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Original Contributions

EARLY BRAIN EDEMA IS A PREDICTOR OF IN-HOSPITAL MORTALITY IN TRAUMATIC BRAIN INJURY

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Abstract—Background: Identifying patients who may progress to a poor clinical outcome will encourage earlier appropriate therapeutic interventions. Brain edema may contribute to secondary injury in traumatic brain injury (TBI) and thus, may be a useful prognostic indicator. **Objective:** We determined whether the presence of brain edema on the initial computed tomography (CT) scan of TBI patients would predict poor in-hospital outcome. **Methods:** We performed a retrospective review of all trauma patients with nonpenetrating head trauma at a Level I Trauma Center. International Classification of Diseases, Ninth Revision codes indicated the presence of brain edema and we evaluated the validity of this pragmatic assessment quantitatively in a random subset of patients. In-hospital mortality was the primary outcome variable. Univariate analysis and logistic regression identified predictors of mortality in all TBI patients and those with mild TBI. **Results:** Over 7200 patients were included in the study, including 6225 with mild TBI. Measurements of gray and white matter CT density verified radiological assessments of brain edema. Patients with documented brain edema had a mortality rate over 10 times that of the entire study population. With logistic regression accounting for Injury Severity Score, Glasgow Coma Scale score, other CT findings, and clinical variables, brain edema predicted an

eightfold greater mortality rate in all patients (odds ratio 8.0, 95% confidence interval 4.6–14.0) and fivefold greater mortality rate for mild TBI patients (odds ratio 4.9, 95% confidence interval 2.0–11.7). **Conclusions:** Brain edema is an independent prognostic variable across all categories of TBI severity. By alerting emergency physicians to patients with poor predicted clinical outcomes, this finding will drive better resource allocation, earlier intervention, and reduced patient mortality. © 2017 Elsevier Inc. All rights reserved.

Keywords—logistic regression; mild traumatic brain injury; mortality; secondary insult

INTRODUCTION

Traumatic brain injury (TBI) is one of the leading causes of death and disability worldwide. TBI serious enough to result in hospitalization or death is projected to affect 10 million people annually, plus an estimated 57 million individuals previously hospitalized with two or more TBIs (1). With such a widespread and increasing prevalence, TBI represents a significant health concern in the United States and worldwide, extracting an enormous socioeconomic burden on both the patients affected and the medical community tasked to manage their care.

Current limitations for accurately predicting clinical outcome in TBI are a particular concern for emergency

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physicians when a poor clinical outcome occurs after mild TBI. Prognostic indices described in existing literature typically assess long-term outcome in patients with moderate to severe TBI (2,3). The currently available prognostic tools for long-term outcomes of mild TBI patients are only modestly accurate (4,5). Fewer data are available for predicting in-hospital outcomes for TBI patients, particularly those with mild TBI. The historical perception that patients with mild TBI are not at risk for poor outcomes makes those patients particularly vulnerable to lack of appropriate early therapeutic intervention.

For the last 40 years, the primary tool used in the clinical assessment and prognosis in patients with TBI has been the Glasgow Coma Scale (GCS), created in 1974 by Teasdale and Jennett (6,7). GCS scores are grouped to divide TBI into three major classifications: mild TBI (score of 13–15), moderate TBI (score of 9–13), and severe TBI (score of 3–8), with respective mortalities of 1.6%, 10.1%, and 84.7% (8). However, Thatcher et al. demonstrated that when based only on GCS score at admission, 23.5% of TBI patients predicted to have poor outcome experienced a good outcome, and 31.4% of those predicted to have good outcome had poor outcomes 1 year later (9). These findings suggest that despite the general correlation between a lower GCS score and poor clinical outcome, presenting GCS alone is unreliable for prognosis of individual TBI patients.

The Brain Trauma Foundation performed a meta-analysis of clinical parameters derived from selected randomized clinical trials to determine long-term outcome predictors in patients with moderate to severe TBI (2). Patient age and computed tomography (CT) imaging findings of compression, effacement, or absence of the basal cisterns, a midline shift, or the presence of traumatic subarachnoid hemorrhage all were associated with less favorable outcome (10,11). Similarly, the IMPACT study analyzed a broad range of variables as prognostic outcome indicators after TBI. These included vital signs, GCS components, demographic parameters, blood serum markers, the presence of secondary injuries, and the mechanism of injury (3). In those analyses, the most powerful prognostic independent variables were age, GCS motor score, pupil response, CT characteristics, and the presence of traumatic subarachnoid hemorrhage. More recent observational, retrospective, and randomized controlled studies have shown moderate predictive value for serum creatinine, osmolality, albumin, glucose, platelets, hemoglobin, and prothrombin time, as well as the more specific neuromarkers B-amyloid, S100B protein, and neuron-specific enolase (12–15).

Previous studies demonstrate that the presence of brain edema is a significant independent prognostic factor

in TBI (16,17). This suggests brain edema may lead to secondary brain damage, which disposes the patient to a less favorable outcome. The additional brain injury stemming from edema may result from local ischemia due to increased intracranial pressure, decreased microcirculatory flow, or neurovascular inflammation (18–21). In addition, the intracellular swelling that characterizes cytotoxic edema after TBI may increase production of reactive oxygen species, known to play an important role in the pathophysiology of TBI (22–25). In this study we aimed to determine whether the presence of brain edema in TBI patients predicts poor clinical outcome across the spectrum of TBI severity, with an emphasis on those with mild TBI. We focused the study to measure the likelihood of successful short-term hospital discharge as this outcome aligns with goals of the emergency and intensive care unit physician during management of the acute TBI patient. Thus, in-hospital mortality was the primary endpoint.

MATERIALS AND METHODS

Study Setting and Design

Institutional Review Boards at Miami Valley Hospital and Wright State University, Dayton, Ohio approved this study. We analyzed data retrospectively obtained from the Trauma Registry at Miami Valley Hospital in Dayton, Ohio, a Level I Trauma Center with an average of 94,000 emergency department (ED) visits per year during the study period. Trained trauma registrars abstracted data from hospital medical records with monthly validation of data reliability, accuracy, and interobserver reliability using a random selection of 5% of patient records. We included in the study records from all trauma patients presenting between May 1, 2005 and July 15, 2010 with documented nonpenetrating head injury. Because the initial GCS score was thought to be a strong predictor of outcome after TBI, patients who were paralyzed prior to GCS assessment were excluded from analysis.

Study Protocol

We queried the Miami Valley Hospital Trauma Registry electronic database to collect data from all patients with documented nonpenetrating head injury on initial presentation. This database is generated from electronic medical records by trauma registrars who are Certified Specialists in Trauma Registries or Registered Health Information Technicians. All selected patients received a head CT examination on initial presentation. The primary independent and outcome variables were the presence or absence of brain edema and discharge status

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