Original Investigation

Dementia Risk After Traumatic Brain Injury vs Nonbrain Trauma
The Role of Age and Severity

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Editorial page 1476

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IMPORTANCE Epidemiologic evidence regarding the importance of traumatic brain injury (TBI) as a risk factor for dementia is conflicting. Few previous studies have used patients with non-TBI trauma (NTT) as controls to investigate the influence of age and TBI severity.

OBJECTIVE To quantify the risk of dementia among adults with recent TBI compared with adults with NTT.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study was performed from January 1, 2005, through December 31, 2011 (follow-up, 5-7 years). All patients 55 years or older diagnosed as having TBI or NTT in 2005 and 2006 and who did not have baseline dementia or die during hospitalization (n = 164 661) were identified in a California statewide administrative health database of emergency department (ED) and inpatient visits.

EXPOSURES Mild vs moderate to severe TBI diagnosed by Centers for Disease Control and Prevention criteria using *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes, and NTT, defined as fractures excluding fractures of the head and neck, diagnosed using *ICD-9* codes.

MAIN OUTCOMES AND MEASURES Incident ED or inpatient diagnosis of dementia (using *ICD-9* codes) 1 year or more after initial TBI or NTT. The association between TBI and risk of dementia was estimated using Cox proportional hazards models before and after adjusting for common dementia predictors and potential confounders. We also stratified by TBI severity and age category (55-64, 65-74, 75-84, and ≥85 years).

RESULTS A total of 51 799 patients with trauma (31.5%) had TBI. Of these, 4361 (8.4%) developed dementia compared with 6610 patients with NTT (5.9%) ($P < .001$). We found that TBI was associated with increased dementia risk (hazard ratio [HR], 1.46; 95% CI, 1.41-1.52; $P < .001$). Adjustment for covariates had little effect except adjustment for age category (fully adjusted model HR, 1.26; 95% CI, 1.21-1.32; $P < .001$). In stratified adjusted analyses, moderate to severe TBI was associated with increased risk of dementia across all ages (age 55-64: HR, 1.72; 95% CI, 1.40-2.10; $P < .001$; vs age 65-74: HR, 1.46; 95% CI, 1.30-1.64; $P < .001$), whereas mild TBI may be a more important risk factor with increasing age (age 55-64: HR, 1.11; 95% CI, 0.80-1.53; $P = .55$; vs age 65-74: HR, 1.25; 95% CI, 1.04-1.51; $P = .02$; age interaction $P < .001$).

CONCLUSIONS AND RELEVANCE Among patients evaluated in the ED or inpatient settings, those with moderate to severe TBI at 55 years or older or mild TBI at 65 years or older had an increased risk of developing dementia. Younger adults may be more resilient to the effects of recent mild TBI than older adults.

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There is controversy regarding the causal link between a single traumatic brain injury (TBI) and the risk of developing dementia. Several studies and meta-analyses[1-5] have not found an association between TBI and risk of dementia. Many previous studies have had notable limitations, including recall bias due to self-reported diagnoses,[6-10] possible reverse causality[11] if patients with dementia have increased risk of TBI, possible confusion with postconcussive syndrome due to transient post-TBI cognitive symptoms,[12,13] or possible confounding if patients with TBI are compared with healthy controls, who may differ in many ways from patients prone to TBI.[13] Even among studies[2,14] that report a positive association between TBI and dementia, marked variability exists in the magnitude of reported risk, which may be due to differences in TBI severity, age of patients, and follow-up period (with some being as short as 2 years) among studies.

According to the Centers for Disease Control and Prevention (CDC), Americans 55 years and older account for more than 60% of all hospitalizations for TBI, with the highest rates of TBI-related emergency department (ED) visits, inpatient visits, and deaths occurring among those 75 years and older (932 per 100 000 population).[15] This number is likely to be an underestimate of the population prevalence of TBI given that many patients with TBI never seek medical attention.[16] Thus, an improved understanding of the effects of a recent TBI sustained in middle-aged or older adulthood on the risk of development of dementia has important public health implications.

