

## Persistent postconcussive symptoms in children and adolescents with mild traumatic brain injury receiving initial head computed tomography

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**OBJECTIVE** The aim of this paper was to evaluate the prevalence of postconcussive symptoms and their relation to health-related quality of life (HRQOL) in pediatric and adolescent patients with mild traumatic brain injury (mTBI) who received head CT imaging during initial assessment.

**METHODS** Patients aged between 5 and 21 years with mTBI (Glasgow Coma Scale scores 13–15) and available Rivermead Post Concussion Questionnaire (RPQ) at 6 months of follow-up in the multicenter, prospectively collected CENTER-TBI (Collaborative European NeuroTrauma Effectiveness Research in TBI) study were included. The prevalence of postconcussive symptoms was assessed, and the occurrence of postconcussive syndrome (PCS) based on the ICD-10 criteria, was analyzed. HRQOL was compared in patients with and without PCS using the Quality of Life after Brain Injury (QOLIBRI) questionnaire.

**RESULTS** A total of 196 adolescent or pediatric mTBI patients requiring head CT imaging were included. High-energy trauma was prevalent in more than half of cases (54%), abnormalities on head CT scans were detected in 41%, and admission to the regular ward or intensive care unit was necessary in 78%. Six months postinjury, 36% of included patients had experienced at least one moderate or severe symptom on the RPQ. PCS was present in 13% of adolescents and children when considering symptoms of at least moderate severity, and those patients had significantly lower QOLIBRI total scores, indicating lower HRQOL, compared with young patients without PCS (57 vs 83 points,  $p < 0.001$ ).

**CONCLUSIONS** Adolescent and pediatric mTBI patients requiring head CT imaging show signs of increased trauma severity. Postconcussive symptoms are present in up to one-third of those patients, and PCS can be diagnosed in 13% 6 months after injury. Moreover, PCS is significantly associated with decreased HRQOL.

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**KEYWORDS** mild traumatic brain injury; pediatric; postconcussive symptoms; CT imaging; Rivermead Post Concussion Symptoms Questionnaire; RPQ; health-related quality of life; HRQOL; trauma

MILD traumatic brain injury (mTBI) is a common injury in children and adolescents that frequently leads to clinical presentation. An epidemiological study including children ranging from 0 to 17 years old requiring medical contact reported an estimated incidence of 304 cases per 100,000 child-years.<sup>1</sup> Ninety-seven percent of included patients in that study were classified as

having mTBI,<sup>1</sup> which was defined according to the American Congress of Rehabilitation Medicine by a Glasgow Coma Scale (GCS) score of 13–15, a maximum loss of consciousness (LOC) of 30 minutes, and posttraumatic amnesia (PTA) less than 24 hours after the brain impact.<sup>2,3</sup> Acute postconcussive symptoms after mTBI can be severe and might include somatic symptoms such as headaches,

**ABBREVIATIONS** CENTER-TBI = Collaborative European NeuroTrauma Effectiveness Research in TBI; ED = emergency department; HRQOL = health-related QOL; GCS = Glasgow Coma Scale; LOC = loss of consciousness; mTBI = mild TBI; PCS = postconcussion syndrome; PTA = posttraumatic amnesia; QOL = quality of life; QOLIBRI = Quality of Life after Brain Injury; RPQ = Rivermead Post Concussion Symptoms Questionnaire; TBI = traumatic brain injury.

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cognitive symptoms such as difficulty concentrating, and affective symptoms such as irritability. In a considerable fraction of patients, symptoms can chronically persist for weeks, months, or even years.<sup>4</sup> The prevalence of prolonged postconcussive symptoms in young patients varies depending on the diagnostic criteria used and the population studied but has been reported to be as high as 31%.<sup>5</sup> Although the knowledge about such postconcussive symptoms in the pediatric and adolescent population has considerably increased over the past years and now includes insights from large, multicenter studies,<sup>5,6</sup> there remains an important subgroup of patients who have not been studied in detail: young mTBI patients requiring head CT during initial assessment following the brain injury. While, to avoid radiation exposure, the majority of adolescents and children do not receive CT imaging after mTBI, it might be nevertheless indicated when, for example, a history of high-energy injury mechanisms, suspicious clinical findings, or other risk factors are present. In such patients, a more severe subtype of mTBI might therefore be present. Mild TBI in general can already have profound negative impacts on the lives of affected adolescents and children.<sup>7</sup> Moreover, young patients experiencing a combination of persistent postconcussive symptoms of somatic, cognitive, and affective nature can be diagnosed with postconcussion syndrome (PCS), a diagnosis encoded in the ICD-10.<sup>8</sup> Between 11% and 55% of adolescents and children have been reported to develop postconcussive symptoms following mTBI.<sup>9</sup> In those patients, the persistent postconcussive symptoms can have serious consequences and could significantly decrease their overall health-related quality of life (HRQOL).<sup>10</sup> The objectives of this study, therefore, were to examine the prevalence of such persistent postconcussive symptoms, to analyze the occurrence of PCS, and to assess its association with HRQOL in the potentially more complicated subgroup of adolescent and pediatric patients who were classified as having mTBI but who required head CT imaging after presenting to the emergency department (ED).

