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Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department With Mild Traumatic Brain Injury:

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Abstract

This 2023 Clinical Policy from the American College of Emergency Physicians is an update of the 2008 “Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting.” A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following questions: 1) In the adult emergency department patient presenting with minor head injury, are there clinical decision tools to identify patients who do not require a head computed tomography? 2) In the adult emergency department patient presenting with minor head injury, a normal baseline neurologic examination, and taking an anticoagulant or antiplatelet medication, is discharge safe after a single head computed tomography? and 3) In the adult emergency department patient diagnosed with mild traumatic brain injury or concussion, are there clinical decision tools or factors to identify patients requiring follow-up care for postconcussive syndrome or to identify patients with delayed sequelae after emergency department discharge? Evidence was graded and recommendations were made based on the strength of the available data. Widespread and consistent implementation of evidence-based clinical recommendations is warranted to improve patient care.

INTRODUCTION

Traumatic brain injuries (TBIs) affect the lives of millions of Americans and represent a serious health care challenge for emergency department (ED) clinicians nationwide.[1] A TBI is caused by an external force to the head or body or a penetrating injury to the head and

is associated with a wide range of functional short- or long-term changes that may affect cognition (eg, memory and reasoning), sensation (eg, sight and balance), language (eg, communication and understanding), and/or emotion (eg, depression, personality changes).[2,3] The initial severity of a TBI may range from "mild," ie, a brief change in mental status or consciousness, to "severe," ie, an extended period of unconsciousness or amnesia after the injury.[3]

In one year alone, EDs in the United States manage more than 25 million injury-related visits, including those for patients with a suspected TBI.[4] In the United States, there were approximately 223,135 TBI-related hospitalizations in 2019 and 64,362 TBI-related deaths in 2020.[5] Recent data indicates that most TBIs occur among adults, with adults age 75 years and older accounting for approximately 32% of TBI-related hospitalizations and 28% of TBI-related deaths.[5] Current data may underestimate the true burden of this injury as people who do not seek medical care after a head injury and patients seen in outpatient, federal, military, or the United States Department of Veterans Affairs (VA) settings may not be included in published reports. Racial and ethnic minorities, people who experience homelessness, people who are in correctional and detention facilities, and survivors of intimate partner violence are groups disproportionately affected by TBI.[6-9] Moreover, people living in rural areas have higher TBI-related mortality rates than those in urban areas.[10-12] Explanations for this disparity may include greater distance to emergency medical care,[13] limited access to a Level I trauma center within 1 to 2 hours of the injury,[14] differing mechanisms of injury,[6] and difficulty obtaining specialized TBI care.[15] Although rates vary by group, overall, suicide (predominantly firearm-related), followed by unintentional falls and unintentional motor vehicle crashes, are the leading mechanisms of TBI-related deaths in the United States.[5,6] Furthermore, unintentional falls are the leading mechanism of TBI-related hospitalizations in the United States.[5]

Approximately 70% to 90% of patients with a head injury and TBI presenting to the ED will be diagnosed with mild traumatic brain injury (mTBI).[16,17] An mTBI is associated with neuronal dysfunction involving a cascade of ionic, metabolic, and physiologic events.[18-21] This cascade and microscopic axonal dysfunction may lead to acute clinical signs and symptoms that evolve during recovery.[3,21] In 2004, the World Health Organization (WHO) Collaborating Centre Task Force on mTBI, the mTBI Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine and the United States Centers for Disease Control and Prevention (CDC) defined mTBI as "an acute brain injury resulting from mechanical energy to the head from external physical forces including (1) 1 or more of the following: confusion or disorientation, loss of consciousness (LOC) for 30 minutes or less, posttraumatic amnesia for less than 24 hours, and/or other transient neurologic abnormalities such as focal signs, symptoms, or seizure; (2) Glasgow Coma Scale (GCS) score of 13 to 15 after 30 minutes postinjury or later on presentation for health care."[22,23] Whereas most patients with mTBI will be treated and discharged from an ED,[24] an estimated 5% to 15% of patients with a head injury will have intracranial injuries on imaging and be classified as having moderate or severe TBI.[25] Roughly 1% of these (more severe TBI) patients will require surgical intervention and fewer will die (0.1%).[25,26]

The costs for all severity levels of TBI are not purely limited to economics. Costs are multifactorial and include dynamic societal, psychosocial, physical, mental, medicolegal, and other quality of life factors that are often challenging to quantify. Further complicating this is the fact that TBI is not solely an acute problem. According to the CDC, the lifetime economic cost of TBI, including direct and indirect costs, was 76.5 billion dollars in the United States in 2010.[27] Although most patients presenting to the ED with mTBI are asymptomatic within a couple of weeks, some patients will have persistent symptoms requiring further care and added expenses.[16,17,28] A 12-month analysis of the health care utilization of 80,004 patients after the diagnosis of mTBI in the United States reported a mean cost of $13,564 (SD=$41,071) involving a combination of inpatient and outpatient services.[29] Prevention and appropriate management of mTBI is critical to reducing the economic and societal burden on the lives of Americans.

Rationale for the Clinical Questions in the 2023 American College of Emergency Physicians (ACEP) Clinical Policy

As variation in mTBI diagnosis and management practices in the United States may contribute to disparities in patient outcomes, widespread and consistent implementation of evidence-based clinical recommendations is warranted.[10,30] To this end, in 2008, the ACEP Clinical Policies Committee published and disseminated the “Clinical Policy: Neuroimaging and Decisionmaking in Adult Mild Traumatic Brain Injury in the Acute Setting.”[31] As research on mTBI has continued to evolve and emerge since 2008, the ACEP Clinical Policies Committee conducted an updated systematic review of the literature to assess any needed changes to the 2008 clinical policy and to determine whether there was a need for additional evidence-based recommendations. The Clinical Policies Committee determined that the recommendations made in the 2008 clinical policy were no longer relevant and did not warrant revision. Therefore, the Clinical Policies Committee identified emerging mTBI research related to clinical decision tools, patients using anticoagulant or antiplatelet medication, and postconcussive syndrome (PCS) that was sufficient to merit clinical application. This document, “Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department with Mild Traumatic Brain Injury” (2023 ACEP clinical policy), is the result of these efforts. This 2023 ACEP clinical policy is comprised of 3 critical questions: 1) In the adult ED patient presenting with minor head injury, are there clinical decision tools to identify patients who do not require a head computed tomography (head CT)?; 2) In the adult ED patient presenting with minor head injury, a normal baseline neurologic examination, and taking an anticoagulant or antiplatelet medication, is discharge safe after a single head CT?; and 3) In the adult ED patient diagnosed with mTBI or concussion, are there clinical decision tools or factors to identify patients requiring follow-up care for PCS or to identify patients with delayed sequelae after ED discharge?

In part because of heterogeneity within the literature in enrolled patient populations, research definitions, and outcomes, there is some inconsistency within studies to determine the need for head CT in patients with suspected mTBI. To provide better insight, we included key word definitions of common terms used throughout the literature to allow for consistency and clarity (Appendix E1, available at http://www.annemergmed.com).

Heterogeneity in the literature has led to challenges in creating evidence-based guidelines on CT usage.[16] However, research on this topic has expanded in recent years. As such, the first critical question examined in this 2023 ACEP clinical policy addresses head CT usage and is the reciprocal of the first question in the 2008 ACEP clinical policy. In 2008, the question asked, "which patients with mTBI should have a non-contrast head CT in the ED?"[31] The updates to this first question were designed to pair with the *Choosing Wisely* campaign. Created by the American Board of Internal Medicine, *Choosing Wisely* promotes the utilization of evidence-based care practices facilitated by improving conversations between clinicians and patients with shared decisionmaking.[32] Based on the work of an ACEP task force in 2013, 10 items were identified for inclusion in the *Choosing Wisely* campaign. The first item recommended clinicians: "Avoid CT scans of the head in ED patients with minor head injury who are at low risk based on validated decision rules."[32] This recommendation is consistent with current research and considered an actionable target to improve the health care value of services delivered, reduce unnecessary procedures and exposure to radiation for patients, and improve direct medical costs.[33]

Coinciding with the aging of the United States population, the number of patients taking anticoagulation and antiplatelet therapies has risen substantially.[34,35] Whereas these medications afford benefits to patients with serious health conditions, research suggests that they may complicate TBI diagnosis and management.[36] As such, the second critical question in this 2023 ACEP clinical policy addresses the safety of discharging a patient with an mTBI taking anticoagulants or antiplatelet medications from the ED after an initial head CT.[35,37] Finally, as evidence concerning the potential for long-term physical, cognitive, and mental health problems after mTBI expands,[28] the third question takes into account the challenge of identifying patients diagnosed with mTBI or concussion who may be at increased risk for PCS or subsequent negative sequelae that requires specialized follow-up care after ED discharge.