The primary goal of our study was to assess the effect of a single recent TBI on the risk of dementia using a novel design that addresses some of the limitations of previous studies. Specifically, we sought to eliminate recall bias by using physician-generated diagnoses of TBI, to minimize reverse causality and misdiagnosis by excluding diagnoses of dementia within 1 year after TBI, and to minimize confounding by comparing patients with TBI with patients with non-TBI trauma (NTT). In addition, we investigated the role of TBI severity and patient age because we hypothesized that although a recent TBI of any severity would increase short-term risk of dementia across all ages, the risk would be greater with increasing TBI severity and increasing age because of increasing brain vulnerability.[17]

Methods

Design and Protocol Approval

This study was approved by the University of California, San Francisco, Human Research Committee, and the need for informed consent was waived because of the use of deidentified administrative data. In this retrospective cohort study, data were derived from the State Inpatient Databases[18] and State Emergency Department Databases[19] for California, which is managed by the Healthcare Cost and Utilization Project (HCUP) and Agency for Healthcare Research and Quality. These data are available to researchers for a fee after they complete a data use agreement. The State Inpatient Databases and State Emergency Department Databases capture all inpatient and ED discharge diagnoses for participating states for each year. California was selected for analysis because it is the most populous state, data for each patient were linked by the HCUP to subsequent inpatient or ED visits before release to researchers in a deidentified fashion, and linked data were available from January 1, 2005, through December 31, 2011.

Patient Selection

Adults 55 years or older were included in the cohort if they were diagnosed as having TBI or NTT during an inpatient or ED visit in 2005 or 2006, did not die during the hospitalization, and did not have a diagnosis of dementia in any discharge diagnosis field.

Exposure

Traumatic brain injury was defined with the CDC criteria[20,21]: *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes 800.0 through 801.9, 803.0 through 804.9, 850.0 through 854.1, or 959.01 in any discharge diagnosis field. Mild TBI was defined according to the CDC criteria[21]: *ICD-9* first 4 digits of 800.0, 800.5, 801.0, 801.5, 803.0, 803.5, 804.0, 804.5, 850.0, 850.1, 850.5, and 850.9 (with a fifth digit of 0, 1, 2, 6, 9, or missing) or 854.0 (with a fifth digit of 1, 2, 6, 9, or missing). Moderate to severe TBI was defined as all nonmild TBI. Non-TBI trauma was defined as fracture, excluding fractures of the head and neck: *ICD-9* codes of 807.0 through 807.9, 812 through 819.9, 822 through 822.9, or 823 through 827.9. Patients with both TBI and NTT during the same hospital visit were classified as having TBI. We conservatively classified patients with multiple subsequent hospital visits based on their first visit only such that a patient who received an in-hospital diagnosis of leg fracture during hospital visit 1 but received an in-hospital diagnosis of TBI during hospital visit 2 was classified as having NTT.

Outcome

The primary outcome was a diagnosis of dementia made during a subsequent ED or inpatient hospitalization. Dementia was defined according to recommendations regarding validated *ICD-9* codes for the diagnosis of dementia in an inpatient setting: *ICD-9* codes 290.0 through 290.9, 331.0 through 331.2, or 294.1 through 294.11 (positive predictive value, 60%-96%; sensitivity, 30%-76%; and specificity, 95%-100%).[22] The follow-up extended through the end of 2011, for a maximum follow-up of 5 to 7 years from the initial hospital visit for trauma in 2005 or 2006. To minimize the chance of reverse causality, misdiagnosis with a potentially resolving postconcussive syndrome,[12] or delirium from medications or other complications of recent trauma, patients were excluded if the diagnosis of dementia was made less than 1 year after the trauma.

Covariates

Information was collected on age, sex, race, comorbidities (depression,[23] delirium,[24] drug or alcohol disorders, and vascular risk factors, including hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, peripheral vascular disease, and cerebrovascular disease), trauma mechanism, health care use, and trauma severity. Income quartile, calculated by the HCUP by matching each patient's zip code to annually updated demographic data,[25] was included as a proxy for socioeconomic status.[26] Comorbidities were based on *ICD-9* dis-

