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ORIGINAL RESEARCH

Prevalence of Cardiovascular Conditions After Traumatic Brain Injury: A Comparison Between the Traumatic Brain Injury Model Systems and the National Health and Nutrition Examination Survey

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BACKGROUND: The purpose of this study is to compare the prevalence of self-reported cardiovascular conditions among individuals with moderate to severe traumatic brain injury (TBI) to a propensity-matched control cohort.

METHODS AND RESULTS: A cross-sectional study described self-reported cardiovascular conditions (hypertension, congestive heart failure [CHF], myocardial infarction [MI], and stroke) from participants who completed interviews between January 2015 and March 2020 in 2 harmonized large cohort studies, the TBI Model Systems and the National Health and Nutrition Examination Survey. Mixed-effect logistic regression models were used to compare the prevalence of cardiovascular conditions after 1:1 propensity-score matching based on age, sex, race, ethnicity, body mass index, education level, and smoking status. The final sample was 4690 matched pairs. Individuals with TBI were more likely to report hypertension (odds ratio [OR], 1.18 [95% CI, 1.08–1.28]) and stroke (OR, 1.70 [95% CI, 1.56–1.98]) but less likely to report CHF (OR, 0.81 [95% CI, 0.67–0.99]) or MI (OR, 0.66 [95% CI, 0.55–0.79]). There was no difference in rate of CHF or MI for those ≤50 years old; however, rates of CHF and MI were lower in the TBI group for individuals >50 years old. Over 65% of individuals who died before the first follow-up interview at 1 year post-TBI were >50 years old, and those >50 years old were more likely to die of heart disease than those ≤50 years old (17.6% versus 8.6%).

CONCLUSIONS: Individuals with moderate to severe TBI had an increased rate of self-reported hypertension and stroke but lower rate of MI and CHF than uninjured adults, which may be due to survival bias.

Key Words: cardiovascular disease ■ congestive heart failure ■ hypertension ■ stroke ■ traumatic brain injury

Cardiovascular disease (CVD) is a leading cause of mortality and health care expenditure in the United States, accounting for nearly 1 million deaths and over $407 billion in direct costs annually.[1] Despite an overall decline in cardiovascular mortality in the past 50 years, significant health care disparities exist in cardiovascular health and outcomes.[2–5] Individuals living with chronic disability, particularly those with disability due to traumatic brain injury (TBI), may be at particularly increased risk for health care disparities. On September 26, 2023, the National Institutes of Health officially recognized individuals with disability as a

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CLINICAL PERSPECTIVE

What Is New?

- Individuals with moderate to severe traumatic brain injury are more likely to report diagnosis of hypertension and stroke compared with the general population.
- Unexpectedly, in those >50 years old, self-reported rate of myocardial infarction and congestive heart failure is lower in those with traumatic brain injury, which may be due survival bias.

What Are the Clinical Implications?

- Individuals living with chronic moderate to severe traumatic brain injury should be screened for common cardiovascular conditions regardless of age to enhance long-term health and functioning.

Nonstandard Abbreviations and Acronyms

NHANES	National Health and Nutritional Examination Survey
TBIMS	Traumatic Brain Injury Model Systems

population with health disparities[6] based on the report of the National Advisory Council on Minority Health and Health Disparities Working Group on Persons Living with Disabilities.[7] This number likely underestimates the burden of TBI as many individuals with mild injuries may not seek care in the emergency department. TBI is increasingly recognized as a chronic health condition rather than a single injury event as many individuals experience some degree of long-term changes in physical, cognitive, or emotional function.[8–13] In 2022, the National Academies of Science, Engineering, and Medicine issued "Traumatic Brain Injury: A Roadmap for Accelerating Progress" that highlighted the need for a comprehensive care model due to insufficient access to high-quality health care and fragmentation of care from the acute to chronic phases.[14]

