



The association between post-concussion symptoms and health-related quality of life in patients with mild traumatic brain injury

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ABSTRACT

A subset of mild traumatic brain injury (mTBI) patients experience post-concussion symptoms. When a cluster of post-concussion symptoms persists for over three months, it is referred to as post-concussion syndrome (PCS). Little is known about the association between PCS and Health-Related Quality of Life (HRQoL) after mTBI. The aims of this study were to assess the implications of PCS on HRQoL six months after mTBI and the relationship between PCS and HRQoL domains. A prospective observational cohort study was conducted among a sample of mTBI patients. Follow-up postal questionnaires at six months after emergency department (ED) admission included socio-demographic information, the Rivermead Post-Concussion Symptoms Questionnaire (RPQ), and HRQoL measured with the 36-item Short-Form Health Survey (SF-36) and the Perceived Quality of Life Scale (PQoL). In total, 731 mTBI patients were included, of whom 38.7% were classified as suffering from PCS. Patients with PCS had significantly lower scores on all SF-36 domains, lower physical and mental component summary scores and lower mean PQoL scores compared to patients without PCS. All items of the RPQ were negatively correlated to all SF-36 domains and PQoL subscale scores, indicating that reporting problems on any of the RPQ symptoms was associated with a decrease on different aspects of an individuals' HRQoL. To conclude, PCS is common following mTBI and patients with PCS have a considerably lower HRQoL. A better understanding of the relationship between PCS and HRQoL and possible mediating factors in this relationship could improve intervention strategies, the recovery process for mTBI patients and benchmarking.

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Introduction

Traumatic brain injury (TBI) represents a substantial burden worldwide and reported annual incidence rates vary from 47 to

849/100,000 in the European population [1]. TBI is defined as “an alteration in brain function, or other evidence of brain pathology, caused by an external force” [2]. The greater part (70–80%) of all TBI cases can be classified as mild TBI (mTBI). Despite the term ‘mild’, many patients experience post-concussion symptoms such as somatic symptoms (e.g. headaches, dizziness, blurred vision, fatigue and sleep disturbances), cognitive complaints (e.g. poor memory, attention and executive difficulties), and behavioral or emotional symptoms (e.g. depression, irritability, anxiety-related disorders, emotional lability) [3]. When a subset of these symptoms persist for over three months [4,5], it is typically referred to as post-concussion syndrome (PCS). In previous literature, the prevalence rates of PCS vary considerably (5–43%), dependent on timing, measurement and classification method used [4–8]. Additionally, van der Naalt et al. have determined an incomplete recovery in almost half mTBI patients

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six months after injury [9]. Generally, the International Classification of Diseases (ICD)-10 [10] or Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV [11] diagnostic criteria are used to determine the presence of PCS. In the literature, PCS continues to be a subject of discussion and remains controversial, because of diverging definitions and classification methods [8], disagreement regarding etiology and no clear impartial neurologic results. Health related quality of life (HRQoL) has been acknowledged as an important outcome, reflecting to what degree a medical condition and its treatment affect the physical, mental and social aspects of someone's life perceived from an individual's perspective [12]. Previous studies have shown that many people suffering from mTBI experience a reduction in HRQoL, because of physical, cognitive and/or emotional impairments [13,14]. Furthermore, PCS may result in loss of functional health, which prohibits return to work after injury and leads to additional economic and societal costs [15] and it may hamper someone's psychosocial functioning [16]. However, the topic of HRQoL and outcomes for people with PCS after mTBI is important and under-researched. Furthermore, to date no large comprehensive study has addressed the association between PCS and HRQoL and its subscales in the general adult mTBI population. This information could also add to the discussion concerning the clinical relevance of PCS; i.e. a strong association between PCS symptoms and a decreased quality of life may indicate that PCS is a clinical relevant syndrome. More insight is needed in the relationship between PCS and HRQoL. Therefore, the objectives of this study were to assess the association between PCS and HRQoL six months after mTBI and the correlation between post-concussion symptoms and HRQoL domains.

