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Plasma D-dimer safely reduces unnecessary CT scans obtained in the evaluation of pediatric head trauma☆,☆☆,★

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ABSTRACT

Purpose: Serum D-dimer has been proposed as a biomarker to aid in the diagnosis of pediatric traumatic brain injury (TBI). We investigated the accuracy of D-dimer in predicting the absence of TBI and evaluated the degree by which D-dimer could limit unnecessary computed tomography scans of the head (CTH).
Methods: Retrospective review of patients with suspected TBI from 2011 to 2013 who underwent evaluation with CTH and quantitative D-dimer. D-dimer levels were compared among patients with clinically-important TBI (ciTBI), TBI, isolated skull fracture and no injury.
Results: Of the 663 patients evaluated for suspected TBI, ciTBI was identified in 116 (17.5%), TBI in 77 (11.6%), skull fracture in 61 (9.2%) and no head injury in 409 (61.7%). Patients with no head injury had significantly lower D-dimer values (1531 ± 1791 pg/μL) compared to those with skull fracture, TBI and ciTBI (2504 ± 1769, 2870 ± 1633 and 4059 ± 1287 pg/μL, respectively, $p < 0.005$). Using a D-dimer value <750 pg/μL as a negative screen, no ciTBIs would be missed and 209 CTHs avoided (39.7% of total).
Conclusion: Low plasma D-dimer predicts the absence of ciTBI for pediatric patient with suspected TBI. Incorporating D-dimer into current diagnostic algorithms may significantly limit the number of unnecessary CTHs performed in this population.
Type of study: Study of diagnostic test.
Level of evidence: I.

Over the last decade, the rate of traumatic brain injury (TBI)-related emergency room visits in children has doubled, currently reaching >600,000 visits annually [1,2]. Fortunately, the number of TBI-related hospital admissions has remained unchanged and TBI-related deaths continue to decline [1,3]. The discrepancy in TBI incidence data highlights the wide spectrum of disease severity in children. Mild TBI, such as concussion or isolated skull fracture, is not acutely life-threatening and treatment overwhelmingly consists of outpatient symptom management [4–6]. Conversely, severe TBI must promptly be treated to avoid severe neurologic damage and/or death. To date, severe TBI remains the leading cause of death and disability in children <18 years old [7].

Currently, computed tomography of the head (CTH) remains the most definitive test to assess the presence and severity of TBI. Concerns over the risks of ionizing radiation [8,9], rising costs [10,11] and potential sedation needs in young children have prompted many clinicians to use CTH judiciously for the assessment of TBI in pediatric patients after blunt head trauma. Several screening algorithms have been developed to help identify patients at very low risk for severe TBI that may safely forego CTH evaluation [12,13]. These screening algorithms, however, rely on complete and accurate history and subjective symptom qualification, which may be lacking or subject to interpretative variation. An objective metric may prove an important addition in the assessment of which pediatric patients warrant a CTH.

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D-dimer is a fibrin degradation product detectable in the blood within minutes of TBI [14]. In a small, single-institution study, quantitative D-dimer was shown to accurately predict the absence of intracranial hemorrhage on CTH in pediatric patients following blunt head trauma [15]. In this study, we aimed to: 1) validate the association of D-dimer and TBI in a larger cohort, 2) establish factors that may limit the accuracy of D-dimer and, 3) determine the degree by which D-dimer may aid in limiting unnecessary CTHs if used as a screening tool for patients with suspected TBI.

1. Methods

We performed a retrospective review of all patients, ≤18 years old, presenting to our facility with suspected TBI from 2011 to 2013 who underwent evaluation with both CTH and quantitative D-dimer. Abstracted data included demographics and presentation details, such as Glasgow Coma Scale (GCS), Injury Severity Score (ISS), mechanism of injury, time from injury to presentation and associated injuries. Patients with prior neurosurgical intervention, epilepsy or coagulation disorders were excluded.

Quantitative D-dimer was a standard laboratory test in our trauma head panel, which included a complete blood count, basic metabolic panel, prothrombin time, partial thromboplastin time and an international normalized ratio (INR). These labs were performed at the time of admission to the emergency room/trauma bay and prior to performing any procedures or obtaining any adjuvant imaging). The trauma head panel was evaluated by the providing practitioner and used as additional data to help determine injury severity. Clinical prediction rules were the primary determinant guiding practitioners in their decision to obtain cross-sectional imaging and D-dimer was considered as supplemental data.