Increased rates of CVD among patients with TBI has been demonstrated in large studies across all TBI severity levels.[15–18] Using administrative data from the Veterans Health Administration and Department of Defense, a cohort study of more than 1.5 million post-9/11 military and veterans found that individuals with TBI were more likely to develop CVD than those without TBI, with highest rates of CVD among those with greater TBI severity.[18] Similarly, analysis of a large institutional registry at a civilian health system identified prior TBI of any severity as risk factor for coronary artery disease and hypertension as well as markers of poor cardiovascular health, such as hyperlipidemia, diabetes, and obesity.[16,17]

Cooccurring CVD may have detrimental impacts on neurologic outcomes in patients with TBI. Individuals with TBI are at increased risk of stroke, both ischemic and hemorrhagic stroke, even years after TBI.[19–22] Similarly, CVD and other cardiovascular risk factors, notably diabetes, hypertension, and obesity in middle age, are associated with increased rates of dementia and cognitive decline in the general (non-TBI) population.[23–27] Individuals with TBI are already at increased risk of long-term cognitive impairments[10] and may be more susceptible to the detrimental impacts of cardiovascular conditions on late life cognitive decline.

Links between TBI and cardiovascular conditions have been demonstrated in various populations including veterans, community civilians and American-style football players.[15,28,29] In many of such studies, the enhanced risk occurs, regardless of age, severity of injury, or indication of premorbid medical diagnosis. Although autonomic dysfunction, neuroinflammation, gut–brain bioaxis, and hypothalamic–pituitary injury exist as biologically plausible contributors, no clear singular explanation has been established at this time.[30] Examining the phenotypes at greatest risk for cardiovascular disease remains a necessary step to defining clinical approaches and interventions and in eventually narrowing identification of causative factors. The National Institute of Disability, Independent Living, and Rehabilitation Research TBI Model Systems (TBIMS) is the world's largest longitudinal data set examining outcomes among those with moderate to severe TBI who require inpatient rehabilitation; thus, the TBIMS is a unique resource from which to examine long-term cardiovascular outcome among those with moderate and severe TBI. The primary objective of this study was to compare the prevalence of self-reported cardiovascular conditions in those with chronic moderate to severe TBI with a propensity-matched control cohort. To date, much of the literature about prevalence of cardiovascular disease has focused on either military populations[18] or civilian cohorts that included individuals with mild TBI/concussion,[16,17] whereas this study will focus exclusively on a well-characterized cohort of civilians with moderate to severe TBI.

METHODS

Participants with TBI were a subset of enrollees in the TBIMS National Database, a multicenter, longitudinal cohort of individuals who receive inpatient rehabilitation for TBI.[31] Inclusion criteria for the TBIMS are age

at injury ≥16 years; moderate–severe TBI (defined as posttraumatic amnesia >24 hours, trauma-related intracranial neuroimaging abnormalities, loss of consciousness >30 minutes, or Glasgow Coma Scale score <13 in the emergency department); and received acute care hospitalization within 72 hours followed by inpatient rehabilitation in designated TBIMS facilities. Currently, there are 16 TBIMS centers throughout the United States. Institutional review board approval is obtained at each study site, and subjects (or their legally authorized representatives) provide informed consent for participation in TBIMS. Individuals enrolled in the TBIMS complete follow-up interviews by phone or mail at 1, 2, 5, 10, and every 5 years thereafter. The interviews include self-reported information about physical and cognitive function, level of disability, participation in the community, and physical and mental health. Questions could be answered by the participant themselves or by proxy interview of their primary caregiver for participants who were unable to answer questions due to cognitive or language impairments from the TBI. Self-reported medical comorbidities were asked at the follow-up interviews and harmonized with the National Health and Nutritional Examination Survey (NHANES; Centers for Disease Control and Prevention, National Center for Health Statistics, 1999) survey questions. Individuals were asked to report diagnoses provided by a doctor or certified health care professional. The data from this study are available upon reasonable request to the TBIMS National Data and Statistical Center.

NHANES is a cross-sectional survey regarding health and nutritional status of a random sample of individuals in the United States and was used as a comparison group for the analysis. For both databases, only individuals interviewed between January 2015 and March 2020 and were age 18 and older at the time of interview were eligible for this analysis. The follow-up interview dates were restricted to March 2020 and earlier to directly correlate with the NHANES survey data and minimize the impacts of the COVID-19 pandemic. Additionally, for those in the TBIMS with multiple follow-up interviews, only the information collected at the last follow-up interview was used in this study to mimic the cross-sectional study design of the NHANES survey.