Materials and methods

Study design

In this study, data were acquired through the Radboud University Brain Injury Cohort Study (RUBICS) [17–20], which is a prospective observational cohort study. Patients who attended the emergency department (ED) of the Radboud University Nijmegen Medical Center (RUNMC) between January 2003 and June 2010 with a diagnosis of mild, moderate or severe TBI were included in the RUBICS database. The clinical data registered in the ED by a neurologist and/or neurosurgeon were entered into the RUBICS databank by a research nurse. Demographic data (age, sex and education), trauma mechanism, hospital admission and length of hospitalization, clinical variables and comorbidities are reflected in the RUBICS databank and follow-up postal questionnaires were utilized to obtain this data. The clinical variables described are the Glasgow Coma Scale (GCS), abbreviated injury scale (AIS) and injury severity score (ISS). The AIS is used to classify and describe the severity of injury to trauma patients in every body region on a six-point ordinal scale [21] and the AIS head (AISH) is classified as the AIS score specific for the head. The ISS [22,23] is derived from the AIS and represents the severity of the trauma. The questionnaires were self-rated by patients or guardians of patients six months after the injury. This study has been approved by the ethical standards committee of the RUNMC. For more details on the RUBICS dataset, see Scholten et al [13] and Haagsma et al [20].

Study participants

In the current study, mTBI was diagnosed by a GCS score of 13–15 in the ED after initial resuscitation or followed by sedation and intubation during resuscitation for non-neurological cause. Exclusion criteria were: being 16 years and younger, no written informed consent given by patients/guardians, abusive use of drugs or alcohol, diagnosed with dementia, unknown address of

the patient, and inability to speak or write Dutch. A total of 731 patients, which were classified as having mTBI and had completed all items of the RPQ at six-month follow-up, were selected for the current analyses.

Post-concussion symptoms and diagnosis of PCS

The RPQ was applied to identify the existence and severity of post-concussion symptoms at six-month follow-up. The RPQ describes 16 post-concussion symptoms frequently identified after TBI including headaches, dizziness, nausea/vomiting, noise sensitivity, sleep disturbance, fatigue, being irritable, feeling depressed or tearful, feeling frustrated or impatient, forgetfulness, poor concentration, taking longer to think, blurred vision, light sensitivity, double vision and restlessness. Patients were asked to assess the severity of these symptoms over the past 24 h compared with the pre-injury situation. The symptoms are rated on a 5-point Likert scale, which covers responses from 0 (not a problem) to 4 (severe problem). A higher total score, which ranges from 0 to 64, on the RPQ represents a higher and more severe number of symptoms to be in place [24]. Rating scores of one did not contribute to the total score of the RPQ as recommended by King et al [24].

In this study, we mapped the symptoms of the ICD-10 diagnostic criteria [25] on the RPQ. Patients were classified as having PCS when they reported three or more of the following symptoms with a rating score of two (mild) or higher: headache, dizziness, fatigue, irritability, insomnia, concentration difficulty, and memory difficulty (Panel 1). Additionally, the ICD-10 diagnostic criteria also requires reduced tolerance to stress, emotional excitement or alcohol as one of the criteria. However, this information is not available in the RPQ nor in the RUBICS database.

Health-related quality of life

The paper-and-pencil version of the 36-Item Short-Form (SF-36) Health Survey (Version 1) [26] was self-rated by the patients included in the databank at six months post-injury. The SF-36 instrument has been validated in a TBI population and has demonstrated good internal consistency and validity [27,28], and is the most used generic HRQoL instrument in TBI research [29]. It is a 36 item multidimensional self-reported survey of patient's health that reflects the physical, mental and social functioning. It consists of eight domains of health status: physical functioning (PF), role limitations related to physical functioning (RP), bodily pain (BP), general health perception (GH), vitality (VT), social functioning (SF), role limitations related to emotional problems (RE), and mental health (MH) [26]. The weighted sums of the item responses for each domain are linearly transformed to a score ranging from 0 to 100. The physical and mental health summary component scores are calculated by first standardizing the patients' scores, specifically by subtracting the subscale means for the general Dutch population sample from each individual's subscale scores and dividing the results by the standard deviation of the Dutch sample to generate Z-scores [30]. Second, to facilitate international comparison, Z-scores

Mapped ICD-10	
Eligible symptoms from the RPQ	At least 3 symptoms from the list below
	Headache
	Dizziness
	Sleep disturbance
	Fatigue
	Being irritable, easily angered
	Forgetfulness, poor memory
	Poor concentration
Cut-off; rating score 2	Three items with score ≥ 2

Panel 1. Classification method regarding Post-Concussion Syndrome. Abbreviations. ICD = International Classification of Diseases.

are multiplied by the subscale factor coefficients for physical and mental health summary component scores of the U.S. sample and summed over eight subscales into the physical and mental health summary component scores. Finally, both sums were re-scaled into T-scores, with a mean of 50 and standard deviation of 10 for the U.S. norm [31]. Mean values of the respondents' completed items in the same scale were used as replacement for the missing values at six months, under one condition that at least 50% of the items within that scale had been completed [26].

