Traumatic Brain Injury as a Risk Factor for Stroke

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Abstract: *TBI is a potential unrecognized stroke risk factor as trauma to the head and neck may increase stroke risk through vascular dissection, (5) microvascular injury, or abnormal coagulation. The aim of the study is to evaluate whether traumatic brain injury may be a risk factor for subsequent ischemic stroke. This study used data of patients presented in Emergency Department in University Hospital Trauma of Tirana from 2012 to 1 December 2015. A total number of 1524 patients were presented in ED. The study cohort included 1524 total trauma subjects, 611 (40.1%) with TBI. The median duration of follow-up was 28 months (interquartile range 14–44), with a total of 18 (1.2%) ischemic strokes identified during this timeframe: 1.8% in the TBI group and 1.3% in the non-TBI trauma group. By having regular medical checkups and knowing the risk, one can focus on what can change and lower the risk of stroke.*

Keywords: stroke, traumatic brain injury, risk factors

1. Introduction

Understanding the epidemiology of TBI, its associated consequences, and the availability and effectiveness of rehabilitation interventions are crucial to improving the quality of life of those with a TBI. The most recent estimates of the burden of TBI suggest a decrease in TBI-related deaths, likely related to fewer motor vehicle-related TBIs (1). In contrast, TBI-related emergency department visits have increased, although this may be due in part to increased awareness of concussions among the general public. Nevertheless, the public health and economic burden of TBI is substantial and primary prevention remains the key public health strategy to reduce the burden of TBI (2). However, because preventing all TBIs is impractical, an imperative for those in public health practice, clinical practice, and research is to design and evaluate effective strategies to mitigate the health effects of TBI. Maintaining a comprehensive and coordinated system of rehabilitation interventions is critical to achieve this end. Substantial progress has been made in identifying effective rehabilitation interventions after a TBI, but considerable work remains to be done. Although previous research has demonstrated the broad effectiveness of a number of TBI rehabilitation services, additional research is needed before evidence-based guidelines can be developed. The heterogeneous nature of TBI injuries and TBI rehabilitation imposes challenges to identifying the specific conclusions that can be translated into recommendations for clinical use. These challenges must be addressed to improve the evidence base before embarking on guideline development. Ischemic stroke and traumatic brain injury (TBI) are common, (3) costly, and leading causes of severe disability in adults (4). In particular, both stroke and TBI are responsible for substantial disability in working-age adults-approximately 20% of strokes and more than 40% of TBI occur in adults younger than 65 years. Identifying novel risk factors has the potential to improve stroke prevention and outcomes. TBI is a potential unrecognized stroke risk factor as trauma to the head and neck may increase stroke risk through vascular dissection, (5) microvascular injury, or abnormal coagulation (6). The aim of the study is to evaluate whether traumatic brain injury may be a risk factor for subsequent ischemic stroke.

2. Material and Methods

This study used data of patients presented in Emergency Department in University Hospital Trauma of Tirana from 2012 to 1 December 2015. A total number of 1524 patients were presented in ED. A prospective cohort study was carried out and the patients were evaluated in three, six and 12 months. We compared TBI patients with non-TBI trauma patients (controls) while accounting for a variety of other variables that may confound the association between TBI and ischemic stroke. Standard protocol approvals, registrations, and patient consents. Adults 18 years or older were entered into our cohort if they survived either an inpatient admission or an emergency department visit for TBI or trauma at any time from 2011 to 2015. The non-TBI trauma group was composed of patients who had a fracture, excluding fractures of the head and neck, in any position on the discharge record. If a patient had both TBI and non-TBI trauma codes or separate visits with both TBI and non-TBI trauma, they were classified as TBI. Individuals with a visit with stroke before TBI or trauma were excluded from the cohort. Similarly, if a patient had multiple TBI or non-TBI trauma visits, they were entered into the cohort with their first visit. The primary outcome was any hospitalization with a discharge diagnosis of ischemic stroke. The primary analysis adjusted for known and possible stroke predictors including demographics, vascular risk factors, comorbidities, trauma severity, and trauma mechanism. Age was divided into quartiles because of the known nonlinear relationship between age and stroke. Vascular risk factors were defined using the single-level clinical classification system. Comorbidities were defined based on diagnosis codes listed on the discharge record. Demographics and baseline characteristics of the TBI and the non-TBI trauma groups were summarized using descriptive statistics. Subsequent stroke was compared by TBI status with Kaplan-Meier estimates and the log-rank test.