Statistical Analysis

TBIMS and NHANES data sets were combined for the purpose of comparing cardiovascular conditions and risk profiles between these 2 populations. Before matching, we reported the summary of patient characteristics for each individual data set. To create a matched sample, individuals were propensity-score matched in a 1:1 ratio, using a caliper distance of 0.01 propensity score units. Matching variables included age, sex, race, ethnicity, education level, year of interview, and current smoking status, all of which have been identified as important variables that may affect development of cardiovascular conditions.[32–35] This technique allowed us to create a matched sample in which individuals from both data sets had similar sociodemographic and lifestyle characteristics. Subsequently, we compared parameters between the NHANES and TBIMS data sets before and after matching to assess the validity of matching process. We also summarized and reported TBI injury severity parameters including Glasgow Coma Scale, and posttraumatic amnesia duration, as well as post-TBI average follow-ups, which were available exclusively for the TBIMS population.

Treating paired participants as random effects in the matched sample, mixed-effect logistic regression models were used to compare prevalence of hypertension, congestive heart failure (CHF), myocardial infarction (MI), stroke, and diabetes between the participants of the TBIMS and the matched control population. Sensitivity analyses were completed to stratify based on age (≤50 years-old versus >50 years old) and time post-injury (<5 years versus ≥5 years post-injury) to assess for whether relationships between TBI and cardiovascular conditions varied by age groups and injury chronicity. The cutoffs for age (50 years-old) and time post-injury (5 years) were chosen because they were close to the mean and median, respectively. Similar to the main analysis, this sensitivity analysis also used mixed-effect logistic regression models with paired participants considered as random effects to compare the prevalence of hypertension, CHF, MI, stroke, and diabetes between the TBIMS participants and the matched control population.

To assess whether there was a survival bias affecting the findings in the TBI cohort, an additional sensitivity analysis was completed in those who were excluded from the TBIMS cohort due to mortality before the 1-year follow-up. We used chi-square test to assess if there is any association between primary and secondary causes of death before the 1-year follow-up with identified age group (ie, ≤50 years and >50 years). This analysis was performed exclusively within the total TBIMS cohort, before implementing the matching criteria with NHANES data.

RESULTS

Population

There were 11 063 individuals from the TBIMS and 15 685 individuals from the NHANES databases in the initial comparison groups (Table S1). A total of 4690 matched pairs were included in this analysis (Figure 1).