The Perceived Quality of Life Scale (PQoL) is also a generic HRQoL instrument, initially developed as a cognitive appraisal of life satisfaction for patients after intensive medical care [32]. The instrument has previously been used in adults with chronic neurologic disability and additionally in stroke and TBI [33,34]. The PQoL showed good internal reliability in a TBI population [35]. The PQoL measures an individuals' satisfaction with his or her functional status on an 11-point scale ranging from 0 (extremely dissatisfied) to 10 (extremely satisfied). It contains 19 items in three different domains (physical health, cognitive health and social health), estimating the level of functioning in 10 different areas, including physical health, thinking and remembering, family relationships, community participation and leisure, work and income, and meaning and purpose of life. The overall PQoL score is established by the mean of the 19 item scores and seen as a measure of global life satisfaction, in which a score of < 7.5 is considered as "Dissatisfied" and a score > 7.5 as "Satisfied" [32]. For our analyses, the mean score (range 0 to 10) was chosen. Hot deck imputation per domain was used to estimate the missing values at six months, provided that at least 50% of the items within that domain had been completed, applying similar scores on the items in that specific domain. This was done because PQoL scores are only allowed to be computed in case of complete information on all items [32].

The PQoL can be divided in physical, social and cognitive subscales. The physical subscale includes physical health (item 1), take care of yourself (item 2), amount of walking (item 4), getting outside the house (item 5) and amount and kind of sleep (item 19). The social subscale consists of see or talk to family and friends (item 8), help from family and friends (item 9), help you give to family and friends (item 10), contribution to community (item 11), work situation (item 12), kind and amount of recreation or leisure (item 13), level or lack of sexual activity (item 14), income meets your needs (item 15), respected by others (item 16), meaning and purpose of your life (item 17) and amount of variety in your life (item 18), and the cognitive subscale entails think and remember (item 3) and carry on a conversation (item 6) [32].

Statistical analysis

Descriptive analyses were conducted on the demographic (age, sex and educational level), trauma mechanism, hospitalization, clinical injury variables and comorbidities. Patients diagnosed with mTBI and who had completed the entire RPQ were included in the analyses. To distinguish on socio-demographic and injury-related variables between mTBI patients experiencing PCS and not experiencing PCS, chi-squared tests (dichotomous variables) and t-tests were applied. Mann Whitney U tests were used to evaluate the differences in SF-36 domain scores and PQoL scores between mTBI patients with and without PCS. Statistical significance was determined by a p-value of $p < .05$. Spearman's correlation coefficients were utilized to evaluate the linear relationship and correlation between the RPQ and the various SF-36 domains and PQoL subscales. Cohen's Set Correlation and Contingency Tables were used to differentiate between strong, moderate and weak correlations. A correlation was considered strong when the coefficient was above 0.5, moderate when the coefficient was between 0.3 and 0.5, and weak when the coefficient was below 0.3

[36]. Missing data for the following variables: education (182 missing), comorbidity (237 missing), and hospital admission (2 missing) were imputed using multiple imputation technique with five datasets. Multiple regression was performed to adjust for differences in case-mix between patients with and without PCS.

All statistical analyses were performed using SPSS version 24 for Windows (IBM SPSS Statistics, SPSS Inc, Chicago, IL).

Results

Patient characteristics

In total, 797 mTBI patients were selected from the RUBICS database, of which 731 were included in this study. There were no significant differences in characteristics between the 731 patients with complete outcome data and the 66 patients with missing items on the RPQ, except that the median age of the 66 patients was significantly higher 54.5 (IQR: 42.75–68, $p < .01$). Table 1 shows the characteristics of our study sample. The median age of the respondents was 44 years and 63% were male. Road traffic accidents (48%) and falls (33%) were the most reported causes of injury. The median ISS and AISH scores were respectively 6 (IQR 4–14) and 2 (IQR 2–2). Forty-five per cent of the patients had no pre-existing disease and 81% received a computed tomography (CT) scan of the head in which no abnormalities were found. Approximately 51% of the mTBI patients were admitted to hospital with an average length of stay of 3 days (range 1 to 8 days). Furthermore, 35 patients (4.8%) were admitted to the intensive care unit (ICU).

