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SHORT COMMUNICATION

MISSED DIAGNOSIS OF TRAUMATIC BRAIN INJURY IN PATIENTS WITH TRAUMATIC SPINAL CORD INJURY

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Objective: **To determine the frequency of missed acute care traumatic brain injury diagnoses in patients with traumatic spinal cord injury, and to examine risk factors for missed traumatic brain injury diagnosis.**

Design: **Prospective magnetic resonance imaging and neuropsychological assessment plus retrospective medical record review, including computed tomography.**

Subjects: **Ninety-two adults with traumatic spinal cord injury recruited from a large, tertiary spinal cord injury program, initially referred from urban teaching hospitals with neurotrauma facilities.**

Methods: **Diagnosis of traumatic brain injury made with clinical neurological indices (i.e., Glasgow Coma Scale, post-traumatic amnesia, and loss of consciousness), neuroimaging (computed tomography and structural magnetic resonance imaging), and neuropsychological tests of attention and speed of processing, memory, and executive function; all measures were validated on a case-by-case basis to rule out confounds. Missed traumatic brain injury diagnoses were made via acute care medical record review and were corroborated by patient/family report where possible.**

Results: **The frequency of missed traumatic brain injury diagnoses in our sample was 58.5%. Missed traumatic brain injury diagnoses were more frequent in injuries sustained outside of a motor vehicle collision (MVC), with 75.0% of acute care traumatic brain injury diagnoses missed in non-MVC patients vs. 42.9% missed in MVC patients. Among patients with non-MVC injuries, a comparable percentage of missed traumatic brain injury diagnoses were observed in patients with cervical (79%) and sub-cervical injuries (80%).**

Conclusion: **In more than half of the traumatic spinal cord injury patients referred for in-patient rehabilitation, acute care diagnoses of traumatic brain injury were missed. A risk factor for missed diagnosis was an injury caused by a mechanism other than an MVC (e.g., falls, assaults), perhaps due to reduced expectations of traumatic brain injury in non-MVC patients. In our research study, we employed multiple assessments to aid diagnosis, which is particularly important for detecting the milder traumatic brain injuries often associated with spinal cord injury; unfortunately, limited resources may preclude a comprehensive diagnostic approach in clinical settings. Our findings point to the need to examine current acute care diagnostic protocols, and to increase vigilance in patients with traumatic injuries sustained outside of an MVC setting.**

Key words: traumatic brain injury; traumatic spinal cord injury; diagnosis.

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INTRODUCTION

Research over the past 30 years has shown that traumatic brain injury (TBI) and traumatic spinal cord injury (SCI) frequently co-occur (1). Recent studies have reported that up to 74% of SCI patients suffer a concomitant TBI during the same event, such as motor vehicle collision (MVC), fall, or sports-related insult (2). Nonetheless, it has been suggested that the clinical diagnosis of TBI in the context of SCI remains underdiagnosed (3). As the presence of a TBI can impede SCI recovery (4, 5) and because a TBI itself often warrants clinical care (6), missing acute care TBI diagnoses in SCI patients likely compromises patient outcomes (7).

There are limited empirical data on the frequency of missed TBI diagnoses in SCI patients. In the only study examining this topic, Tolonen et al. (2) prospectively examined a sample of 31 SCI patients referred to a national rehabilitation hospital in Helsinki, Finland. They found that of the 23 patients diagnosed with concomitant TBI and SCI, only 9 had received an acute care brain injury diagnosis, with 60.9% of TBI diagnoses therefore missed. This important finding has yet to be corroborated, which is particularly important given that patient management strategies for TBI vary considerably across institutions (6).

Anecdotally, our group has also suspected that TBI diagnoses may be missed in SCI patients. Historically, patients in our SCI clinical program have shown symptoms of TBI despite not being diagnosed with brain injury in acute care; this can result in deleterious consequences including reduced therapeutic gains made during rehabilitation (4). Therefore, the primary objective of our study was to determine the frequency of missed acute care TBI diagnoses in a large, prospectively collected sample of traumatic SCI patients ($n = 92$). A secondary objective was to assess whether any subgroups of SCI patients were at elevated risk of missed diagnosis.

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METHODS

The research ethics board at Toronto Rehab, now part of the University Health Network, approved this study; all procedures followed the guidelines established by this board.

