making it difficult to use as a scale for severity. The Rotterdam score, modified from the Marshall score, is based only on the combination of NCCT findings, such as the presence of subarachnoid or intraventricular hemorrhage, effacement of the basilar cisterns, midline shift >5 mm, presence of subdural hemorrhage, and absence of epidural hemorrhage, in an effort to predict 6-month mortality. The Rotterdam score is a well-standardized and validated tool [25]. Other prognostic tools exist that incorporate similar imaging features, such as the International Mission for Prognosis and Analysis of Clinical Trials in TBI prognostic model for severe TBI [26] and the Traumatic Coma Data Bank [27].

MRI

Pulse sequences used for TBI imaging in MRI include conventional T1-weighted, T2-weighted (T2W), T2W fluid-attenuated inversion recovery (FLAIR), T2*-gradient-echo (GRE), and diffusion-weighted imaging (DWI). Susceptibility-weighted imaging (SWI) is rapidly becoming added to routine TBI MRI protocols [28,29].

MRI is not currently indicated as a primary evaluation tool for acute TBI mainly because of logistics in scanning these patients emergently and resource availability. However, despite the lack of high-level evidence, the current practice is to perform MRI in patients with acute TBI when results on NCCT are normal and there are persistent unexplained neurologic findings [30] (class I recommendation). MRI is recognized as providing prognostic information that is important for clinical management [22]. MRI has been shown to be more sensitive when directly compared with NCCT for detecting all stages of epidural and subdural hematomas, nonhemorrhagic cortical contusions, brain stem injuries, and particularly for the detection of hemorrhagic and nonhemorrhagic axonal injuries in the white matter (evidence level Ib) [31-37]. T2W and T2W FLAIR sequences have been shown to be more sensitive than NCCT in detecting subacute subarachnoid hemorrhage, small subdural hematoma, brain contusions, and brain stem injuries (evidence levels Ib—II) [31-33,35-38]. Modern T2W FLAIR techniques are comparable with or more sensitive than NCCT for all stages of subarachnoid hemorrhage (evidence level II) [31,39-42]. T2W FLAIR has also been shown to be comparable with NCCT in detecting posttraumatic intraventricular hemorrhage (evidence level III) [43]. T2* GRE has been shown to be equivalent to NCCT in detecting acute intracranial hemorrhage and

significantly more sensitive than NCCT for detecting subacute and chronic hemorrhage (evidence levels Ib—II) [44,45]. DWI has been shown to be not only sensitive to acute parenchymal contusions, but it also often may permit visualization of both axonal injuries and fat emboli not otherwise easily appreciated on T2W FLAIR or T2* GRE sequences. DWI also has a direct and established positive correlation with various commonly used clinical outcome scales (evidence level II) [46-51]. DWI is also critical in the assessment of secondary brain ischemia related to acute infarction from brain herniation or vascular injury. Currently, there is no scientific evidence necessitating the administration of gadolinium-based intravenous contrast agents for conventional MRI in the setting of TBI (class IIb recommendation). Contrast does not improve the conspicuity of acute brain injury; however, a few small studies have shown that posttraumatic contusions enhance in their subacute stages, similar to infarctions, most likely related to blood-brain barrier disruption and inflammation [52,53].

MRI has clear limitations for use in the setting of acute TBI, including limited availability, longer imaging times, sensitivity to patient motion, incompatibility with certain medical and life-support devices (eg, pacemakers, nerve stimulators, ferromagnetic intracranial aneurysm clips, most routinely used ventilators) and occult ferromagnetic foreign bodies [28]. Moreover, whether increased sensitivity in detecting these abnormalities leads to changes in patient treatment and outcomes is a matter of active debate [50,54-58].

Diffuse Axonal Injury (DAI). The pathology of DAI is characterized histologically by axonal injury primarily in the parasagittal white matter, corpus callosum, and dorsal upper brain stem and other regions of the brain [59-61]. Conflicting results are noted within the large body of literature devoted to correlating T2W, T2W FLAIR, T2* GRE, and SWI abnormalities thought to represent cerebral contusions or axonal injuries to patient outcomes.