The prevalence of PCS in this population according to our criteria was 38.7%, which defines a total of 283 patients as experiencing PCS six months after the injury. Patients with PCS were significantly more often female, had a lower education, were more likely to be injured by assault compared with other causes of injury, had higher ISS and AISH scores, were more likely to be hospitalized and had a higher RPQ total score (Table 1).

PCS and Health-related quality of life

SF-36 – Table 2 shows the median SF-36 and PQoL scores for mTBI patients with and without PCS six months post-injury. Patients with mTBI and PCS had significantly lower scores on all domains of the SF-36 compared to mTBI patients without PCS. The lowest mean score for mTBI patients with PCS compared to patients without PCS was reported on the role limitations related to physical functioning domain, which represents problems with work / daily activities as a result of physical health (mean: 40, SD: 42 vs. mean: 82, SD: 33, $p < .001$). The median physical component summary score was 44 (IQR 35–53) and 56 (IQR 49–59), respectively for patients with PCS and without PCS ($p < .001$). Furthermore, the median mental component summary score was 43 (IQR 32–52) for patients experiencing PCS and 54 (IQR 50–58) for patients without PCS ($p < .001$) (Appendix A).

PQoL – The median PQoL score for patients with PCS was 6.7 (IQR 5.3–7.8) and significantly lower compared to the median PQoL of patients without PCS (8.6 (IQR 7.7–9.5), $p < .001$) (Appendix B). Approximately, 45% of patients with PCS were dissatisfied with their functioning (PQoL < 7.5), whereas only 14% of patients without PCS were dissatisfied with their functioning.

After adjusting for case-mix differences, there were still significant differences between patients with and without PCS.

Correlation of RPQ with SF-36

In Fig. 1 the Spearman's correlation coefficients of the RPQ items and the eight domains of the SF-36 are shown. All items of

Table 1
Characteristics of the study population.

	Total	PCS	No PCS	P-value
N	731	283	448	
Gender (male)	463 (63.3%)	161 (56.9%)	302 (67.4%)	<.01
Age ¹ (years)	44 (27–57)	45 (31–56)	43 (26–57)	.14
Education				<.01
Primary education	21 (2.9%)	6 (2.1%)	15 (3.3%)	
Secondary education	336 (46.0%)	142 (50.2%)	194 (43.3%)	
Higher professional education	108 (14.8%)	32 (11.3%)	76 (17.0%)	
Academic education	84 (11.5%)	18 (6.4%)	66 (14.7%)	
Unknown	182 (24.9%)	85 (30.0%)	97 (21.7%)	
Injury Mechanism				.03
Road traffic accident	351 (48.0%)	139 (49.1%)	212 (47.3%)	
Fall	240 (32.8%)	96 (33.9%)	144 (32.1%)	
Sports	77 (10.5%)	19 (6.7%)	58 (12.9%)	
Assault	41 (5.6%)	22 (7.8%)	19 (4.2%)	
Other/Unknown	22 (3.0%)	7 (2.6%)	14 (3.3%)	
Injury severity				
ISS ¹	6 (4–14)	8 (5–16)	5 (4–13)	<.01
AISH ¹	2 (2–2)	2 (2–3)	2 (1–2)	<.01
Head AIS 3	93 (12.7%)	42 (14.8%)	51 (11.4%)	
Head AIS 4	57 (7.8%)	30 (10.6%)	27 (6.0%)	
Head AIS 5	11 (1.5%)	6 (2.1%)	5 (1.1%)	
Comorbidity ²				<.01
No pre-existing disease	329 (45.0%)	102 (36.0%)	227 (50.7%)	
1 comorbid disease	92 (12.6%)	36 (12.7%)	56 (12.5%)	
2 comorbid disease	33 (4.5%)	13 (4.6%)	20 (4.5%)	
3 or more comorbidities	40 (5.5%)	24 (8.5%)	16 (3.6%)	
Unknown	237 (32.4%)	108 (38.2%)	129 (28.8%)	
CT scan				.20
No CT scan	46 (6.3%)	18 (6.4%)	28 (6.3%)	
CT scan, no abnormalities	591 (80.8%)	223 (78.8%)	368 (82.1%)	
CT scan, abnormalities	94 (12.9%)	42 (14.8%)	52 (11.6%)	
Hospitalization ²				
Hospital admission	373 (51.0%)	180 (63.6%)	193 (43.1%)	<.01
Number of days hospitalized ¹	3 (1–8)	4 (1–9)	3 (1–6)	.37
ICU admission	35 (4.8%)	22 (7.8%)	13 (2.9%)	<.01
GCS ¹	15 (14–15)	15 (14–15)	15 (15–15)	<.01
13	40 (5.5%)	22 (7.8%)	18 (4.0%)	
14	152 (20.8%)	71 (25.1%)	81 (18.1%)	
15	539 (73.7%)	190 (67.1%)	349 (77.9%)	
RPQ total score ¹	4 (0–15)	18 (12–28)	0 (0–4)	<.01