## Methods

### Study Design and Patient Selection

For the present study, data from the Collaborative European NeuroTrauma Effectiveness Research in TBI (CENTER-TBI) core study was analyzed. CENTER-TBI is a multicenter, observational, longitudinal cohort study of patients with a clinical diagnosis of TBI (all severities) and, notably, the indication for head CT imaging (defined at the discretion of each study center), who presented to a participating study center within 24 hours after the injury. Patients for the CENTER-TBI core study were enrolled from December 2014 to December 2017 in 59 centers across Europe and Israel.<sup>11,12</sup> The study protocol was approved by national and local ethics committees for each recruiting site (<https://www.center-tbi.eu/project/ethical-approval>), and informed consent was obtained by the legal representative or next of kin for all enrolled patients. For this analysis, we included all pediatric and adolescent patients between the ages of 5 and 21 years from the CENTER-TBI core study database who presented with

mTBI (GCS scores 13–15) and had completed the Rivermead Post Concussion Symptoms Questionnaire (RPQ) at 6 months postinjury.

### Data Collection

Data were accessed through the clinical study data management tool Neurobot (INCF-Neurobot, RRID: SCR\_017004). The CENTER Core version 2.1 was used for this study. The variables age, sex, GCS score at admission, seizures, intubation, reason for admission, reason for CT imaging, presence of any intracranial abnormalities on initial CT brain imaging (CT abnormalities), post-traumatic amnesia (PTA), LOC, major extracranial injury, admission to the ICU, high-energy trauma and RPQ and Quality of Life After Brain Injury (QOLIBRI) scores at 6 months were collected. Major extracranial injury was defined as an abbreviated injury scale score of at least 3 in any body region. High-energy trauma was defined as an accelerating/decelerating trauma of high velocity or falls > 1 m. The variable “CT abnormality” refers to any trauma-related abnormality found on CT imaging.

### Outcome Measurements

#### Rivermead Post Concussion Symptoms Questionnaire

The RPQ was used to assess the presence and severity of postconcussive symptoms following mTBI.<sup>13</sup> This assessment instrument evaluates 16 different symptoms that can be divided into 3 categories: somatic symptoms (headaches, blurred vision, double vision, noise sensitivity, light sensitivity, dizziness, nausea, sleep disturbances, and fatigue), affective symptoms (irritability, depression, frustration, and restlessness), and cognitive symptoms (forgetfulness, poor concentration, and slowed thinking). Patients rate the severity of each symptom on a 5-point Likert scale (not experienced at all [0], no more of a problem [1], a mild problem [2], a moderate problem [3], and a severe problem [4]). Patients were specifically instructed to rate the severity of their symptoms over the last 7 days in comparison with their preinjury levels, thus giving the instrument a time and an event anchor.<sup>14</sup> For the analysis, scores 0 and 1 were combined into one category as proposed in previous works,<sup>13,15,16</sup> yielding a 4-point scale ranging from currently absent symptoms (0), mild symptoms (2), moderate symptoms (3), and severe symptoms (4). The total RPQ score was calculated by adding the scores of each RPQ symptom to a sum, with a maximum total score of 64. The presence of PCS was defined according to ICD-10 criteria, which meant that patients had to experience at least 3 of the following symptoms: headaches, dizziness, sleep disturbance, fatigue, being irritable/easily angered, forgetfulness/poor memory, and poor concentration.<sup>8</sup> As there is currently no consensus on whether to include only symptoms of at least moderate severity (rating score  $\geq 3$ ) or even of mild severity (rating score  $\geq 2$ ) when assessing patients for PCS, the prevalence of PCS was analyzed for both definitions in this study.

#### Health-Related Quality of Life

To assess HRQOL, the QOLIBRI questionnaire was used, which consists of 37 items covering 6 aspects of dis-

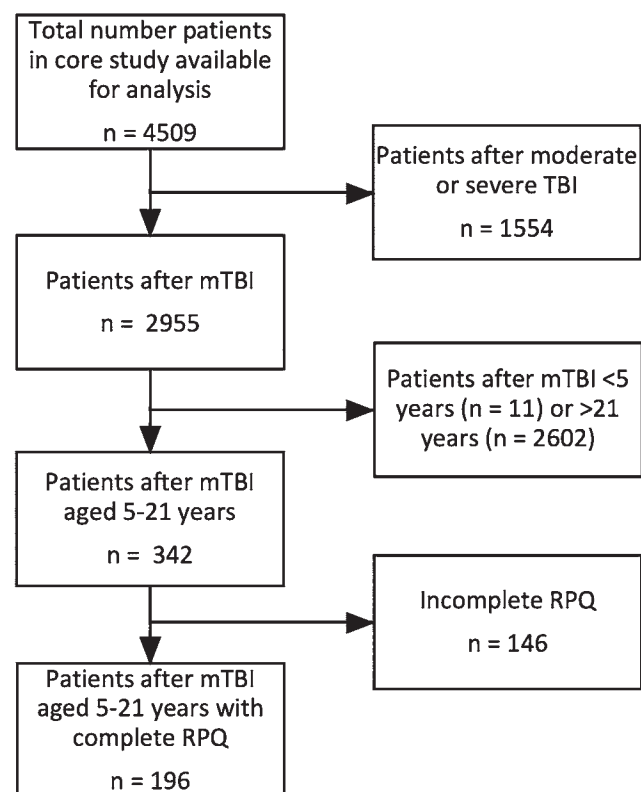


FIG. 1. Flowchart of patient selection.