Participants

The initial sample comprised 100 adults who were consecutively recruited from the inpatient Spinal Cord Rehabilitation Program at Toronto Rehab, University Health Network and met the inclusion and exclusion criteria of the study. Patients were accepted into the program from acute care hospitals throughout Ontario, with a majority of patients arriving from urban teaching hospitals with a neurotrauma unit. All patients were 2- to 6-months post-SCI. Subjects were included in the study if they had a clinically diagnosed traumatic SCI, were between 18 and 55 years of age, and had sufficient data to provide a definitive TBI diagnosis. Exclusion criteria included pre-morbid neurological and/or psychotic disorder, a known prior TBI, and an acquired language impairment that precluded neuropsychological testing. Of the 100 patients eligible for inclusion, 8 withdrew from the study, leaving a study sample of 92 participants

The demographics of the SCI sample were similar to those in other adult studies of SCI (8, 9), with a mean age of 35.8 years (standard deviation; SD 11.6), mean education of 12.9 years (SD 2.4) and a predominantly male (73.9%) population.

Materials

Clinical neurological indices of brain injury: Glasgow Coma Scale (GCS) score, presence of post-traumatic amnesia (PTA), and occurrence of loss of consciousness (LOC) were obtained retrospectively from medical records. All but 3 patients (or 3.3% of our sample) had information on at least one neurological index.

Neuroimaging: (*i*) Clinical computed tomography (CT) scan reports were retrospectively obtained from medical records. (*ii*) Magnetic resonance imaging (MRI) was prospectively collected for the study. The MRI protocol was tailored for detection of milder TBIs, including a T2* gradient echo sequence that is sensitive to microbleeds and a T2 FLAIR sequence sensitive to post-traumatic diffuse axonal injury. Scans were read by neuroradiologists with experience in TBI, including mild TBI.

Neuropsychological measures: The battery employed conventional clinical measures. All tests were free of upper extremity function requirements, except for the Wisconsin Card Sorting Test, which was adapted (Table I).

Procedures

Outcome measures were collected retrospectively and prospectively. Prospective measures, MRI and neuropsychological assessment, were undertaken between 2- and 6-months post-injury. These assessments were undertaken outside the acute care window, while participants were enrolled in the in-patient Spinal Cord Injury Program (which we note may have reduced our ability to detect some TBI cases due to symptom resolution). Retrospective medical record review was undertaken to collect GCS scores, presence of PTA and presence of LOC. Information on factors that could confound a TBI diagnosis was also collected, including intoxication, hypoxia, medication use at the time of injury, a history of substance abuse and learning disorder.

For the purposes of the study, we conservatively operationalized our diagnosis of TBI with a view to minimizing type I errors, both for incidence rate of TBI and for missed diagnoses. The necessary and sufficient conditions for a diagnosis of TBI were as follows: (*i*) two or more positive findings on the clinical neurological scales, with a GCS threshold of 13 or less, PTA of any duration and LOC of any duration; and/or (*ii*) a positive CT report for TBI with evidence of hemorrhage; and/or (*iii*) an explicit and unambiguous neuroradiologist diagnosis of TBI on MRI scan and/or (*iv*) on neuropsychological testing, a disparity between current neuropsychological function measures and estimated pre-morbid IQ; the minimum gap was 2 z-scores below pre-morbid IQ on at least one current measure or 1.5 z-scores below pre-morbid IQ on at least two measures of current functioning.

We sought to verify the validity of each diagnostic measure by identifying potential confounds that could give rise to a false-positive TBI diagnosis. For neurological indices, such confounds included intoxication, substance-use or hypoxia at the time of injury, or intubation. For neuropsychological assessment, pre-morbid and co-morbid factors included psychoactive medications (e.g., opioids), English as a second language, history of learning disorder or attention deficit hyperactivity disorder, and acquired or pre-morbid language disorders. All variables with confounds were excluded from analyses in a pairwise fashion. This approach allowed compromised variables to be removed without eliminating entire cases. For example, in the instance of an invalid GCS score, only the GCS variable would be removed from analyses while other measures would still be included for diagnosis. Patients that showed no evidence of TBI or who contained a combination of no evidence of TBI and confounded evidence (e.g., a GCS of 13 at the scene of the accident, but with high levels of alcohol; or loss of consciousness, but possible hypoxia) were classified as SCI with no TBI.

Finally, a case was classified as a "missed diagnosis" if the results of the current study revealed a definitive diagnosis of TBI, and if medical records from acute care either contained no diagnosis of TBI or contained an explicit statement indicating a patient had not sustained a TBI. Clinical corroboration was obtained for this classification, where possible, by each patient's overseeing neuropsychologist (CB). This corroboration with patients and/or family members provided a secondary check on the validity of our classifications, and there were no discrepancies between our classifications of missed TBI diagnosis and patient/family reports.

Data analysis

Statistical analyses were performed with SPSS version 20 (SPSS Inc., Chicago, IL), with significance set at $\alpha < 0.05$ for all analyses. The clinical characteristics of the full sample and TBI-positive patients were compared using chi-square analyses for categorical variables, and student t-tests for continuous variables. χ^2 analysis was used to compare the frequency of missed TBI diagnoses between sub-groups.