Abbreviations. ISS=Injury Severity Score; AISH=Abbreviated Injury Scale of the Head; AIS=Abbreviated Injury Scale; CT=Computed Tomography; ICU=Intensive Care Unit; GCS=Glasgow Coma Scale; RPQ=Rivermead Post-Concussion Symptoms Questionnaire; TBI=traumatic brain injury.

¹Data are displayed as median, with the first and third quartile given within brackets.

²Comorbidity was defined as the presence of any co-existing diseases or disease processes additional to injury that the TBI patients sustained. The following diseases were assessed as comorbid disease: asthma, chronic bronchitis, chronic non-specific lung disease (not questioned), heart disease, diabetes, back hernia or chronic backache, osteoarthritis, rheumatoid arthritis, and cancer. ³Hospital or IC admission for one day or more after arrival at emergency department.

the RPQ were negatively correlated to the SF-36 domains, indicating that reporting problems on any of the RPQ items is associated with a decrease on different aspects of an individuals' HRQoL. The strongest negative correlation (-0.671, $p < .001$) was found between fatigue and the vitality (VT) domain of the SF-36. Double vision was determined as having the weakest correlations with all domains. Moreover, fatigue was observed as having a strong negative correlation with all domains except for role limitations related to emotional problems (RE) and mental health (MH). All correlations were statistically significant on a $p < .001$ level.

Correlation of RPQ with PQoL

The Spearman's correlation coefficients of the RPQ items and the three PQoL subscales are shown in Fig. 2. All the items of the RPQ were negatively correlated with the PQoL subscales. All correlations were statistically significant on a $p < .001$ level. The strongest correlation (-0.621, $p < .001$) was found between forgetfulness and the PQoL cognitive subscale. Double vision was observed as having the weakest correlation with all subscales, which is in line with the SF-36 domain correlations.

Discussion

The objectives of this paper were to elucidate the association between PCS and HRQoL six months after mTBI and the correlation between the RPQ items with SF-36 domains and PQoL subscale scores. Almost 40% of our mTBI cohort were experiencing PCS six months post-injury and PCS was negatively associated with HRQoL as measured with both the SF-36 and PQoL. MTBI patients with PCS had a 20% lower HRQoL on average, compared with mTBI patients without PCS. Almost half of mTBI patients with PCS were dissatisfied with their functioning. When adjusting for possible confounding effects of baseline differences between the two groups, it was shown that PCS decreases HRQoL. Additionally, significant negative correlations between all RPQ items and SF-36 domains and PQoL subscale scores were found, indicating that reporting problems on any of the RPQ items was associated with a decrease on different aspects of an individual's HRQoL. These results are in line with previous literature, where Emanuelson et al. have found a significant correlation between higher rates of symptoms and low SF-36 scores in patients 16–60 years of age living in western Sweden [14]. However, they did not use the RPQ to assess post-concussion symptoms. Patients could only rate each symptom as existing (yes) or non-existing (no), which meant they weren't able to identify the severity of post-concussion symptoms and they didn't use the term PCS throughout their paper. Patients with mTBI and PCS had lower SF-36 scores on all domains compared to the Dutch population norm [30]. However, when looking at patients without PCS, mean SF-36 scores were higher on all domains compared to the Dutch population norm. This is in line with a previous study by Scholten et al. where it was reported that respondents with mTBI reached outcomes comparable to the Dutch population norm on all the SF-36 domains at one year follow-up [13]. In previous literature, a reduction of HRQoL was found for mTBI patients [13], nevertheless there is a gap in the literature concerning the factors that cause this reduction. This study shows that a decrease in HRQoL for mTBI patients could be affected by PCS. We adjusted for the most important factors, however, there may also be an intricate role of other factors influencing the relationship between PCS and HRQoL. Both, the reporting of post-concussion symptoms with the RPQ and functional impairments with the SF-36 may be mediated by pre-injury psychological, personality, psycho-social factors and the severity of the injury [29,37,38]. Additionally, 14% of patients without PCS demonstrated dissatisfaction with their functioning, which implies that other factors play a role. Several limitations have been encountered during this study. Firstly, an abundance of information was requested from TBI patients to acquire the RUBICS database, which may have resulted in lower quality responses. Secondly, RPQ, SF-36 and PQoL were all reported through self-administration. For HRQoL self-report is inherent in the concept. However, as the general population already had difficulties to fill out the SF-36 in its entirety [38], this might be even more complex for the TBI population; these

