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Clinical Trajectories of Comorbidity Associated With Military-Sustained Mild Traumatic Brain Injury: Pre- and Post-Injury

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Background and Objective: In the US military, traumatic brain injury (TBI) is of distinct importance, at home and in the deployed setting, and is considered a "signature injury of the wars in Afghanistan and Iraq." Since 2000, an estimated 468 424 service members (SMs) have been diagnosed with at least one TBI. We examined the clinical trajectories of a group of 18 comorbidities before and after a military-sustained mild TBI (mTBI). **Methods:** Without making assumptions on causality, a group of 18 conditions often co-occurring with mTBI were identified through literature review and TBI subject matter workgroup consensus. Using data from Military Health System Data Repository, we identified SMs whose first lifetime military mTBI occurred between October 1, 2016, and October 30, 2019. Correlation analyses were used to determine the linear relationship between comorbidities prior to and after mTBI diagnosis. Changes in the period prevalence of comorbidities was calculated. **Results:** We identified 42 018 SMs with a first lifetime military mTBI, of which 77.6% had at least one comorbidity. Identified SMs were mostly young (46.1% ages 18-24 years), male (81.4%), and White (64.1%). Up to 180 days prior to an mTBI, the most frequently identified conditions were sleep-related conditions (21.7%), headaches (19.4%), posttraumatic stress disorders (PTSDs) (17.8%), anxiety disorders (11.3%), and cervicogenic disorders (eg, cervicalgia) (10.9%). In the period following mTBI diagnosis, the prevalence of diagnosed conditions increased, especially for visual disturbances (327.2%), cognitive conditions (313.9%), vestibular conditions (192.6%), those related to headache (152.2%), and hearing (72.9%). Sleep-related conditions showed moderate positive correlation with a group of co-occurring conditions, led by cognitive conditions ($\phi c = 0.50$), anxiety disorders ($\phi c = 0.42$), PTSDs ($\phi c = 0.43$), and headaches and related conditions ($\phi c = 0.38$). **Conclusion:** Results indicate that caring for SMs with mild TBI requires a holistic approach, one that considers the complex nature of SM conditions, prior to sustaining their mTBI, as well as after injury. We found a complex correlation of conditions that suggest SMs with mTBI are undergoing a multifaceted experience, one that may require the development of a targeted multidimensional clinical practice recommendation and practice. **Key words:** *anxiety, comorbidities, correlation, depression, mild TBI, military, PTSD, sleep, traumatic brain injuries, vestibular*

IN THE UNITED STATES, traumatic brain injury (TBI), a traumatically induced structural injury or a physiological disruption of brain function as a result of an external force, has long been considered a significant public health issue, contributing to significant deaths annually and considered a major cause of disability.[1–3] In the US military, TBI is of distinct importance, both at home and in the deployed setting, and was considered a "signature injury" of the wars in Afghanistan and Iraq. Since 2000, an estimated 453 919

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service members (SMs) have been diagnosed with at least one TBI.[4] Mild TBI (mTBI), characterized by an alteration of consciousness lasting less than 24 hours after injury, reported loss of consciousness of up to 30 minutes, or memory loss lasting less than 24 hours, accounts for some 84.5% of all Military TBIs, with moderate, severe, and penetrating TBIs accounting for the rest.[4]

Serving in the US military requires meeting a number of standards, including age, physical performance, educational attainment, and a combination of height and weight criteria, as well as stringent medical requirements.[5] These factors and adherence to health guidelines during service are thought to establish a military cohort healthier than the average citizen, often termed the healthy soldier effect.[6] Evidence of SMs and veterans being generally healthier and having lower mortality than their civilian counterparts came from World War II veterans[7] and Gulf War veterans studies.[8,9] There is now concern of an erosion of this effect among recent veterans, especially among those with military deployments in support of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND).[9] In addition to repeat and prolonged deployments to theater, morbidity from the battlefield, including the higher survivability of otherwise deadly blast exposures, frequently resulting in TBI, has further eroded the healthier than average profile of SMs.[10] Even though most mTBI patients are expected to fully recover,[11] some develop long-term disabilities.[12] Caring for SMs with TBI, especially those with mTBI, has been challenging for clinicians, given the frequent co-occurrence of other conditions obscuring the presentation of mTBI and necessitating a holistic approach. Scientific inquiry has now expanded to examine the copresentation and prevalence of conditions among those newly injured.[13–15]

Multiple studies have found that a high percentage of SMs, who sustained a TBI, also report other conditions, including posttraumatic stress disorder (PTSD), headache, musculoskeletal pain, depression, anxiety, and auditory dysfunction. Over half of those returning from deployments between 2009 and 2011 had a diagnosis of TBI, PTSD, head, neck, or back pain.[16] Auditory dysfunction, namely hearing loss and tinnitus, as well as headache-related conditions, was also found to co-occur with TBI.[14,15]

The purpose of this study was to measure the prevalence of a large spectrum of co-occurring conditions among the entire population of SMs newly diagnosed with mTBI. Furthermore, the study uses a causality agnostic approach, aimed at directly informing clinical practice in the Military Health System (MHS). We sought to measure the prevalence of prominent conditions such as PTSDs, headaches, anxiety, visual disturbances, and depressive disorders, pre- and postdiagnosis of mTBI. This study aims to identify correlations and prevalence proportion of conditions that co-occur with mTBI over time in a representative military cohort to improve clinicians' and administrators' ability to provide adequate care and anticipate the healthcare needs of SMs and veterans.