T2* GRE imaging has been shown to be very sensitive to microhemorrhages within the brain, which are associated with acute, early subacute, and chronic stages of DAI (evidence level II) [62-66]. The presence of traumatic microhemorrhages in DAI has been correlated with the presenting GCS (evidence level III) [62,67]; however, the number of these microhemorrhages, although helpful for the accurate diagnosis of DAI, is not currently thought to be associated with injury severity or outcomes (evidence level II) [51,68]. More recently, the multicenter Transforming Research and Clinical Knowledge in Traumatic Brain Injury study found the presence of both a contusion and >4 foci of hemorrhagic axonal injury on MRI to be an independent prognostic predictor after adjustment for NCCT findings and other demographic and clinical factors [69].

SWI uses both the magnitude component of the T2* GRE data and the phase of the MRI signal to both improve contrast and increase sensitivity for cerebral microhemorrhages [70]. It is an extremely sensitive technique for depicting intracranial blood products of various stages and deoxyhemoglobin within cerebral veins. Two studies have reported that SWI is 3 to 6 times more sensitive than T2* GRE in detecting hemorrhagic axonal injuries in children with moderate to severe TBI (evidence level II) [71,72]. Hemorrhagic axonal injuries are very rare in mild TBI.

Although a few studies have demonstrated that DWI is not as sensitive to axonal shear injuries as T2* GRE, DWI demonstrates additional white matter abnormalities not seen on either T2W FLAIR or T2* GRE sequences, which may represent a different type of axonal injury (evidence level II) [48,73].

Summary

For patients presenting with acute moderate to severe TBI:

1. NCCT is the first line of imaging in the acute phase and can predict mortality and unfavorable outcomes in these patients (class I recommendation).
2. MRI may be indicated in acute TBI when results on NCCT are normal and there are persistent unexplained neurologic findings (class I recommendation).
3. MRI, more specifically T2* GRE and SWI, is very sensitive to microhemorrhages within the brain. Whether the number and volume of these microhemorrhages, although important for the accurate diagnosis of DAI, are associated with injury severity or outcomes remains inconclusive (class IIa recommendation).

EVIDENCE AND RECOMMENDATIONS FOR IMAGING IN ACUTE MILD TBI

There has been increasing public awareness and concern regarding the magnitude and impact of mild TBI. The vast majority of patients with TBI are classified as having mild injuries and do not require any special medical treatment. One of the challenges is the fact that there is no clear consensus on the definition of what constitutes mild TBI. In fact, the terminology is confusing. Terms used include *concussion*. For the purposes of this white paper, we include in our definition of mild TBI any traumatic event affecting the patient's head and brain such as impact, rotation, deceleration, blast, or forceful blow causing a brief alteration of mental status such as confusion, disorientation, brief loss of consciousness, or memory loss. Although patients with mild TBI generally achieve full recovery, it is not uncommon for these patients (6%—10%) to have imaging

evidence of intracranial injury, referred to as "complicated" mild TBI [74-79]. Worse functional outcomes have been reported in patients with mild TBI who have imaging evidence of intracranial injury compared with patients with mild TBI who do not have imaging evidence of intracranial injury [74,80]. In the acute setting, an immediate challenge facing physicians in managing patients with TBI is to identify patients with potentially significant intracranial injury. Various guidelines regarding diagnosis and management of mild TBI have been published. One of the challenging aspects of obtaining accurate surveillance data and standardized epidemiology data is the lack of an accepted standardized definition of mild TBI and limited understanding of the consequences of mild TBI. For example, the Centers for Disease Control and Prevention and the American College of Emergency Physicians use a GCS score of 14 or 15 to define mild TBI, excluding patients with GCS scores of 13 from mild TBI [20], while others state that results on NCCT must be normal as a part of the definition of mild TBI [14,81,82].

