HHS Public Access

Author manuscript

J Head Trauma Rehabil. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:

J Head Trauma Rehabil. 2020 ; 35(5): E436–E440. doi:10.1097/HTR.0000000000000561.

Severity of Traumatic Brain Injury in Older Adults and Risk of Ischemic Stroke and Depression

Aparna Vadlamani, MPH[1], **Jennifer S. Albrecht, PhD**[1]

[1]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, United States

Abstract

Objective: Risk of ischemic stroke and depression is elevated among older adults following traumatic brain injury (TBI), yet little is known about how the severity of TBI influences risk. Thus, our objective was to assess the association between severity of the index TBI and risk of ischemic stroke and depression in a sample of older adults treated for TBI.

Design: Retrospective cohort study.

Setting: R Adams Cowley Shock Trauma Center

Participants: Adults aged ≥65 years treated for TBI between 2006-2010 who survived to hospital discharge and could be linked to their Medicare administrative claims data with continuous enrollment for at least 6 months pre-TBI and 12 months post-TBI.

Main Measures: First dates of ischemic stroke and depression available in Medicare claims were used to exclude individuals with a past history. Next, we separately assessed the association between TBI severity and time to first stroke and depression using Cox proportional hazards models.

Results: Among 132 patients without pre-existing history of stroke, high TBI severity was associated with increased risk of stroke compared to low TBI severity (adjusted hazard ratio (HR) 6.68, 95%CI 2.49-17.94). Among 163 patients without pre-existing history of depression, high TBI severity was not significantly associated with increased risk of depression compared to low TBI severity (adjusted HR 1.90, 95%CI 0.94-3.84).

Conclusion: In this group of older adults with TBI, higher TBI severity was associated with increased risk of ischemic stroke, but not depression. These results suggest that increased monitoring of older adults with moderate-severe TBI for stroke may be warranted.

Keywords

TBI; stroke; depression; older adults

Address correspondence to: Aparna Vadlamani, Department of Epidemiology and Public Health, University of Maryland School of Medicine, MSTF 360, 10 South Pine Street, Baltimore, MD 21201, United States, Telephone: 410-706-0064 avadlamani@som.umaryland.edu.

Background

Traumatic brain injury (TBI) is often perceived as a single event; however, evolving perspectives suggest that TBI may be a chronic disease process.[1] TBI triggers chronic inflammatory and immune responses that can result in persistent and lifelong health problems affecting the brain and other organ systems with non-reversible, permanent consequences.[1,2] Mechanisms of disease development following TBI include damage to the blood-brain barrier, neuronal loss, increased oxidative stress, and neuroendocrine dysfunction.[1,3]

Increased risk of chronic and acute disease following TBI among younger adults has been reported, however most studies have not been able to examine the role of TBI severity. For example, prevalence of psychiatric disorders is elevated following TBI with one of the most common disorders being depression.[1,4,5] While several studies have reported increased prevalence of depression following TBI, few have examined the impact of TBI severity and fewer still have been conducted among older adults. One study conducted among younger adults reported a higher frequency of major depressive disorder among patients with TBI compared to non-TBI controls, however, in this small sample (n=91), there were no significant differences in depression by TBI severity.[6] In contrast, a study conducted in a mixed age population using large administrative claims data reported slightly higher risk of psychiatric illness over the 6 months post-injury among individuals with moderate to severe TBI compared to those with mild TBI.[7]

Fewer studies have examined ischemic stroke following TBI, however increased risk has been reported. In a study conducted among Medicare beneficiaries hospitalized with TBI, we reported a 30% increase in the risk of ischemic stroke, however, we did not have information on TBI severity. A similar study conducted in a mixed age population with TBI reported increased risk of any stroke (included hemorrhagic stroke) in the 3 months, 1 year, and 5 years post TBI, but also lacked information on TBI severity.[8]

Although increased risk of ischemic stroke and depression following TBI is well-established, the impact of TBI severity on these outcomes is less clear, particularly in older adults. Understanding the effects of TBI severity on ischemic stroke and depression can better inform care and management for older adults who may require additional resources to optimize their recovery based on severity of the TBI, compared to their younger counterparts. Thus, we aimed to assess the association between TBI severity and onset of ischemic stroke and depression following TBI in older adults using data from a Level 1+ trauma center linked to Medicare administrative claims. We hypothesized that the risk of ischemic stroke and depression will be higher in older adults with higher index TBI severity compared to those who experience low index TBI severity.