METHODS

Using the official Department of Defense (DOD) TBI case definition, we identified all SMs from the MHS Data Repository, containing the SMs' electronic health record (EHR), whose first military lifetime mTBI occurred between October 1, 2016, and October 30, 2019. The period met 3 conditions: 1) most recent data available, 2) contained 12 months of data for patients (6 prior to mTBI and 6 post-diagnosis), and 3) reflected the current operating environment of the MHS. An mTBI case is defined as per official DOD case definition, where an mTBI is denoted by the patient's first military admission or outpatient encounter containing an *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) TBI defining code in the first 10 diagnostic position codes in ambulatory care encounters or first 20 diagnostic position codes in inpatient stays (see Supplemental Digital Content Appendix 1, available at: http://links.lww.com/JHTR/A789). Due to significant physiological differences as well as clinical presentation, moderate, severe, and penetrating TBIs were excluded from current analyses. Additional details are published elsewhere.[17]

Using a causality agnostic approach, conditions often co-occurring with mTBI were identified through TBI subject matter expert (SME) consensus and review of the literature.[13–15,18–36] First, an initial list of conditions was created based on literature pertaining to TBI-related comorbidities and literature directly identified by a group of SMEs from the Traumatic Brain Injury Center of Excellence (TBICoE), a Defense Health Agency Center of Excellence. TBI SMEs representing primary care, sports medicine, military medicine, neurosurgery, neurorehabilitation, and clinical pharmacy used the modified Delphi method to review and validated the identified list of conditions and corresponding *ICD-10-CM* codes. Identified conditions were categorized into clinically related groups, with additional *ICD-10-CM* codes added based on clinical relevance.[37] Identified codes were then used to query the patient's EHR to flag conditions of interest. Areas of nonconsensus in group assignments were adjudicated in group meetings until consensus was achieved. Categorization of conditions was based on mTBI symptom groups utilized in TBICoE clinical products, which are congruent with other symptom groupings published in the literature, including anxiety/mood, cervical, cognitive, headache, visual/oculomotor, sleep, and vestibular.[38,39] Ultimately, 18 category groupings were established including alcohol and substance abuse disorders, anxiety disorders, cervicogenic disorders, cognitive conditions, depression and related conditions, headache and related conditions, hearing-related conditions, nausea/vomiting, neuroendocrine disorders, PTSDs, psychosocial conditions, seizure-related conditions, suicidal ideation/homicidal ideation (SI/HI), sleep-related conditions, vestibular-related conditions, and visual disturbances. A separate group of neurologic conditions not elsewhere classified (eg, anesthesia of the skin), and psychiatric conditions not elsewhere classified (eg, psychotic disorders and somatoform disorders), were also analyzed.

Statistical analyses

We evaluated the prevalence of each condition at 4 intervals: 180 to −1 days (6 months to −1 day), 0 to 30 days (0-1 month) post, 0 to 90 days (0-3 months) post, and 0 to 180 days (0-6 months) post-incident mTBI diagnosis. Since the cohort is measured at multiple time periods, the McNemar test for paired data was used to compare changes in the prevalence of diagnoses pre-mTBI to post-mTBI. All analyses shown, comparing pre-mTBI diagnosis to post-mTBI diagnosis, are unadjusted given that pre-/post-analyses are conducted within the same subjects. To reduce risk of multiple comparisons, equivalent pre- to post-periods were compared. Cohen's g statistic was used to estimate the effect size difference between these periods. Cramer's V correlation coefficient was used to create correlation matrices between conditions. Odds ratios (ORs) comparing odds of conditions being present post-mTBI diagnosis compared with the pre-mTBI diagnosis period are shown. Analyses and tabulations were prepared using the software R (R Core Team, 2021). This study was approved by the US Army Public Health Review Board (DV-15-04).

RESULTS

Between October 1, 2016, and October 30, 2019, we identified 42 018 active duty and activated reserve/guard SMs diagnosed with their first military mTBI. Among those, 77.6% were diagnosed with at least one condition in the 180 days (6 months) prior to their mTBI diagnosis and 180 days (6 months) following their diagnosis. While most identified mTBI SMs were male (81.4%), those with any other condition were more likely to be female than those with no other diagnosed conditions (19.5% vs 15.7%, respectively, $P < .001$). White non-Hispanic SMs represented the largest group (50.2%), and Black or African American SMs were more likely to have a diagnosed condition (14.5% vs 10.0%, respectively, $P < .001$), as were army SMs (59.6% vs 49.9%, $P < .001$) and older SMs (see Table 1).