CT

Although results on NCCT are normal in the majority of patients with mild TBI, NCCT remains the imaging investigation of choice for the detection of potential surgical brain injuries in this category of patients [21,83] (class I recommendation). When rules such as the New Orleans Criteria (NOC), Canadian CT Head Rule (CCHR), or National Emergency X-Ray Utilization Study (NEXUS-II) are used to select patients for NCCT, the sensitivity of NCCT to detect brain injuries requiring neurosurgical intervention is considered to be almost 100% [84] (evidence level Ib). A prospective study in 2,152 patients with mild TBI reported that NCCT has a very high negative predictive value (99.7%) for excluding significant intracranial injury; thus, patients can be safely discharged home without admission in the absence of other significant extracranial injuries or neurologic symptoms (evidence level Ib) [85].

Although NCCT has a high negative predictive value, few patients with negative results on NCCT may have imaging evidence of intracranial injury on MRI. NCCT has limited sensitivity for nonhemorrhagic axonal injury or hypoxic ischemic encephalopathy. Thus, patients with neurologic abnormalities or deterioration should be observed closely despite negative results on NCCT. Negative results on imaging studies, including brain MRI, do not predict accurately which patients remain symptomatic for postconcussive symptoms weeks or months after trauma [86-89].

Which Patients With Mild TBI Can Safely Avoid Head NCCT? Although NCCT scanning is widely available and an effective and efficient imaging test, it leads to radiation exposure and additional costs. A variety of prediction rules have been developed to determine which patients with mild TBI are at high risk for having intracranial injury and to reduce the unnecessary use of NCCT scans. The NOC, CCHR [78], NEXUS-II [90], and the National Institute for Health and Care Excellence [91] rules are 4 major prediction rules (Table 3). Using various clinical variables to increase the pretest probability of having intracranial injury on NCCT among patients with mild TBI increases sensitivity, thus safely avoiding NCCT for those who are at low risk for having brain injury.

MRI

The routine use of brain MRI for the detection of injury in the setting of acute mild TBI is not supported at the present time by 6 high-quality clinical practice guidelines (class IIb recommendation) [21]. However, MRI may be indicated in acute TBI when results on NCCT are normal and there are persistent unexplained neurologic findings, such as new-onset, progressive, or worsening symptoms (class I recommendation). In complicated acute mild TBI, MRI has been shown to be more sensitive for the detection of all stages of subarachnoid hemorrhage, extra-axial collections, contusions, and axonal injuries when directly compared with NCCT, as outlined above. The Transforming Research and Clinical Knowledge in Traumatic Brain Injury study reported that 27% of patients with mild TBI with normal results on NCCT had MRI abnormalities [69].

Although MRI is more sensitive than NCCT, many symptomatic patients with mild TBI have normal results on conventional MRI. A study directly comparing NCCT and early MRI for acute mild TBI revealed additional findings on MRI in one-third of patients; however, there were no changes in management on the basis of these additional MRI findings [92]. No studies to date have demonstrated a significant impact of early MRI for acute mild TBI on the emergent disposition of patients with mild TBI (evidence level II) [93,94].

Summary

For patients presenting with acute mild TBI:

1. NCCT remains the imaging of choice in the acute phase. NCCT has a high negative predictive value for excluding the need for neurosurgical intervention in patients with mild TBI (class I recommendation).
2. The NOC, CCHR, and NEXUS-II are 3 major prediction rules that identify patients with mild TBI who can safely avoid NCCT (class I recommendation).
3. Despite the higher sensitivity of MRI for detecting axonal injury among patients with mild TBI, the routine use of

Table 3. Three major predictive rules used to determine which patients with mild TBI are at high risk for having intracranial injury and should undergo NCCT

	New Orleans Criteria	Canadian CT Head Rule	National Emergency X-Ray Utilization Study	NICE
Inclusion criteria	Only GCS score 15 blunt trauma LOC Headache Vomiting Age > 60 y Alcohol or drug intoxication Amnesia Visible trauma above clavicle Posttraumatic Seizure*	GCS score 13–15 blunt trauma GCS score < 15 at 2 h after trauma Open or depressed skull fracture Sign of skull base fracture Age ≥ 65 y Amnesia for ≥30 min ≥2 episodes of vomiting Dangerous mechanism†	GCS score 15 resulting from blunt head trauma	GCS score 14 Signs of basal skull fracture Neurologic deficit Vomiting Amnesia before impact >30 min Posttraumatic seizures Coagulopathy Dangerous mechanism Age > 64 y
References	Haydel et al [79]	Stiell et al [78]	Mower et al [90]	NICE [91]

Note: GCS = Glasgow Coma Scale; NCCT = noncontrast CT; LOC = loss of consciousness; NICE = National Institute for Health and Care Excellence; TBI = traumatic brain injury.