Defining Mild TBI Controversy

Despite being a common injury, there is a significant discrepancy in the literature and among medical societies regarding the definition of mTBI, and no consensus definition for mTBI currently exists. Various government and medical societies have sought to define mTBI, including the following: American Congress of Rehabilitation Medicine; American College of Occupational and Environmental Medicine; Brain Trauma Foundation; CDC; American College of Sports Medicine; American Medical Society for Sports Medicine; WHO; International Conference on Concussion in Sport; National Academy of Medicine, formerly called the Institute of Medicine; American Academy of Neurology; Eastern Association for the Surgery of Trauma; Ontario Neurotrauma Foundation, and ACEP. All have used varying definitions, and there is debate regarding whether the term concussion is synonymous with mTBI or if concussion is a subset of mTBI. In the published literature, concussion, mild or minor head trauma, and mild head injury are often used interchangeably.[17,38] The Ontario Neurotrauma Foundation Concussion/mTBI Guideline published in 2018 noted that "all concussions are considered to be an mTBI; however, mTBI is distinguished from concussion when there is evidence of intracranial injury on conventional neuroimaging, or there is a persistent neurologic deficit."[39] The WHO defined these separately, and their definition of

mTBI also includes intracranial injury not requiring surgery.[40] However, many practicing clinicians would not necessarily agree that positive findings on imaging would equate to a "mild" TBI. In patients with a GCS score of 13, which many define as mTBI, there have been reports of a higher incidence of injuries requiring surgical intervention, and in subsets of mTBI with a GCS score of 13 and intraparenchymal lesions, patients have reportedly performed poorer on neuropsychological evaluations more consistent with those in moderate TBI groups.[31,41,42] One author, Stein, even titled a report, "Minor Head Injury: 13 is an Unlucky Number," in reference to the increased problems associated with a GCS score of 13.[41] The VA and Department of Defense (DoD) definition of mTBI and concussion from 2016, which is currently under revision, includes normal structural imaging if obtained.[43] In the 2015 CDC Report to Congress, mTBI is referenced to include normal structural imaging, LOC <30 minutes, posttraumatic amnesia 0 to 1 day, and a GCS score of 13 to 15.[44] The CDC report also acknowledged that the use of GCS alone can lead to misclassification of TBI and even individual characteristics of severity criteria (ie, for mild, moderate, or severe), when used alone, cannot accurately predict severity and outcomes.[44,45] The VA/DoD's most updated version of its definition of TBI no longer recommends the use of GCS to diagnose TBI.[43] Since there is no universal definition for mTBI, we chose to stay consistent with the ACEP 2008 adult mTBI clinical policy by once again addressing blunt head injury patients age 16 years or older with a GCS score of 14 or 15 and improvement to a GCS score of 15 at 2 hours postinjury if the initial GCS score was 14 with or without a history of the following: LOC, amnesia, or disorientation presenting for evaluation within 24 hours.[31] A GCS score of 13 will not be considered mTBI for the purposes of this guideline because many experts and authors note a higher or moderate risk in this group as previously discussed (see mTBI in Definitions E1). In this 2023 ACEP clinical policy, the term mTBI and concussion may be used interchangeably unless otherwise stated. The term "mild" in mTBI is used primarily in reference to the diagnosis of mild traumatic brain injury, whereas the term "minor" is used frequently to describe the mechanism of injury and not the diagnosis. Many studies that were graded and reviewed used similar terminology. The articles were graded and interpreted based on how mTBI was defined by the authors. Most patients in the studies examined for this guideline had a GCS score of 14 or 15; however, when studies included patients with a GCS score of 13, this is addressed in the prose.

METHODOLOGY

This ACEP clinical policy was developed by emergency physicians with input from medical librarians and a patient safety advocate and is based on a systematic review and critical, descriptive analysis of the medical literature and is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[46]

Search and Study Selection

This clinical policy is based on a systematic review with a critical analysis of the medical literature meeting the inclusion criteria. Searches of PubMed, SCOPUS, Embase, Web of Science, and the Cochrane Database of Systematic Reviews were performed by a librarian. Search terms and strategies were peer reviewed by a second librarian. All searches were limited to human studies published in English. Specific key words/phrases, years used in the

searches, dates of searches, and study selection are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Two subcommittee members independently read the identified abstracts to assess for possible inclusion. Of those identified for potential inclusion, each full-length text was reviewed for eligibility. Those identified as eligible were subsequently abstracted and forwarded to the committee's methodology group (emergency physicians with specific research methodological expertise) for methodological grading using a Class of Evidence framework (Appendix E2).

Assessment of Risk of Bias and Determination of Classes of Evidence

Each study identified as eligible by the subcommittee was independently graded by 2 methodologists. Grading was done with respect to the specific critical questions; thus, the Class of Evidence for any study may vary according to the question for which it is being considered. For example, an article that is graded an "X" because of "inapplicability" for one critical question may be considered perfectly relevant for another question and graded I to III. As such, it was possible for a single article to receive a different Class of Evidence grade when addressing a different critical question.

Design 1 represents the strongest possible study design to answer the critical question, which relates to whether the focus was therapeutic, diagnostic, prognostic, or meta-analysis. Subsequent design types (ie, Design 2 and Design 3) represent weaker study designs, respectively. Articles are then graded on dimensions related to the study's methodological features and execution, including but not limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, generalizability, data management, analyses, congruence of results and conclusions, and potential for conflicts of interest.

Using a predetermined process that combines the study's design, methodological quality, and applicability to the critical question, two methodologists independently assigned a preliminary Class of Evidence grade for each article. Articles with concordant grades from both methodologists received that grade as their final grade. Any discordance in the preliminary grades was adjudicated through discussion, which involved at least one additional methodologist, resulting in a final Class of Evidence assignment (ie, Class I, Class II, Class III, or Class X) (Appendix E3). Studies identified with significant methodologic limitations and/or ultimately determined to not be applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. However, the content in these articles may have been used to formulate the background and to inform expert consensus in the absence of evidence. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Based on the strength of evidence for each critical question, the subcommittee drafted the recommendations and supporting text, synthesizing the evidence using the following guidelines:

Level A recommendations.—Generally accepted principles for patient care that reflect a high degree of scientific certainty (eg, based on evidence from one or more Class of Evidence I or multiple Class of Evidence II studies that demonstrate consistent effects or estimates).

Level B recommendations.—Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate scientific certainty (eg, based on evidence from one or more Class of Evidence II studies or multiple Class of Evidence III studies that demonstrate consistent effects or estimates).

Level C recommendations.—Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of adequate published literature, based on expert consensus. In instances where consensus recommendations are made, “consensus” is placed in parentheses at the end of the recommendation.

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 consistency of results, the uncertainty of effect magnitude, and publication bias, among others, might lead to a downgrading of recommendations. When possible, clinically oriented statistics (eg, likelihood ratios [LRs], number needed to treat) are presented to help the reader better understand how the results may be applied to the individual patient. This can assist the clinician in applying the recommendations to most patients but allow adjustment when applying to patients with extremes of risk (Appendix E4).

Evaluation and Review of Recommendations

Once drafted, the policy was distributed for internal review (by members of the entire committee), followed by an external expert review and an open comment period for all ACEP membership. Comments were received during a 60-day open comment period, with notices of the comment period sent electronically to ACEP members, published in *EM Today*, posted on the ACEP website, and sent to other pertinent physician organizations. The responses were used to further refine and enhance this clinical policy, although responses do not imply endorsement. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology, methodology, or the practice environment changes significantly.

Application of the Policy

This policy is not intended to be a complete manual on the evaluation and management of adult patients with mTBI but rather a focused examination of critical questions that have particular relevance to the current practice of emergency medicine. The potential benefits

and harms of implementing recommendations are briefly summarized within each critical question.

It is the goal of the Clinical Policies Committee to provide evidence-based recommendations when the scientific literature provides sufficient quality information to inform recommendations for a critical question. When the medical literature does not contain adequate empirical data to inform a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline provides clinical strategies for which medical literature exists to inform the critical questions addressed in this policy. ACEP funded this clinical policy.

Scope of Application.—This guideline is intended for physicians working in EDs.

Inclusion Criteria.—The guideline is intended for adults with blunt head injury (Q1/Q2), or adults diagnosed with mild traumatic brain injury or concussion (Q3).

Exclusion Criteria.—This guideline is not intended for patients with a history of a bleeding disorder, pregnant patients, patients with a primary presentation of a seizure disorder, pediatric patients, patients with an obvious open or penetrating head injury, or patients with unstable vital signs with multisystem trauma.

CRITICAL QUESTIONS

1. In the adult ED patient presenting with minor head injury, are there clinical decision tools to identify patients who do not require a head CT?

Patient Management Recommendations

Level A recommendations.—Use the Canadian CT Head Rule (CCHR) to provide decision support and improve head CT utilization in adults with a minor head injury (Table 1).

Level B recommendations.—Use the National Emergency X-Radiography Utilization Study (NEXUS) Head CT decision tool (NEXUS Head CT) or the New Orleans Criteria (NOC) to provide decision support in adults with minor head injury; however, the lower specificity of the NEXUS Head CT and NOC compared with CCHR may lead to more unnecessary testing (Table 1).

Level C recommendations.—Do not use clinical decision tools to reliably exclude the need for head CT in adult patients with a minor head injury on anticoagulation therapy or antiplatelet therapy exclusive of aspirin.

