Prevalence of Cerebral Microhemorrhage following Chronic Blast-Related Mild Traumatic Brain Injury in Military Service Members Using Susceptibility-Weighted MRI

E. Lotan, C. Morley, J. Newman, M. Qian, D. Abu-Amara, C. Marmar, and Y.W. Lui

ABSTRACT

BACKGROUND AND PURPOSE: Cerebral microhemorrhages are a known marker of mild traumatic brain injury. Blast-related mild traumatic brain injury relates to a propagating pressure wave, and there is evidence that the mechanism of injury in blast-related mild traumatic brain injury may be different from that in blunt head trauma. Two recent reports in mixed cohorts of blunt and blast-related traumatic brain injury in military personnel suggest that the prevalence of cerebral microhemorrhages is lower than in civilian head injury. In this study, we aimed to characterize the prevalence of cerebral microhemorrhages in military service members specifically with chronic blast-related mild traumatic brain injury.

MATERIALS AND METHODS: Participants were prospectively recruited and underwent 3T MR imaging. Susceptibility-weighted images were assessed by 2 neuroradiologists independently for the presence of cerebral microhemorrhages.

RESULTS: Our cohort included 146 veterans (132 men) who experienced remote blast-related mild traumatic brain injury (mean, 9.4 years; median, 9 years after injury). Twenty-one (14.4%) reported loss of consciousness for <30 minutes. Seventy-seven subjects (52.7%) had 1 episode of blast-related mild traumatic brain injury; 41 (28.1%) had 2 episodes; and 28 (19.2%) had >2 episodes. No cerebral microhemorrhages were identified in any subject, as opposed to the frequency of SWI-detectable cerebral microhemorrhages following blunt-related mild traumatic brain injury in the civilian population, which has been reported to be as high as 28% in the acute and subacute stages.

CONCLUSIONS: Our results may reflect differences in pathophysiology and the mechanism of injury between blast- and blunt-related mild traumatic brain injury. Additionally, the chronicity of injury may play a role in the detection of cerebral microhemorrhages.

ABBREVIATIONS: CMH—cerebral microhemorrhages; CTE—chronic traumatic encephalopathy; mTBI—mild traumatic brain injury; TBI—traumatic brain injury

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following acute and subacute blunt mTBI have reported that the frequency of SWI-detected cerebral microhemorrhages (CMH) ranged from 19% to 28%. A few recent works have suggested a lower prevalence in military personnel with chronic mTBI compared with civilians, though these studies were of mixed cohorts, including both blast- and blunt-related TBI and a range of injury severity. Riedy et al and Liu et al found an approximately 3%–4% prevalence of CMH in subjects with a mixed history of blast- and blunt-related mTBI. The true prevalence of CMH in blast-related mTBI is not known. The purpose of the current study was to characterize CMH in military service members with chronic blast-related mTBI.

MATERIALS AND METHODS

Participants and Measures

Subjects in this study were drawn from an ongoing prospective study of military veterans performed at the NYU Langone Medical Center. The study was approved by the local institutional review board. All participants provided written informed consent. Inclusion criteria for this study were the following: military service in Operation Enduring Freedom, Operation Iraqi Freedom, and/or Operation New Dawn; between 18 and 70 years; and clinical diagnosis of mTBI in conjunction with close proximity to a blast explosion without concomitant blunt traumatic head injury based on the Department of Veterans Affairs and the Department of Defense definition of mTBI (including altered mental state for <24 hours and no or <30 minutes loss of consciousness) as elicited by the Ohio State University TBI Identification Method—Short Form. Subjects were excluded with a history of comorbid major neurologic disorder or systemic illness, a history of severe drug use disorder, psychosis, suicidality, homicidality, a history of prior moderate or severe head injury, or contraindications to MR imaging. All participants completed a formal, self-report measure of postconcussive symptoms. Symptom severity and quantity were measured using the Concussion Symptom Inventory, a list of 12 symptoms that are graded in severity by the patient on a 5-point Likert scale. The maximum Concussion Symptom Inventory score is 72, indicating maximum overall symptom severity. Additionally, to assess the impact of headache, we used the Headache Impact Test-6 score. This score ranges between 36 and 78, with larger scores reflecting greater impact and a score of >50 considered an abnormal finding. All participants were administered the 2-factor model from the Wechsler Adult Intelligence Scale, 2nd ed, which uses vocabulary and matrix reasoning subtests to estimate intelligence quotient.