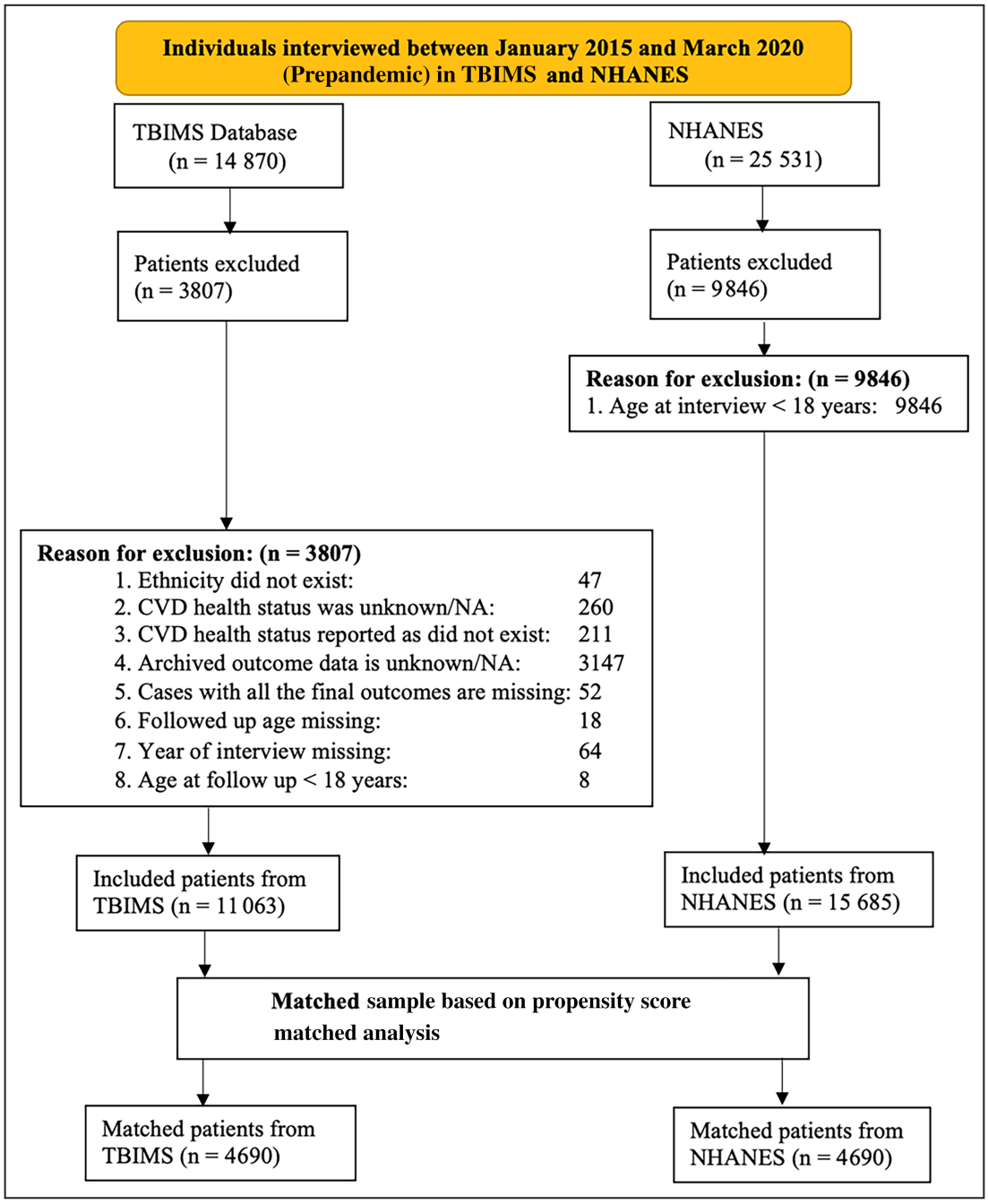

Figure 1. Flow chart for participant inclusion.
CVD indicates cardiovascular disease; NA, not available; NHANES, National Health and Nutrition Examination Survey; and TBIMS, Traumatic Brain Injury Model Systems.

There were no significant differences in age, sex, body mass index, race, ethnicity, education level, and cigarette smoking status between groups in the matched cohort (Table 1). For those with TBI, the median initial Glasgow Coma Scale score was 11 (interquartile range: 6–14) and median duration of posttraumatic amnesia days was 17 (interquartile range: 5–32) days, indicating that TBI severity was overall moderate to severe. Median time post-injury was 5 (interquartile range: 2–10) years.

Overall Prevalence of Cardiovascular Conditions

Figure 2 shows the odds ratio (OR) for self-report of cardiovascular conditions and diabetes in those enrolled in the TBIMS study compared with the NHANES.