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charge codes from the index visit for each patient. Vascular risk factors were generated using these HCUP single-level clinical classification system codes[27]: 98 and 99 for hypertension, 53 for hyperlipidemia, 49 and 50 for diabetes, 100 and 101 for coronary artery disease, 114 for peripheral vascular disease, and 109 or 113 for cerebrovascular disease. Other comorbidities were identified using the following *ICD*-9 codes: 296.2 through 296.36 or 311 for depression,[23] 292.81 or 293.0 or 293.9 for delirium, 291 through 291.99 or 303 through 303.93 for alcohol disorders or dependence, and 292 through 292.99 or 304 through 304.99 for drug disorders or dependence. Trauma mechanism was coded using major external cause of injury group codes (E codes)[28] and then divided into 4 categories: falls, vehicle crashes, assault, and other or unknown. Health care use data included total hospital visits and total trauma visits per patient during the follow-up period, including the index visit, as well as the location of the index visit (ED or inpatient). Trauma severity was defined according to the New Injury Severity Score,[29] a composite score that takes into account a patient's 3 most severe injuries regardless of anatomical location and has been reported as an excellent predictor of mortality, particularly in patients with head or neck trauma.[30]

Statistical Analysis

All statistical analyses were performed using STATA software, version 13.1.[31] Summary statistics were generated for baseline characteristics and demographics of TBI and NTT groups and compared using the *t* test or χ^2 test. We compared the risk of developing dementia according to TBI status using Kaplan-Meier estimates. Patients were not censored at death because this information was not provided by the HCUP and deidentification precluded linkage to national death data. To evaluate the effect of potential confounders, we adjusted analyses using Cox proportional hazards modeling that included all covariates listed above. In preplanned analyses, to test for a dose response and to investigate our theory regarding aging and brain vulnerability, we assessed for interaction between age and TBI severity and then performed further analyses stratified by TBI severity and age category (55-64, 65-74, 75-84, and ≥85 years). Given our inability to censor at death, 3 additional post hoc analyses were performed after excluding all dementia-free patients with TBI and NTT who were not seen alive (did not have an ED or inpatient visit recorded in the database) within 1 year, 6 months, and 30 days of the end of the follow-up period. To test the robustness of our primary result and study design, we performed 4 additional post hoc sensitivity analyses: (1) excluding patients with multiple trauma visits for TBI or NTT, (2) moving patients into the TBI group if they sustained a TBI any time during the follow-up period, (3) comparing patients with single vs multiple TBIs during the follow-up period, and (4) including patients with dementia diagnoses less than 1 year after the index visit.

Results

After excluding patients with a dementia diagnosis less than 1 year after the initial trauma (n = 4187), the cohort included 164 661 trauma patients, of whom 51 799 (31.5%) had TBI. The median duration of follow-up was 6 years (interquartile range, 0.4-0.5 years). A total of 10 971 patients (6.7%) were diagnosed as having dementia during follow-up. Baseline patient characteristics are reported in **Table 1**. Compared with the TBI group, the NTT group was younger, had a higher proportion of women, had less cerebrovascular disease, and had trauma mechanisms less commonly due to vehicle collisions or assault. The rate of falls was equivalent for patients with TBI and NTT.

Those with TBI were more likely to be diagnosed as having dementia compared with the NTT group (4361 [8.4%] vs 6610 [5.9%], $P < .001$). The mean time from trauma to dementia diagnosis was 3.2 years and was shorter in the TBI group compared with the NTT group (3.1 vs 3.3 years, $P < .001$).

In the unadjusted model, TBI was significantly associated with dementia diagnosis (hazard ratio [HR], 1.46; 95% CI, 1.41-1.52; $P < .001$). Individual adjustment for each covariate changed the HR by less than 10% except for age (model adjusted for age category; HR, 1.25; 95% CI, 1.20-1.30; $P < .001$). Nonetheless, TBI remained significantly associated with dementia diagnosis in the final model adjusted for all covariates (HR, 1.26; 95% CI, 1.21-1.32; $P < .001$).

A significant interaction was found between TBI severity and age category (fully adjusted model, TBI severity × age category, $P < .001$) such that moderate to severe TBI was associated with increased dementia risk across all ages, whereas mild TBI became a relatively more important dementia predictor with increasing age (**Table 2**). There was, however, an unexpected attenuation of dementia risk after severe TBI with increasing age such that the trend toward a dose response was reversed among the oldest old (≥85 years of age). Exclusion of all dementia-free patients who were not seen alive within 1 year of the end of the follow-up period resulted in the expected trend toward a dose response (**Table 3** and **Figure**). Analyses excluding dementia-free patients not seen alive within 6 months or within 30 days of the end of follow-up produced similar results.