MR Imaging

Participants were imaged at 3T (Skyra; Siemens, Erlangen, Germany) using a 20-channel head coil. SWI was performed with the following parameters: TR = 29 ms, TE = 20 ms, flip angle = 15°, slice thickness = 2 mm, intersection gap = 0 mm, FOV = 158 × 220 mm, matrix = 261 × 448, generalized autocalibrating partially parallel acquisition factor = 2. Conventional MR imaging, including T1-weighted imaging, T2-weighted imaging, T2-weighted FLAIR imaging, and diffusion-weighted imaging, was also performed. SWI and conventional MR imaging sequences were reviewed independently by 2 neuroradiologists (1 second-year neuroradiology fellow [E.L.] and 1 attending neuroradiologist with >10 years of experience [Y.W.L.]). Susceptibility-weighted images were reviewed for quality in terms of susceptibility seen in expected locations such as venous structures and calcification of the choroid plexus, or for the presence of any artifacts. The presence of CMH was determined using the Greenberg criteria, including a round or ovoid signal at least half the size of a pixel and the presence of any susceptibility seen in expected locations such as venous structures or periventricular interfaces. No other structural abnormalities were identified. No images demonstrated artifacts warranting exclusion.

Table 1: Demographic and clinical characteristics (N = 146)*

| Variable               | No.  | %   |
|------------------------|------|-----|
| Ethnicity              |      |     |
| White                  | 84   | 57.5|
| Hispanic               | 31   | 21.2|
| African American       | 17   | 11.6|
| Asian                  | 9    | 6.2 |
| Other                  | 5    | 3.4 |
| Tours of duty          |      |     |
| 0                      | 7    | 4.8 |
| 1                      | 55   | 37.7|
| 2                      | 48   | 32.9|
| 3                      | 19   | 13.0|
| ≥4                     | 17   | 11.6|
| Episodes of blast-related mTBI |  |     |
| 1                      | 77   | 52.7|
| 2                      | 41   | 28.1|
| ≥3                     | 28   | 19.2|
| Hypertension           | 19   | 13.0|

Note: —WASI-II indicates Wechsler Adult Intelligence Scale, 2nd ed; IQ, intelligence quotient; HIT-6 = Headache Impact Test-6; CSI = Concussion Symptom Inventory.

Table 2: Demographic and clinical characteristics (N = 146)*

| Variable              | Mean | SD  |
|-----------------------|------|-----|
| Time since mTBI (yr)  | 9.4  | 6.2 |
| Deployment time (yr)  | 5.7  | 3.5 |
| WASH-II IQ (standard score) | 106.6 | 13.3 |
| HIT-6 score           | 45.8 | 9.3 |
| CSI                   | 12.5 | 14.0|

Note: The maximum CSI and HTI-6 score is 72, indicating maximum symptom severity. The maximum WASH-II IQ is 160.

RESULTS

One-hundred forty-six subjects were identified with a history of blast-related mTBI (132 men, 14 women). Demographic and clinical data for the present sample are reported in Tables 1 and 2. The mean age was 32.8 ± 7.4 years (median, 31 years; range, 22–66 years). The time interval from the last injury to MR imaging ranged from 1 to 31 years (mean, 9.4 ± 6.2 years; median, 9 years). Sixty-nine subjects (47.3%) had ≥2 episodes. Twenty-one (14.4%) reported loss of consciousness with their injury of <30 minutes, and 85.6% had altered mental status. Subjects had a normal distribution of IQ and demonstrated mild headache pain and postconcussive symptoms (Tables 1 and 2). No CMH were detected by either neuroradiologist. One subject (1%) had cerebellar ectopia, 7 (5%) had developmental venous anomalies, 48 (33%) had some degree of white matter abnormality (ie, T2 hyperintensity), 3 (2%) had arachnoid cysts, and 54 (37%) had sinus disease. No other structural abnormalities were identified. No images demonstrated artifacts warranting exclusion.
Table 3: Prevalence of CMH in civilian and military populations