Methods

Study Design and Data Source

This was a retrospective analysis of adults aged ≥65 years who were treated for TBI at the R Adams Cowley Shock Trauma Center (STC) between 2006-2010 and survived to hospital

discharge. The STC is an urban level 1+ trauma center treating 33% of all trauma cases in Maryland.[9] Injury and demographic characteristics came from the STC Registry (STR).

The sample was further limited to patients with a valid social security number. We attempted to link eligible patients to one of two Medicare administrative datasets obtained from the Centers for Medicare and Medicaid (CMS) Chronic Conditions Warehouse (CCW) database. The CCW contains Medicare files for fee-for-service institutional and non-institutional claims, enrollment and eligibility files, and costs.[10] Our two datasets comprised a 5% random sample for years 2006–2012 and 100% of Medicare beneficiaries hospitalized with TBI between 2006–2010. We required six months of continuous Medicare coverage pre-TBI and at least 12 months of continuous coverage post-TBI. Coverage included Medicare parts A and B, no C (Medicare Advantage). Criteria for a successful linkage were 1) a valid social security number, name, and date of birth and 2) hospitalization for TBI (100% sample) or appearance in the 5% random sample if the TBI did not result in admission to hospital. We worked with CMS to link the identifiable information from the STR to the encrypted beneficiary id number in the claims data.

Traumatic Brain Injury (TBI) Severity

All STC admissions during the study period with a TBI diagnosis were included in this study. The abbreviated injury scale (AIS) score is an anatomic measure of injury severity in six specified regions; head, face, spine, thorax, and upper and lower extremities.[11] In each of these anatomic regions, injury severity is scored from 1 to 6, with 1 indicating mild injury and 6 indicating a fatal injury. For the purpose of this study we were specifically interested in the abbreviated injury scale-head (AIS-H) score, which measures injury severity in the head and neck.[11] AIS scores were obtained from the STR. TBI was defined as an AIS-H >0, not including injury of the neck. TBI severity defined by the AIS-H and dichotomized as low (≤2) and high (>2) severity. The Glasgow Coma Scale (GCS) score is a measure of neurologic impairment and is based on eye, verbal, and motor response.[12] While the GCS is often used as a measure of TBI severity, in this study we used the AIS-H to measure injury severity as it has been shown to be a more accurate measure among older adults.[12]

Outcomes

Our primary outcomes were incident ischemic stroke (defined by ICD-9-CM codes 410.00-410.02, 410.10-410.12, 410.20-410.22, 410.30-410.32, 410.40-410.42, 410.50-410.52, 410.60-410.62, 410.70-410.72, 410.80-410.82, 410.90-410.92, 411.10, 411.1, 411.81, 411.89, 412, 413.0, 413.1, 413.9, 414.00-414.07, 414.12, 414.2-414.4, 414.8, and 414.9) and depression (defined by ICD-9-CM codes 296.20-296.26, 296.30-296.36, 296.51-296.56, 296.60-296.66, 296.89, 298.0, 300.4, 309.1, and 311) post-TBI. For the stroke cohort, we used the date of first diagnosis of stroke available in the CCW to exclude beneficiaries with a prior history of stroke and followed people forward from the TBI to date of first stroke. Beneficiaries were censored at data of first stroke or end of follow-up. We excluded beneficiaries with a stroke that occurred within two weeks of the index TBI to minimize the potential for reverse causality. We used a similar approach to create the depression cohort.

Statistical Analysis

We assessed differences in clinical and demographic characteristics between TBI severity groups using Pearson's chi-square for categorical variables and Student's t test for continuous variables. Additionally, we assessed differences in clinical and demographic characteristics for each outcome using Pearson's chi-square for categorical variables and Student's t test for continuous variables. We calculated unadjusted incidence rates and 95% confidence intervals (CI) for each outcome, stratified by TBI severity. Variables associated with each outcome at $p<0.05$ were included in our final regression models. The association between TBI severity and each outcome was estimated using Cox proportional hazards modeling, adjusting for variables associated with each outcome (separate models) and treating death as a competing risk. We tested the proportional hazards assumptions as well. We reported hazard ratios (HR) and 95% CI. All analyses were performed using SAS software version 9.4 (SAS Institute, Cary NC) and a p-value of <0.05 was considered statistically significant. This study was approved by the Institutional Review Board of the University of Maryland, Baltimore.