Table 1. Comparison Between Cohorts After Propensity Score Matching

	NHANES N=4690	TBIMS N=4690	*P* value
Age at time of interview, y; mean±SD	52.3±17.3	52.1±16.6	0.58
Sex, n (%)			0.79
Female	1641 (35.0%)	1629 (34.7%)	
Male	3049 (65.0%)	3061 (65.3%)	
Body mass index (kg/m^2); mean±SD	28.9±6.5	29.0±6.6	0.22
Race, n (%)			0.22
White	2688 (57.3%)	2590 (55.2%)	
Black	1068 (22.8%)	1116 (23.8%)	
Asian/Pacific Islander	230 (4.9%)	233 (5.0%)	
Other	704 (15.0%)	751 (16.0%)	
Ethnicity, n (%)			0.63
Non-Hispanic	3825 (81.6%)	3807 (81.2%)	
Hispanic	865 (18.4%)	883 (18.8%)	
Education, n (%)			0.18
Completed high school	3642 (77.7%)	3587 (76.5%)	
Less than high school	1048 (22.3%)	1103 (23.5%)	
Current cigarette smoker, n (%)	1845 (39.3%)	1934 (41.2%)	0.061
TBI injury severity			
Glasgow Coma Scale score; mean±SD; median; IQR	…	9.99±4.5; 11 (6–14)	
Posttraumatic amnesia days; mean±SD; median, IQR	…	21.7±21.2; 17 (5–32)	
Years post-TBI: mean±SD; median; IQR	…	8.2±6.4; 5; (2–10)	
Cardiovascular disease estimates, n (%)			
Hypertension	1926 (41.1%)	2109 (45.0%)	
Heart failure	240 (5.1%)	196 (4.2%)	
Heart attack	322 (6.9%)	218 (4.6%)	
Stroke	293 (6.2%)	475 (10.1%)	
Diabetes	735 (15.7%)	800 (17.1%)	

IQR indicates interquartile range; NHANES, National Health and Nutrition Examination Survey; TBI, traumatic brain injury; and TBIMS, Traumatic Brain Injury Model Systems.

Individuals with TBI were more likely to report hypertension (OR, 1.18 [95% CI, 1.08–1.28]) and stroke (OR, 1.70 [95% CI, 1.56–1.98]) but less likely to report CHF (OR, 0.81 [95% CI, 0.67–0.99]) or MI (OR, 0.66 [95% CI, 0.55–0.79]) compared with matched controls. There was no significant difference in diabetes between groups (OR, 1.11 [95% CI, 0.99–1.24]).

Differences in Cardiovascular Disease Prevalence Based on Age at Interview and Time Post Injury

Separate models were completed for those ≤50 years old or younger and those >50 years old at time of interview (Figure 3A). In both groups, individuals with TBI had increased risk of hypertension and stroke compared with matched controls; however, the effect was greater in the younger cohort, as evident from the marginally nonoverlapping 95% CIs. In those ≤50 years old, there was no difference in CHF (OR, 1.11 [95% CI, 0.66–1.89]) or MI (OR, 1.13 [95% CI, 0.69–1.87]) but lower rates of both CHF (OR, 0.79 [95% CI, 0.64]) and MI (OR, 0.62 [95% CI, 0.51–0.75]) were noted in those with TBI for the subgroup >50 years old.

Sensitivity analyses were additionally completed to assess impact of time post-TBI at time of interview (Figure 3B). Only stroke was noted to be elevated in those with TBI compared with the control cohort regardless of time post-injury; however, the effect was more pronounced in those <5 years post-TBI (OR, 2.73 [95% CI, 2.07–3.59]) versus those ≥5 years post-injury (OR, 1.34 [95% CI, 1.12–1.62]). Hypertension was elevated in those within 5 years post-TBI (OR, 1.49 [95% CI, 1.28–1.74]), but there was no difference between groups for those ≥5 years post-injury. Rate of CHF was higher in those with TBI <5 years post-injury (OR, 1.41 [95% CI, 1.01–1.96]) but lower in those ≥5 years post-injury (OR, 0.60 [95% CI, 0.47–0.77]). There was no significant difference in MI in those <5 years post-injury (OR, 0.83 [95% CI, 0.60–1.13]), but rate of MI was lower