| Authors                | Population     | Mechanism of mTBI | Prevalence of CMH | Time since mTBI | MRI              | Voxel Size (mm) |
|------------------------|----------------|-------------------|-------------------|-----------------|------------------|-----------------|
| van der Horn et al (2017) | Civilian       | Blunt             | 15/54 (28%)       | 33 days         | SWI (3T)        | 0.9 × 0.9 × 2   |
| Trifan et al (2017)    | Civilian       | Blunt             | 26/150 (17%)      | 29 months       | SWI (3T)        | 0.5 × 0.5 × 2   |
| Toth et al (2018)      | Civilian       | Blunt             | 1/13 (8%)         | 2 years         | SWI (3T)        | 1.0 × 0.9 × 1.5 |
| Huang et al (2015)     | Civilian       | Blunt             | 23/111 (21%)      | 25 days         | SWI (3T)        | 0.5 × 0.5 × 2   |
| Wang et al (2014)      | Civilian       | Blunt             | 32/165 (19%)      | ≤3 days         | SWI (3T)        | 0.7 × 0.7 × 1.2 |
| Yuh et al (2013)       | Civilian       | Blunt             | 23/98 (23%)       | 12 days         | T2*-weighted GRE (1.5/3T) | NA              |
| Topal et al (2008)     | Civilian       | Blunt             | 4/40 (10%)        | <1 day          | T2*-weighted GRE (1.5T) | NA              |
| Tate et al (2017)      | Military members | Mixed blunt and blast | 9/77 (12%)       | 309 days        | SWI (3T)        | 1.0 × 0.9 × 1.5 |
| Liu et al (2016)       | Military members | Mixed blunt and blast | 18/559 (3%)      | 1325 days       | SWI (3T)        | 0.5 × 0.9 × 1.5 |
| Riedy et al (2016)     | Military members | Mixed blunt and blast | 29/768 (4%)      | 1381 days       | SWI (3T)        | 0.5 × 0.9 × 1.5 |
| Current study (2018)   | Military members | Blast             | 0/146 (0%)        | 9 years         | SWI (3T)        | 0.5 × 0.6 × 2   |

Note: —NA indicates not applicable; GRE, gradient recalled-echo.

**DISCUSSION**

In this cohort of 146 veterans with exposure to chronic blast-related mTBI, with approximately half exposed to multiple blast episodes in multiple tours during 5 years of deployment time, no foci of CMH were detected at 3T MR imaging using SWI. The overall prevalence of CMH in our cohort of well-characterized subjects with a history of chronic military blast-related mTBI was low compared with previous reports of civilian blunt-related mTBI.21-24,34-36 There is a mix of literature and findings in terms of the mechanism of injury (blunt or mixed population of blunt- and blast-related mTBI), prevalence of CMH, variable cohorts (military or civilian), variable time since injury, and the MR imaging techniques used for CMH detection. The literature is summarized in Table 3.3,4,21-26,34-36 Our findings are in keeping with Liu et al25 and Riedy et al3 who reported 3%–4% prevalence of chronic blast-related mTBI CMH that we report may suggest a substantially lower prevalence of CMH in this cohort of subjects with blast-related mTBI compared with previous reports, primarily in civilian chronic blunt-related mTBI.34,35 and may reflect differences in the mechanism and pathophysiology of injury. However, due to possible degradation of CMH with time, the chronicity of injury may play a role in the detection of CMH, and future studies will be needed to assess the prevalence of CMH in the more acute settings.

Limitations of this study include a retrospective self-report of injury, though a prospective study including acutely injured subjects is challenging due to the limitations of MR imaging availability in remote military sites. Furthermore, the Ohio State University TBI Identification Method is considered a reliable and valid tool for assessing TBI and was selected on the basis of its high interrater reliability.28 An additional limitation is the variability of the time since injury compared with the previous studies, particularly because there is evidence that CMH may evolve.

**CONCLUSIONS**

We found that no individuals in the 146 subjects with chronic blast-related mTBI had evidence of CMH on 3T SWI. This finding may suggest a substantially lower prevalence of CMH in this cohort of subjects with blast-related mTBI compared with previous reports, primarily in civilian chronic blunt-related mTBI.34,35 and may reflect differences in the mechanism and pathophysiology of injury. However, due to possible degradation of CMH with time, the chronicity of injury may play a role in the detection of CMH, and future studies will be needed to assess the prevalence of CMH in the more acute settings.

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