Results

We successfully linked 416 older adults treated for TBI at the STC between 2006–2012 to their Medicare administrative claims. After applying continuous enrollment eligibility criteria, 259 beneficiaries remained and formed our study sample (Table 1). The mean age of the study sample was 79.5 and the sample was predominantly female (58%) and white (80%). There was high prevalence of hypertension (91%), anemia (69%), and ischemic heart disease (64%).

There were 132 beneficiaries in our stroke cohort. Of these, 67 (51%) had low TBI severity and 65 (49%) had high TBI severity. Among those with low TBI severity, there were 5 (7%) stroke events. Among those with high TBI severity, there were 21 (32%) stroke events. Absolute risk of ischemic stroke was greater for those in the high TBI severity group compared to those in the low TBI severity group (25.1/100 person-years (95% CI 13.4-38.5) vs 3.2 /100 person-years (95% CI 1.3-7.7). Following adjustment for chronic kidney disease (CKD), high TBI severity was associated with increased risk of stroke compared to those with low TBI severity (HR 6.68, 95% CI 2.49-17.94). There were no violations of the proportional hazards assumptions.

There were 163 beneficiaries in our depression cohort. Of these 163 beneficiaries, 67 (41%) had low TBI severity and 96 (59%) had high TBI severity. Among those with low TBI severity, there were 11 (16%) depression events. Among those with high TBI severity, there were 28 (29%) depression events. Absolute risk of depression was slightly greater for those in the high TBI severity group compared to those in the low TBI severity group (1.9/100 person years (95% CI 1.6-2.3) vs 1.4/100 person-years (95% CI 1.1-1.8). Following adjustment for Alzheimer's disease and related dementias (ADRD) and CKD, high TBI severity was not significantly associated with increased risk of depression compared to low TBI severity (HR 1.90, 95% CI 0.94-3.84). There were no violations of the proportional hazards assumptions.

Discussion

In this study of older adults treated for TBI at a trauma center, higher TBI severity was associated with increased risk of stroke, but not depression. These findings add to the literature on the impact of TBI severity on risk of outcomes among older adults and can inform prevention and treatment efforts.

Secondary effects of TBI such as reduction of cerebral blood flow can lead to ischemia, with level of risk correlated with severity of TBI.[13] This is consistent with reports of increased risk of acute ischemic stroke, but less is known about longer-term implications or whether the same mechanism is involved.[14] One study reported that acute respiratory distress syndrome during the initial TBI episode was associated with significantly increased risk of ischemic stroke during a five-year follow-up, suggesting a possible pathway.[15] Additionally, there is a high prevalence of hypertension and ischemic heart disease in this cohort of older adults, both of which facilitate atherosclerotic events that can lead to increased risk of stroke.[16] This is seen more so in older adults due to increased exposure time to age-related changes in vascular function, such as large artery stiffness, although neither ischemic heart disease or hypertension were significantly associated with stroke here.[16] This study provides evidence that anatomic TBI severity, as measured by AIS score, is associated with long-term risk of ischemic stroke among older adults.

Although TBI is a well-established risk factor for depression, prior history of neuropsychiatric disorders seems to be the strongest risk factor, with TBI severity playing little or no role.[7,17,18] Results from this study are consistent with previous literature suggesting no association between TBI severity and depression risk and extend results to older adults.[6,7,19–21]

To the authors knowledge, this study represents the first linkage between trauma registry records and Medicare data, linking detailed injury-level information with long-term follow up available in claims data. Linkages such as this could be used in future work to elucidate associations between baseline injury characteristics and long-term outcomes, including economic outcomes.

Nonetheless, there are limitations to note when interpreting our findings. Our linkage was limited to a small number of individuals treated at a single urban trauma center who were either present in the 100% sample of hospitalized beneficiaries or were part of the 5% random sample and met our coverage criteria. Consequently, individuals with Medicare advantage, commercial insurance, the uninsured, and those who did not have continuous coverage are not represented. The impact these exclusions would have on results is hard to predict but suggests that results should be validated in other cohorts. Another limitation is the possible inclusion of beneficiaries who had depression but were not diagnosed during our six-month pre-TBI period. However, given that pre-existing depression is a risk factor for post-TBI depression and we saw no effect of severity, any missed cases were likely equally distributed between the low and high severity groups.