Table I. *List of neuropsychological measures*

Cognitive domain tested	Neuropsychological measure
Estimated pre-morbid intelligence quotient	Wechsler Test of Adult Reading (WTAR) (10)
Attention and speed of processing	Wechsler Adult Intelligence Scale 3rd edition (WAIS-III): Digit Span Forwards and Backwards (11); Symbol Digit Modalities Test (SDMT) (12)
Memory	Wechsler Memory Scale 3rd edition (WMS-III): Logical Memory Delayed Recall sub-test; Family pictures 2 (13)
Executive function	WAIS-III Similarities sub-test (11); Wisconsin Card Sorting Test (14)

RESULTS

Forty-one of 92 patients were classified as TBI-positive using our diagnostic criteria. Approximately one third of cases were classified as TBI-positive on the basis of acute care CT scan and approximately one third were classified with neurological indices. MRI diagnoses accounted for an additional 24% , with the rest diagnosed by neuropsychological testing.

Addressing the primary objective of the study, Table II illustrates that of the 41 patients identified as TBI-positive through our study diagnostic measures, nearly 60% did not receive an acute care diagnosis of TBI. χ^2 analyses revealed no significant differences or trends towards significance between the full sample and the TBI-positive patients with respect to sex, mechanism of injury, level of injury, American Spinal Injury Association (ASIA) Impairment Score (AIS), and frequency of CT scan completion; *t*-tests revealed no significant differences on age or education.

With regard to the second objective of the study, Table II illustrates the injury characteristics of TBI-positive patients whose TBI diagnoses were missed. With respect to mechanism of injury, although there were nearly equal numbers of TBI-positive patients with MVC and non-MVC injuries, there was over 1.5 times the number of missed diagnoses in non-MVC cases ($n=15$, or 37% of all TBI-positive patients) vs. MVC cases ($n=9$, or 22% of all TBI-positive patients). χ^2 analysis revealed a significant difference between these subgroups (χ^2 (1, $n=41$) $=4.361$; $p<0.05$; Cramer's V $=0.426$).

Table II illustrates that the percentage of the cervical injuries that were TBI-positive, but missed (60.9%), was broadly comparable to the percentage of TBI-positive sub-cervical injuries that were missed (53.3%), with no significant differences in frequency observed (χ^2 (1, $n=41$) $=0.212$; $p=0.646$; Cramer's V $=0.075$). Moreover, when the entire group of SCI patients with missed TBI-positive diagnoses was examined ($n=24$), there were more patients that had a missed diagnosis and a cervical injury (14/24 or 58%) than a sub-cervical injury (8/24 or 33%). These findings are surprising given that there is strong clinical suspicion of TBI in cervical injuries (3). However, a closer inspection of these data reveals that the finding is explained by mechanism of injury. There was a higher percentage of MVC injuries in the sub-cervical group (66.7%) as compared to the cervical group (39.1%). Indeed, when considering missed diagnoses with respect to level of injury, and in the context of mechanism of injury, Table III illustrates that sub-cervical patients showed marginally greater absolute percentages of missed diagnoses than cervical patients, although these differences did not reach statistical significance for MVC injuries (χ^2 (1, $n=19$) $=0.090$; $p=0.764$; Cramer's V $=0.090$) or non-MVC injuries (χ^2 (1, $n=19$) $=0.005$; $p=0.946$; Cramer's V $=0.015$).

With regard to other factors that potentially could have influenced missed diagnosis, severity of the SCI injury, as measured by AIS scores, did not have a significant effect (χ^2 (3, $n=41$) $=1.154$; $p=0.764$; Cramer's V $=0.168$). There was also no effect of whether or not CT scans were performed. We examined whether the groups differed in the number of acute care CT scans performed, surmising that fewer CT scans might have been performed in patients with a missed TBI diagnosis. Of the 24 patients for whom TBI diagnoses were missed, 16 patients (66.7%) underwent CT imaging. Of the 17 SCI patients for whom TBI diagnoses were caught, 14 patients (82.4%) underwent CT imaging. These differences in proportion between the groups were not significant (χ^2 (1, $n=41$) $=1.247$; $p=0.263$; Cramer's V $=0.185$). Lastly, we examined age. An independent samples *t*-test revealed no significant difference in age between TBI-positive patients with vs. without an acute care TBI diagnosis, nor a trend towards significance (t (39, $n=41$) $=0.099$; $p=0.922$; Cohen's $d=0.031$).