Resources (Appendix E6):

- Canadian CT Head Rule:[47] https://www.mdcalc.com/canadian-ct-head-injury-trauma-rule
- New Orleans/Charity Head Trauma/Injury Rule:[48] https://www.mdcalc.com/new-orleans-charity-head-trauma-injury-rule
- NEXUS Head CT:[49] https://bit.ly/NEXUSHeadCT

Potential Benefit of Implementing the Recommendations:

- Decreased costs and decreased radiation exposure because of the potential for fewer head CT scans.
- Potential for decreased ED length of stay and improved patient flow because of the potential for fewer head CT scans.

Potential Harm of Implementing the Recommendations:

- To the extent that decision rules lack specificity, there is potential for increased radiation to patients from unnecessary CT scans as well as increased health care costs and resource use. It is important to apply the available decision tools only to the appropriate patient population, as defined by the inclusion and exclusion criteria of the studies. An inappropriate application can lead to both over-triage and unnecessary CT use, as well as under-triage and missed injuries. Additionally, the identification of injuries that are not clinically important may lead to unnecessary additional downstream medical care costs and hospitalizations.

Key words/phrases for literature searches: brain concussion, brain injury, closed head injury, concussion, commotio cerebri, craniocerebral trauma, head injury, head trauma, instrument, mild traumatic brain injury, mTBI, minor head injury, traumatic brain injury, biological marker, biomarker, clinical assessment tool, clinical decision, clinical decision instrument, clinical decision tool, clinical decision rule, clinical prediction instrument, clinical prediction tool, clinical prediction rule, cognitive aid, decision support instrument, decision support system, decision support technique, screening aid, rule, screening tool, tool, brain computed tomography, brain CT, brain imaging, head computed tomography, head CT, multidetector computed tomography, x-ray computed tomography, and variations and combinations of the key words/phrases. Searches included January 2008 to search dates of January 16 and 21, 2020, March 9 and 11, 2020, and June 7 and 8, 2022.

Study Selection: One thousand two hundred sixteen articles were identified in the searches. Thirty-five articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, zero Class I studies, 5 Class II studies, and 5 Class III studies were included for this critical question (Appendix E5).

In the current practice of emergency medicine, clinical decision tools have become more commonplace in the attempt to improve patient safety and encourage responsible resource

utilization. One area that has seen considerable research in developing clinical decision tools is minor traumatic head injury. The two most well-studied and well-validated clinical decision tools are the CCHR, as initially developed by Stiell et al[47] in 2001, and the NOC, developed at Charity Hospital by Haydel et al[48] in 2000. These and other clinical decision tools tend to have similar criteria that can help physicians recognize high-risk patients.

Informed by prior studies primarily based on trauma registry data, two foundational studies were published in the early 2000s that led to a more robust validation of the CCHR and NOC. Stiell et al,[47] in a Class II study, performed a derivation and internal validation study prospectively evaluating 3,121 patients aged 16 years or older who had a minor head injury, which was defined as an initial ED GCS score of 13 to 15 plus either witnessed LOC, definite amnesia or witnessed disorientation. Patients were excluded if there was no clear trauma history (ie, primary seizure or syncope), obvious penetrating skull injury or depressed skull fracture, acute focal neurologic deficit, unstable vital signs from trauma, seizure before ED assessment, bleeding disorder, or use of oral anticoagulants, patients returning for repeat assessment of same injury, or pregnancy. Qualifying patients were assessed for 22 standardized clinical findings based on history and examination. The primary outcome measure was the need for neurosurgical intervention, and the secondary outcome was clinically important brain injury (CIBI). The need for neurologic intervention was defined as death within 7 days because of a head injury or the need for any procedures within 7 days (eg, craniotomy, skull fracture elevation, intracranial pressure monitoring, or intubation for head injury shown on head CT). Clinically important brain injury was defined as any acute intracranial finding revealed on CT that would normally require admission to the hospital and neurologic follow-up. Sixty-seven percent (2,078 of 3,121) of the patients had a CT to assess secondary outcomes, but surrogate measures, including telephone follow-up with neurologic assessment, were used in place of a negative CT to assess the primary outcome measure. In patients who were neurologically intact, clinically unimportant lesions included solitary contusions less than 5 mm in diameter, localized subarachnoid blood less than 1 mm thick, smear subdural hematomas less than 4 mm thick, isolated pneumocephaly, or closed depressed skull fractures, not through the inner table. A set of 7 questions stratified as high-risk and medium-risk factors was developed. The high-risk factors were 100% sensitive (95% confidence interval [CI] 92% to 100%) and 68.7% specific (95% CI 67% to 70%) for predicting the need for neurologic intervention, which would have required only 32.2% of patients to undergo CT. The medium-risk factors were 98.4% sensitive (95% CI 96% to 99%) and 49.6% specific (95% CI 48% to 51%) for predicting CIBI, which would have required only 54.3% of patients to undergo CT. The authors concluded that CT in minor head injury is indicated in patients with 1 of 5 high-risk factors, ie, failure to reach a GCS score of 15 within 2 hours of injury, suspected open skull fracture, a sign of basal skull fracture, vomiting more than once, or age greater than 64 years.

Similarly, a Class III study from Haydel et al[48] in 2000 prospectively assessed patients with a minor head injury to develop and validate clinical criteria in what is now commonly known as the NOC. The authors included 1,429 patients who presented to the ED after a minor head injury with a GCS score of 15, a normal brief neurologic examination (ie, normal cranial nerves, normal strength, and sensation of arms and legs) and a history of LOC or amnesia. Patients who declined CT and had concurrent injuries precluding the use of CT

or reported no LOC or amnesia for the traumatic event were excluded. In the derivation phase, 520 patients were included, and 6.9% (95% CI 4.2% to 9.6%) had an abnormal CT. The CT was considered abnormal if it showed an acute traumatic intracranial lesion (ie, a subdural, epidural, or parenchymal hematoma; subarachnoid hemorrhage; cerebral contusion; or depressed skull fracture). In the validation phase, 909 patients were included, and 6.3% (95% CI 4.7% to 7.8%) had a positive CT. All patients with a positive CT had 1 or more of 7 findings: headache, vomiting, age over 60 years, drug or alcohol intoxication, deficits in short-term memory, physical evidence of trauma above the clavicles, and posttraumatic seizure. In this group, the sensitivity of these 7 factors was 100% (95% CI 95% to 100%), and the specificity was 25% (95% CI 22% to 28%).

Apart from the CCHR and the NOC, the NEXUS Head CT decision instrument (NEXUS Head CT) has additionally shown promise as a clinical decision tool. First proposed in 2002, Mower et al[49] completed the 10-year prospective observational NEXUS study in 2015. Published in 2017, the Class II study[49] evaluated 8 high-risk criteria (ie, evidence of skull fracture, scalp hematoma, neurologic deficit, abnormal level of alertness, abnormal behavior, persistent vomiting, coagulopathy, and age 65 or greater) that were applied to patients 16 years and older who presented to the ED with blunt head trauma and underwent a head CT. Patients with penetrating trauma, presentation >24 hours after injury, patients undergoing imaging unrelated to trauma, or those patients transferred with known intracranial injuries were excluded. Patients with the absence of all 8 criteria were considered at low risk of intracranial injury and deemed safe to omit from head CT imaging, whereas patients meeting one or more of the criteria were considered high risk. All ED patients with acute blunt head trauma who received a head CT were eligible. The ordering physicians were cautioned from using decision tools as a sole determinant, and the ultimate decision to omit or perform imaging was made by the treating provider (not by study protocol). To account for verification bias, the study performed a 3-month follow-up on a cohort of 368 consecutive patients with a blunt head injury that had not been imaged to assess the potential effects. The primary outcome was the need for neurosurgical intervention, and the secondary outcome was CIBI using the same definition as Steill et al[47] (2001). For this study, 11,770 patients were enrolled with completed imaging, and 420 required neurosurgical intervention. The NEXUS Head CT identified all 420 high-risk patients requiring neurosurgical intervention, demonstrating a sensitivity of 100% (95% CI 99.1% to 100%) and a specificity of 24.9% (95% CI 24.1% to 25.7%). Sensitivity and specificity for high-risk patients with CIBI were 99% (95% CI 98% to 99.6%) and 25.6% (95% CI 24.8% to 26.4%), respectively. The NEXUS Head CT correctly assigned low-risk status to 2,823 of 11,350 patients not requiring neurosurgical intervention (specificity 24.9% [95% CI 24.1% to 25.7%]). None of the 2,823 required intervention resulting in a negative predictive value (NPV) of 100% (95% CI 99.9% to 100%). The NEXUS Head CT correctly assigned low-risk status to 2,815 of 11,003 patients without significant intracranial injury (specificity 25.6% [95% CI 24.8 to 26.4%]). In patients deemed low risk by the NEXUS Head CT, significant injuries were not present in 2,815 of the 2,823 patients resulting in an NPV of 99.7% (95% CI 99.4% to 99.9%). Mower et al[49] then further compared this NEXUS Head CT study group population with patients also meeting CCHR inclusions and exclusions

(N=7,759 patients). The NEXUS Head CT had good sensitivity but was less specific than the CCHR (Table 2).