In conclusion, among older adults with TBI, an AIS-H score of 3 or greater was associated with significantly increased risk of ischemic stroke during a minimum one-year follow-up.

These results suggest that increased monitoring of these individuals for stroke may be warranted.

Acknowledgments

Conflicts of Interest and Sources of Funding:

The authors have no conflicts of interest. Ms. Vadlamani is supported by the National Institutes of Health grant T32AG000262 (Magaziner, PI). Dr. Albrecht was supported by AHRQ grant K01HS024560.

References

1. Masel BE, DeWitt DS. Traumatic brain injury: a disease process, not an event. Journal of neurotrauma 2010;27(8):1529–1540. [PubMed: 20504161]
2. Corrigan JD, Hammond FM. Traumatic brain injury as a chronic health condition. Archives of Physical Medicine and Rehabilitation. 2013;94(6):1199–1201. [PubMed: 23402722]
3. Povlishock JT, Katz DI. Update of neuropathology and neurological recovery after traumatic brain injury. The Journal of head trauma rehabilitation. 2005;20(1):76–94. [PubMed: 15668572]
4. Holsinger T, Steffens DC, Phillips C, et al. Head injury in early adulthood and the lifetime risk of depression. Archives of general psychiatry 2002;59(1):17–22. [PubMed: 11779276]
5. Kreutzer JS, Seel RT, Gourley E. The prevalence and symptom rates of depression after traumatic brain injury: a comprehensive examination. Brain Inj. 2001;15(7):563–576. [PubMed: 11429086]
6. Jorge RE, Robinson RG, Moser D, Tateno A, Crespo-Facorro B, Arndt S. Major depression following traumatic brain injury. Archives of general psychiatry. 2004;61(1):42–50. [PubMed: 14706943]
7. Fann JR, Burington B, Leonetti A, Jaffe K, Katon WJ, Thompson RS. Psychiatric illness following traumatic brain injury in an adult health maintenance organization population. Archives of general psychiatry. 2004;61(1):53–61. [PubMed: 14706944]
8. Chen YH, Kang JH, Lin HC. Patients with traumatic brain injury: population-based study suggests increased risk of stroke. Stroke. 2011;42(10):2733–2739. [PubMed: 21799162]
9. MIEMSS Annual Report 2015–2016. In. Vol 20172016.
10. (CMS) CfMaMS. About chronic conditions data Warehouse. https://www.ccwdata.org/web/guest/about-ccw. Accessed November 1, 2018.
11. Rating the severity of tissue damage. I. The abbreviated scale. Jama. 1971;215(2):277–280. [PubMed: 5107365]
12. Kehoe A, Rennie S, Smith JE. Glasgow Coma Scale is unreliable for the prediction of severe head injury in elderly trauma patients. Emergency medicine journal : EMJ 2015;32(8):613–615. [PubMed: 25280479]
13. Bramlett HM, Dietrich WD. Pathophysiology of cerebral ischemia and brain trauma: similarities and differences. Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism. 2004;24(2):133–150.
14. Kowalski RG, Haarbauer-Krupa JK, Bell JM, et al. Acute Ischemic Stroke After Moderate to Severe Traumatic Brain Injury: Incidence and Impact on Outcome. Stroke. 2017;48(7):1802–1809. [PubMed: 28611087]
15. Chen GS, Liao KH, Bien MY, Peng GS, Wang JY. Increased Risk of Post-Trauma Stroke after Traumatic Brain Injury-Induced Acute Respiratory Distress Syndrome. Journal of neurotrauma. 2016;33(13):1263–1269. [PubMed: 26426583]
16. Miller AP, Navar AM, Roubin GS, Oparil S. Cardiovascular care for older adults: hypertension and stroke in the older adult. Journal of geriatric cardiology : JGC. 2016;13(5):373–379. [PubMed: 27594862]
17. Albrecht JS, Barbour L, Abariga SA, Rao V, Perfetto EM. Risk of Depression after Traumatic Brain Injury in a Large National Sample. Journal of neurotrauma. 2019;36(2):300–307. [PubMed: 29808770]

18. Albrecht JS, Kiptanui Z, Tsang Y, et al. Depression among older adults after traumatic brain injury: a national analysis. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry. 2015;23(6):607–614. [PubMed: 25154547]

