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Risk of severe and repetitive traumatic brain injury in persons with epilepsy: A population-based case–control study

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ABSTRACT

Background: While traumatic brain injury (TBI) can lead to epilepsy, individuals with preexisting epilepsy or seizure disorder (ESD), depending on the type of epilepsy and the degree of seizure control, may have a greater risk of TBI from seizure activity or medication side effects. The joint occurrence of ESD and TBI can complicate recovery as signs and symptoms of TBI may be mistaken for postictal effects. Those with ESD are predicted to experience more deleterious outcomes either because of having a more severe TBI or because of the cumulative effects of repetitive TBI.

Methods: We conducted a case–control study of all emergency department visits and hospital discharges for TBI from 1998 through 2011 in a statewide population. The severity of TBI, repetitive TBI, and other demographic and clinical characteristics were compared between persons with TBI with preexisting ESD (cases) and those without (controls). Significant differences in proportions were evaluated with confidence intervals. Logistic regression was used to examine the association of the independent variables with ESD.

Results: During the study period, 236,164 individuals sustained TBI, 5646 (2.4%) of which had preexisting ESD. After adjustment for demographic and clinical characteristics, cases were more likely to have sustained a severe TBI (OR = 1.49; 95% CI = 1.38–1.60) and have had repetitive TBI (OR = 1.54; 95% CI = 1.41–1.69).

Conclusion: The consequences of TBI may be greater in individuals with ESD owing to the potential for a more severe or repetitive TBI. Seizure control is paramount, and aggressive management of comorbid conditions among persons with ESD and increased awareness of the hazard of repetitive TBI is warranted. Furthermore, future studies are needed to examine the long-term outcomes of cases in comparison with controls to determine if the higher risk of severe or repetitive TBI translates into permanent deficits.

1. Introduction

Epilepsy is a well-documented sequel to traumatic brain injury (TBI) [1–10]. However, epilepsy can lead to TBI; the incidence of epilepsy-induced TBI depends on the type of epilepsy and the degree of seizure control [11–14]. Individuals with generalized tonic–clonic, atonic, and myoclonic seizures are at a greater risk of seizure-related injuries, as are those with uncontrolled (i.e., more frequent) seizures [11,12]. The majority of TBI sustained by individuals with epilepsy are mild to moderate in severity [15–18].

Annually, ~1.7 million Americans sustain TBI with 275,000 hospitalizations and 52,000 deaths [19,20]. Depending on the severity, TBI can lead to chronic and long-term disability; ~40% of TBI survivors develop functional deficits within a year [21,22]. One concern in TBI research has been the cumulative effect of repetitive TBI. Having sustained one TBI event increases the risk of subsequent TBI events [23–25]. Cumulative insult from repetitive TBI can lead to fatal second impact syndrome or chronic traumatic encephalopathy when the brain does not recover sufficiently before a subsequent TBI [26–29]. In the case of mild TBI, when acute signs and symptoms are subtle or easily ignored, recovery time may be insufficient.

Those individuals with epilepsy who sustain TBI may be at a greater risk of deleterious outcomes either because the TBI is more severe or because repetitive TBI leads to cumulative brain insult [13,30]. The cooccurrence of the two neurological conditions complicates the recovery trajectory as it may be difficult to distinguish postictal effects from the signs and symptoms of mild head injury. While the relationship between epilepsy and seizure-related injuries has been described, the potential for more severe TBI and repetitive TBI is not adequately documented. The primary purpose of this study was to identify risk characteristics in a population with TBI that discriminate persons with preexisting epilepsy (cases) from persons without preexisting epilepsy (controls). We hypothesized that cases have higher severity and are more likely to have repetitive TBI compared with controls.

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2. Methods

2.1. Study population

This case–control study used data collected by the South Carolina (SC) TBI Surveillance System to assess the relationship between epilepsy and severity and repetitiveness of TBI. South Carolina state law requires all nonfederal hospitals and emergency departments (EDs) to provide Uniform Billing (UB-04) data to the Division of Research and Statistics (DRS) of the SC Budget and Control Board. The SC TBI Surveillance System assembles data from ED visits, hospital discharges, and mortality for all individuals with a diagnosis of TBI. The SC TBI Surveillance System has conducted validation studies and determined that the discharge diagnoses reported via Uniform Billing are accurate representations of the diagnoses assigned by clinicians during the encounter. The earliest recorded TBI for each individual in the SC TBI Surveillance System is considered the index TBI. All individuals sustaining a TBI from 1998 to 2011 were eligible for the study.

2.2. Exclusions

Repeat admissions for the same TBI (defined as 2 TBI events in the same person less than 7 days apart) were excluded in order to avoid double counting of individuals who were transferred between hospitals or sought care at multiple hospitals for the same TBI. Based on data from chart reviews with the TBI surveillance data, we found that most repeat admissions within 7 days were transfers or encounters for the same injury due to persistent effects of the TBI. Also excluded were 98 individuals with evidence of late effects of TBI at the index TBI, 15,900 observations with missing or invalid external cause of injury codes, and 202 observations with missing or invalid date of birth, leaving an effective sample size of 236,164 individuals with TBI (Fig. 1).