Table 2 shows changes in period prevalence of grouped conditions pre- and post-incident mTBI diagnosis. In the 180 days prior to the diagnosis of mTBI, sleep-related conditions were most frequently diagnosed (21.7%), followed by headache and related conditions (19.4%), PTSDs (17.8%), anxiety disorders (11.3%), and cervicogenic disorders (10.9%). In the first 180 days following mTBI diagnosis, inclusive of diagnosis day, patients had 3.11 the odds of a headache or related condition (95% CI 3.01-3.21; eg, migraine, cluster headache, and tension-type headache), compared with pre-mTBI diagnosis. The prevalence of cognitive conditions (eg, disorientation, symptoms related to cognitive function and awareness, altered mental status, slurred speech, and other speech disturbances) showed a statistically significant increase, as well as a large effect size, post-mTBI diagnosis (OR 4.91; 95% CI 4.69-5.14; $g \geq 0.25$), increasing from 6.2% prior to mTBI diagnosis, to 24.6% post-diagnosis. Other notable, albeit less prevalent conditions were those related to visual disturbance, increasing from 2.5% to 11.5% post-mTBI (OR 5.07; 95% CI 4.73-5.43; $g \geq 0.25$). Prevalence of conditions related to the vestibular system increased from 4.7% pre- to 18.4% post-mTBI diagnosis (OR 3.87; 95% CI 3.68-4.08; $g \geq 0.25$). Sleep-related conditions remained a concern, increasing from 21.7% prevalence prior to mTBI diagnosis to 36.3% post-mTBI (OR 2.05; 95% CI 1.99-2.12; $g \geq 0.25$) (see Table 2).

Correlation matrices in Figure 1 show the correlation between the paired co-occurrence of conditions split into 4 periods: pre-mTBI diagnosis (−180 to −1 days), and post-mTBI diagnosis: first 30 days inclusive of TBI diagnosis date (0-1 month), first 90 days (0-3 months), and first 180 days inclusive of TBI diagnosis date (0-6 months). We conservatively used a correlation coefficient of 0.1 to 0.29 to show weak positive correlation, 0.3 to 0.49 to show moderate positive correlation, and above 0.5 to indicate strong positive correlation. In the 180 days prior to the diagnosis of mTBI, excluding day of mTBI diagnosis, sleep-related conditions were more likely to co-occur in patients with PTSDs ($\phi c = 0.40$), anxiety disorders ($\phi c = 0.34$), and depression and related conditions ($\phi c = 0.25$). Anxiety disorders and PTSDs also showed a moderate positive correlation ($\phi c = 0.38$) (see Fig 1A). In the first 30 days following mTBI diagnosis, inclusive of TBI diagnosis day, relationships strengthened, and a few new relationships appeared, especially related to cognitive conditions. A moderate positive correlation between cognitive conditions and sleep-related conditions presented ($\phi c = 0.44$), as well as weaker correlations with vestibular conditions ($\phi c = 0.34$), headache

TABLE 1 *Demographic characteristics of newly injured SMs with mTBI according to presence of other conditions*

	No other conditions ***n*** **(%)**	**Any other condition** ***n*** **(%)**	**Total** ***n*** **(%)**
Category	9426 (22.4)	32 592 (77.6)	42 018 (100.0)
Sex[a]			
Male	7949 (84.3)	26 235 (80.5)	34 184 (81.4)
Female	1477 (15.7)	6357 (19.5)	7834 (18.6)
Race[a]			
White non-Hispanic	4582 (48.6)	16 524 (50.7)	21 106 (50.2)
Hispanic	1216 (12.9)	4248 (13.0)	5464 (13.0)
Black non-Hispanic	1035 (11.0)	5208 (16.0)	6243 (14.8)
Asian/Pacific Islander	241 (2.6)	947 (2.9)	1188 (2.8)
American Indian/Alaska Native	61 (0.6)	276 (0.9)	337 (0.8)
Other	331 (3.5)	1275 (3.9)	1609 (3.8)
Missing	1957 (20.8)	4114 (12.6)	6071 (14.4)
Status[a]			
Active duty	8717 (92.5)	30 701 (94.2)	39 421 (93.8)
Reserve/guard	709 (7.5)	1891 (5.8)	2597 (6.2)
Rank[a]			
Cadet	1088 (11.5)	1422 (4.4)	2510 (6.0)
Enlisted officer, junior (E1-E4)	5209 (55.3)	14 382 (44.1)	19 591 (46.6)
Enlisted officer, senior (E5-E9)	2100 (22.3)	12 471 (38.3)	14 571 (34.7)
Officer, junior (O1-O4)	656 (6.9)	1754 (5.4)	2410 (5.7)
Officer, senior (O5-O10)	256 (2.7)	1774 (5.4)	2030 (4.8)
Warrant officer	68 (0.7)	758 (2.3)	826 (2.0)
Other	49 (0.5)	31 (0.1)	80 (0.2)
Age[a]			
18-24	5907 (62.7)	13 445 (41.2)	19 352 (46.1)
25-34	2502 (26.5)	9032 (27.7)	11 534 (27.5)
35-44	780 (8.3)	7231 (22.2)	8011 (19.1)
45-64	200 (2.1)	2829 (8.7)	3029 (7.2)
Unknown	37 (0.4)	55 (0.2)	92 (0.2)
Service[a]			
Army	4700 (49.9)	20 352 (62.4)	25 052 (59.6)
Air force	1826 (19.4)	4007 (12.3)	5833 (13.9)
Marine corps	1510 (16.0)	3798 (11.6)	5308 (12.6)
Navy	1337 (14.2)	4227 (12.9)	5564 (13.2)
Other	53 (0.6)	208 (0.6)	261 (0.6)

Abbreviations: mTBI, mild traumatic brain injury; SMs, service members.
[a]χ^2 test: $P < .001$.