ease-specific HRQOL after TBI (cognition, self, daily life and autonomy, social relationships, emotions, and physical problems).<sup>17</sup> The QOLIBRI instrument is a health-related, disease-specific, internationally validated instrument to assess HRQOL in patients after brain injury.<sup>17,18</sup> The responses to each questionnaire item were summed to the QOLIBRI total score ranging from 0, meaning worst, to 100, meaning best possible HRQOL (<https://qolibrinet.com/scoring/>). A QOLIBRI total score of 60 or greater represents good HRQOL; a score below 60 indicates an unsatisfactory outcome with an increased risk for one or even two psychiatric disorders.<sup>18</sup>

### Statistical Analysis

Baseline demographic and clinical variables are presented as the median and IQR for continuous variables and numbers and percentages for categorical variables. Correlation between total RPQ scores and total QOLIBRI scores were tested using Spearman's rank-sum test. Differences in QOLIBRI total scores between patients with and without PCS were tested using the nonparametric Mann-Whitney U-test. The level of significance was set at  $p < 0.05$ . All analyses were conducted with the statistical software R (version 3.6.1, <https://www.r-project.org/>).

## Results

### Patient Characteristics

Among recruited CENTER-TBI core study participants, 342 mTBI patients were between the age of 5 and

TABLE 1. Characteristics of the study population

Characteristic	Value
Demographic characteristics	
Median age, yrs [IQR]	17 [14–19]
Sex (male)	142 (72)
Stratum	
ED	44 (22)
Admission	96 (49)
ICU	56 (29)
High-energy trauma	106 (54)
Preinjury health status	
Previous history of headaches	10 (5)
Previous psychiatric history	8 (4)
Previous TBI	24 (12)
Clinical presentation	
GCS score 15	144 (73)
PTA	102 (52)
LOC	114 (58)
Major extracranial injury	37 (19)
CT abnormalities	80 (41)
Influence of alcohol & drugs	
Blood alcohol >80 mg/dL	6 (3)
Drug abuse	5 (3)

Values represent the number of patients (%) unless stated otherwise.

21 years at the time of enrollment, of whom 196 patients (60%) completed the RPQ at 6 months after the brain impact and were included in this study (Fig. 1). These patients were enrolled at 32 different centers across Europe and by definition of the CENTER-TBI core study inclusion criteria had undergone head CT scanning during their initial assessment in the ED. The median age was 17 years (IQR 14–19 years, range 6–21 years), and 72% of included patients were male. A GCS score of 15 was recorded for 144 patients (73%). LOC and PTA were very common in this cohort, in 58% and 52% of patients, respectively. Overall, 54% of patients were involved in a high-energy trauma, and 19% additionally had major extracranial injuries with an abbreviated injury scale score  $\geq 3$ . Three patients had seizures (1 partial, 1 generalized, and 1 status epilepticus). Of all patients, 22% were discharged home from the ED, while 49% and 29% were admitted to the regular ward and ICU, respectively (Table 1). Among patients admitted to the regular ward, 77% were admitted for clinical observation of TBI, 15% due to abnormalities on CT scanning, 5% due to extracranial injuries requiring medical care at the hospital, and 3% for unknown/other reasons. ICU patients were admitted for the following reasons: 54% due to the need for frequent neurological observations, 27% due to mechanical ventilation, 9% due to extracranial injuries, 4% due to neurological deterioration, 4% for observation after neurosurgery, 2% for invasive vital parameter monitoring, and 1% for unknown/other reasons. Twenty-five patients (13%) underwent intubation during their hospital stay.