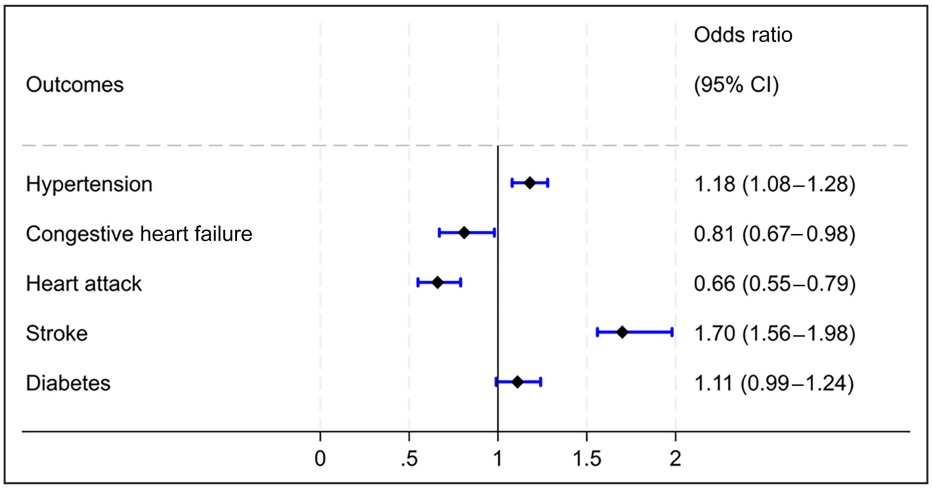

Figure 2. Odds of cardiovascular outcomes for those in the Traumatic Brain Injury Model Systems cohort compared with National Health and Nutrition Examination Survey cohort.

in those at least 5 years post-TBI (OR, 0.59 [95% CI, 0.48–0.74]).

Mortality Within First Year After TBI

There are notable differences in mortality during the first year following TBI based on age (Table 2). Of those who suffered a TBI at age ≤50, 4.5% died before the 1-year follow-up; whereas 20.1% of those >50 at time of injury died before the first-year follow-up. Individuals >50 years old were more likely to have cause of death administrative codes for ischemic heart disease (8.6% versus 2.8%), other heart conditions such as heart failure (9.0% versus 5.8%), or cerebrovascular disease (4.4% versus 1.4%) listed as the primary cause of death on the death certificate than the younger cohort.

DISCUSSION

In this propensity matched case–control study, we compared the self-reported prevalence of 5 cardiovascular conditions among a sample of individuals with moderate-to-severe TBI to a national community-based sample. Our findings indicated—after matching for several confounders including age—that individuals with TBI were more likely than their general population peers to report having been diagnosed with hypertension and stroke. Stratified analyses by age indicated that the greater odds of these 2 conditions were most pronounced relative to the general population among younger persons (≤50 years old) and those within 5 years of injury. These findings are generally consistent with prior literature showing elevated risk of long-term cardiovascular and related conditions following

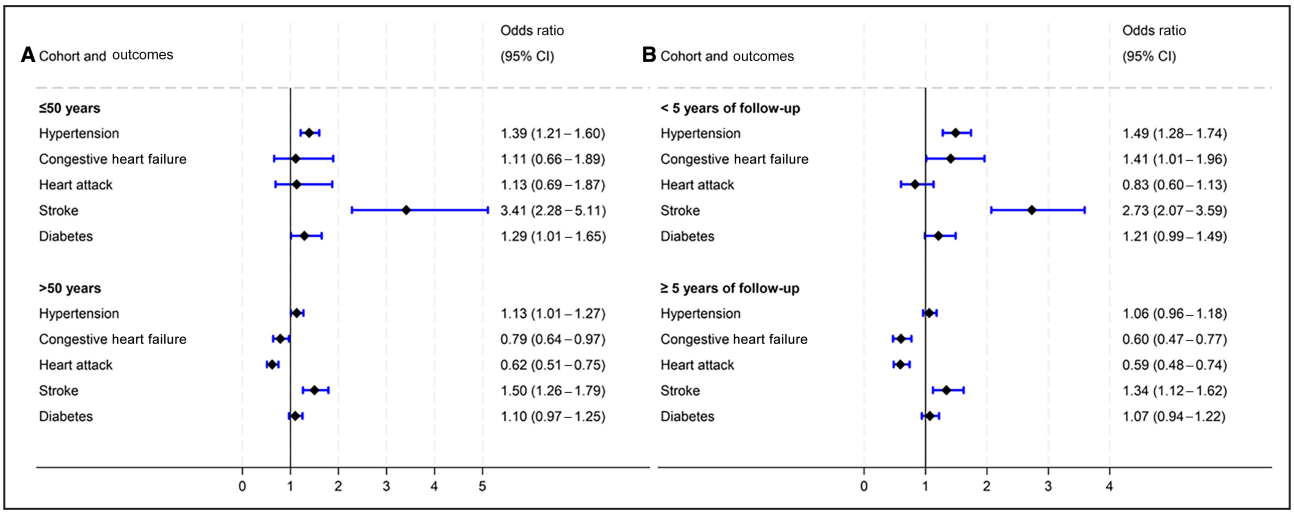

Figure 3. Results of sensitivity analyses to assess the impact of age at time of interview (A) and time post-injury (B) on odds of cardiovascular disease prevalence in those with history of traumatic brain injury.