Further sensitivity analyses to test the robustness of our primary result produced similar findings. After excluding all patients with additional trauma visits (for TBI or NTT) during the follow-up period (n = 37 417), single TBI was associated with significantly increased risk of dementia compared with single NTT (fully adjusted HR, 1.26; 95% CI, 1.19-1.32; $P < .001$). After excluding all patients with NTT and subsequent TBI (n = 6748) and then stratifying patients based on NTT vs single TBI vs more than 1 TBI during the follow-up period, the risk of dementia after single TBI was virtually equivalent to that reported in the primary analysis (fully adjusted HR, 1.25; 95% CI, 1.20-1.31; $P < .001$), but the risk of dementia after more than 1 TBI was doubled (fully adjusted HR, 1.56; 95% CI, 1.45-1.69; $P < .001$). After recategorizing all patients with NTT and subsequent TBI during the follow-up period as patients with TBI, TBI at any time during the follow-up period was associated with significantly increased risk of dementia compared with NTT without subsequent TBI (fully adjusted HR, 1.41; 95% CI, 1.36-1.48; $P < .001$). Last, when dementia diagnoses rendered less than 1 year after the index trauma were included, TBI was as-

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Table 1. Baseline Patient Characteristics by TBI Status[a]

Characteristic	NTT (n = 112 862)	TBI (n = 51 799)	*P* Value
Age, mean (SD) y	70.8 (10.8)	73.2 (11.1)	
Age group, y			
55-64	40 444 (35.8)	14 697 (28.4)	<.001
65-74	27 991 (24.8)	11 618 (22.4)	
75-84	29 113 (25.8)	15 603 (30.1)	
≥85	15 314 (13.6)	9881 (19.1)	
Female sex	76 131 (69.1)	29 057 (56.9)	<.001
Race/ethnicity			
White	75 467 (66.9)	34 142 (65.9)	<.001
African American	3820 (3.4)	2002 (3.9)	
Hispanic	14 691 (13.0)	6225 (12.0)	
Asian	4148 (3.7)	3301 (6.4)	
Other or missing	14 736 (13.1)	6129 (11.8)	
Median income quartile			
First (poorest)	25 613 (23.2)	10 135 (20.1)	<.001
Second	26 675 (24.2)	12 055 (24.0)	
Third	29 663 (26.9)	14 134 (28.1)	
Fourth (wealthiest)	28 360 (25.7)	14 015 (27.8)	
ICD-9 comorbidities at index visit			
Hypertension	34 729 (30.8)	17 997 (34.7)	<.001
Hyperlipidemia	10 819 (9.6)	4889 (9.4)	.34
Diabetes mellitus	15 382 (13.6)	7092 (13.7)	.73
Coronary artery disease	8972 (8.0)	5105 (9.9)	<.001
Peripheral vascular disease	1308 (1.2)	581 (1.1)	.51
Cerebrovascular disease	2386 (2.1)	1973 (3.8)	<.001
Depression	3492 (3.1)	1606 (3.1)	.94
Delirium	414 (0.37)	224 (0.43)	<.05
Drug disorder or dependence	437 (0.4)	169 (0.3)	.06
Alcohol disorder or dependence	1237 (1.1)	1136 (2.2)	<.001
Trauma mechanism			
Fall	74 986 (66.4)	34 404 (66.4)	<.001
Vehicle collision	9890 (8.8)	7454 (14.4)	
Assault	815 (0.7)	1562 (3.0)	
Other or missing	27 171 (24.1)	8379 (16.2)	
Health care use			
Index visit location of ED	76 512 (67.8)	35 269 (68.1)	.23
Total inpatient or ED visits, mean (SD)[b]	4.8 (6.2)	5.2 (7.0)	<.001
Total inpatient or ED visits for TBI or trauma, mean (SD)[b]	1.32 (0.70)	1.30 (0.72)	<.001
New Injury Severity Score, mean (SD)	5.0 (3.7)	7.8 (5.9)	<.001
TBI frequency			
1 TBI anytime during study period	5743 (5.1)	44 440 (85.8)	<.001
>1 TBI anytime during study period	1005 (0.89)	7359 (14.2)	

Abbreviations: ED, emergency department; *ICD-9*, *International Classification of Diseases, Ninth Revision*; NTT, non-TBI trauma; TBI, traumatic brain injury.