TABLE 2 *Period prevalence of select conditions pre- and post-incident mTBI diagnosis* (n = 32 592)

Condition or condition group	*ICD-10-CM* diagnosis codes	Pre-mTBI diagnosis	Post-mTBI diagnosis			Pre- and post-prevalence *n* (%)	Odds ratio (95% CI)
		−180 to −1 d	0 to 30 d	0 to 90 d	0 to 180 d	−180 to 180 d	Post/pre
Alcohol and substance abuse disorders	F10.00-F10.99, F11.0-F11.99	2128 (5.1)	1820 (4.3)	2316 (5.5)	2713 (6.5)[a,b]	3516 (8.4)	1.29 (1.22-1.37)
Anxiety disorders	F40.0-F41.9, F45.2-F45.4, R45.0, R45.1,R45.4-R45.7, R45.82	4741 (11.3)	4858 (11.6)	6816 (16.2)	8009 (19.1)[a,c]	9788 (23.3)	1.85 (1.78-1.92)
Cervicogenic disorders	S13-S13.9XXS, M54.2	4560 (10.9)	5009 (11.9)	6693 (15.9)	7755 (18.5)[a,c]	9866 (23.5)	1.86 (1.79-1.93)
Cognitive conditions	R41.0-R41.9, R45.87, R47-R47.9	2620 (6.2)	7445 (17.7)	9508 (22.6)	10 346 (24.6)[a,d]	11 169 (26.6)	4.91 (4.69-5.14)
Depression and related conditions	F32-F32.9, F34-F34.9, R4.3, R45.81, R45.83, R45.84, R45.86	2620 (6.2)	2131 (5.1)	3092 (7.4)	3874 (9.2)[a,c]	5015 (11.9)	1.53 (1.45-1.61)
Headache and related conditions	G43.001-G43.119, G43.70-G43.719, G43.90-G43.919 G44.0-G44.099, G44.201, G44.209, G44.211, G44.219, G44.221, G44.219, G44.301-G44.329, G44.4-G44.41, G44.81-G44.89, M79.2, R51, M54.81	8168 (19.4)	14 374 (34.2)	16 816 (40.0)	18 010 (42.9)[a,d]	20 603 (49.0)	3.11 (3.01-3.21)
Hearing-related conditions	H90.0-H90.A32, H91-H91.93, H93.11-H93.239	2349 (5.6)	3166 (7.5)	4378 (10.4)	5161 (12.3)[a,d]	6410 (15.3)	2.36 (2.25-2.49)
Nausea/vomiting	R11-R11.2	3254 (7.7)	1473 (3.5)	2521 (6.0)	3596 (8.6)[a,b]	6119 (14.6)	1.11 (1.06-1.17)
Neuroendocrine disorders	E23.0	12 (0.0)	9 (0.0)	14 (0.0)	17 (0.0)	21 (0.0)	1.41 (0.67-3.05)
Other neurologic conditions	R20.0-R20.9, R27.0, R48.2	1424 (3.4)	784 (1.9)	1395 (3.3)	1944 (4.6)[a,c]	3037 (7.2)	1.38 (1.29-1.48)
Other psychiatric conditions	F23, F30.0-F30.9, F31.0-F31.9, F45-F45.9, F48-F48.9, R45, R45.8, R45.89	1413 (3.4)	1389 (3.3)	2294 (5.5)	2949 (7.0)[a,c]	3828 (9.1)	2.17 (2.03-2.32)
Posttraumatic stress disorder	F43.0-F43.9	7484 (17.8)	7404 (17.6)	9559 (22.7)	10 944 (26.0)[a,d]	12 640 (30.1)	1.63 (1.57-1.68)

(continues)

TABLE 2 *Period prevalence of select conditions pre- and post-incident mTBI diagnosis* (n = *32 592*) (Continued)

Condition or condition group	*ICD-10-CM* diagnosis codes	Pre-mTBI diagnosis	Post-mTBI diagnosis			Pre- and post-prevalence *n* (%)	Odds ratio (95% CI)
		−180 to −1 d	0 to 30 d	0 to 90 d	0 to 180 d	−180 to 180 d	Post/pre
Psychosocial conditions	T74-T74.01XS, T74.02-T74.02XS, T74.1-T74.12XS, T74.2-T74.22XS, T74.3-T74.32XS, T74.4-T74.4XXS, T74.5-74.52XS, T74.6-74.62XS, T74.9-T74.92XS, T76-76.92XS, Z55-Z55.9, Z56.9, Z59-59.9, Z62-Z62.9, Z63.0-Z63.9, Z65.4, Z65.5, Z69-Z69.82	3299 (7.9)	2202 (5.2)	3460 (8.2)	4444 (10.6)[a,b]	6141 (14.6)	1.39 (1.32-1.46)
Seizure-related conditions	G40-G40.B19	144 (0.3)	120 (0.3)	181 (0.4)	230 (0.5)[a,c]	295 (0.7)	1.60 (1.30-1.97)
Sleep-related conditions	F51-F51.9, G47-G47.9, Z72.820-Z72.9, R53.1, 53.8, 53.82, 53.83, G25.81	9131 (21.7)	10 750 (25.6)	13 690 (32.6)	15 259 (36.3)[a,d]	17 170 (40.9)	2.05 (1.99-2.12)
Suicidal ideation/ homicidal ideation	R45.85-R45.851, T14.91-T14.91XS	944 (2.2)	572 (1.4)	904 (2.2)	1209 (2.9)[a,b]	1910 (4.5)	1.29 (1.18-1.41)
Vestibular-related conditions	H81-H81.93, R26.0-R26.81, R42, I69.998	1972 (4.7)	4205 (10.0)	5888 (14.0)	6730 (16.0)[a,d]	7740 (18.4)	3.87 (3.68-4.08)
Visual disturbances	H51.111-H52.5, H53.0-H53.9, H55.00, H55.81, H55.82	1047 (2.5)	2895 (6.9)	4147 (9.9)	4816 (11.5)[a,d]	5520 (13.1)	5.07 (4.73-5.43)