Table II. *Absolute numbers and percentages of missed acute-care diagnoses based on injury mechanism, level of SCI injury and SCI injury severity*

Group/sub-group	TBI-positive *n*	Missed diagnoses in acute care *n* (%)
All TBI-positive cases	41	24 (58.5)
Mechanism of injury		
Total MVC	21	9 (42.9)
Total non-MVC	20	15 (75.0)
Falls	15	12 (80.0)
Other[a]	5	3 (60.0)
Level of SCI		
Total cervical	23	14 (60.9)
Total sub-cervical	15	8 (53.3)
Thoracic	13	7 (53.8)
Lumbar	2	1 (50.0)
Multi-level[b]	3	2 (66.7)
AIS		
AIS A	17	9 (52.9)
AIS B	3	2 (66.7)
AIS C	8	4 (50)
AIS D	13	9 (69.2)

[a]Other comprises mechanisms such as sports-related insults and being struck against or by an object.
[b]Patients that had multi-level injuries were not also classified as cervical or sub-cervical patients.
SCI: traumatic spinal cord injuries; MVC: motor vehicle collision; AIS: American Spinal Injury Association Impairment Score.

Table III. *Number of patients injured during an MVC or other mechanism and the number and percentage of each with missed acute care TBI diagnoses at each level of injury*

	Total *n*	Total missed *n* (%)
MVC injuries	19	7 (36.8)
Cervical	9	3 (33)
Sub-cervical	10	4 (40)
Non-MVC injuries	19	15 (78.9)
Cervical	14	11 (79)
Sub-cervical	5	4 (80)
All injuries	41	24 (58.5)

Patients with multi-level injuries were not included in the above analysis.
MVC: motor vehicle collision; TBI: traumatic brain injuries.

DISCUSSION

Our study addressed the preliminary empirical evidence and the clinical concern that TBI diagnoses are missed in patients with traumatic SCI. The results validate that clinical concern is indeed warranted: 58.5% of TBI diagnoses in our Canadian sample were missed in acute care. Our findings are similar to those reported by Tolonen and colleagues (2), who found that 60.9% of acute care TBI diagnoses were missed in their smaller Finnish sample of 31 patients with SCI.

The absolute percentages in Table II indicate that TBI diagnosis was less frequently missed in MVC patients than in patients injured during other events, such as falls or sports-related insults. This may be because MVC-related injuries raise greater suspicion of TBI, given that the high impact velocities associated with an MVC contribute to concomitant bodily injuries, which may flag a more serious injury (15).

An explanation for missed diagnoses is the insensitivity of conventional TBI diagnostic tools to the milder brain injuries that are commonly sustained in patients with SCI (5). In our study, we used a combination of carefully validated diagnostic approaches to maximize sensitivity and specificity of our diagnosis, including an MRI acquisition protocol tailored to milder TBIs, with a sequence for detection of microbleeds (16). Given current limitations to diagnosis of milder brain injuries, use of multiple approaches to diagnosis is probably optimal, although perhaps unlikely where clinical resources are limited.

Davidoff et al. (17) reported several decades ago a dearth of clinical collection of PTA and LOC data. In the current study, many cases were missing this information as well as GCS scores. More systematic collection and recording of this information would likely improve sensitivity and specificity of TBI diagnosis, provided that validity of measurement is also confirmed in each case. However, we found that even when these data were collected, a formal diagnosis of TBI was still frequently absent from medical records and, to our knowledge, never conveyed directly to patients.

Our study had several methodological limitations. First, our prospective data collection (MRI and neuropsychological assessment) occurred in the sub-acute stages of injury. The results may, therefore, underestimate the incidence of TBI in our sample because of the opportunity for symptom resolution prior to data collection. Second, our sub-group analyses concerning mechanism, level and severity of injury were limited by power. Further studies with larger sample sizes in these sub-groups should be undertaken to confirm the findings. Third, we did not have information on injury severity for all TBI patients and could thus only speculate on the contribution of TBI injury severity to our findings. For example, the increased risk of missed diagnosis in non-MVC patients could be attributable to a higher number of milder TBIs, which are harder to diagnose. Fourth, and related, our information on prior history of TBI was based on self-report. It is possible that patients forgot or were unaware of prior TBIs in this sub-group, especially mild TBIs. If true, this may have increased type-I (or false-positive) errors for missed diagnosis in our sample. Finally, all of our classifications of patients into the TBI-negative group relied on null findings; this type of classification leaves our study vulnerable to type-II (or false negative) errors in our initial diagnostic classifications, though would not necessarily have affected the missed-diagnosis rate.

In conclusion, our findings suggest that missed acute care brain injury diagnoses in patients with traumatic SCI are prevalent. Type of injury – MVC – appears to increase the likelihood of detection of brain injury, perhaps due either to more severe TBIs being associated with MVCs that require acute care medical management or to the clinical expectation of brain injury in such events. Injury mechanism appears to be a better indicator of missed diagnosis than level of injury.

The present study emphasizes the importance of considering the presence of dual diagnosis in all SCI patients and using multiple diagnostic methods, ideally at more than one time-point, for assessing the presence of TBI. Where clinical diagnostic resources for TBI are limited, flagging at-risk patients for future follow-up may help to minimize missed diagnoses.

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