### CT Indications and Findings

Because indication for head CT imaging was an inclu-

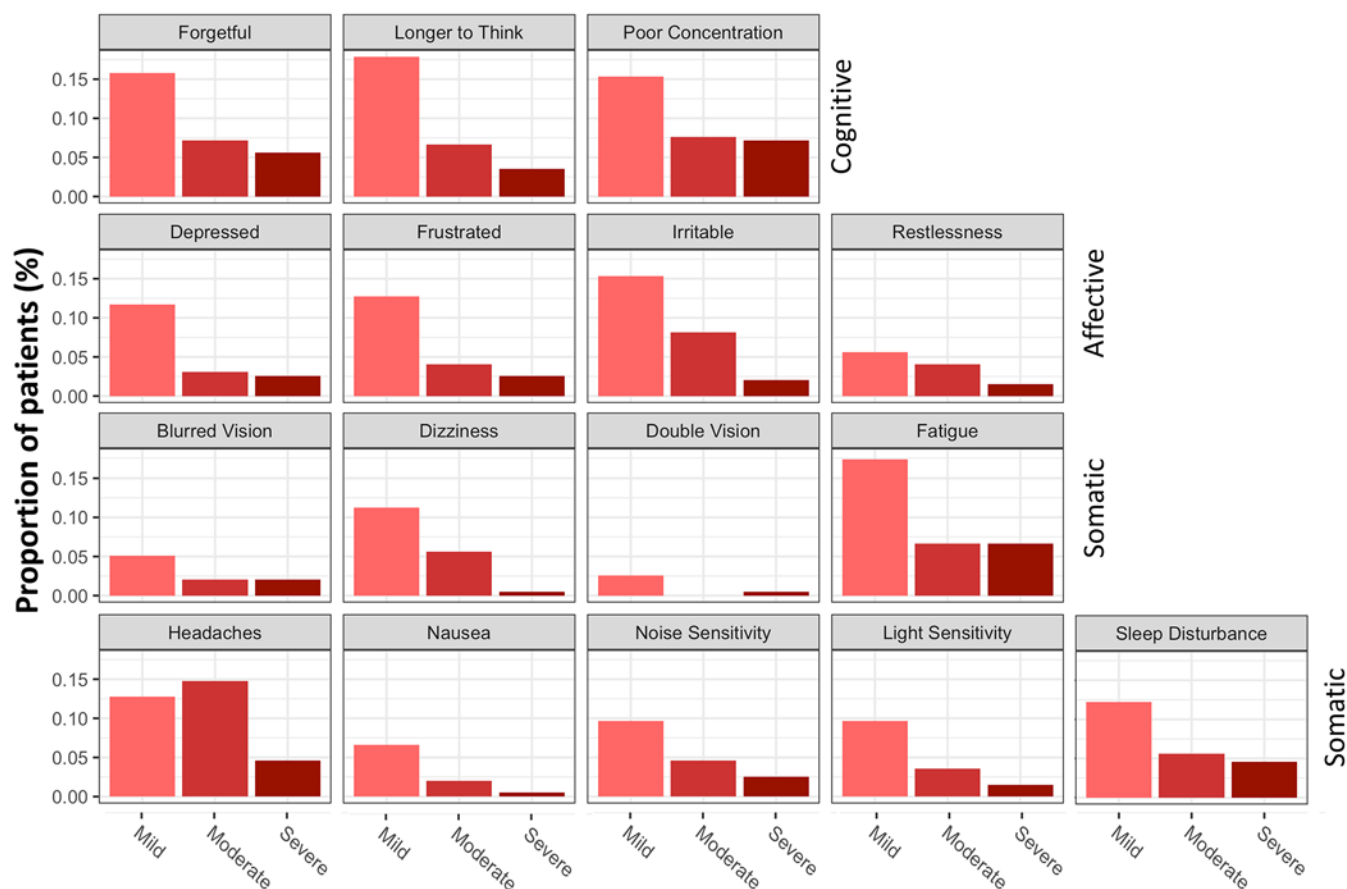


FIG. 2. Prevalence of mild, moderate, or severe postconcussive symptoms. Figure is available in color online only.

sion criterion for the CENTER-TBI core study, all patients in this analysis had available head CT images. In this context, a GCS score of 15 plus the presence of risk factors such as high-energy trauma was stated as the main indication for obtaining a CT scan in 42% of patients. In 32%, a GCS score lower than 14 led to the decision for head CT imaging. Other reasons included presence of a head wound in 19%, exclusion of abnormalities before discharge in 12%, and suspicion of maxillofacial injuries in 6% of cases. Importantly, multiple reasons for one patient could be entered into the study database. Taken together, CT abnormalities were detected in 41% of patients. These included skull fractures (32%), contusions (16%), subarachnoid hemorrhages (16%), epidural hematomas (13%), acute subdural hematomas (10%), traumatic axonal injuries (7%), mass lesions (3%), and cisternal compressions (2%). In two patients, a midline shift was present. Intraventricular hemorrhage and subdural collection mixed density were detected in 1 patient each.

#### Prevalence of Postconcussive Symptoms and Occurrence of PCS

The prevalence of mild, moderate, or severe postconcussive symptoms was assessed at 6 months after mTBI in our adolescent and pediatric patient cohort (Fig. 2). More than one-third of patients (36%) reported having at least one of the 16 symptoms assessed in the RPQ with at least

moderate severity. When including symptoms of mild severity, this number exceeded 60% (Fig. 3). The most commonly reported symptoms were headaches, fatigue, poor concentration, and forgetfulness (i.e., poor memory). At least one of the 9 somatic symptoms of at least moderate severity was reported by 30% of patients, while 20% had at least one of the 3 cognitive and 4 psychological symptoms. These numbers increased to 54% for any somatic symptom, 40% for any cognitive symptom, and 37% for any psychological symptom when including mild symptoms. Among patients reporting postconcussive symptoms at 6 months, the median number of moderate or worse symptoms was 2 (IQR 2–4) and 5 (IQR 2–7) for mild or worse symptoms. By our definition requiring at least 3 moderate RPQ symptoms on the basis of ICD-10 criteria, 26 patients (13%) were classified as having PCS 6 months after injury. Notably, this number substantially increased to 34% when applying the definition that at least 3 symptoms of at least mild severity were required. There were no significant differences in the frequency of any RPQ symptoms between patients admitted to the hospital and those discharged home from the ED (39% vs 27%,  $p = 0.22$ ). Similarly, the presence of PCS did not differ significantly between those groups regardless of which definition was used (PCS score  $\geq 2$ : 36% vs 25%,  $p = 0.20$ ; and PCS score  $\geq 3$ : 14% vs 11%,  $p = 0.87$ ). When comparing patients with CT abnormalities with those without them, we found a higher pro-