For the standard trauma lab head panel, 0.8 mL of whole blood was collected in ethylenediamine tetra-acetic tubes. The plasma was separated and D-dimer was measured using an Alere Triage® D-Dimer antibody-based capillary detection system according to the manufacturer's instructions.

Head injuries were broadly classified into 4 groups according to attending radiologist final CT scan report and the patient's clinical course:

1) TBI: defined as intracranial hemorrhage or contusion, cerebral edema, traumatic infarction, diffuse axonal injury, shearing injury or depressed skull fracture by ≥ the bone thickness in accordance with previous definitions [13]
2) Clinically-important TBI (ciTBI): defined as TBI resulting in death, neurosurgical intervention, intubation >24 h or hospital admission >2 nights as previously defined by the Pediatric Emergency Care Applied Research Network (PECARN) [13]
3) Isolated skull fracture: defined as a nondisplaced skull fracture in the absence of any TBI findings
4) No head injury: defined as no injury identified on cranial cross-sectional imaging

Given that D-dimer is known to rapidly rise after injury and return to baseline levels after 24–36 h [16], we sought to determine if timing from injury to presentation would affect the accuracy of D-dimer in predicting the absence of TBI on CTH. To measure this, we generated receiver operator curves (ROC) with D-dimer values of those with and without ciTBI who presented within 6, 12 and 48 h after injury using GraphPad Prism 6. Area under the curve (AUC) was calculated and compared with the Mann–Whitney *U* test for significance.

Statistical significance was calculated with χ^2 for bivariate categorical variables, Student's *t* test for continuous variables and ANOVA for multivariate analysis.

2. Results

A total of 663 patients met inclusion criteria and were analyzed in the study (Fig. 1). ciTBI was identified in 116 patients (17.5%), TBI in 77 (11.6%), isolated skull fracture in 61 (9.2%) and no head injury in 409 (61.7%). The average age was 7.1 ± 5.0 years and approximately two

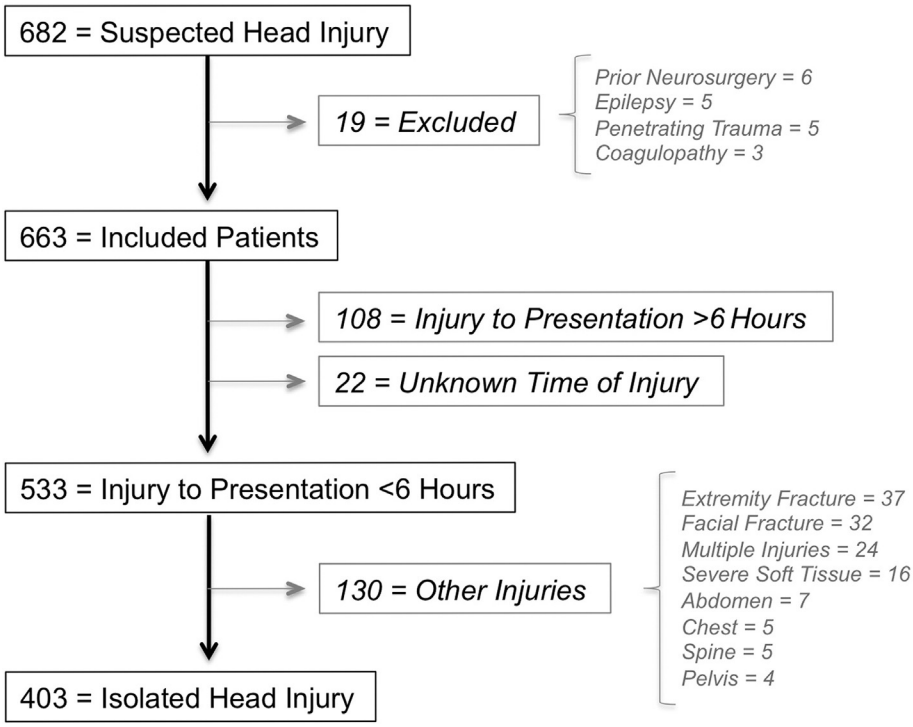

Fig. 1. Study population. 682 patients presented to our institution with suspected head injuries. 19 patients were excluded because of prior neurosurgical intervention ($n = 6$), history of epilepsy ($n = 5$), penetrating trauma ($n = 5$) and history of coagulopathy ($n = 3$). Of the 663 patient who met the study inclusion criteria, 108 presented >6 h from injury or had unknown times from injury and were excluded from subsequent D-dimer analysis. A subgroup analysis of D-dimer was performed on patients with isolated head injuries. 130 patients were excluded from the subgroup analysis because of the presence of other injuries.