Subsequently, several studies have evaluated the performance of both the CCHR and NOC in a variety of settings.[50-53] Stiell et al[50] in a Class II study from 2005, applied these 2 decision tools to a prospective cohort in 9 Canadian community and academic EDs. In this study, 1,822 patients with a GCS score of 15 were included, and both the CCHR and the NOC had 100% sensitivity (95% CI 63% to 100%) for predicting the need for neurosurgical intervention. However, the CCHR was more specific at 76.3% (95% CI 74% to 78%) versus 12.1% (95% CI 11% to 14%) for the NOC. Similarly, for CIBI, the CCHR and the NOC had similar sensitivity (100% versus 100%; 95% CI 96% to 100%), but again the CCHR was more specific at 50.6% (95% CI 48% to 53%) versus 12.7% (95% CI 11% to 14%) for the NOC. In patients with a GCS score of 15, the CCHR showed improved rates of CT usage versus the NOC, respectively (CCHR 52.1% [95% CI 50% to 54%] versus NOC 88% [95% CI 86% to 89%]).

A Class II study by Smits et al[51] examined the CCHR and the NOC at 4 university hospitals in the Netherlands. The decision tools were applied to 3,181 consecutive adult patients along with an adaptive model in patients with a GCS score of 13 to 14 or a GCS score of 15 plus one of the risk factors identified by the decision rules. A neurosurgical intervention occurred in 17 patients (0.5%), and clinically important CT findings (any intracranial traumatic CT finding or depressed skull fracture) were present in 243 patients (7.6%). The original CCHR had a sensitivity for identifying neurosurgical intervention of 100% (95% CI 64.6% to 100%) and a specificity of 37.2% (95% CI 34.1% to 40.4%), whereas the original NOC had a sensitivity of 100% (95% CI 34.2% to 100%) and a specificity of 5.3% (95% CI 2.5% to 8.3%). For the identification of a clinically important CT finding, the CCHR had a sensitivity of 84.5% (95% CI 78.1% to 89.3%) and a specificity of 38.9% (95% CI 35.6% to 42.3%), whereas the NOC had a sensitivity of 97.7% (95% CI 92.1% to 99.4%) and a specificity of 5.5% (95% CI 2.6% to 8.7%). In this study, the discrepancy between the sensitivities for the NOC and CCHR for clinically important CT findings is most likely because of a more demanding or comprehensive definition for external injury defined in the NOC compared with a more overall potentially severe definition with CCHR, which does not allow for the inclusion of findings such as minor abrasions. Additionally, Smits et al[51] defined “clinically important CT finding” differently by including “any intracranial traumatic finding” on CT, such as depressed skull fractures. In contrast, the 2005 study by Stiell et al[50] did not consider the following as clinically important: neurologically intact patients with any one of the following: 1) solitary contusion <5 mm, 2) localized subarachnoid hemorrhage (SAH) <1 mm, smear subdural hematoma (SDH) <4 mm, or closed depressed skull fracture (not through the inner table).

A Class II systematic review by Easter et al[25] examined the accuracy of symptoms and signs in adults with minor head trauma to identify those with severe intracranial injuries. Included in this systematic review were specific pooled data from 14 studies involving 23,079 patients with a prevalence of severe intracranial injury of 7.1% (95% CI 6.8% to 7.4%) and a prevalence of injuries leading to death or the need for neurosurgical intervention of 0.9% (95% CI 0.78% to 1%). In patients with minor head injury with LOC, amnesia, or

disorientation, the CCHR demonstrated a sensitivity of 99% (95% CI 78% to 100%) and specificity of 40% (95% CI 34% to 46%) for severe intracranial injury. In the same patient population, the NOC had a sensitivity of 99% (95% CI 90% to 100%) and specificity of 13% (95% CI 8.1% to 22%). The absence of all features of the CCHR lowered the probability of a severe intracranial injury to 0.31% (95% CI 0% to 4.7%) when accounting for the pooled study prevalence of 7.1%. Similarly, in the absence of all features of the NOC, the probability was 0.61% (95% CI 0.08% to 6%).

In a Class III study by Ro et al,[52] 7,131 consecutive patients were enrolled in a prospective cohort involving 5 academic EDs in South Korea to study the CCHR, the NOC, and the NEXUS Head CT. Of the 696 patients meeting the CCHR eligibility requirements, the CCHR was 79.2% sensitive (95% CI 70.8% to 86.0%) and 41.3% specific (95% CI 37.3% to 45.5%) for detecting CIBI. Of the 657 patients meeting the eligibility requirement for the NOC, the NOC was 91.9% sensitive (95% CI 84.7% to 96.5%) and 22.4% specific (95% CI 19% to 26.1%). Sensitivities reported were much lower than in previous studies for CIBI; however, specificity remained similar. The sensitivity for CIBI with the NEXUS Head CT was 88.7% (95% CI 85.8% to 91.2%), and specificity was 46.5% (95% CI 44.5% to 48.5%). The NEXUS Head CT sensitivity for neurosurgical intervention was 95.1% (95% CI 90.1% to 98%), and specificity was 41.4% (95% CI 39.5% to 43.2%). Although the NEXUS Head CT was shown to reduce overall imaging in this trial, it also missed cases requiring neurosurgical intervention. Sensitivities for neurosurgical intervention were similar to previous reports at 100% for the CCHR and the NOC, as all the patients with a need for neurosurgical intervention by the CCHR and the NOC were identified. This study suffered from selection bias as only 8.2% of the patients screened for enrollment were evaluated in the subsequent underpowered intersection cohort that included 588 patients.

Bouida et al,[53] in a Class III comparison study from Tunisia, prospectively enrolled 1,582 patients in an observational cohort of patients with a mild head injury, comparing the CCHR and the NOC. The sensitivity and specificity for patients requiring neurosurgical intervention were 100% (95% CI 90% to 100%) and 60% (95% CI 44% to 76%) for the CCHR, and 82% (95% CI 69% to 95%) and 26% (95% CI 24% to 28%) for the NOC. Sensitivity and specificity for clinically significant head CT findings were 95% (95% CI 92% to 98%) and 65% (95% CI 62% to 68%) for the CCHR and 86% (95% CI 81% to 91%) and 28% (95% CI 26% to 30%) for the NOC. Although there were significant limitations applied to this study regarding loss of screened patients and data, the proportion of patients imaged, the definition of clinically significant head CT findings, and follow-up, it did support the fact that decision tools may have performance patterns that change depending on the setting and population in which they are used. When adjusting for patients with a GCS score of 15 in this trial, the sensitivity for the CCHR was 100% (95% CI 86% to 100%), and the sensitivity for the NOC was 96% (95% CI 88% to 100%); specificities were 58% (95% CI 55% to 61%) and 26% (95% CI 23% to 28%), respectively.

Certain subsets of head-injured patients present additional concerns that may exclude them from established decision tools, such as those on anticoagulant or antiplatelet medications (excluding aspirin as a sole agent) and older patients. All 3 decision tools necessitate imaging in older patients regardless of other risk factors. Similarly, older patients (65 years

and older in the CCHR and the NEXUS Head CT and 60 years and older in the NOC) were considered high risk for CIBI, but data on age as an independent variable are limited.

Probst et al,[54] in a Class III multicenter study, enrolled a prospective cohort of 9,070 adult patients presenting with blunt head trauma who underwent CT imaging based on the clinical judgment of the treating physician (not by study protocol). Among this population, 1,323 (14.6%) were on either aspirin, clopidogrel, warfarin, or combination therapy, and most (77.5%) had a GCS score of 15. Compared with patients without any coagulopathy, the relative risk of significant intracranial injury was 1.29 (95% CI 0.88 to 1.87) for patients on aspirin alone, 0.75 (95% CI 0.24 to 2.30) for those on clopidogrel alone, and 1.88 (95% CI 1.28 to 2.75) for those on warfarin alone. The relative risk of significant intracranial injury was 2.88 (95% CI 1.53 to 5.42) for patients receiving both aspirin and clopidogrel combination therapy. Additionally, the increased risk in patients receiving warfarin or those receiving both aspirin and clopidogrel persisted across most subgroup analyses. Given these results, clinicians would be prudent in having a lower threshold for imaging in these high-risk patients. Furthermore, whereas nonvitamin K antagonist oral anticoagulants (NOACs) have not been well studied in head trauma,[55,56] given the increased risk conferred by other nonaspirin anticoagulants, these patients are likely at higher risk for significant intracranial injury as well. Almost all studies reviewed included some patients on aspirin, but that particular antiplatelet agent by itself was not considered to be a factor in clinical decisionmaking.

As for intoxication, the NOC included drug or alcohol intoxication as a higher-risk feature. In the study,[48] intoxication was defined as history from the patient or a witness and suggested by findings on examination like speech changes or odor on breath. Laboratory testing was only ordered by physician discretion. The derivation and validation studies for the CCHR and the NEXUS Head CT, although having included intoxicated patients, did not rely specifically on intoxication as a risk factor but relied on a GCS score of <15 or an abnormal level of alertness, respectively, as risk factors. In a Class III study, Easter et al[57] (2013) enrolled a prospective cohort of intoxicated adults with minor head injury presenting to an urban academic trauma center over a one-year period. A total of 283 patients were enrolled, with a GCS score of ≥14, the majority with a GCS score of 15 (80%). Clinically important injuries requiring admission or neurosurgical follow-up were identified in 23 patients (8% [95% CI 5% to 12%]). Although LOC and headache were associated with clinically important injury, the CCHR only had a sensitivity of 70% (95% CI 47% to 87%), and the NEXUS Head CT had a sensitivity of 83% (95% CI 61% to 95%). Given these results, whereas the presence of certain features, such as headache, may raise suspicion for significant injuries, the absence of high-risk criteria in the CCHR and the NEXUS Head CT cannot alone eliminate the need for CT in intoxicated patients.