Abbreviations: *ICD-10-CM*, *International Classification of Diseases, Tenth Revision, Clinical Modification*; mTBI, mild traumatic brain injury.
[a] $P < .001$; McNemar test for paired data and unadjusted prevalence; odds ratios are calculated comparing pre-mTBI period (−180 to −1 days) and post-mTBI period (0 to 180 days) for same cohort.
[b] Cohen's (g) effect size estimate—low: 0.05 < 0.15.
[c] Cohen's (g) effect size estimate—medium: 0.15 < 0.25.
[d] Cohen's (g) effect size estimate—large: ≥0.25.

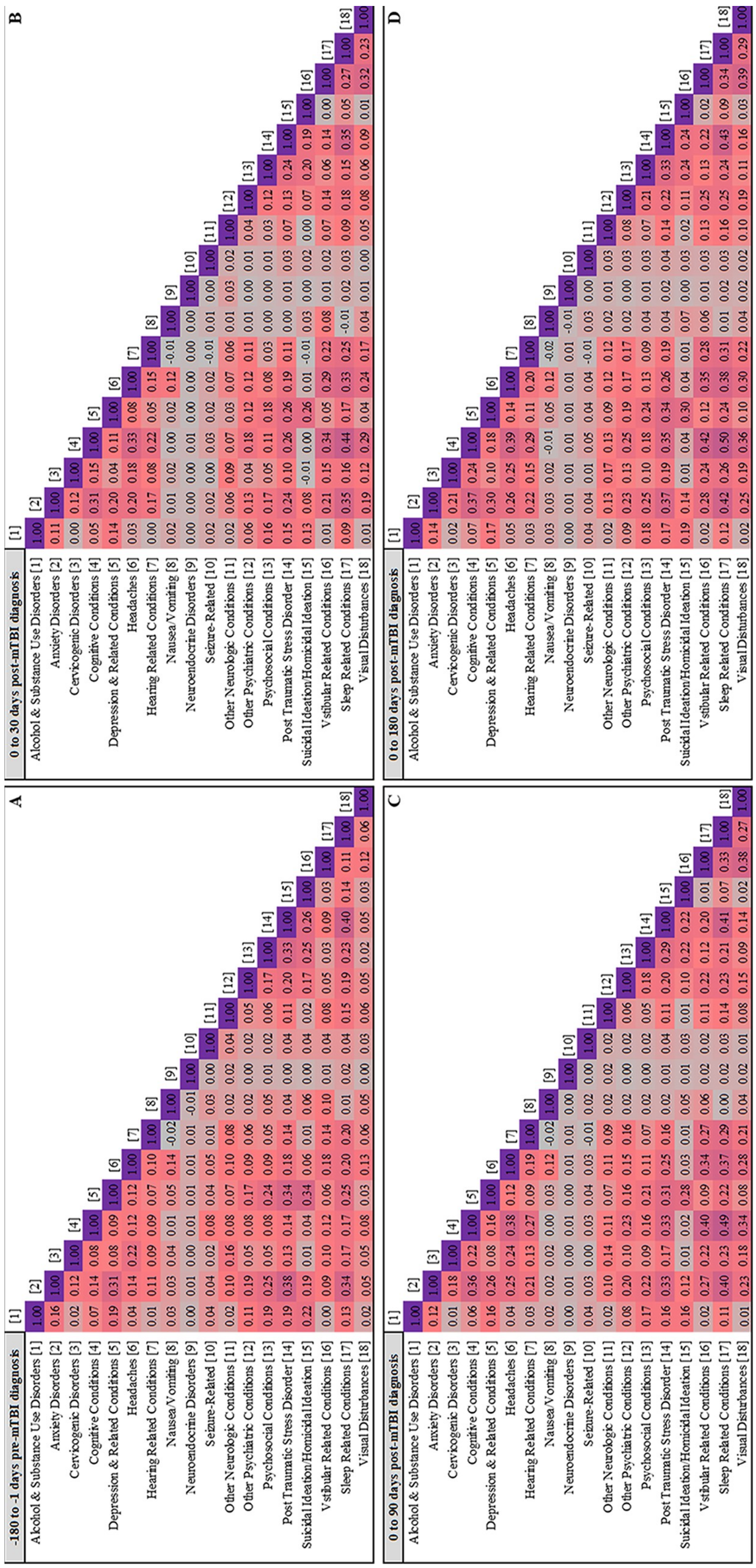

Figure 1. Correlation matrix of patients diagnosed with any condition by time. (A) −180 to −1 days (6 months) prior to mTBI. (B) 0 to 30 days (1 month) post-mTBI diagnosis. (C) 0 to 90 days (3 months) post-mTBI diagnosis. (D) 0 to 180 days (6 months) post-mTBI diagnosis.