3. Results

The study cohort included 1524 total trauma subjects, 611 (40.1%) with TBI. The median duration of follow-up was 28 months (interquartile range 14–44), with a total of 18 (1.2%) ischemic strokes identified during this timeframe: 1.8% in the TBI group and 1.3% in the non-TBI trauma group. The patients with TBI were slightly younger than controls (mean age 50.5 vs 54.8 years), less likely to be female (44.2% vs 50.2%), and had a higher mean injury severity score (4.6 vs 4.1). Kaplan-Meier survival curves for survival free from ischemic stroke after TBI and non-TBI trauma are illustrated in the figure 1. The TBI group was more likely to be hospitalized for ischemic stroke than the non-TBI trauma group (log-rank test, $p < 0.01$). After adjustment for all covariates TBI was associated with ischemic stroke hospitalization (hazard ratio [HR]=1.41, 95% CI 1.28–1.59). This association only changed slightly when covariate groups were serially added: demographics only (HR=1.32, 95% CI 1.31–1.42), addition of vascular risk factors (HR=1.40, 95% CI 1.29–1.56), addition of comorbidities (HR 1.43, 95% CI 1.38–1.54), and addition of injury severity and trauma mechanism (HR=1.37, 95% CI 1.29–1.48).

We found a robust association between TBI visits and subsequent hospitalization for ischemic stroke, even after adjusting for a number of potential confounding variables. The magnitude of this association was substantial and was similar to the association between the leading stroke risk factor, hypertension and ischemic stroke. Given the higher prevalence of TBI in this trauma population, TBI was responsible for more ischemic stroke than hypertension. The TBI–ischemic stroke association persisted in secondary analyses after accounting for a variety of variables and assumptions that may alter the stroke-TBI relationship. Despite the robust association of TBI and ischemic stroke, the absolute ischemic stroke risk difference between TBI and non-TBI trauma patients in this low-risk cohort is small. Nonetheless, if further research definitively established TBI as a novel stroke risk factor, this would stimulate research to understand stroke pathophysiology after TBI and inform stroke prevention efforts in this young population with few vascular risk factors (7).

We found a similar association between ischemic stroke and TBI as in other studies (8). We also found that the ischemic stroke–TBI association was similarly unaffected by accounting for potential confounders such as trauma severity and trauma mechanism. Interestingly, we found that the difference in ischemic stroke risk between the TBI and non-TBI trauma groups was not just attributable to a high early risk in patients with TBI. The risk of stroke after TBI persisted even when excluding cases of stroke within 60 days of trauma. We also found that the TBI-stroke association was of considerably greater magnitude in the population younger than 50 years (OR 1.61) vs those 50 years and older (OR 1.33), suggesting that TBI may be uniquely important in younger patients. If the association between TBI and ischemic stroke is causal, a number of potential pathways may explain this relationship (9.10). Although other novel pathophysiologic pathways may have a role, it is also possible that patients with TBI may accrue conventional vascular risk factors at a faster rate than patients with non-TBI trauma because of a more sedentary lifestyle after TBI. This study has a number of important limitations (11,12). First, inaccuracy in administrative diagnosis coding may affect both stroke and TBI diagnoses. For example, sequelae of TBI could lead to a misdiagnosis of ischemic stroke based on neuroimaging studies. If this was the case, we would have expected a stronger association between TBI and ischemic stroke in any position on the record compared with the association between TBI and ischemic stroke as the principal diagnosis because principal position diagnoses generally have a higher specificity. However, we found a similar association between TBI and stroke regardless of the stroke's position on the claim, thus suggesting that the results are not attributable to diagnostic inaccuracy. Similarly, it is possible that patients presenting with focal neurologic symptoms after a seizure related to their TBI are misdiagnosed with stroke (13,14). Prospective cohort and/or population-based, cross-sectional studies are needed to confirm the association, explore potential mechanisms for the association between TBI and ischemic stroke, and carefully characterize the clinical features of both TBI and subsequent stroke, including both TBI and stroke mechanism, size, and location.

4. Conclusions

Knowing the risk factors for stroke is the first step in preventing a stroke. Some risk factors can be changed or treated, but others can't. By having regular medical checkups and knowing the risk, one can focus on what can change and lower the risk of stroke. Intervening factors that have been shown to influence outcomes must be considered when interpreting research examining the effectiveness of rehabilitation. Aside from the type and severity of a TBI, and the medical care received, recovery from TBI is influenced by factors including individual patient characteristics, social-environmental factors, and access to rehabilitation services.

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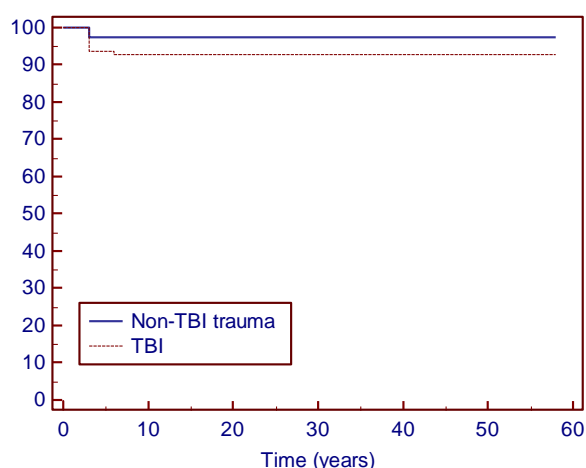
Figure 1: Stroke free survival in traumatic brain injury (TBI) and non-TBI trauma patients