Summary

Recognizing the growing emphasis of value-based care, clinical decision tools have gained attention as potential solutions for preserving patient safety whereas decreasing costs and using fewer resources. The CCHR and the NOC, along with the NEXUS Head CT, demonstrate excellent sensitivity regarding the timely identification of significant

intracranial injury. With well-demonstrated sensitivities of close to 100% (CCHR 95% CI 92% to 100%, NOC 95% CI 95% to 100%, NEXUS Head CT 95% CI 95.3% to 99.1%) for significant intracranial injury, the CCHR, NOC, and NEXUS Head CT can effectively aid in determining which patients do not need a head CT.[47-49] The CCHR has higher specificity than the NOC; however, both have some limitations in specificity that may inhibit substantial reductions in CT imaging. Although some studies have shown decreases in head CT imaging with the application of a clinical decision tool,[58] others have shown no change or even an increase in use.[59,60] As with any clinical decision tool, those that address head injury must be applied to the population in which they were developed and validated. For example, applying these rules to higher volumes of lower-risk populations could lead to increased specificity, whereas applying these rules to higher volumes of higher-risk populations (less low risk) could lead to decreased specificity. Inclusion criteria for these rules restrict their use, and the CCHR and the NOC are only valid when applied to patients who have had LOC or amnesia, or disorientation and who are not on anticoagulants. Although several other clinical decision tools exist for determining the need for head CT in minor head injury, none have been studied well enough to be included in this policy. In conclusion, the NEXUS Head CT or NOC have similar sensitivities to the CCHR in providing decision support. However, as most studies show that the NEXUS Head CT and NOC have lower specificity in adults (which may lead to more unnecessary testing), the CCHR is the more favored tool.

Future Research

Future research may help provide a broader application of clinical decision tools for mTBI or improved specificity or, ideally, both. For example, the ability to apply a decision tool for a patient on an anticoagulant or antiplatelet therapy (exclusive of aspirin) or a patient who is intoxicated has some limitations, as previously noted. Perhaps there are some CT scans performed in these patient populations that are unnecessary. Serum biomarkers, such as S-100 calcium binding protein or brain-specific glial fibrillary acidic protein, may add additional information. The addition of biomarker information may then be combined with patient history and examination features or components of existing clinical decision tools, with the potential for increased specificity and decreased CT utilization. However, at this point, strong data on biomarker use with or without other decision tools is lacking and limited by the availability of these tests. Additionally, more recent work with EEG-based artificial intelligence derived algorithms may lead to improved diagnostic capabilities.[61,62] Future studies should also investigate whether subsets of patients with coagulopathy, advanced age, NOAC, or newer antiplatelet agent treatments or intoxication may safely avoid imaging after minor blunt head trauma.

2. In the adult ED patient presenting with minor head injury, a normal baseline neurologic examination, and taking an anticoagulant or antiplatelet medication, is discharge safe after a single head CT?

Patient Management Recommendations

Level A recommendations.—None specified.

Level B recommendations.—Do not routinely perform repeat imaging in patients after a minor head injury who are taking anticoagulants or antiplatelet medication and are at their baseline neurologic examination, provided the initial head CT showed no hemorrhage.

Do not routinely admit or observe patients after a minor head injury who are taking anticoagulants or antiplatelet medications, who have an initial head CT without hemorrhage, and who do not meet any other criteria for extended monitoring.

Level C recommendations.—Provide instructions at discharge that include the symptoms of rare, delayed hemorrhage after a head injury (Consensus recommendation).

Consider outpatient referral for assessment of both fall risk and risk/benefit of anticoagulation therapy (Consensus recommendation).

Resources (Appendix E6):

Discharge instructions and other materials for patients

- CDC Mild Traumatic Brain Injury and Concussion: Information for Adults: https://www.cdc.gov/traumaticbraininjury/pdf/TBI_Patient_Instructions-a.pdf
- CDC educational materials for adults with mTBI: https://www.cdc.gov/traumaticbraininjury/mtbi_guideline.html

Fall risk screening and assessment for providers and fall prevention materials for patients

- CDC Algorithm for Fall Risk Screening, Assessment & Intervention: https://www.cdc.gov/steadi/pdf/STEADI-Algorithm-508.pdf
- CDC fall prevention materials for patients: https://www.cdc.gov/steadi/patient.html
- CDC Stay Independent Brochure: https://www.cdc.gov/steadi/pdf/STEADI-Brochure-StayIndependent-508.pdf

Potential Benefit of Implementing the Recommendations:

- A decrease in medical costs by avoiding unnecessary medical imaging or hospital observation, or admission.
- Avoid inpatient health care-associated complications by avoiding excessive duration of stay in the ED or hospital.
- A decrease in length of stay for patients who could go home early from the ED without repeat imaging or prolonged observation.

Potential Harm of Implementing the Recommendations:

- A missed case of posttraumatic intracranial hemorrhage that could have benefited from early intervention.

Key words/phrases for literature searches: brain concussion, brain injury, closed head injury, concussion, commotio cerebri, craniocerebral trauma, mild traumatic brain injury, minor head injury, mTBI, traumatic brain injury, anticoagulant, anticoagulant therapy, antiplatelet, antiplatelet medication, direct thrombin inhibitor, factor Xa inhibitor, apixaban, aspirin, betrixaban, clopidogrel, coumarin, dabigatran, dabigatran etexilate, dipyridamole, edoxaban, fondaprinux sodium, heparin, heparinoids, lepirudin, prasugrel, low molecular weight heparin, NOAC, nonvitamin K antagonist oral anticoagulant, rivaroxaban, ticlopidine, tinzaparin sodium, warfarin, brain computed tomography, CT scan, head computed tomography, head CT, x-ray computed tomography, and variations and combinations of the key words/phrases. Searches included January 2008 to search dates of January 16 and 22, 2020, March 9 and 11, 2020, and June 7 and 8, 2022.

Study Selection: Three hundred seventy-six articles were identified in the searches. Forty-one articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, zero Class I studies, one Class II study, and 7 Class III studies were included for this critical question (Appendix E5).

As the United States population continues to age, there is an increasing prevalence of anticoagulant and antiplatelet use. Most indications are for atrial fibrillation, cardiac valve replacement, and thromboembolic disease.[63] Older patients are also more prone to closed head injury, predominantly from falls.[64] The presence of these drugs, including NOACs, is associated with increased morbidity and mortality from intracranial hemorrhage (ICH). Antiplatelet agents are no safer in some series.[65] Therefore, the threshold for initial imaging after minor head trauma in patients on either anticoagulants or antiplatelet agents is very low because of the consequences of potentially missing an early hemorrhage.

The risk of spontaneous ICH in association with anticoagulation is well described. Because of the higher incidence of significant intracranial injuries after blunt head trauma in patients on warfarin versus nonanticoagulated patients (3.9% versus 1.5%), the liberal use of neuroimaging on initial presentation is advocated.[54] Although NOACs have lower incidence of ICH (2.6% versus 10.2% for vitamin K antagonists [VKAs]), it is still higher than in patients without any anticoagulation.[66] Even though most clinicians agree on the need for an initial CT scan of the brain,[31] many are concerned about the possibility of delayed ICH in patients on anticoagulants or antiplatelet agents, which has been cited to be as high as 6%.[67,68] European guidelines suggest that all patients on anticoagulants should undergo a period of routine observation after a head injury, regardless of clinical presentation.[69] More recently, the value of observation has been questioned,[70] but not the need for repeat imaging. With the lack of national consensus guidelines regarding the need for repeat imaging, there are a variety of approaches to these patients, including a serial neurologic examination, observation, or hospital admission versus immediate discharge. Because of the risk of delayed hemorrhage, many physicians subject these patients to repeat brain imaging after a brief period (4 to 6 hours) of observation before discharge, even with a normal neurologic examination.

Therefore, this clinical policy aims to clarify if a single CT scan is adequate (or acceptable) to exclude an ICH after blunt head trauma. The population included adult patients who regularly took anticoagulants (eg, warfarin and NOACs) or antiplatelet agents (eg, clopidogrel and ticagrelor). Although the studies included any adult patients, the predominant population ended up being aged over 60. The focus was on a safe ED discharge that avoided any subsequent clinically significant outcome because of ICH, such as cranial surgery or death, after the initial visit related to the original injury. The main exclusion from this clinical policy recommendation is the concomitant use of aspirin; there were not enough cases to make a recommendation for that particular antiplatelet agent.

The literature search and recommendations were limited to include only minor head injury. This included any blunt head trauma that could be severe enough to cause temporary LOC, posttraumatic amnesia, or disorientation and have a minimum GCS score of 14 on presentation to the ED.[47,71] We only included cases of isolated blunt head trauma in adults at the minimum age of 14 years or older. Further review of the literature revealed a single Class II study and 3 Class III studies that reported data pertinent to answering the critical question.