*If none present, safely avoid NCCT (sensitivity, 97%–100%).

†If none present, avoid NCCT (sensitivity, 98.4%).

brain MRI for the detection of injury in the setting of acute mild TBI is not supported at the present time (class IIb recommendation). However, MRI may be indicated in particular instances when there are persistent neurologic, cognitive, and behavioral symptoms, such as new-onset, progressive, or worsening symptoms (class I recommendation).

4. No studies to date have demonstrated a significant impact of early MRI for acute mild TBI on the emergent disposition of patients with mild TBI.

EVIDENCE AND RECOMMENDATIONS FOR FOLLOW-UP IMAGING IN TBI

A small subset of patients with mild TBI experience persistent symptoms, including posttraumatic headache, sleep disturbance, disorders of balance, cognitive impairment, fatigue, and mood disorders [95-97]. It is challenging to identify which patients are at high risk for prolonged postconcussive symptoms and long-term sequelae.

CT

Although there is strong consensus that NCCT is the first line of imaging for patients with TBI, the guidelines on the use of routine repeated NCCT after the initial admission NCCT study remain controversial. There has been conflicting evidence, with some reporting benefit and others emphasizing cost with limited benefit. Follow-up NCCT is indicated for any trauma patient with neurologic deterioration (class I recommendation). Generally, routine follow-up NCCT is supported for moderate to severe TBI (evidence level II) [98] or anticoagulated patients with abnormalities on initial NCCT because repeat NCCT can detect clinically meaningful changes in such patients [99]. One prospective study at a level I trauma center revealed that no patients with mild TBI underwent neurosurgical intervention after repeated head CT [100]. According to a comprehensive meta-analysis evaluating 10,501 patients in 41 studies, the evidence suggests that repeat NCCT in patients with mild TBI and negative findings on initial CT results in a change in management for only a minority of patients [101] (2.3% for prospective studies and 3.9% for retrospective studies) (evidence level Ia). Thus, data do not support the routine practice of repeat head CT for mild TBI (class III recommendation). In particular, patients with mild TBI with convexity subarachnoid hemorrhages, small subdural hemorrhages, small intracranial hemorrhages, and small convexity contusions (all defined as <10 mL) may not require repeat NCCT in the absence of neurologic decline [100].

MRI

MRI may be indicated as a follow-up imaging study in acute TBI when results on NCCT are normal and there are persistent unexplained neurologic findings, such as

new-onset, progressive, or worsening symptoms (class I recommendation). The foregoing sections describe the evidence and recommendations for its use in mild and moderate to severe TBI.

Summary

In terms of follow-up imaging for acute TBI:

1. Repeat NCCT is supported for patients with neurologic deterioration, patients with moderate to severe TBI, as well as patients receiving anticoagulation therapy with initial CT abnormalities (class I recommendation).
2. Repeat NCCT in patients with mild TBI results in management changes for only a minority of patients, typically those with complicated mild TBI. The routine practice of repeat NCCT is therefore not supported for patients with mild TBI with negative results on initial NCCT (class III recommendation).
3. MRI may be indicated as a follow-up imaging study in acute TBI only in limited instances when results on NCCT are normal and there are persistent unexplained neurologic findings, such as new-onset, progressive, or worsening symptoms (class I recommendation).