Table 2. Primary Cause of Death for Those With Traumatic Brain Injury Who Died Before First Follow-Up Interview at 1 Year Post-Injury, Stratified By Age Group

Primary cause of death	≤50 y	>50 y	*P* value
No. died/no. injured (percent mortality)	504/11165 (4.5%)	1094/5435 (20.1%)	
Ischemic heart disease	14 (2.8%)	94 (8.6%)	<0.001
Other form of heart disease	29 (5.8%)	99 (9.0%)	
Cerebrovascular disease	7 (1.4%)	48 (4.4%)	
Other cause	336 (66.7%)	683 (62.4%)	
Unknown	118 (23.4%)	170 (15.5%)	

TBI.[11,15–17,36] Similar to the current findings, one study of 404 individuals with moderate to severe TBI 10 years prior found that hypertension was noted as the most common medical condition, affecting nearly one third of the participants.[11] The findings of increased risk of stroke in the TBIMS cohort compared with the propensity-matched control cohort in the NHANES database is consistent with the existing literature. In one study of 1410 individuals with TBI of all severities, median 10.2 (interquartile range: 5.2–17.8) years post-injury, those with any severity of TBI had a 1.32 (95% CI, 1.06–1.63) increased risk of stroke. Furthermore, those with definite TBI (consistent with moderate–severe TBI) were 2.20 (95% CI, 1.04–4.64) more likely to have a stroke than those without TBI.[22] Heart disease, hypertension, hyperlipidemia, and diabetes are known risk factors for stroke in the general population,[37] and cooccurring cardiovascular conditions with TBI may further increase the risk of stroke in this population.

The current study was unable to assess the timing of diagnosis of the cardiovascular conditions in relation to the TBI diagnosis in order to directly compare the 2 databases used; therefore, we are unable to determine any particular directionality of the relationship—that is, either the TBI leads to increased risk of hypertension or those with hypertension were more likely to suffer a TBI. One study of individuals without previously diagnosed cardiovascular or neuropsychiatric conditions found that individuals with TBI of any severity had increased risk of hypertension and stroke compared with uninjured controls matched on age, sex, and race, suggesting a potential causative role for TBI for these conditions. Similar to this study, the increased risk was noted even in those aged 18 to 40 years old, who had even greater risk for developing these conditions compared with their matched controls.[17]