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

[b] Total inpatient or ED visits are mean per participant during follow-up period, including index visit.

sociated with an increased risk of dementia compared with NTT (HR, 1.37; 95% CI, 1.32-1.42; $P < .001$).

Discussion

Among a large cohort of patients with trauma evaluated in the ED or inpatient setting, we found an association between TBI sustained in middle-aged and older adulthood and the development of dementia. Stratification by age and TBI suggested that moderate to severe TBI was associated with risk of dementia in patients 55 years and older, whereas mild TBI was associated with risk of dementia among older patients.

Nearly all previous studies[2,3,6-8,13,32] of TBI and dementia risk have compared patients with TBI with the general popu-

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Table 2. Association Between TBI and Risk of Dementia Stratified by Age and TBI Severity[a]

Patient Group	No. of Patients	HR (95% CI)	*P* Value
Aged 55-64 y (reference NTT)	40 444		
Mild TBI	4670	1.11 (0.80-1.53)	.55
Moderate to severe TBI	10 027	1.72 (1.40-2.10)	<.001
Aged 65-74 y (reference NTT)	27 991		
Mild TBI	2810	1.25 (1.04-1.51)	.02
Moderate to severe TBI	8808	1.46 (1.30-1.64)	<.001
Aged 75-84 y (reference NTT)	29 113		
Mild TBI	2800	1.21 (1.08-1.36)	<.005
Moderate to severe TBI	12 803	1.27 (1.19-1.36)	<.001
Aged ≥85 y (reference NTT)	15 314		
Mild TBI	1443	1.25 (1.09-1.44)	<.005
Moderate to severe TBI	8438	1.14 (1.06-1.24)	<.005

Abbreviations: HR, hazard ratio; NTT, non-TBI trauma; TBI, traumatic brain injury.

[a] Model adjusted for sex, race, income, comorbidities, trauma mechanism, health care use, and injury severity.

Table 3. Association Between TBI and Risk of Dementia Stratified by Age and TBI Severity, Excluding Patients Not Seen Alive Within 1 Year of the End of Follow-up[a]

Patient Group	No. of Patients	HR (95% CI)	*P* Value
Aged 55-64 y (reference NTT)	10 281		
Mild TBI	1226	1.08 (0.77-1.49)	.66
Moderate to severe TBI	2769	1.65 (1.35-2.02)	<.001
Aged 65-74 y (reference NTT)	8607		
Mild TBI	850	1.22 (1.02-1.47)	.03
Moderate to severe TBI	2750	1.50 (1.33-1.68)	<.001
Aged 75-84 y (reference NTT)	10 025		
Mild TBI	938	1.26 (1.13-1.42)	<.001
Moderate to severe TBI	4347	1.38 (1.29-1.47)	<.001
Aged ≥85 y (reference NTT)	4218		
Mild TBI	422	1.25 (1.09-1.44)	<.005
Moderate to severe TBI	2278	1.31 (1.21-1.41)	<.001

Abbreviations: HR, hazard ratio; NTT, non-TBI trauma; TBI, traumatic brain injury.

[a] Model adjusted for sex, race, income, comorbidities, trauma mechanism, health care use, and injury severity. "Seen alive" indicates the exclusion of patients who did not have an emergency department or inpatient visit recorded in the database.

lation. This study design may account for the observation that some have found a marked attenuation of risk of post-TBI dementia after multivariate adjustment.[32] There may, however, be additional unique characteristics of TBI-prone patients that increase their risk of dementia and are unmeasured confounders in these studies (ie, risk-taking behavior and poor judgment). Additional limitations of prior studies[12,13] include possible reverse causality, misdiagnosis due to a resolving postconcussive syndrome, or misdiagnosis due to delirium from medications or other complications of recent trauma if dementia is diagnosed too soon after TBI. For example, a study[11] of TBI and risk of Parkinson disease reported that patients in the early stages of disease are more likely to fall and incur a TBI in the months preceding the diagnosis of Parkinson disease. Similarly, a large population-based study[13] that assessed dementia-free survival in patients with TBI compared with the general population found a 3-fold increased risk of dementia after mild TBI. The mean time from TBI to dementia diagnosis, however, was just 1 year, raising the possibility of reverse causality or misdiagnosis. Last, many studies reporting a lack of association between TBI and dementia have relied on self-report[1-3] (raising concern for recall bias), have used a report of head injury[3-5] to approximate a history of TBI (raising concern for misdiagnosis), or have provided insufficient longitudinal follow-up.[2,14]