EVIDENCE AND RECOMMENDATIONS FOR IMAGING IN SUBACUTE TO CHRONIC TBI

Chronic sequelae of repetitive TBI among military personnel and civilians such as athletes have been increasingly recognized in the past several years. Repetitive concussion or mild TBI, a condition sometimes referred to as "chronic traumatic encephalopathy," represents a form of brain atrophy and dementia thought to be related to repeated head injury. The underlying biologic mechanism of this condition is poorly understood and is an area of active investigation. Pathologically, this condition is characterized by aggregation of hyperphosphorylated tau and neurofibrillary tangles, along with diffuse axonal disruption and loss. The clinical presentation of chronic traumatic encephalopathy is also very poorly defined, lacks consensus, and may (or may not) include the following symptoms: visual and auditory deficits, impairment in attention, orientation, memory, language, information processing, posttraumatic epilepsy, cognitive behavioral problems, as well as posttraumatic stress disorder [102]. The neuropathology of subjects with this condition often reveals the presence of various proteins, including tau and neurofibrillary tangle formation, which suggests overlapping features of this condition and Alzheimer's dementia, frontotemporal degeneration, and Lewy body disease [103].

The main goals of imaging patients with chronic TBI are to better characterize any injuries, enhance understanding of persistent symptoms, prognosticate, provide education, and identify the need for specialist referral.

CT

NCCT is an adjunctive study in patients with chronic TBI. NCCT may show focal atrophy in a regionally susceptible area of the brain, such as the anterior temporal lobes, medial temporal lobes, or inferior frontal lobes among patients with TBI. Some studies have reported ventricular enlargement and sulcal dilatation among patients with severe TBI in the chronic stage that may be correlated with neuropsychologic outcomes [104,105].

MRI

MRI is the primary imaging modality for subacute to chronic TBI (evidence level II) [29] and has been repeatedly shown to be very sensitive for detecting and characterizing brain injuries, particularly brain atrophy in the chronic stages. However, MRI is typically recommended only in the presence of new, persistent, or worsening symptoms in subacute to chronic TBI because only then are MRI changes clinically meaningful (class I recommendation). Studies comparing CT and MRI often suffer from CT and MRI studies' being obtained at different times (NCCT is typically performed in the ED, and MRI is performed at a later time, often a few days to a few weeks after injury). Despite these limitations, MRI, in particular SWI, shows approximately 30% more TBI lesions compared with admission CT (evidence level II) [105]. For chronic moderate to severe TBI, the number, size, and location of MRI abnormalities have been correlated with the severity of TBI and have been used to predict clinical outcomes among patients with early posttraumatic vegetative state (evidence level II) [106]. Currently, there are no large prospective studies that address long-term neurocognitive outcomes in patients with mild TBI who are imaged using conventional MRI sequences in the subacute to chronic stages after injury (evidence level III) [107-110].

Cerebral Atrophy. Cerebral atrophy has been reported after all severities of TBI, but the literature is more complete for moderate to severe TBI (evidence levels II—III) [112-115]. Three-dimensional isotropic short—echo time spoiled gradient-recalled echo and magnetization-prepared rapid gradient-echo sequences have been used to assess TBI-associated brain atrophy in numerous studies (evidence levels II—III) [110,115-118]. A number of studies have correlated post-TBI atrophy with severity of injury (such as admission GCS score, duration of coma, and Glasgow Outcome Scale score) (evidence levels II—III) [111,119] and others with functional outcomes (evidence levels II—III) [112,114,120,121]. However, the association with

functional outcomes is less well correlated, with only weak correlations elucidated to date between the patterns of atrophy and their neurocognitive sequelae [115,118].

Summary

1. MRI is recommended only in the presence of new, persistent, or worsening symptoms in patients with subacute to chronic TBI. Only MRI changes appear to be clinically meaningful (class I recommendation).