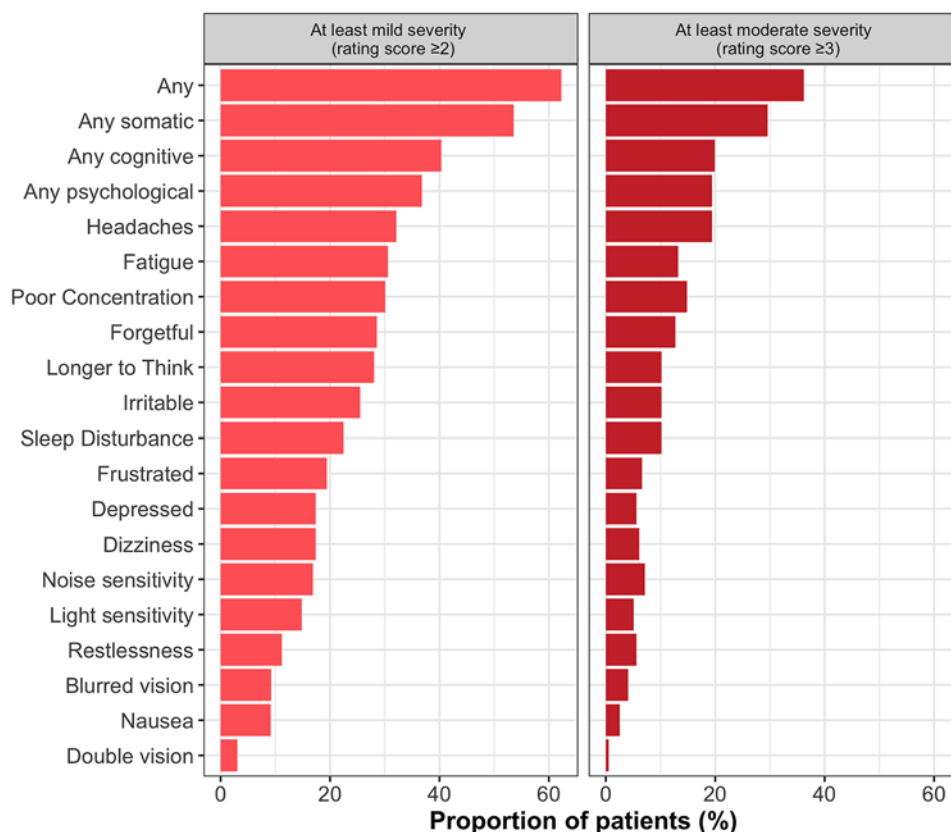


FIG. 3. Symptoms assessed in the RPQ with at least mild or moderate severity. Figure is available in color online only.

portion of patients reporting any RPQ symptom (44% vs 30%,  $p < 0.001$ ). However, when applying the definitions for PCS, no significant differences between those groups were detected (PCS score  $\geq 2$ : 36% vs 34%,  $p = 0.87$ ; and PCS score  $\geq 3$ : 19% vs 10%,  $p = 0.77$ ).

### PCS and Quality of Life

A total of 172 patients (88%) included in this study completed a QOLIBRI assessment at 6 months of follow-up. The median QOLIBRI total score was 82 (IQR 68–91), representing good quality of life (QOL). In 67 patients (34%) with PCS considering at least mild severity, the median QOLIBRI total score was 66 (IQR 53–76). Of those, 23 patients (34%) had a QOLIBRI total score  $< 60$ , representing unsatisfactory HRQOL. Patients without PCS following this classification ( $n = 129$ , 66%) reported a median QOLIBRI total score of 86 (IQR 79–94), which was significantly higher than that for patients with PCS considering at least mild severity ( $p < 0.001$ ). As opposed to patients with PCS, only 4 patients (3%) without PCS had a QOLIBRI rating  $< 60$ . When applying the definition of at least 3 symptoms of moderate severity, similar results were obtained. Patients classified as having PCS ( $n = 26$ ) had a median QOLIBRI total score of 57 (IQR 49–72), and 14 of those 26 patients (54%) reported a QOLIBRI total score  $< 60$ . Patients without PCS following this classification ( $n = 170$ , 87%) had a median QOLIBRI total score of 83 (IQR 73–92), which was significantly higher than that of the patients with PCS, with a significant dif-

ference between these two groups ( $p < 0.001$ ). Only 13 patients (8%) without PCS reported a QOLIBRI total score  $< 60$ . For both severity cutoffs, this means that patients with PCS have lower HRQOL than do patients without PCS. Moreover, total RPQ scores and QOLIBRI total scores showed a significant, moderately strong negative correlation ( $r = -0.62$ ,  $p < 0.001$ ). No significant differences in median QOLIBRI total scores could be found between patients admitted to the hospital and those discharged home after ED presentation (82 [68–91] vs 81 [70–90],  $p = 0.80$ ). Likewise, the median QOLIBRI total score was similar between patients with and without CT abnormalities (82 [IQR 68–91] vs 81 [IQR 68–90],  $p = 0.77$ ).