Table 2
Data on health-related quality of life at six months after mTBI.

	PCS				No PCS				Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)*
	N	Observed range	Mean (SD)	Median (IQR)	N	Observed range	Mean (SD)	Median (IQR)		
SF-36 (0-100)										
Physical Functioning	277	0-100	68.9 (27.9)	75 (50-95)	432	0-100	88.7 (20.4)	100 (90-100)	19.8 (16.2-23.4)	15.2 (11.7-18.8)
Role Physical	279	0-100	40.0 (42.1)	25 (0-75)	437	0-100	82.2 (33.1)	100 (75-100)	42.2 (36.7-47.8)	36.4 (30.7-42.1)
Bodily Pain	283	0-100	58.8 (25.6)	62 (41-74)	446	0-100	82.8 (21.5)	100 (72-100)	24.0 (20.5-27.4)	20.3 (16.7-24.0)
General Health	281	5-100	56.9 (22.0)	57 (40-72)	442	6-100	77.6 (18.5)	80 (67-92)	20.7 (17.7-23.6)	19.1 (16.0-22.1)
Vitality	283	0-100	49.2 (18.7)	50 (40-65)	443	15-100	73.0 (16.7)	75 (60-85)	23.8 (21.2-26.4)	22.2 (19.5-25.0)
Social Functioning	283	0-100	61.5 (27.0)	63 (50-87.5)	447	25-100	89.7 (16.1)	100 (75-100)	28.2 (25.0-31.3)	25.9 (22.6-29.2)
Role Emotional	279	0-100	58.2 (42.3)	67 (0-100)	438	0-100	92.6 (22.6)	100 (100-100)	34.4 (29.7-39.2)	31.9 (26.9-36.9)
Mental Health	283	0-100	62.2 (20.3)	64 (48-76)	443	28-100	81.7 (13.7)	84 (76-92)	19.6 (17.1-22.0)	19.1 (16.5-21.7)
Physical CS	271	9-69	43.2 (11.4)	44 (35-53)	423	16-70	52.5 (9.0)	56 (49-59)	9.2 (7.7-10.8)	7.3 (5.8-8.9)
Mental CS	271	7-66	41.1 (12.5)	43 (32-52)	423	16-73	52.7 (7.5)	54 (50-58)	11.6 (10.1-13.1)	11.6 (10.0-13.2)
PQoL (0-10)	192	1-10	6.5 (1.9)	6.7 (5.3-7.8)	347	0-10	8.4 (1.5)	8.6 (7.7-9.5)	1.9 (1.6-2.2)	1.6 (1.2-1.9)

*Variables adjusted for: gender, age, education, ISS, comorbidity, hospital admission, GCS and yes/no PCS. Abbreviations. mTBI = mild Traumatic Brain Injury; PCS = post-concussion syndrome; IQR = interquartile range; CI = confidence interval; SF-36 = Short-Form-36; Physical CS = physical component score; Mental CS = mental component score; PQoL = Perceived Quality of Life; ISS = Injury Severity Score; GCS = Glasgow Coma Scale.