EVIDENCE AND RECOMMENDATIONS FOR IMAGING IN PEDIATRIC TBI

CT

Mild TBI is a common reason for children to visit the ED [122]. Although NCCT is the standard diagnostic test for acute TBI for both adults and children, increasing public awareness and concern regarding ionizing radiation exposure demands judicious use of NCCT for children with mild TBI. Although the magnitude of risk for future development of malignant neoplasm from a single head CT study is expected to be very low, children are at greater risk than adults because the pediatric brain is more sensitive to ionizing radiation than the adult brain because of a larger proportion of actively dividing cells and the longer life span for radiation-induced tumor development [123-125]. In addition, radiation exposure to the lens of the eye from NCCT increases the risk for developing cataracts later in life [126]. Technical innovation and efforts to reduce radiation dose have led to broad clinical applications of various adaptive statistical iterative reconstruction tools for trauma patients. The reconstruction algorithms contributed to the reduction of radiation dose for body CT by 20% in trauma patients [127]. The ACR [12], working in collaboration with the Society of Pediatric Radiology, has successfully launched the Image Gently® campaign to many radiology communities, focusing on minimizing radiation exposure to pediatric patients for all clinical applications aligning with the concept of "as low as reasonably achievable" (http://www.imagegently.org).

Which Pediatric Patients With TBI Can Safely Avoid Head NCCT? With the goal of reducing unnecessary NCCT in children, several clinical decision rules have been tested in an effort to identify pediatric patients who do not need NCCT, including the Canadian Assessment of Tomography for Childhood Head Injury rule [128,129], the Children's Head Injury Algorithm for the Prediction of Important Clinical Events rule [130], and the Pediatric Emergency Care Applied Research Network (PECARN) rule [131]. A recent review of these and other rules applied in pediatric populations concluded that the PECARN rule appears to be the best validated rule for both children and infants. It has the largest study cohort, the highest sensitivity, and acceptable specificity for clinically significant intracranial injuries, although further validation of the PECARN rule is necessary [132].

PECARN derived and validated clinical prediction rules that identify both younger and older children at very low risk for clinically important TBI after mild blunt head trauma. In such patients, CT scans may safely be avoided. A total of 25 EDs participated in the PECARN study to detect "severe injury mechanisms" among younger and older children, enrolling a total of 42,412 patients. Overall, 367 children had clinically important TBI (0.9%). Of the 1,327 children <2 years of age with severe injury mechanisms, 4 (0.3%) had clinically important TBI, as did 12 of the 1975 children ≥2 years of age (0.6%) [23].

The planned subanalysis of the PECARN study reviewed the utilization of CT and outcomes of two groups of children: (1) children who were clinically observed before NCCT and (2) children who were not clinically observed before NCCT. The clinically observed group had a lower use of NCCT by 3.9%. However, the rate of clinically significant injury was similar between the two groups, 0.75% for the observed group and 0.87% for the non-observed group (evidence level I). For children with mild TBI (GCS scores of 14 and 15), clinical observation before making a decision to obtain NCCT is therefore an effective strategy in reducing unnecessary radiation exposure for young children (class IIa recommendation). Additional studies will be necessary to determine the optimal duration of clinical observation to measure the impact on CT utilization, the total length of the ED stay, as well as the overall costs [133].

Another prospective study with 1,306 children with mild TBI demonstrated that 49% of subjects were observed in the ED, and 20% underwent CT scans [134]. After adjusting for time from injury, patient age, gender, physician type, and study month, every additional hour of ED observation time was associated with a commensurate decrease in the CT rate for children in all risk groups (evidence level II). All 8 children with significant injuries underwent immediate CT. ED observation time was associated with a time-dependent reduction in head CT rate, with no delay in the diagnosis of a significant TBI. In this instance, increasing clinical observation led to decreased radiation dose without substantial harm to children with mild TBI.

MRI

Conventional brain MRI has advantages over NCCT, including lack of ionizing radiation and superior detection

Table 4. Summary of recommendations for neuroimaging in patients with TBI

Modality or Sequence	TBI Indication	Recommendation
Noncontrast head CT	First-line test for acute mild, moderate, and severe TBI	Class I
Noncontrast head CT	Repeat assessment in acute TBI with neurologic deterioration	Class I
Noncontrast head CT	Judicious use in pediatric mild TBI	Class I
Noncontrast head CT	Repeat assessment of mild TBI with negative initial NCCT results	Class III
CTA of the brain	Suspected vascular trauma	Class IIa
Brain MRI without contrast	Acute or subacute TBI when initial or follow-up NCCT is negative with unexplained neurologic findings	Class I
T2* and SWI MRI sequences	Acute, early subacute, and chronic stages of diffuse axonal injury	Class IIa
Brain MRI with contrast	Can aid in visualizing subacute brain contusions	Class IIb
Advanced neuroimaging*	Mild TBI with negative conventional CT and MRI	Class IIb