19. Jorge RE, Robinson RG, Starkstein SE, Arndt SV. Depression and anxiety following traumatic brain injury. The Journal of neuropsychiatry and clinical neurosciences. 1993;5(4):369–374. [PubMed: 8286933]

20. Rogers JM, Read CA. Psychiatric comorbidity following traumatic brain injury. Brain injury. 2007;21(13-14):1321–1333. [PubMed: 18066935]

21. Whelan-Goodinson R, Ponsford J, Johnston L, Grant F. Psychiatric disorders following traumatic brain injury: their nature and frequency. The Journal of head trauma rehabilitation. 2009;24(5):324–332. [PubMed: 19858966]

Table 1.

Baseline characteristics of adults ≥65 years and treated for traumatic brain injury (TBI) at the R Adams Cowley Shock Trauma Center (2006-2012) by TBI severity[1], N=259

	Total (N=259)	Low TBI Severity (N=102)	High TBI Severity (N=157)	p-value[2]
Age (mean, SD)	79.5 (7.8)	79.1 (8.0)	79.7 (7.7)	<0.001
Sex (n,%)				
Female	150 (58.0)	59 (57.8)	91 (58.0)	
Male	109 (42.0)	43 (42.2)	66 (42.0)	0.98
Race (n,%)				
White	208 (80.3)	86 (84.3)	122 (77.7)	
Black	33 (12.7)	10 (9.8)	23 (14.7)	
Other	18 (7.0)	6 (5.9)	12 (7.6)	0.42
Glasgow Coma Scale score				
≥13	209 (80.7)	91 (89.2)	118 (75.2)	
9-12	33 (12.7)	8 (7.8)	25 (15.9)	
≤8	17 (6.6)	3 (2.9)	14 (8.9)	0.02
Deaths (n,%)	24 (9.3)	2 (2.0)	22 (14.0)	0.001
Comorbidities (n,%)				
Acute myocardial infarction (AMI)	24 (9.3)	6 (5.9)	18 (11.5)	0.13
Alzheimer's disease and related dementias	78 (30.1)	25 (24.5)	53 (33.8)	0.11
Anemia	179 (69.1)	65 (63.7)	114 (72.6)	0.13
Chronic kidney disease (CKD)	69 (26.6)	29 (28.4)	40 (25.5)	0.60
Congestive heart failure	107 (41.3)	44 (43.1)	63 (40.1)	0.63
Diabetes	98 (37.8)	35 (34.3)	63 (40.1)	0.35
Depression	89 (34.4)	33 (32.3)	56 (35.7)	0.58
Hypertension	235 (90.7)	88 (86.3)	147 (93.6)	0.05
Ischemic heart disease	166 (64.1)	62 (60.8)	104 (66.2)	0.37
Stroke	81 (31.5)	32 (31.4)	49 (31.6)	0.97

[1] TBI severity defined as low (AIS-H <3) and high (AIS-H ≥

[2] p-values were calculated using Pearson's chi-square test for categorical variables and Student's t test for continuous variables, significant at p<0.05

Table 2.

Number of events and person-time at risk in ischemic stroke and depression cohorts by traumatic brain injury (TBI) severity among adults aged ≥ 65 years and treated at the R Adams Cowley Shock Trauma Center (2006-2012)

	Count of Events	Time to Event in days (Median, IQR)
Ischemic stroke (N=132)		
Low TBI severity	5	899 (629-1080)
High TBI severity	21	386 (54-706)
Depression (N=163)		
Low TBI severity	11	761 (386-994)
High TBI severity	28	453 (95-819)

Table 3.

Unadjusted and adjusted hazard ratios (95% confidence intervals) of association between traumatic brain injury (TBI) severity and risk of ischemic stroke and depression among adults aged ≥ 65 years and treated at the R Adams Cowley Shock Trauma Center (2006-2012)

	Unadjusted	Adjusted
Ischemic stroke (N=132)		
Low TBI severity	Reference	Reference
High TBI severity	6.59 (2.47-17.62)	6.68 (2.49-17.94) *
Depression (N=163)		
Low TBI severity	Reference	Reference
High TBI severity	2.10 (1.04-2.03)	1.90 (0.94-3.84) **

* Adjusted for chronic kidney disease

** Adjusted for chronic kidney disease and Alzheimer's disease and related dementias