### Discussion

Mild TBI represents one of the most common injuries in the young population, but only a small minority of patients will undergo CT scanning in an effort to avoid potentially harmful radiation in this particular patient population. The analysis of patient characteristics in our cohort showed that adolescents and children who require CT imaging indeed form a more severe and complex subgroup of mTBI patients. More than half of the patients in this study were involved in high-energy trauma, and abnormalities on CT imaging were detected in 41%. Nearly 30% of patients were primarily admitted to the ICU in this cohort, which is notable because the TBI was classified at presentation as mild in all patients. This might reflect the higher

injury severity in this particular group of patients, and possible explanations for the high ICU admission rate despite mTBI include the high prevalence of concurrent extracranial injuries. While previous reports of postconcussive symptoms focused on young mTBI patients in general and thus included only a small portion of patients who underwent head CT scanning (and/or excluded them altogether when detecting abnormalities on CT imaging), with head CT imaging as an inclusion criterion, the CENTER-TBI study offers the unique possibility for analyzing this particular subgroup of adolescents and children as a separate entity.

For young mTBI patients who require head CT imaging during initial postinjury assessment, we report a high prevalence of postconcussive symptoms. One-third of patients reported at least 1 symptom of at least moderate severity 6 months after brain injury. Thirteen percent of patients met the criteria for our more demanding definition of PCS that considered only at least moderate symptoms, which falls well into the range of results from previous studies that included pediatric mTBI patients in general.<sup>4,19,20</sup> It is noteworthy that reported prevalence rates vary greatly between such studies due to, for example, different time intervals used until the assessment of PCS. Because postconcussive symptoms are reported to decrease over time, a high prevalence of such symptoms can typically be observed in studies in which the assessment has been performed within the first few weeks after the brain injury.<sup>9,21</sup> Nevertheless, most studies have evaluated persistent postconcussive symptoms and PCS between 4 and 12 weeks after mTBI. In our current study, however, a much longer time interval of 6 months was used. Despite this substantial difference, we still report comparable PCS prevalence rates (13% and 34%), indicating that adolescent and pediatric mTBI patients with an indication for head CT imaging might have a higher symptom burden. Although not significantly different, patients discharged home from the ED compared with patients admitted to the hospital or ICU had a slightly lower frequency of having any RPQ symptoms (27% vs 39%) and a slightly lower PCS score (discharge to home: 25% [PCS score  $\geq 2$ ] and 11% [PCS score  $\geq 3$ ] vs discharge to hospital or ICU: 36% [PCS score  $\geq 2$ ] and 14% [PCS score  $\geq 3$ ]). These findings highlight the importance of triage in the ED after mTBI also for adolescents and children. Nevertheless, they might also indicate that young mTBI patients with normal findings on head CT imaging might be prone to rapid discharge from the ED while still having a relevant risk of developing PCS, which might leave them undertreated.

Somatic symptoms were very common in our study (30% of children and adolescents) and this number increased to more than 50% when including also mild symptoms. Naturally, when including mild symptoms, the results are likely to be less specific and more susceptible to confounding influences, as mild somatic symptoms such as mild headaches and fatigue are also common in non-injured individuals.<sup>22–24</sup> The high prevalence of symptoms of moderate and severe severity in adolescents and children with mTBI and an indication for head CT imaging, however, emphasizes the presumption that mTBI in this subgroup might not be so “mild” after all but can have se-

rious long-term sequelae. We found a higher proportion of patients reporting any RPQ symptom in patients with CT abnormalities. However, when applying the stricter definition of PCS, no significant differences could be detected, indicating that differences in postconcussive symptoms between those groups were, if at all, very subtle. However, it is important to emphasize that due to the limited patient numbers, all abnormal CT findings were grouped into the variable “CT abnormality” and results might thus be somewhat blunted. Further studies with larger patient numbers are needed to address the question whether certain findings on CT are closer associated with RPQ and PCS than others.

HRQOL after mTBI has been the topic of various publications, mostly focusing on the adult population.<sup>25</sup> In adolescent and pediatric mTBI patients, fewer prior studies on HRQOL exist. Howell et al. investigated postconcussion QOL and symptom burden in 176 young mTBI patients who completed a 30-day follow-up QOL questionnaire and uncovered that age was not significantly associated with physical or psychosocial QOL ratings. They also pointed out that impaired QOL outcome might identify children and adolescents at risk for persistent symptoms after concussions.<sup>26</sup> A further analysis investigating the association between HRQOL and postconcussive symptoms in 1722 nonconcussed children aged 8–12 years identified a negative correlation between good HRQOL and postconcussion symptoms that were experienced by the noninjured children due to daily stressors.<sup>27</sup> Similarly, by evaluating long-term HRQOL 2.7 years after concussion in young mTBI patients aged 8–18 years, it could be shown that children’s premorbid attention and mood are relevant for outcome and need to be assessed in clinical settings to prevent and treat long-term psychosocial postconcussion problems.<sup>28</sup>

In our study, adolescent and pediatric patients with PCS had significantly lower QOLIBRI total scores, indicating lower or even unsatisfactory HRQOL compared with young patients without PCS. Those findings are in line with the results from another previous study showing that HRQOL is influenced across several domains (e.g., physical, emotional, social, school) in patients with PCS.<sup>10</sup> In addition, the reported significant correlation between the RPQ and QOLIBRI total scores in our study illustrates the close association between postconcussive symptoms and HRQOL, and therefore demonstrates the clinical importance of recognizing postconcussive symptoms in this particular subgroup of adolescents and children who underwent CT imaging after mTBI. Interestingly, there were no significant differences in total QOLIBRI scores between admitted or discharged patients and patients with and without CT abnormalities. As mentioned above, further studies need to investigate whether this is true for all CT findings when not grouped together. While there are some preliminary promising therapeutic approaches such as brief cognitive therapy and other medical and nonmedical interventions that could be effective and beneficial in children and adolescents with persistent postconcussive symptoms,<sup>29,30</sup> further high-quality studies are needed to more closely investigate the possible impact and efficacy of these interventions.<sup>29</sup>