Note: CTA = CT angiography; NCCT = noncontrast CT; SWI = susceptibility-weighted imaging; TBI = traumatic brain injury.
*Advanced neuroimaging: MRI diffusion tensor imaging, blood oxygen level–dependent functional MRI, MR spectroscopy, perfusion imaging, PET/single-photon emission CT, and magnetoencephalography (discussed in AJNR Am J Neuroradiol 2015;00:000-000).

of small TBI lesions; however, particularly in pediatric patients who may require sedation for MRI evaluation, NCCT currently remains routine in the assessment of acute traumatic head injury. In cases of suspected pediatric nonaccidental trauma, MRI may be useful to identify multiple injuries and injuries of varying age, as well as hypoxic ischemic injury [124,125]. MRI can detect injuries not seen on NCCT; however, NCCT should not be deferred to await MRI in a symptomatic child.

In particular, SWI was reported to detect 30% more TBI-related lesions compared with NCCT and MRI (evidence level III) [105]. A retrospective case-control study of 101 infants with nonaccidental trauma using SWI revealed that presence of microhemorrhage on SWI combined with ischemic injury predicted poor outcomes in children with nonaccidental trauma (evidence level III) [135]. Another case-control study of pediatric TBI using DWI reported that apparent diffusion coefficient values of the peripheral (normal-appearing) white matter were significantly reduced in children with severe TBI with poor outcomes compared with patients with severe TBI with good clinical outcomes [50].

EVIDENCE AND RECOMMENDATIONS FOR FOLLOW-UP IMAGING IN PEDIATRIC TBI

The use of routine (or scheduled) follow-up NCCT has questionable value for adult patients with TBI and is even less supported for children with TBI. One retrospective study of 268 children with TBI who underwent follow-up NCCT within 24 hours of the initial NCCT study concluded that repeat NCCT is recommended only in patients with epidural, subdural, and parenchymal hematomas, whereas repeated imaging may be less likely to alter the clinical management scheme in patients with subarachnoid hemorrhage, intraventricular hemorrhage, DAI, and isolated skull fractures without clinical deterioration [136].

IMAGING PREDICTION OF OUTCOMES IN PEDIATRIC TBI

A prospective longitudinal study by Levin et al [86] enrolling pediatric patients with mild TBI demonstrated that patients with abnormal CT findings had significantly worse episodic memory, slower cognitive processing, and poor performance in calculating and reading than those with no CT abnormalities.

Systematic review of pediatric TBI indicates that postconcussion symptoms persist in children with mild TBI with lower cognitive ability and intracranial pathology on imaging (evidence level II) [137]. Despite reports that the number and volume of SWI lesions are correlated with clinical outcomes (evidence level III) [135,138], this remains an area of intensive investigation to produce higher levels of evidence.

Summary

1. Head trauma is a common reason for children to visit EDs. Judicious use of NCCT for children with mild TBI is recommended (class I recommendation).
2. Although NCCT is the standard diagnostic test for acute moderate to severe TBI in pediatric patients, increasing clinical observation in the ED can obviate the need for NCCT without substantial harm in children with mild TBI (class IIa recommendation).
3. MRI is more sensitive in detecting TBI lesions and avoids ionizing radiation to the brain or lens of the eye and may be particularly helpful in cases of nonaccidental trauma. Further research is needed to determine which pediatric patients with mild TBI, if any, should undergo MRI as routine care.

TAKE-HOME POINTS

- Neuroimaging plays a critical role in the evaluation of patients with TBI. The imaging recommendations for patients with TBI are summarized in Table 4.
- NCCT remains the first line of imaging for patients with TBI, with MRI being recommended in specific situations listed in Table 4.
- NCCT should be used with caution in the pediatric TBI population because of the risks associated with ionizing radiation.
- TBI imaging is a rapidly evolving field, and a number of the recommendations presented will be updated in the future to reflect the advances in medical knowledge.

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APPENDIX

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