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Short communication

Antithrombotic agents intake prior to injury does not affect outcome after a traumatic brain injury in hospitalized elderly patients

Jessica Julien [a,b], Ghusn Alsideiri [c], Judith Marcoux [d], Mohammed Hasen [e], José A. Correa [f], Mitra Feyz [g], Mohammed Maleki [d], Elaine de Guise [a,b,h,*]

[a] Department of Psychology, University of Montreal, Canada
[b] Centre de recherche interdisciplinaire en réadaptation du Montréal métropolitain (CRIR), Canada
[c] Montreal Neurological Institute & Hospital, McGill University, Canada
[d] Neurology and Neurosurgery Department, McGill University Health Centre, Canada
[e] University of Dammam, Saudi Arabia
[f] Department of Mathematics and Statistics, McGill University, Canada
[g] Traumatic Brain Injury Program, McGill University Health Centre, Canada
[h] Research Institute-McGill University Health Center, Canada

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ABSTRACT

Background: The purpose of this study is to investigate the effect of risk factors including International Normalized Ratio (INR) as well as the Partial Thromboplastin Time (PTT) scores on several outcomes, including hospital length of stay (LOS) and The Extended Glasgow Outcome Scale (GOSE) following TBI in the elderly population. *Methods*: Data were retrospectively collected on patients ($n = 982$) aged 65 and above who were admitted post TBI to the McGill University Health Centre-Montreal General Hospital from 2000 to 2011. Age, Injury Severity Score (ISS), Glasgow Coma Scale score (GCS), type of trauma (isolated TBI vs polytrauma including TBI), initial CT scan results according to the Marshall Classification and the INR and PTT scores and prescriptions of antiplatelet or anticoagulant agents (AP/AC) were collected. *Results*: Results also indicated that age, ISS and GSC score have an effect on the GOSE score. We also found that taking AC/AP has an effect on GOSE outcome, but that this effects depends on PTT, with lower odds of a worse outcome for those taking AC/AP agents as the PTT value goes up. However, this effect only becomes significant as the PTT value reaches 60 and above. *Conclusion*: Age and injury severity rather than antithrombotic agent intake are associated with adverse acute outcome such as GOSE in hospitalized elderly TBI patients.

1. Introduction

In 2011 in Canada, individuals aged 65 years old and over accounted for 15% of the population. By 2031, it is projected that they will account for one quarter of Canada's entire population [1]. The tendency is comparable to the United States where approximately one in five individual is expected to be 65 years or older in 2030 [2]. The elderly population is at greater risk of sustaining traumatic brain injury (TBI), with approximately 30% of people aged 65 years or older falling each year, and one fifth of the falls requiring medical care [3]. In Canada, falls are the leading cause of injury for individuals in this age bracket and also contribute to a significant burden on the health care system. Direct health care costs for falls are estimated at $2 billion annually [4]. In a previous study, falling was found to be the main cause of hospitalized TBI patients over 70 years old (52%), followed by vehicle accidents (32.7%) and work accidents (10.3%) [5].

Anticoagulants are frequently used in seniors [6] and with the aging of the population, clinicians will see more and more patients using anticoagulants. But this class of medication in the context of TBI may cause difficult dilemma for clinicians who have to balance the risk of intracranial bleed with the risk of thrombo-embolic complications. Benefits of chronic anticoagulation have been documented in some clinical population [7,8] but there is still a lack of consensus regarding the risks of this medication in TBI patients. There are some studies which suggested that mortality and morbidity in elderly patients taking anticoagulation medication is worse than without this pharmacological treatment before trauma [9,10]. A recent study has demonstrated that normalization of International Normalized Ratio (INR) was associated with

* Corresponding author at: Université de Montréal, Campus de Laval, 1700, rue Jacques-Tétreault, bureau 6230, Laval, QC H7N 0B6, Canada.
E-mail address: elaine.de.guise@umontreal.ca (E. de Guise).

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decreased mortality in isolated TBI patients with acute traumatic anticoagulopathy [11]. Moreover, therapeutic anticoagulation with warfarin, rather than warfarin use itself, is associated with adverse outcomes after TBI in elderly patients [12]. Previous studies have also shown that anticoagulation is associated with a higher risk of bleeding after TBI, a higher frequency of isolated head trauma, a higher risk of intracranial hemorrhage, and a higher mortality rate [13,14]. Being on anticoagulant also significantly increases the mortality of a traumatic intracranial bleed [15,16].

However, controversial outcomes were reported from studies in the anticoagulated TBI population [9,17–19]. In some studies, no increase in mortality is reported in anticoagulated trauma patients when controlling for the GCS and ISS [17–19]. The controversies may be caused by several factors not systematically controlled in all studies, such as the sample size, the age and the severity of the TBI or the absence of INR upon admission to confirm anticoagulation [18]. For example, a systematic review done recently has revealed that the incidence of delayed intracranial hemorrhage is low among patients on warfarin with minor head injuries [20]. They also suggested that differences in the risk of delayed intracranial hemorrhage were related to the difference among age groups [20]. Moreover, age differences among groups were present in studies that compared TBI patients using warfarin with nonusers [21] as well as differences in comorbidities [9,18] and mechanisms of injury [9,13]. These differences led Pieracci and colleagues [12] to suggest that all these variables account for a worse outcome instead of the anticoagulation effect per se.