and related conditions (ϕc = 0.33), and hearing-related conditions (ϕc = 0.22). Visual disturbances showed moderate positive correlation with vestibular-related conditions (ϕc = 0.32), cognitive conditions (ϕc = 0.29), and weak correlation with sleep-related conditions (ϕc = 0.23) (see Fig 1B). Extending the period to the first 90 days following mTBI, of note is the borderline strong positive correlation between cognitive-related conditions and those related to sleep (ϕc = 0.49) and the moderate positive correlation between the co-occurrence of cognitive conditions and vestibular-related conditions (ϕc = 0.40) (see Fig 2C). Extending the period even further to the first 180 days following mTBI diagnosis, the relationships between conditions strengthened further. A cluster of conditions correlated with cognitive conditions emerged, namely sleep-related conditions (ϕc = 0.50), vestibular conditions (ϕc = 0.42), headache conditions (ϕc = 0.39), visual disturbances (ϕc = 0.36), and PTSDs (ϕc = 0.35) (see Fig 1D).

Figure 2 organizes new diagnoses of conditions of interest into their period prevalence to show the temporal change in new diagnoses of conditions across 3 periods prior to mTBI: −180 to −31 days, −30 to −15 days, and −14 to −1 days (the day just before mTBI diagnosis) and 3 periods post-mTBI diagnosis: 0 to 30 days, 31 to 90 days, and 91 to 180 days. For this figure, periods were chosen to better differentiate the chronological range of the patient's diagnoses, underscoring the proportion of those diagnosed just before the patient's first military mTBI. As reported previously, in the first 180 days prior to mTBI diagnosis, sleep-related conditions were present in 21.7% of patients, with 9.2% of those diagnosed in the 2 weeks prior to mTBI diagnosis. Headaches, diagnosed in 19.5% of the cohort prior to mTBI diagnosis, include 32.8% of those diagnosed in the 2 weeks prior to mTBI diagnosis. PTSD was another condition reported frequently at 17.9%, with 9.5% of those diagnoses diagnosed in the 2 weeks prior to