The only Class II study, Nishijima et al,[72] is a multicenter retrospective observational study of adults (18 years of age and older) with a blunt traumatic injury. Although ultimately 1,064 patients were enrolled, most, 932 (87.6%), qualified as a patient with minor TBI who presented with a GCS score of 15, and 752 (70.7%) had head trauma above the clavicles. Out of the 1,064 patients, 1,000 (94%) received a CT scan of the head, with 43 on concomitant aspirin. All 930 patients found to have normal initial CT scans were followed for 14 days, either as inpatients or outpatients. Of the 687 patients on warfarin, 4 (0.6% [95% CI 0.2% to 1.5%]) had delayed ICHs, with none requiring neurosurgical intervention, but 2 cases resulted in death. None of the 243 patients on clopidogrel had delayed ICH, with one death due to an unknown cause. Although a small number of patients were lost to follow-up, the authors concluded that delayed ICH after a negative initial head CT scan is very rare in patients on warfarin or clopidogrel and that these patients do not warrant admission for observation or immediate reversal of anticoagulation. Of note, only a small number of patients (43 total) in both groups (warfarin and clopidogrel) were on concomitant aspirin, but the drug did not seem to be associated with initial or delayed ICH.

There were 2 Class III studies that mainly looked at warfarin rather than NOACs. The first, Menditto et al,[73] is a prospective case series of patients 14 years of age and older with a minor head injury on warfarin who had an initial negative head CT scan. All were observed for approximately 24 hours and had a repeat CT scan before discharge. Although 5 of 87 patients (6% [95% CI 1% to 11%]) had an intracranial injury on the second CT scan, only one required neurosurgical intervention for a subdural hematoma. An additional two patients who had a negative second CT scan at discharge returned several days later with subdural hematomas. The authors concluded that they support the European Federation of Neurological Sciences' recommendation of a 24-hour observation accompanied by a repeat CT scan for all anticoagulated patients with a minor head injury. Based on this protocol, one patient in 87 identified will require neurosurgical intervention. Limitations in this study

included no blinded outcome assessment or adjudication of outcomes. Approximately 10% of qualifying subjects refused the second scan but follow-up showed they did well.

The second Class III study looking at warfarin also had some patients on heparin. Kaen et al,[74] is a prospective single center study of patients with a mild head injury, GCS score of 14 to 15, age >16 years, with or without LOC or posttraumatic amnesia on anticoagulant therapy (warfarin or heparin) who had an initial normal CT scan of the head. All patients were admitted and observed for 24 hours with serial neurologic exams. At 20 to 24 hours post initial CT scan, a repeat scan was performed. Out of 137 patients, only 2 (1.4% [95% CI 1.0% to 1.8%]) showed hemorrhagic lesions on repeated imaging. Neither patient required neurosurgical intervention nor adjustment of anticoagulation. Both patients were subsequently discharged without neurologic sequelae. Of note, 3 patients were concomitantly on aspirin.

Three subsequent Class III studies looked at NOACs in addition to patients on warfarin. The first of these, Cipriano et al,[75] is a single center prospective observational study that followed a cohort of adults on oral anticoagulant therapy who sustained a blunt head injury associated with an initial ED GCS score of 13 to 15 regardless of LOC. Out of the 206 patients, 121 were on VKAs, and 85 were on NOACs. Because 183 of the 206 patients did not have an immediate ICH (initial negative CT), and 5 patients were lost to follow-up, the final analysis group consisted of 178 patients. Of the 178 patients with normal CT head exams, dispositions included: immediate discharge without 24-hour observation (16), admission for medical reasons unrelated to the ICH (12), or observation for 24 hours prior to discharge (150). Out of the 150 patients who were observed, only 3 (2% [95% CI 0 to 4.2%]) had neurologic deterioration, but they all had a second CT scan that was also negative for ICH. Ultimately, out of the 178 patients followed for 30 days, only 3 (1.7% [95% CI 0 to 3.6%]) had a positive CT scan for delayed ICH, with one death (0.6% [95% CI 0.5% to 1.7%]) and none required neurosurgical intervention. Although the study had some patients lost to follow-up, the only delayed hemorrhage of clinical importance was the one death in a patient that had already been admitted and experienced early neurologic deterioration. The other caveat noted in this study is that most patients were observed before discharge.

The second study including patients on NOACs and VKAs was a retrospective observational, cross-sectional study of single site enrolled adult patients with mTBI after a negative head CT scan at admission and repeated 24 hours later.[76] Late ICH occurred in 5 (4.5%) of the 111 patients on VKA and 4 (4%) of the 99 patients on NOACs. None were on antiplatelet agents, and none required surgery. They also included a control group of 475 nonanticoagulated patients with mTBI that were propensity score matched. Only one of those patients had a delayed ICH that required surgery for a subdural hematoma. Limitations of the study include that it was a retrospective experience at a single referral site with a low incidence of disease, thereby limiting the power of the study.

The last Class III study including NOACs and VKAs was a retrospective study of 178 patients on either NOACs or VKAs, as well as an additional 2 individuals on heparin.[77] Patients were observed prior to a repeat scan at least 12 hours after the

traumatic event. Although only 4 patients developed delayed ICHs, none died nor required neurosurgical intervention. In fact, during the 24-hour surveillance, several patients became agitated or confused from nontrauma-related issues, questioning the benefit of short-term hospitalization.

The largest collection of patients with mTBI, which included only those on NOACs, and no cases of VKAs, followed a protocol where after an initial CT scan, all patients were observed for 24 hours, with most having a repeat CT scan of the head.[78] Although observational and retrospective, this Class III multicenter trial found delayed ICH on CT in 14 of 916 patients (1.5%) rescanned; no patient died nor required neurosurgical intervention. An additional 424 patients were discharged without rescanning at physician discretion. All of those patients fared well, except one returned at 8 days with delayed ICH and subsequently died. In spite of the observational nature of the study and lack of mandatory repeat scanning, the incidence of delayed ICH, especially requiring neurosurgical intervention, is less than 1%. Therefore, in patients on NOACs who sustain mTBI, repeating a CT of the head after an initial second scan in well appearing patients has an extremely low yield for actionable findings.

There was an additional study that looked at the antiplatelet agent aspirin in patients 65 years and older with an isolated mild head injury and initial negative head CT.[79] All patients presented with a GCS score of 15 and were on low-dose aspirin prophylaxis, primarily for cardiovascular reasons. Out of 100 patients, 4 (4%) had delayed ICH, one of which required neurosurgical decompression, and another died. Because of these findings, the authors advocate longer observation and/or repeat imaging for elderly patients on low-dose aspirin. This may have implications for patients on dual anticoagulant and antiplatelet therapy, possibly necessitating greater caution.

Taken together, all these studies suffer from limited patient numbers along with potential selection biases. Overall, there was a paucity of patients on aspirin, with or without concomitant anticoagulants, in these studies, as well as limited numbers of patients on NOACs. Regardless, collectively these studies all support the notion that delayed ICH after blunt head trauma in neurologically intact patients on anticoagulant or antiplatelet therapy is rare (Table 3). Even if delayed ICH does occur, it tends not to be clinically significant and rarely necessitates neurosurgical intervention. The data suggest that patients on anticoagulants, or antiplatelet agents, with a normal initial head CT after blunt trauma and who are neurologically intact can be safely discharged. Most studies included a brief observation period, which is fortunate for research follow-up but ultimately unnecessary because of the lack of ICHs or neurologic deterioration during that additional period. Because of the potential for up to approximately 5% of these patients to develop delayed ICH, clear discharge instructions with return precautions are warranted. Most studies did not state if patients had their anticoagulant or antiplatelet medication withheld for the first few hours or days after the injury, which would require weighing the chance of repeat trauma (fall) or lack of good social support for home observation. However, with the low incidence of delayed ICH, there is not a strong argument for withholding these medications if the patients are not suspected to be supratherapeutic.

Summary

Anticoagulants (VKA and NOACs), and to some extent, antiplatelet agents, are associated with a higher risk of ICH after mild head trauma. Initial neuroimaging should be sufficient to exclude any clinically significant injuries in patients who appear otherwise neurologically intact at baseline. Based on the lack of increased delayed ICH, patients who are neurologically intact can be safely discharged without the need for repeat imaging or observation admission specifically for a head injury. The most concerning study that looked at aspirin was by Tauber et al,[79] suggesting that patients, especially those that are elderly on antiplatelet agents as opposed to anticoagulants and at high risk (LOC, amnesia, or GCS <15), may require some sort of observation if the choice is made to avoid repeat CT scanning. Another caveat is that these patients, especially those requiring ongoing physical or cognitive assistance, should have someone who can assist them with following discharge care instructions and/or helping provide a safe environment during their recovery.[80-82]

Future Research

Future research should focus on predictive factors for a higher risk of decompensation, along with the use of preinjury aspirin, for the few patients who do sustain delayed ICH after minor head injury. Other important questions include the assessment of potential patient subgroups that could benefit from holding medication or reversal of anticoagulation after trauma. Also, based on the low incidence of ICH on initial imaging, the research could focus on trying to reduce unnecessary CT scanning on the initial presentation for these patients. Quantification of the economic benefit of reduced repeat imaging and observation times is needed. Finally, the role of shared decisionmaking needs to be better evaluated.