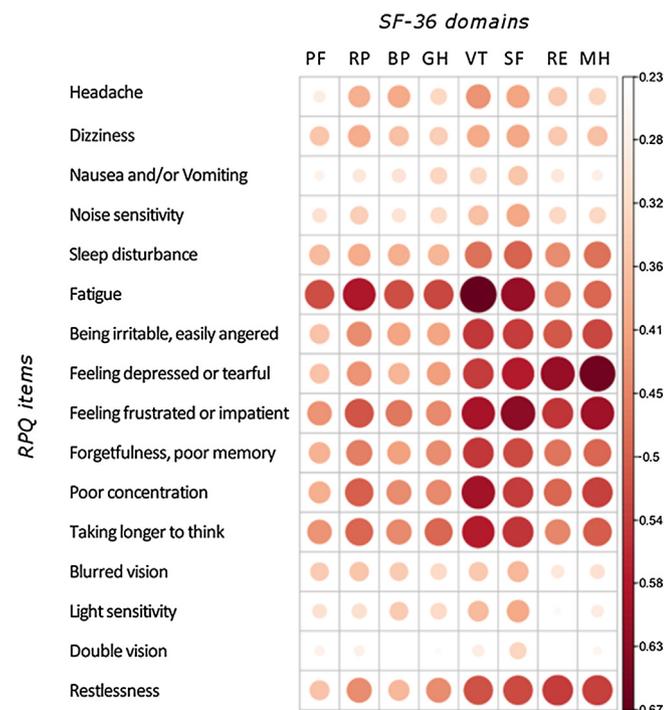


Fig. 1. Correlation RPQ items and SF-36 domains. Abbreviations. SF-36Short-Form-36; RPQRivermead Post-Concussion Symptoms Questionnaire.

patients may experience cognitive problems and may have more difficulties answering complicated and extensive questions. Concerning the RPQ, previous research has revealed that self-report might lead to under- or over-reporting of symptoms [39].

By asking explicitly for the existence of symptoms patients might furthermore be made aware of a symptom they would have otherwise not reported or they may not understand the meaning of a symptom and may just simply endorse it anyway [39]. Researchers have questioned whether the sensitivity and specificity of most instruments (e.g. RPQ) are sufficient for mTBI patients, because they have been developed for more severe cases of TBI [29]. Stulemeijer et al. have shown that additional extracranial injuries could also have an impact on lowered SF-36 scores [40]. Furthermore, even though questionnaires are very convenient in the clinical and research context, the RPQ alone cannot be used to diagnose PCS, a full clinical evaluation by a health professional is necessary. Lastly, the cohort data were collected in an academic hospital where it is more likely that patients with severe trauma have been admitted to the ED, which is shown in the high percentage of patients admitted to the hospital (51%). Additionally, no pre-injury data with the exception of pre-existing comorbidity was available in the dataset. Therefore, the cohort is likely to not be representative for the overall mTBI population. This study gives us more information on PCS and the association with HRQoL, which could ultimately lead to a better comprehension of recovery and burden of PCS after mTBI. A better understanding of the relationship between PCS and HRQoL and possible mediating factors in this relationship could improve intervention strategies and the recovery process. TBI outcome covers a broad spectrum of HRQoL [38] and more knowledge about the specific effects on the HRQoL domains will justify future decisions concerning quality of life measures and interventions. Nevertheless, the role of mediating factors in the relationship between PCS and generic and disease-specific HRQoL is not clear. For future studies it would be interesting to look at the role of pre-injury psychological, personality and psychosocial factors which may influence both, the report of post-concussion symptoms and physical, mental and social functioning measured with the SF-36.

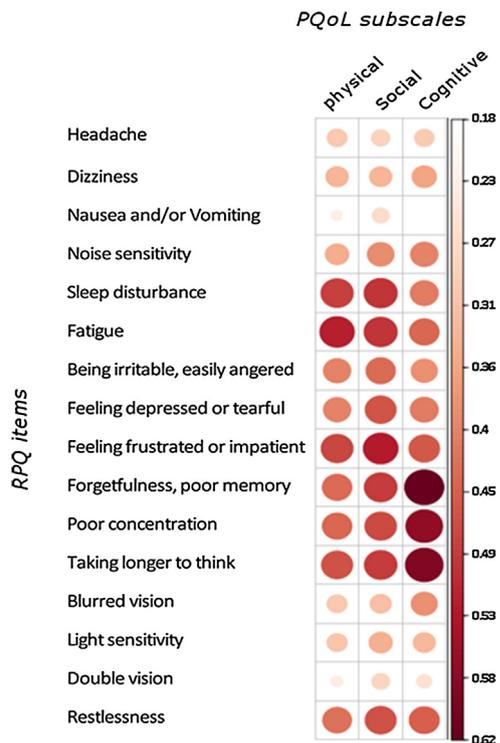


Fig. 2. Correlation RPQ items and PQL subscales. Abbreviations. RPQ = Rivermead Post-Concussion Symptoms Questionnaire; PQL = Perceived Quality of Life.