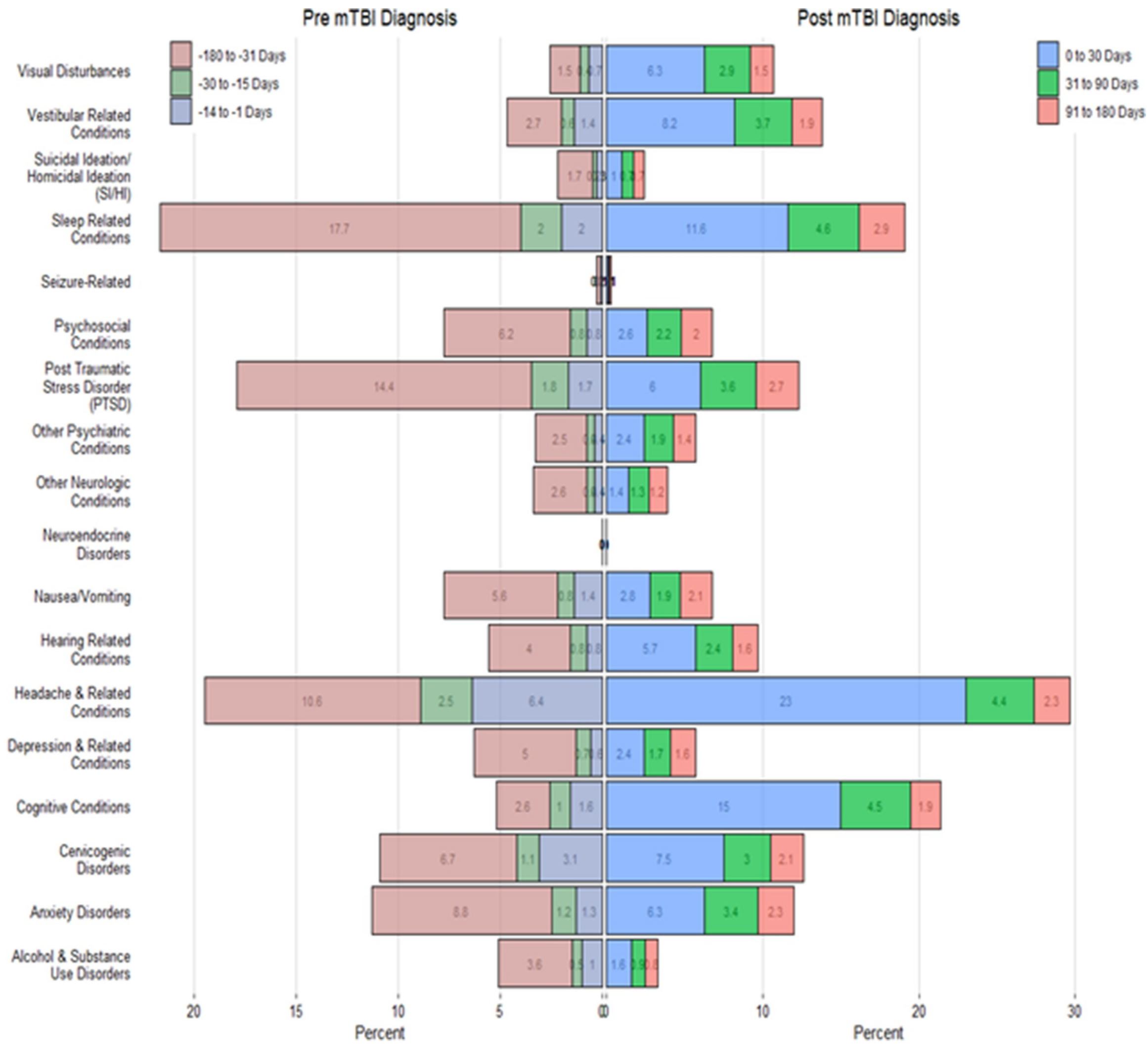

Figure 2. Incidence of conditions pre- and post-diagnosis of mTBI (180 days prior to and 180 days later). This figure is available in color online (www.headtraumarehab.com).

mTBI diagnosis. Following sleep, headache, and PTSD, anxiety and cervicogenic disorders rounded up the top 5 most prevalent conditions pre-mTBI diagnosis. In the first 180 days following mTBI diagnosis, headache-related conditions were newly diagnosed among 29.7% of patients, with 77.4% of those diagnosed in the first 30 days. Cognitive conditions increased as well, with 21.4% of patients newly diagnosed. Cervicogenic disorders were newly diagnosed among 12.6% of patients, with 59.5% of those diagnosed in the first 30 days. Similarly, anxiety disorders were diagnosed among 12.0% of patients, with 52.5% diagnosed in the first 30 days following mTBI diagnosis (see Fig 2).

DISCUSSION

This study was intended to show the existing health profile of all SMs newly sustaining an mTBI as well as explore changes in the prevalence of conditions that co-occur with mTBI and contrast preexisting conditions to those being diagnosed concurrently with the patient's mTBI. Although the conditions examined relate to brain injury, this study was intended to be causality agnostic, intending to capture the comorbidity profile of a representative cohort of mTBI patients before and after their injury. Information may be used to characterize the medical and psychological profile of SMs diagnosed with mTBI to inform treatment approaches. Three in 4 newly injured SMs with mTBI had at least one condition prior to or following mTBI diagnosis, much higher than the 5.9% prevalence of any mental health condition among a sample of SMs across the entire force.[40] Our period prevalence estimates of PTSD (30.1%) among those with mTBI are higher than the 5% PTSD prevalence at follow-up visits among nondeployed SMs and 8% combat deployers across the force.[40] In contrast our prevalence estimates for depression and related conditions (11.9%) are lower than the 15.2% reporting a major depressive episode among 18- to 25-year-olds in the American public.[41] Sleep-related conditions, headaches, and PTSDs were common prior to mTBI, and there was a significant increase in cognitive conditions, vestibular-related conditions, visual disturbances, hearing-related conditions, and headache and related conditions acutely post-mTBI. We further found that PTSDs, anxiety disorders, depression and related conditions, and sleep-related conditions had moderate positive correlation pre- and post-mTBI. Clustering studies have found a similar co-occurrence of conditions such as anxiety, depression, PTSD, and other emotional symptoms.[42] PTSD prior to mTBI was found among 17.8% of our cohort, increasing to 26.0% post-mTBI, markedly higher than the 8.5% indicating probable PTSD in the Health Related Behaviors Survey (HRBS). While PTSD's co-occurrence with mTBI may be a function of deployment, combat, or blast exposure, data suggest PTSD remains a comorbidity of mTBI even after major combat operations have ended. At 180 days following an SM's first military mTBI, we can expect a complex patient presentation, one containing a myriad of conditions, making for an ever-changing patient presentation along the SM's rehabilitation pathway.

The high prevalence of sleep-related conditions, pre- and post-mTBI, was a notable, yet anticipated, finding. In their broad, retrospective cohort study of all active-duty army soldiers, Caldwell et al[43] found an overall incidence of insomnia and sleep apnea to be 11.0% and 5.1%, respectively, reaching 19.2% among those with combat exposures. Those with a history of mTBI specifically were 15% more likely to report sleep disorders, and even higher (219%) if they indicated PTSD. Similarly, our study found moderate correlation between sleep-related conditions and anxiety, cognitive conditions, PTSD, and, to a lesser extent, depression. The relationships strengthened over time suggesting a cumulative effect. We found a high prevalence of sleep-related conditions prior to mTBI and after its diagnosis. Prior to their mTBI, 11.3% of SMs had a diagnosed anxiety disorder, slightly lower than the 14.2% probable generalized anxiety disorder prevalence in the most recent DOD HRBS.[44] Among our mTBI cohort, 6.1% had a diagnosis of depression prior to mTBI, increasing to 9.2% following its diagnosis, slightly below the 9.4% reported military-wide.[45] PTSD prior to mTBI was found among 17.8% of our cohort, increasing to 26.0% post-mTBI, markedly higher than the 8.5% indicating probable PTSD in the HRBS. Capturing the entire period, pre- and post-mTBI, prevalence increased to 23.3% having a diagnosis of anxiety, 11.9% having a diagnosis of depression, and 30.1% having a diagnosis of PTSD. While PTSD's co-occurrence with mTBI may be a function of deployment, combat, or blast exposure, data suggest PTSD remains a comorbidity of mTBI even after major combat operations have ended. At 180 days following an SM's first military mTBI, we can expect a complex patient presentation, one containing a myriad of conditions, making for an ever-changing patient presentation along the SM's rehabilitation pathway.