1. In the adult ED patient diagnosed with mild traumatic brain injury or concussion, are there clinical decision tools or factors to identify patients requiring follow-up care for postconcussive syndrome or to identify patients with delayed sequelae after ED discharge?

Patient Management Recommendations

Level A recommendations.—None specified.

Level B recommendations.—None specified.

Level C recommendations.—Consider referral for patients with PCS and the following potential risk factors: female sex; previous preconcussive psychiatric history; GCS score <15; etiology of assault, acute intoxication; LOC; and preinjury psychological history such as anxiety/depression.

Do not use current diagnostic tools (including biomarkers) to reliably predict which patients are at risk for PCS.

Provide concussion-specific discharge instructions and selected outpatient referrals of patients at high risk for prolonged PCS (Consensus recommendation).

Resources (Appendix E6):

Discharge instructions and other materials for patients

- CDC Mild Traumatic Brain Injury and Concussion: Information for Adults https://www.cdc.gov/traumaticbraininjury/pdf/TBI_Patient_Instructions-a.pdf
- CDC educational materials for adults with mTBI: https://www.cdc.gov/traumaticbraininjury/mtbi_guideline.html

Potential Benefit of Implementing the Recommendations:

- The ability to predict and screen for patients at risk for PCS allows for early recognition and potential interventions such as referral to multidisciplinary concussion programs or modifications in post-visit behaviors.

Potential Harm of Implementing the Recommendations:

- Missing “clinically important findings” or associated injuries could lead to increased morbidity and mortality if a tool used is poorly proven.
- Misapplication of a tool for patients inappropriately identified as high-risk individuals could result in an excessive patient concern, anxiety, or unneeded interventions adding to costs.

Key words/phrases for literature searches: brain concussion, brain injury, closed head injury, commotio cerebri, concussion, head injury, head trauma, mild traumatic brain injury, mTBI, minor head injury, traumatic brain injury, clinical criteria, clinical decision, clinical decision instrument, clinical decision rule, clinical decision tool, clinical prediction instrument, clinical prediction rule, clinical prediction tool, decision support instrument, decision support techniques, cognitive aid, screening aid, screening tool, screening marker, screening criteria, biomarkers, postconcussive syndrome, delayed sequelae, emergency care, emergency department, and variations and combinations of the key words/phrases. Searches included January 2008 to search dates of January 17 and 22, 2020, March 9 and 11, 2020, and June 7 and 8, 2022.

Study Selection: Three hundred ninety-three articles were identified in the searches. Fifty-two articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, zero Class I studies, zero Class II studies, and 9 Class III studies were included for this critical question (Appendix E5).

Several studies examined multiple modalities to predict the likelihood of PCS, symptoms of PCS, and/or delayed sequelae after ED discharge. There would be a direct clinical benefit in the development of a single parsimonious bedside tool to risk stratify individuals in the ED for referral to neuropsychiatric clinical follow-up or the ability to predict potentially protracted symptoms and sequelae. Following mTBI, there is an ill-defined subset of patients whose prolonged course postinjury results in increased morbidity associated with decreased function at home: while driving, at work, and on the athletic field during sporting activities. However, studies of prolonged or long-term follow-up are limited, and resolution

of time courses for PCS have varying agreement.[83,84] Each compiled and assessed study attempts to delineate this subgroup, working with variable definitions and mixed tools, for the assessment and stratification of at-risk, postdischarge, mTBI patients presenting to the ED.

The 9 included studies are all Class III and vary in their definition of mTBI, making a singular generalizable recommendation on this patient group difficult. Included studies differ in their decision tools, the variable nature, and often unclear baseline neurocognitive status before the injury, inclusion criteria, duration of follow-up, and outcome definitions. The patient populations, as defined across the range of articles, are heterogeneous, along with variable study methodologies. A recurrent challenge in this research is in the definitions related to PCS. Criteria standards vary for PCS and therefore serve to alter adhered to definitions and nomenclature across various studies. In addition, the total symptom duration for the PCS is not well understood, resulting in variable periods of follow-up for all the included studies.

Of the included studies, many used a battery of tests conducted in the ED with an objective follow-up assessment tool to predict the risk of PCS based on patient characteristics and examination variables. Subbian et al[85] conducted a Class III prospective observational study of 66 ED patients with blunt head trauma and a clinical diagnosis of isolated mTBI made by the treating physician. In the ED, a battery of robotic-assisted tests was performed assessing proprioceptive, visuomotor, visuospatial, and executive functions on inception. Three weeks postinjury, patients were contacted to complete the Rivermead Post-Concussion Symptoms Questionnaire (RPQ) to assess for the presence of symptoms consistent with PCS. The RPQ consists of 16 symptoms associated with concussion that are assessed on a severity scale from 0 to 4 based on subjective symptoms at the time of administration.[86] Of the 66 enrolled, 42 completed both the initial assessment and the subsequent follow-up questionnaire, and ultimately 40 were included in the final analysis.[85] The area under the curve (AUC) for the entire battery of tests was 0.72 (95% CI 0.54 to 0.90), and the AUC for visuomotor and proprioceptive performance was 0.80 (95% CI 0.65 to 0.95) and 0.71 (95% CI 0.53 to 0.89), respectively.[85] Although this study was prospective with sound methodology, this was a labor-intensive single-centered study with a small number of patients enrolled and followed through to completion. The assessment battery required careful training and assessment with the use of a robotic-assisted device to ensure the initial and follow-up evaluations were performed adequately and in accordance with the study design. This would be challenging in standard ED settings to perform routinely, as most EDs are not equipped with such a testing apparatus.

Sheedy et al,[87] in a Class III prospective case series using a convenience sample from a single hospital in Australia, applied a similar methodology as in the study by Subbian et al.[85] Enrolled patients were assessed by a battery of tests at inception, including neuropsychological functioning, acute pain scores, and postural stability. In the subsequent telephone follow-up at 3-months postinjury, patients were assessed with the RPQ. Patients with neuropsychological defects, acute pain, or postural instability at the time of ED assessment were statistically associated with continued postconcussive symptoms at 3 months. Using a regression formula, a simple measure within the ED—immediate and

delayed recall of 5 words and a visual analog scale (VAS) score of acute headache—resulted in 80% sensitivity and 76% specificity for the prediction of postconcussive symptoms at 3 months. The study was small, single-centered, and based primarily on a convenience sample, so it is, therefore difficult to secondarily generalize to other ED populations.

Multiple other studies included in this review contained results derived from datamining reassessments of larger studies that were not initially designed to answer the primary question of concern for the emergency physician. In a Class III study by Booker et al,[88] data was used from a larger cohort to perform an observational study of mTBI in the ED using the SHEFfield Brain Injury After Trauma study to assess long-term disability using the RPQ and the Rivermead Post-Injury Follow-up Questionnaire. Of the 1,322 patients initially approached, 575 mTBI patients were analyzed and enrolled in the multivariate analysis. Female gender, previous psychiatric history, GCS score of <15, etiology of assault, and alcohol intoxication were associated with prolonged symptoms and worse outcomes in recovery.

A Class III trial by Kraus et al[89] performed a secondary analysis of a larger cohort using the RPQ and indicators of health services used and social disruptions at 3- and 6-months postdischarge of mTBI patients versus those without injury. The RPQ symptoms, health service utilization, and 5 indicators of social disruption or function were found to be higher in the mTBI group, indicating significant morbidity in this cohort. These problems may persist for at least 6 months and this study shows the need for not only continued medical care, but also the potential need for social assistance with things such as driving support, employment issues, and financial assistance during recovery.

In a Class III secondary analysis of a larger trial, Ponsford et al[90] (2019) assessed 343 individuals with mTBI out of a larger cohort of the NET trial involving 31 Australian EDs. Each enrolled participant completed the RPQ, the Anxiety scale of the Hospital Anxiety and Depression Scale (HADS), and the Quality of Life (QOL)—Short Form. Three or more postconcussive symptoms were reported in 18.7% of the participants, most frequently fatigue (17.2%) and forgetfulness (14.6%). Predictors of postconcussive symptoms included the following: preinjury psychological issues, LOC, and having no recall of receiving information regarding brain injury from the ED.

Before the aforementioned study, a Class III study using a secondary analysis of a larger study by Ponsford et al[91] (2012) compared 123 patients with mTBI with 100 trauma controls recruited and assessed in the ED and followed up at 1 week and 3 months postinjury. Multiple outcome measures were used which included a self-reported PCS measured by the ImPACT Post-Concussion Symptom Inventory (22 postconcussive symptoms) with a severity scale, a cognitive battery including 5 test modules (attention, verbal memory, visual memory, processing speed, reaction time); pre injury and postinjury SF-36; the Mini-International Neuropsychiatric Interview (MINI); a pain VAS; HADS; posttraumatic stress disorder Checklist Specific (PCLS); Revised Social Readjustment Rating Scale; and questions regarding narcotic use and litigation. Mild TBI predicted PCS at 1-week postinjury with the following: female gender, premorbid psychiatric history, and increased HADS anxiety, whereas at 3 months, anxiety and age were better predictors of PCS in

mTBI. Potentially focusing on patients with notable anxiety after mTBI or a history of anxiety might be helpful. Prospective interventions with outcomes assessing this and other factors would be of much interest.