In our study, by comparing trauma patients with and without TBI,[34] we tried to account for potential unmeasured confounders and mitigated the possibility of reverse causality because it is unlikely that patients in an early stage of dementia would be more prone to a TBI than a traumatic limb injury. Other strengths of our study design were excluding dementia diagnoses less than 1 year after TBI and using validated *ICD*-9 code hospital-based diagnoses of TBI. Last, by conservatively classifying TBI and NTT based on the index visit only (an intent-to-treat model), we were able to approximate risk of a single TBI. Given the lack of data about prior TBIs, we chose this model as our primary study design rather than a design that accounted for patients with multiple TBIs during the follow-up period because such exclusion was considered arbitrary. Our additional post hoc sensitivity analyses, however, in which we excluded patients with multiple traumas, stratified based on single vs multiple TBIs, or patients with NTT moved into the TBI group at any point during follow-up if they were diagnosed as having TBI, all returned similar results and further confirmed the robustness and validity of our study design meant to quantify risk of a single recent TBI.

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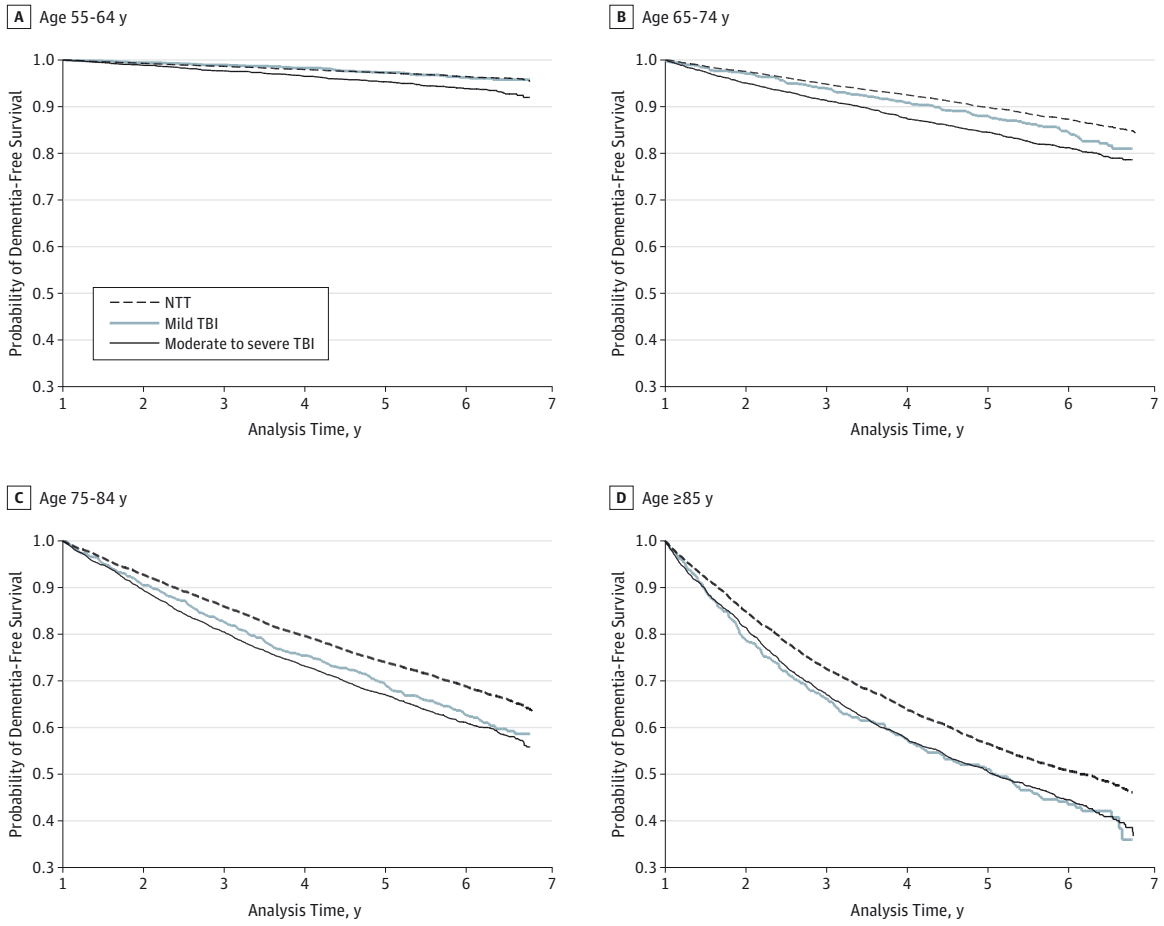
Figure. Kaplan-Meier Plots for Dementia-Free Survival After Nontraumatic Brain Injury Trauma (NTT), Mild Traumatic Brain Injury (TBI), or Moderate to Severe TBI