2.3. Definitions

Traumatic brain injury was defined using the International Classification of Disease 9th revision, Clinical Modification (ICD-9-CM) diagnosis codes for fracture of the vault of the skull (800.x), fracture of the base of the skull (801.x), other skull fractures (803.x), multiple fractures involving skull (804.x), intracranial injury without skull fracture (850.x–854.x), and head injury, unspecified (959.01) [31–33]. Preexisting epilepsy or seizure disorder (ESD) was defined using the ICD-9-CM diagnosis codes for epilepsy (345.x) or seizure not otherwise specified (780.39) recorded at the time of the index TBI. International Classification of Disease 9th revision, Clinical Modification coding instructions specify that neither of these codes should be used for provoked seizures (resulting from a known cause) or seizures occurring within the first week after TBI as specific ICD-9-CM codes exist for those situations. Late effects of TBI were identified based on ICD-9-CM code 907.0. Demographic and clinical variables were ascertained at the time of the index TBI (Table 1). Traumatic brain injury severity was obtained by translating the ICD-9-CM codes into Abbreviated Injury Scale (AIS) scores using ICDMAP-90 software [34,35]. The AIS is an anatomic measure of injury severity that classifies over 2000 injuries according to the body region of injury (e.g., head, chest, and extremity), type of structure injured (e.g., nerve, vessel, and bone), location of injury within the body region (e.g., femur, tibia, and talus), and nature of injury (e.g., abrasion, burn, and crush). The AIS grades each injury according to its associated threat to life on an ordinal scale from one (minor) to six (unsurvivable) [34]. Severity scores assigned by the ICDMAP-90 software have very good reliability when compared with medical records 75% of the time [36]. Specifically, TBI cases with more than one diagnosis of TBI were assigned the diagnosis that yielded the highest AIS score for the head region. Severity of TBI was classified on the basis of the AIS score as “severe” with a score of 4–6, “moderate” with a score of 3, and “mild” with a score of 2. The software does not assign an AIS score of 1 for TBI. Repetitive TBI was defined as the occurrence of a subsequent TBI at least 7 days after the index TBI. Payer status included uninsured (self-pay), Medicare, Medicaid, other government programs, and commercial insurance. County of residence was classified as rural, urban, or out of state according to the federal Metropolitan Statistical Area designation [37,38]. Persons treated and released from the EDs and never admitted for the same event were defined as ED encounters. The cause of the index TBI (Appendix A) was classified as violence, fall, transportation-related, struck by/against, poisoning/adverse drug event, sport-related, environmental factors, and all other based on ICD-9-CM External Cause of Injury codes (E-codes). Concomitant injury was defined as the presence of injury in body regions other than the head by counting the remaining eight AIS body regions with assigned values of AIS of 2 or more.

The ICD-9-CM codes were further used to identify comorbid conditions (based on a modified Elixhauser Comorbidity Scale grouping that specifically excluded epilepsy and seizure disorders from the comorbidity categories) present at the time of the index TBI [39]. These comorbid

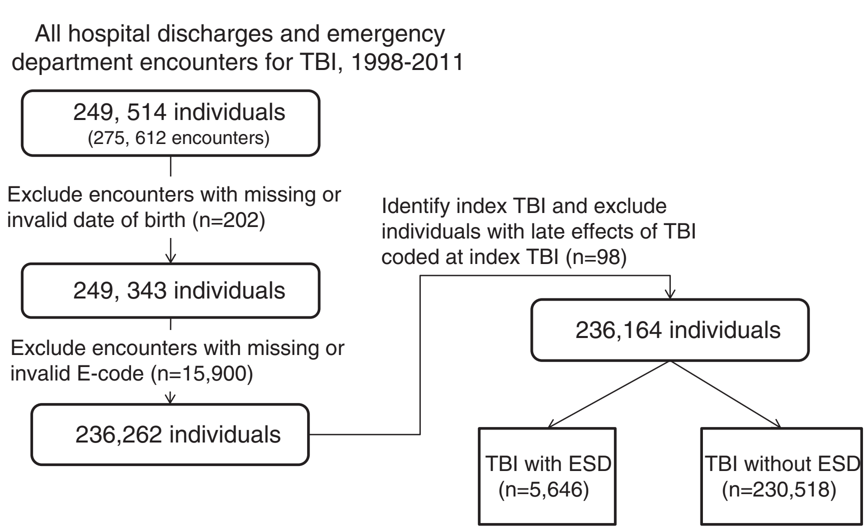

Fig. 1. Derivation of study cohort.