In a 2017 Class III study, Scheenen et al[92] performed a subgroup analysis of a larger prospective cohort study. The 820 patients with mTBI were evaluated to compare patient characteristics and associations in those with persistent postconcussive symptoms at 2 weeks post-ED discharge. It was found that female gender and psychological factors such as coping styles, depression, anxiety, and posttraumatic stress disorder symptoms best predicted the identification of patients at risk for persistent symptoms.

In an alternative approach to this question, Su et al[93] conducted a Class III retrospective cohort study in patients with isolated mTBI from 4 institutions in China by assessing the plasma biomarker high-sensitivity C-reactive protein (hs-CRP) at baseline and 1, 2, 3 months after initial TBI. The endpoints included persistent PCS, persistent psychological problems (depression and anxiety), and persistent physiological problems (frequent headaches, nausea, insomnia, dizziness, and fatigue [at least one/week]), and persistent cognitive impairments. Elevated baseline hs-CRP was associated with a statistically significant increase in persistent PCS, (odds ratio [OR] 2.72; 95% CI 1.61 to 4.59), persistent psychological problems (OR 1.54; 95% CI 1.06 to 2.22), and persistent cognitive impairment (OR 1.69; 95% CI 1.14 to 2.51). However, elevated hs-CRP levels were not associated with persistent physiological problems (OR 1.33; 95% CI 0.91 to 1.96). The study had a small loss to follow-up (less than 10%) but is only based on 213 patients and has yet to be reproduced on a larger scale to be better externally validated.

The only imaging study included in this review was a Class III prospective cohort study by Lange et al[94] performed at a Level 1 Trauma Center in Canada. The study evaluated 108 ED patients recruited following mTBI or orthopedic injuries without brain injury (72 mTBI and 36 controls) and determined the ability of diffusion tensor imaging (DTI) magnetic resonance imaging (MRI) to predict PCS based on changes in the microstructural architecture of the white matter. Ultimately the study found no ability for the novel imaging modality to discern PCS in patients from those without.

Summary

Postconcussion syndrome is a poorly understood clinical entity that requires increased medical and social resources and is associated with significant morbidity, particularly concerning neurocognitive functioning. The ability to predict at-risk individuals in the ED after an inciting mTBI may have implications for postdischarge interventions. These might include, but are not limited to, postdischarge precautions regarding limitation in physical and cognitive activity, avoidance of activities that exacerbate symptoms, and referral to multidisciplinary teams for early interventions. However, most of these interventions still have unknown efficacy in reducing any potential negative impact on quality of life. In this review, 9 articles with Class III evidence were included assessing the predictive ability of ED screening modalities and diagnostic entities. Multiple studies assessed a battery of cognitive testing performed in the ED particularly concerning pain, visuospatial and visuomotor functioning at onset, and found an association between the performance in

these tests and subsequent development of PCS. These studies all suffer from the same methodological limitations as secondary analyses of larger cohorts and demonstrate only interesting associations without any ability to discern causation. In addition, the studies demonstrate an association between psychiatric comorbidity, particularly defined as anxiety and depression, and the development of persistent PCS. Formal diagnostic testing has shown limited promise with hs-CRP, although this was a small study and DTI MRI was not useful.

Future Research

Future research should include prospective randomized or observational cohort trials of ED patients presenting with and without mTBI to delineate the risk factors, duration, demographics, patient-oriented outcomes like quality of life, and natural progression of PCS among a diverse cohort of patients that present to an ED. In addition, it would be beneficial to determine the contribution of health disparities (eg, race, sex, socioeconomic factors) on the differences in the development and mitigation of PCS. A fruitful venture for research will include the evaluation of early neurocognitive interventions of patients at high risk for persistent PCS to determine if early recognition and treatment reduces morbidity along with ascertaining which, if any, of the appropriate neurocognitive battery of tests are expedient, reliable, accurate, and feasible to the ED clinician evaluating mTBI and screening for PCS. The role of newer imaging modalities such as transcranial ultrasound, positron emission tomography, or alternative MRI protocols must be investigated to determine if there are imaging predictors of PCS. The role of biomarkers in the identification of patients with PCS or their possible roles in assessing disease progression or healing must also be better investigated. Finally, additional studies are needed to better determine the necessity and impact of postdischarge precautions, the assessment and treatment of physical and cognitive symptoms with neurocognitive interventions, and the assessment of other efforts to decrease the incidence and symptomatology of PCS to improve long-term outcomes, especially among high-risk groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Clinical decision tools. (Used with permission).

	Canadian CT Head Rule[47]	New Orleans Criteria[48]	NEXUS Head CT[49]
High-risk features for predicting patients with CIBI	Any one of: • Failure to reach GCS score of 15 within 2 hours of injury • Suspected open skull fracture • Signs of basal skull fracture • Vomiting more than once • Age greater than 64 y	Any one of: • Headache • Vomiting • Age over 60 y • Drug or alcohol intoxication • Deficits in short-term memory • Physical evidence of trauma above the clavicles • Posttraumatic seizure	Any one of: • Evidence of skull fracture • Scalp hematoma • Neurologic deficit • Abnormal level of alertness • Abnormal behavior • Persistent vomiting • Coagulopathy • Age 65 y or greater
Exclusion Criteria	• Age <16 y • Blood thinners • Seizure after injury	• GCS score of <15 • Age ≥3 y	• GCS score of <15

CIBI, clinically important brain injury; *CT*, computed tomography; *GCS*, Glasgow Coma Scale.

Table 2.

Comparison studies.

Study	Patients enrolled	Patients with CIBI	Sensitivity for CIBI (95% CI)	Specificity for CIBI (95% CI)
Stiell et al[50] Class II	1,822	97 (5.3%)	CCHR: 100% (96% to 100%) NOC: 100% (96% to 100%)	CCHR: 50.6% (48% to 53%) NOC: 12.7% (11% to 14%)
Smits et al[51] Class II *different definition of CIBI	3,181	243 (7.6%)	CCHR: 84.5% (78.1% to 89.3%) NOC: 97.7% (92.1% to 99.4%)	CCHR: 38.9% (35.6% to 42.3%) NOC: 5.5% (2.6% to 8.7%)
Easter et al[25] Class II Systematic review	23,079	1,639 (7.1%)	CCHR: 99% (78% to 100%) NOC: 99% (90% to 100%)	CCHR: 40% (34% to 46%) NOC: 13% (8.1% to 22%)
Mower et al[49] Class II *comparison cohort, not overall NEXUS Head CT cohort	7,759	306 (3.94%)	CCHR: 98.4% (96.2% to 99.5%) NEXUS Head CT: 97.7% (95.3% to 99.1%)	CCHR: 12.3% (11.6% to 13.1%) NEXUS Head CT: 33.3% (32.3% to 34.4%)
Ro et al[52] Class III **data from original cohort outcomes compared with results of original articles **this study also has data for intersection cohort N=588 for all 3 tools	7,131	692 (9.7%)	CCHR: 79.2% (70.8% to 86.0%) NOC: 91.9% (84.7% to 96.5%) NEXUS Head CT: 88.7% (85.8% to 91.2%)	CCHR: 41.3% (37.3% to 45.5%) NOC: 22.4% (19% to 26.1%) NEXUS Head CT: 46.5% (44.5% to 48.5%)
Bouida et al[53] Class III	1,582	218 (13.8%)	CCHR: 95% (92% to 98%) NOC: 86% (81% to 91%)	CCHR: 65% (62% to 68%) NOC: 28% (26% to 30%)

CCHR, Canadian Head CT Rule; *CIBI*, clinically important brain injury; *CT*, computed tomography; *NOC*, New Orleans Criteria.

Table 3.

Comparison of incidence of delayed ICH and neurosurgical (NS) intervention after initial negative CT scan in all 8 studies.

Study	Blood Thinner	N	Delayed ICH (NS Intervention)	% Incidence (95% CI)
Nishijima et al[72]	Warfarin	687	4 (0)	0.6% (0.2% to1.5%)
	Clopidogrel	243	0 (0)	0% (0 to 1.5%)
Menditto et al[73]	Warfarin	87	5 (1)	5.6% (2.5% to 12.8%)
Kaen et al[74]	Warfarin or Heparin	137	2 (0)	1.4% (0.4% to 5.2%)
Cipriano et al[75]	Warfarin	99	1 (0)	1.0% (0.2% to 5.5%)
	NOACs	79	2 (0)	2.5% (0.7% to 8.8%)
Covino et al[76]	Warfarin	111	5 (0)	4.5% (1.9% to 10.1%)
	NOACs	99	4 (0)	4.0% (1.6% to 9.9%)
Duarte-Batista et al[77]	Warfarin	52	4 (0)	2.3% (0.9% to 5.7%)
	NOACs	124		2.3% (0.8% to 5.6%) *
Turcato et al[78]	NOACs	916	14 (0)	1.5% (0.9% to 2.6%)
Tauber et al[79]	Aspirin	100	4 (1)	4% (1.6% to 9.8%)

* Total 178 patients because 2 were on heparin