The association between TBI severity and risk of dementia stratified by age and excluding dementia-free patients who did not have an emergency department or inpatient visit recorded in the database within 1 year of the end of follow-up. Sample sizes are per Table 3.

Major theories regarding the mechanism linking TBI and dementia include (1) the triggering of a progressive neurodegenerative cascade, (2) the acceleration of an established neurodegenerative cascade, and (3) a static brain injury that reduces cognitive reserve.[35,36] Given the relatively short duration of follow-up in this study (5-7 years), we are unable to comment on a possible role of TBI in triggering a de novo neurodegenerative cascade, but our results could theoretically lend support to either of the other 2 proposed theories. Whether a person with TBI recovers cognitively or develops dementia, however, is likely dependent on multiple additional risk and protective factors, ranging from genetics and medical comorbidities to environmental exposures and specific characteristics of the TBI itself. Furthermore, certain factors may combine with TBI synergistically to increase the risk of neurodegenerative disease in a more than additive fashion.[37,38]

We found that moderate to severe TBI is a risk factor for developing dementia among adults 55 years and older, whereas mild TBI is a risk factor for adults 65 years and older. Increasing mortality after TBI with increasing age,[1,39,40] however, may mask the risk of dementia, particularly after moderate to severe TBI in the oldest-old population—a hypothesis supported by our analyses censoring patients who were not seen alive within 1 year, 6 months, or 30 days of the end of follow-up. Overall, the interaction with age and TBI severity suggests that younger patients may be more resilient to the effects of recent mild TBI or may take longer to manifest symptoms of dementia.

A limitation of this study is the use of retrospective inpatient and ED administrative health data. Sources of error may include misdiagnosis by the health care professional or miscoding by the hospital billing staff. Specifically, inpatient *ICD-9* diagnostic codes are relatively insensitive for the diagnosis of dementia.[22,41-43] Thus, although our study may underestimate dementia risk, this pattern should be equal between patients with TBI and NTT and would not be expected to bias the magnitude of the association.

Additional limitations include the lack of data on family history, educational status, prior operations or illnesses, prior TBIs before the index visit, details of treatment during the index visit, relatively short duration of follow-up, inability to cen-

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sor at death, lack of outpatient data, and the possibility that patients who present to the ED or are hospitalized for TBI may differ from those who do not seek medical attention.[16] By comparing patients with TBI with patients with NTT, we controlled for any additional deleterious systemic effects of trauma on the nervous system, such as an increase in peripheral inflammatory markers, that may further increase risk of dementia.[44] Last, because our goal was to assess risk of dementia after a recent TBI sustained in middle-aged or older adulthood, these data do not address the important issue of whether a single mild TBI sustained in adolescence or young adulthood increases the risk of dementia.

Conclusions

We found that mild TBI sustained at 65 years or older or moderate to severe TBI sustained at 55 years or older may significantly increase the risk of developing dementia. Given the high rates of TBI in the population, primary prevention of TBI, which in this study was overwhelmingly (66.4%) due to falls, is critical. The effect of mild TBI sustained in middle age or earlier deserves further study during a longer period of follow-up. In addition, further research is needed to understand the mechanisms of post-TBI dementia to inform secondary preventive strategies.

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Study concept and design: Gardner, Burke, Yaffe.
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Drafting of the manuscript: Gardner, Burke, Yaffe.
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