In light of previous studies, larger studies are necessary to refine the evaluation of outcomes, especially with regards to the level of anticoagulation. In addition, using the patients' admission International Normalized Ratio (INR) as well as the Partial Thromboplastin Time (PTT) scores values to document anticoagulation is robust and innovative. The objective of this study is to investigate the effect of risk factors including INR and PTT scores on outcome following TBI. We hypothesized that higher levels of INR and PTT combined with the use of antithrombotic agents will be associated with longer length of stay in acute care setting and a worse outcome following acute care hospitalization, when controlling for age and TBI severity.

2. Methods

2.1. Participants

All patients aged 65 and above with a diagnosis of TBI admitted to the McGill University Health Centre – Montreal General Hospital (MUHC-MGH) between 2000 and 2011 were included in this study. They were identified using the Trauma Registry and the TBI program database. Patients not admitted or seen only at the emergency department were not included in this study. In this study, we were interested to the outcome of hospitalized patients. We performed a retrospective study of all charts (in-patient hospital charts) and excluded patients where (1) charts were missing or were incomplete after multiple attempts to locate them (2) no outcome information was collected. The institutional research ethics board approved this retrospective study.

2.2. Variables measured

2.2.1. Demographic characteristics

Gender and age were collected from the medical charts.

2.2.2. Medical and accident related characteristics

The Glasgow Coma Scale score (GCS) upon admission to the emergency room was used to determine TBI severity. A GCS score of 13–15 indicates a mild TBI, 9–12 a moderate TBI, while a score of 3–8 a severe TBI. Also, the Injury Severity Scores (ISS) was obtained from patient charts. The type of trauma was also collected in the medical charts (isolated TBI vs polytrauma including TBI which correspond to at least three injury sites) as well as the presence or absence of traumatic intracranial hemorrhage (TICH). Initial CT scan results were classified according to the Marshall Classification by a neurosurgeon blind to the testing procedure as part of the clinical evaluation. This classification includes (1) no visible intracranial pathology; (2) cisterns present; midline shift: 0–5 mm and/or lesion densities present; no high/mixed density lesions >25 ml; (3) cisterns compressed or absent; midline shift:0–5 mm; no high/mixed density lesions >25 ml; (4) midline shift >5 mm; no high/mixed density lesions >25 ml; (5) evacuated mass lesion (any lesion surgically evacuated) (6) non evacuated mass lesion (high/mixed density lesions >25 ml, not surgically evacuated [22]. Qualitative information regarding the type (intracerebral, subarachnoid and skull base fracture) and the sites of cerebral injuries were obtained: (1) basal-frontal, (2) prefrontal, (3) non-basal frontal (dorsolateral), (4) left and (5) right temporal, (6) occipital. The International Normalized Ratio (INR) as well as the Partial Thromboplastin Time (PTT) were collected as well as prescriptions of antiplatelet or anticoagulant agents (AP/AC).

2.2.3. Outcome variables

Length of stay (LOS).

LOS was defined as the number of days the patient remained hospitalized in the acute care setting from admission to discharge.

The Extended Glasgow Outcome Scale (GOSE).

The GOSE assesses global outcome [23]. For analysis, the values of this scale were collapse and reverse-coded from best to worse outcome into five categories, (1) scores of 7 or 8 correspond to good recovery referring to normal participation in social, vocational and physical life. (2) Scores of 5 or 6 indicate moderate disability describing the patient as independent but physically or cognitively disabled and requiring an altered physical, social, psychological or vocational environment for participation.(3) Patients with severe disabilities receive scores of 3 or 4 and are totally dependent in managing a normal or modified environment whereas (4) a score of 2 corresponds to a vegetative state reflecting total dependency with no awareness of the environment. (5) Patients who died receive a score of 1.The multidisciplinary team rated each patient on this scale at the time of his or her discharge.

2.3. Statistical analysis

Descriptive statistics are presented as means and standard deviations for variables in an interval scale when we had evidence that the values follow an approximately Normal distribution; otherwise medians and inter-quartile range (IQR) are reported. For categorical variables we report counts and percentages.

To investigate the marginal effect of the risk factors gender, age, ISS, GCS, TICH, Marshall Classification scores. INR, PTT and AP/AC agents variables on the GOSE scores, we used the proportional odds, or cumulative logits, regression model to take into account the ordinal nature of the coding for this outcome. Results for these analyses are reported as odds ratios (OR) and 95% confidence intervals (CI). To investigate the marginal effect of the same risk factors on hospital LOS we used regression models for competing risks. Considering death during hospitalization and other discharge destinations as mutually exclusive events, they can be treated as competing risks. These models allow to take into account information on those who die at the hospital and those who are eventually dis-

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