We note several limitations to our study. First, while CENTER-TBI included patients of all ages, pediatric and adolescent patients were underrepresented as participating centers were mainly general hospitals and not specialized pediatric centers. Therefore, the sample size is relatively small when compared with the older patient cohort in the CENTER-TBI study. Due to the CENTER-TBI study design that requires all patients to have undergone CT imaging at admission at the clinician's indication, no control group that did not receive CT imaging is available for comparison. Moreover, no comparable study with the indication for CT imaging as an exclusion criterion is available in the literature to create a historical control group. Furthermore, a nonresponse bias limiting external validity is possible, as a considerable proportion of patients were lost to follow-up (40%). Patients lost to follow-up were slightly older (median 18 [IQR 16–20] years vs 17 [IQR 14–19] years;  $p = 0.004$ ) and had fewer CT abnormalities (29% vs 41%,  $p = 0.02$ ). There were no differences in regard to sex distribution, care stratum, presence of high-energy trauma, GCS score of 15, or major extracranial trauma. While our study showed no significant differences between patients with and without CT abnormalities in the primary outcome measures (PCS and QOLIBRI), the smaller proportion of CT abnormalities in those lost to follow-up is a noteworthy limitation. Results from our study also need to be interpreted with caution when considering the assessment tool used. The RPQ was initially validated in adolescents and adults aged 16 years and older.<sup>13</sup> It has been suggested to remain a basic common data element in TBI research as it correlates with cognitive impairment,<sup>13,14,31</sup> although it remains a controversial assessment tool that might, among other concerns, be prone to recall bias as patients might underestimate postconcussive-like symptoms they experienced before the injury. Lastly, the use and utility of simple change scores (i.e., those that solely consider the changes between baseline and follow-up scores), for diagnosis of postconcussive symptoms in children have recently been questioned.<sup>32</sup> While the RPQ is supposed to be answerable by younger children, sequencing of symptoms on a time axis as required by the RPQ is considered to be difficult for children aged < 7 years.<sup>33</sup> However, having included only 7 patients (3.6%) aged 6 years and 7 patients (3.6%) aged 7 years, results of these participants potentially only had a minor impact on the overall result. Nevertheless, the results from this study should merely be seen as an exploratory analysis. Likewise, due to the limited patient numbers, we did not perform predictive modeling and our results are therefore not intended to prognosticate PCS in young mTBI patients. However, our results support the fact that further studies designed to acquire a better understanding of postconcussive symptoms are needed, as those symptoms might be highly prevalent in children and adolescents with mTBI and directly affect patients' HRQOL.

## Conclusions

In this analysis of the multicenter, prospectively collected CENTER-TBI data set, we found a high prevalence of 30% to 60% of postconcussive symptoms at 6 months

postinjury in adolescents and children with mTBI who underwent CT imaging on presentation to the hospital. Depending on the definition, 13%–34% of patients were classified as experiencing a PCS. These patients had a significantly decreased HRQOL compared with patients without PCS.

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## Appendix

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## References

- Schneider AJ, Shields BJ, Hostetler SG, et al. Incidence of pediatric traumatic brain injury and associated hospital resource utilization in the United States. *Pediatrics*. 2006; 118(2):483–492.
- Kay T, Harrington DE, Adams R, et al. Definition of mild traumatic brain injury. *J Head Trauma Rehabil*. 1993;8(3): 86–87.
- Sussman ES, Pendharkar AV, Ho AL, Ghajar J. Mild traumatic brain injury and concussion: terminology and classification. *Handb Clin Neurol*. 2018;158:21–24.
- Barlow KM, Crawford S, Stevenson A, et al. Epidemiology of