Our study was also able to identify some 4.5% of newly injured mTBI patients with a diagnosis of SI/HI, to include suicide attempt. Fonda et al[46] found that veterans deployed to OEF/OIF/OND who sustained TBI were 3.76 times more likely to attempt suicide compared with those without a TBI, after adjusting for demographic characteristics. Importantly, about 83% of that association was mediated by co-occurring psychiatric conditions, with PTSD having the largest impact. In our cohort, the 6-month post-mTBI correlation between SI/HI and PTSD ($\phi c = 0.24$), depression $\phi c = 0.30$), and other psychosocial conditions ($\phi c = 0.24$) showed low to moderate positive correlation. This further suggests the need to closely monitor SI among newly injured patients, especially those with a diagnosis of PTSD and/or depression.

This study's results, together with existing literature, show mTBI does not exist in isolation among our military's SMs and suggest a rather arduous recovery pathway for mTBI patients. This complex profile of the TBI patient seems to extend beyond active duty. Veterans with an mTBI in the LIMBIC-CENC cohort also had high rates of depression symptoms, pain, and sleep apnea risk compared with those without TBI up to 10 years following injury.[47] Taylor et al[48] also found that the majority of OEF/OIF veterans diagnosed with TBI using Veterans Health Administration services also had a diagnosed mental disorder and more than half had both PTSD and chronic pain. Our findings are particularly striking given our young cohort, as almost half of the mTBI SMs with any other condition were younger than 24 years. Knowledge of common co-occurring conditions and their evolution and correlations over time can help guide clinicians in monitoring their presence and ensuring appropriate and timely management to maximize recovery. Awareness and focus, particularly on the domains that show marked changes post-mTBI diagnosis, including vision (OR = 5.07; 95% CI 4.73-5.43), cognitive (OR = 4.91; 95% CI 4.69-5.14), vestibular (OR = 3.87; 95% CI 3.68-4.08), hearing (OR = 2.36; 95% CI 2.25-2.49), and headache (OR = 3.11; 95% CI 3.01-3.21), represent potential areas of early intervention, calling for proactive evaluation and treatment if indicated.

LIMITATIONS

As with any study, this study has strengths and limitations. First, there are strengths to using MHS data for this study. Unlike other study designs, especially surveys reliant on sampling, this study examined the entire population of SMs with their first lifetime military mTBI, aiding in its generalizability to the entire military population. This study uses a total of 1 year of data, thus setting the time bounds of identifying conditions, and estimates must be understood with this limitation in place. This was intentional to recreate the population most likely to present acutely after mTBI and allow time from incident diagnosis for co-occurring conditions to meet diagnostic criteria. Second, SMs with undiagnosed mTBIs, or conditions diagnosed outside of the MHS, may not appear in our data, thus leading to underestimation. This limitation is partly tapered by the results of a review of DOD and service-specific policies aimed at improving the documentation of TBI, which showed that these policies significantly improved the number of identified TBIs. Furthermore, our analyses are not adjusted for population distribution, hence may not be generalizable to other military populations.[49] A third limitation is the surveillance effect, whereby SMs with newly diagnosed mTBI may be more likely to be diagnosed with comorbid conditions than prior to their mTBI diagnosis, even if conditions are not causal. While changes in diagnoses following mTBI reflect a clinical reality, it is possible that some conditions diagnosed post-mTBI were undocumented prior to its diagnosis. This bias is particularly relevant post-mTBI diagnosis, as patients return for follow-up care, increasing the likelihood of conditions to be identified. Fourth, some of these preexisting conditions, such as SI, depression, PTSD, and alcohol and substance abuse disorders, are known to have stigma as a barrier to care utilization, likely influencing their diagnosis, and presence in our data. Fifth, conditions examined herein were considered clinically well-established in the literature and among experts; however, other conditions, directly or indirectly associated with TBI, may have been present, but not captured by our query. Additionally, condition groups studied here were defined based on specific *ICD-10-CM* codes provided in Table 2, and other studies may have applied different coding methodology for each condition compared with our analyses.

IMPLICATIONS FOR FUTURE RESEARCH

Due to the vast, interconnected functions that the brain controls, injuries to the brain can result in a wide variation in the presentation of conditions in the short and long-term. This study aimed to quantify the disease burden placed on our SMs by capturing the intricate dynamic between mTBI and other concurrent conditions. We found that a large proportion of mTBI SMs are afflicted with other conditions, especially following mTBI, making for a complex patient profile. The MHS, commanders, administrators, and clinicians should continuously monitor for comorbidities, extend the timeline of observation, identify comorbid clusters, and determine the elevated risk associated with mTBI and specific conditions within this population. Monitoring conditions associated with TBI within the US military population is necessary to acknowledge the complexity of the TBI patient and to improve our understanding of how these conditions impact TBI care and recovery. This information may allow for appropriation of funds and resources to provide adequate treatment for the wide range of conditions that occur with mTBI. Additionally, knowledge of the most common conditions associated with mTBI may allow for the prevention of adverse outcomes and chronic mTBI sequela by providing clinicians with evidence to guide their approach to treatment and management of mTBI.

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