Surprisingly, we observed a counterintuitive protective effect of TBI for MI and CHF for those >50 years old, which may be influenced by survival bias among persons who die acutely post-TBI. Prior studies of cardiovascular outcomes following TBI used broader definitions to capture cardiovascular comorbidities than this study. Izzy and colleagues had studied overall prevalence of coronary artery disease, including those both with and without MI,[16,17] and Stewart and colleagues included acute coronary heart disease, previous coronary heart disease, cardiac arrest, ischemic stroke/transient ischemic attack/documented atherosclerotic cerebrovascular disease, peripheral arterial disease, coronary procedures, and peripheral arterial procedures in their definition of CVD.[18] We found that roughly 20% of those >50 years old at time of injury died before the 1-year follow-up interview and, therefore, were not included in the analytic sample whereas only 4.5% of those age ≤50 at time of injury died within the first year. Cardiovascular causes of death, namely MI and "other form of heart disease," which includes CHF, accounted for 17.6% of the causes of death before the 1-year post-injury follow-up in those >50 years old. These subjects were excluded from this study due to lack of 1-year follow-up data. Furthermore, survival bias—that is, the competing risk of death—could have also influenced the difference in results seen between those <5 years post-injury compared with those ≥5 years post-injury. It has been found that individuals living with chronic moderate to severe TBI have a 2.25 times higher mortality rate than the uninjured individuals even many years post-injury and causes of death are typically unrelated to the underlying neurologic injury.[38,39] For example, one retrospective cohort study using a statewide hospital discharge database found that individuals who were previously hospitalized for TBI were more likely to die of cardiac conditions (standardized mortality ratio, 3.34 [95% CI, 3.10–3.58]) within 90 months of hospital discharge than those without TBI,[13] and another study of 2140 individuals surviving at least 1 year after moderate to severe TBI found that cardiovascular conditions were the primary cause of death led by ischemic heart disease (12.3%) followed by "other heart disease" (8.8%).[40] The true prevalence of MI and CHF may be underestimated in the TBI cohort because, in order to directly compare the 2 cohorts, we included only data from the last interview available and not information regarding cause of death. For example, if someone reported not having an MI at their last follow-up interview but died of an MI before their next scheduled follow-up time period, they would be considered to not have the MI in this analysis. Though survival bias could also affect the NHANES cohort, the TBIMS cohort may be more greatly affected by this selection bias due to excess mortality within the first year after moderate to severe TBI, particularly mortality due to cardiovascular conditions.[41,42]

The findings from this study highlight the importance of early screening for and management of cardiovascular risk factors in individuals with chronic TBI, particularly those of younger age not typically thought to be

at risk for these conditions. Though this study was not designed to infer causality between TBI and cardiovascular conditions, our results provide evidence for an increase in stroke and hypertension burden experienced among persons living with TBI. Furthermore, this study also showed that the increased risk of these cardiovascular conditions was greatest within the first 5 years after TBI. These findings highlight the need for routine screening for markers of cardiovascular health following TBI regardless of age to address modifiable risk factors to decrease long-term morbidity early after injury. To date, there are no clinical practice guidelines for screening of cardiovascular risks following TBI, in contrast to the clear clinical practice guidelines established for individuals with traumatic spinal cord injury who are similarly at increased risk for CVD. The most updated Clinical Practice Guidelines for management of those with spinal cord injury recommend initial screening for obesity, hyperlipidemia, hypertension, and diabetes before discharge from inpatient rehabilitation and at regular intervals following discharge.[43] Similar guidelines are needed to best address cardiovascular health following TBI.

Limitations and Strengths

The current study had limitations that reveal opportunities for future research. We cannot draw conclusions about the risk for developing cardiovascular conditions due to TBI, nor can our results speak to the potential impact of TBI in either the worsening of preexisting cardiovascular conditions. Furthermore, all diagnoses were self-reported and not verified against medical records. This data acquisition method is subject to not only problems inherent in self-report (eg, limitations in memory or health knowledge) but may also reflect false negatives associated with lack of care (ie, some individuals may have CVD but were never diagnosed by a doctor). Nonetheless, our characterization of prevalence of cardiovascular conditions in TBI, carefully compared with population data, provides a strong argument for close monitoring and treatment in TBI, particularly as individuals age with chronic brain injury. Strengths of our study include the very large sample and well-matched comparison group with a TBI group reflecting a range of demographics to provide an estimate of overall prevalence. However, selection bias associated with TBIMS eligibility criteria (eg, admission to specified acute care and rehabilitation facilities) cannot be discounted. Because certain demographic groups have poorer access to care, and because these groups may also be at higher risk for CVD, our prevalence estimates to some degree may be underestimated. Finally, we do not have an orthopedic trauma control group, preventing investigation into whether these associations were related to the overall traumatic event or to the TBI.

CONCLUSIONS

TBI is a common condition that has been shown to be associated with poorer cardiovascular health. Our study provides evidence for greater prevalence of hypertension and stroke in persons with moderate to severe TBI, particularly those who are younger. Efforts to apply existing guidelines for the prevention of CVD to the health assessment and management of persons with TBI should be strengthened. Further research into the mechanisms and directionality of cause between TBI and cardiovascular health will also offer potential treatment and preventive approaches.

ARTICLE INFORMATION

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Disclosures

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Supplemental Material

Table S1

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