- postconcussion syndrome in pediatric mild traumatic brain injury. *Pediatrics*. 2010;126(2):e374–e381.
5. Zemek R, Barrowman N, Freedman SB, et al. Clinical risk score for persistent postconcussion symptoms among children with acute concussion in the ED. *JAMA*. 2016;315(10):1014–1025.
  6. Babcock L, Byczkowski T, Wade SL, et al. Predicting postconcussion syndrome after mild traumatic brain injury in children and adolescents who present to the emergency department. *JAMA Pediatr*. 2013;167(2):156–161.
  7. Fineblit S, Selci E, Loewen H, et al. Health-related quality of life after pediatric mild traumatic brain injury/concussion: a systematic review. *J Neurotrauma*. 2016;33(17):1561–1568.
  8. *The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research*. World Health Organization; 1992.
  9. Davis GA, Anderson V, Babl FE, et al. What is the difference in concussion management in children as compared with adults? A systematic review. *Br J Sports Med*. 2017;51(12):949–957.
  10. Novak Z, Aglipay M, Barrowman N, et al. Association of persistent postconcussion symptoms with pediatric quality of life. *JAMA Pediatr*. 2016;170(12):e162900.
  11. Maas AIR, Menon DK, Adelson PD, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol*. 2017;16(12):987–1048.
  12. Maas AIR, Menon DK, Steyerberg EW, et al. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI): a prospective longitudinal observational study. *Neurosurgery*. 2015;76(1):67–80.
  13. King NS, Crawford S, Wenden FJ, et al. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *J Neurol*. 1995;242(9):587–592.
  14. Bodien YG, McCrea M, Dikmen S, et al. Optimizing outcome assessment in multicenter TBI trials: perspectives from TRACK-TBI and the TBI Endpoints Development Initiative. *J Head Trauma Rehabil*. 2018;33(3):147–157.
  15. Eyres S, Carey A, Gilworth G, et al. Construct validity and reliability of the Rivermead Post-Concussion Symptoms Questionnaire. *Clin Rehabil*. 2005;19(8):878–887.
  16. Crossen MC, Winkler EA, Yue JK, et al. Development of a prediction model for post-concussive symptoms following mild traumatic brain injury: a TRACK-TBI pilot study. *J Neurotrauma*. 2017;34(16):2396–2409.
  17. von Steinbuechel N, Petersen C, Bullinger M, QOLIBRI Group. Assessment of health-related quality of life in persons after traumatic brain injury—development of the Qolibri, a specific measure. *Acta Neurochir Suppl*. 2005;93:43–49.
  18. Truelle JL, Koskinen S, Hawthorne G, et al. Quality of life after traumatic brain injury: the clinical use of the QOLIBRI, a novel disease-specific instrument. *Brain Inj*. 2010;24(11):1272–1291.
  19. Ewing-Cobbs L, Cox CS Jr, Clark AE, et al. Persistent postconcussion symptoms after injury. *Pediatrics*. 2018;142(5):142.
  20. Barlow KM, Crawford S, Brooks BL, et al. The incidence of postconcussion syndrome remains stable following mild traumatic brain injury in children. *Pediatr Neurol*. 2015;53(6):491–497.
  21. Eisenberg MA, Meehan WP III, Mannix R. Duration and course of post-concussive symptoms. *Pediatrics*. 2014;133(6):999–1006.
  22. Abu-Arafeh I, Razak S, Sivaraman B, Graham C. Prevalence of headache and migraine in children and adolescents: a systematic review of population-based studies. *Dev Med Child Neurol*. 2010;52(12):1088–1097.
  23. Philipp J, Zeiler M, Wöber C, et al. Prevalence and burden of headache in children and adolescents in Austria—a nationwide study in a representative sample of pupils aged 10–18 years. *J Headache Pain*. 2019;20(1):101.
  24. Petersen S, Bergström E, Brulin C. High prevalence of tiredness and pain in young schoolchildren. *Scand J Public Health*. 2003;31(5):367–374.
  25. Filbay S, Pandya T, Thomas B, et al. Quality of life and life satisfaction in former athletes: a systematic review and meta-analysis. *Sports Med*. 2019;49(11):1723–1738.
  26. Howell DR, Wilson JC, Kirkwood MW, Grubenhoff JA. Quality of life and symptom burden 1 month after concussion in children and adolescents. *Clin Pediatr (Phila)*. 2019;58(1):42–49.
  27. Paniccia M, Ippolito C, McFarland S, et al. Health-related quality of life in non-concussed children: a normative study to inform concussion management. *Dev Neurorehabil*. 2020;23(8):534–541.
  28. Plourde V, Yeates KO, Brooks BL. Predictors of long-term psychosocial functioning and health-related quality of life in children and adolescents with prior concussions. *J Int Neuropsychol Soc*. 2018;24(6):540–548.
  29. Winkler R, Taylor NF. Do children and adolescents with mild traumatic brain injury and persistent symptoms benefit from treatment? A systematic review. *J Head Trauma Rehabil*. 2015;30(5):324–333.
  30. McNally KA, Patrick KE, LaFleur JE, et al. Brief cognitive behavioral intervention for children and adolescents with persistent post-concussive symptoms: a pilot study. *Child Neuropsychol*. 2018;24(3):396–412.
  31. King NS. Emotional, neuropsychological, and organic factors: their use in the prediction of persisting postconcussion symptoms after moderate and mild head injuries. *J Neurol Neurosurg Psychiatry*. 1996;61(1):75–81.
  32. Mayer AR, Stephenson DD, Dodd AB, et al. Comparison of methods for classifying persistent post-concussive symptoms in children. *J Neurotrauma*. 2020;37(13):1504–1511.
  33. Orbach Y, Lamb ME. Young children's references to temporal attributes of allegedly experienced events in the course of forensic interviews. *Child Dev*. 2007;78(4):1100–1120.

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## Author Contributions

Conception and design: Younsi, Riemann. Acquisition of data: Younsi, Riemann. Analysis and interpretation of data: Younsi, Riemann, Voormolen, Rauen. Drafting the article: Younsi, Riemann, Voormolen, Rauen. Critically revising the article: Zweckberger, Unterberg. Reviewed submitted version of manuscript: Younsi, Riemann. Approved the final version of the manuscript on behalf of all authors: Younsi. Statistical analysis: Younsi, Riemann. Administrative/technical/material support: Younsi, Zweckberger, Unterberg. Study supervision: Younsi, Zweckberger, Unterberg.

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