Conclusions

To conclude, PCS is common after mTBI and patients suffering from PCS have a considerably lower HRQoL. These findings highlight that better assessment and intervention strategies for PCS are needed, because intervention and support strategies can be targeted more appropriately when mTBI patients with PCS are detected shortly after sustaining the injury [40]. More insight is needed in the role of pre-injury psychological, personality and psychosocial factors that may influence both the report of post-concussion symptoms and physical, mental and social functioning.

Author disclosure statement

The authors have declared that no competing interests exist.

The ethical standards committee of the Radboud University Medical Center has approved the RUBICS study. Written informed consent was obtained from all patients in this study.

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Supplementary data

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References

- [1] Brazinova A, Rehorcikova V, Taylor MS, Buckova V, Majdan M, Psota M, et al. Epidemiology of traumatic brain injury in Europe: a living systematic review. *J Neurotrauma* 2016.
- [2] Menon DK, Schwab K, Wright DW, Maas AI. Demographics, clinical assessment working group of the, I., interagency initiative toward common data elements for research on traumatic brain, I. And psychological, H. (2010). Position statement: definition of traumatic brain injury. *Arch Phys Med Rehabil* 2010;91:1637–40.
- [3] American Congress of Rehabilitation Medicine (ACRM). Definition of mild traumatic brain injury. 1993.
- [4] Hiploylee C, Dufort PA, Davis HS, Wennberg RA, Tartaglia MC, Mikulis D, Hazrati LN, Tator CH. Longitudinal study of postconcussion syndrome: not everyone recovers. *J Neurotrauma* 2016.
- [5] Ruff RM. Mild traumatic brain injury and neural recovery: rethinking the debate. *NeuroRehabilitation* 2011;28:167–80.
- [6] Leddy JJ, Sandhu H, Sodhi V, Baker JG, Willer B. Rehabilitation of concussion and post-concussion syndrome. *Sports Health* 2012;4:147–54.
- [7] King NS, Kirwilliam S. The nature of permanent post-concussion symptoms after mild traumatic brain injury. *Brain Impair* 2013;14:235–42.
- [8] Voormolen DC, Cnossen MC, Polinder S, von Steinbuechel N, Vos PE, et al. Divergent classification methods of post-concussion syndrome after mild traumatic brain injury: prevalence rates, risk factors and functional outcome. *J Neurotrauma* 2018.
- [9] van der Naalt J, Timmerman ME, de Koning ME, van der Horn HJ, Scheenen ME, Jacobs B, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. *Lancet Neurol* 2017;16:532–40.
- [10] World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: WHO; 1993.
- [11] American psychiatric association diagnostic and statistical manual of mental disorders. 4th edn. Washington, DC: text revised; 2000.
- [12] Cnossen MC, Polinder S, Vos PE, Lingsma HF, Steyerberg EW, Sun Y, Ye P, Duan L, Haagsma JA. Comparing health-related quality of life of Dutch and Chinese patients with traumatic brain injury: do cultural differences play a role? *Health Qual Life Outcomes* 2017;15:72.
- [13] Scholten AC, Haagsma JA, Andriessen TM, Vos PE, Steyerberg EW, van Beeck EF, Polinder S. Health-related quality of life after mild, moderate and severe traumatic brain injury: patterns and predictors of suboptimal functioning during the first year after injury. *Injury* 2015;46:616–24.
- [14] Emanuelson I, Andersson Holmkvist E, Bjorklund R, Stalhammar D. Quality of life and post-concussion symptoms in adults after mild traumatic brain injury: a population-based study in western Sweden. *Acta Neurol Scand* 2003;108:332–8.
- [15] Daneshvar DH, Riley DO, Nowinski CJ, McKee AC, Stern RA, Cantu RC. Long term consequences: effects on normal development profile after concussion. *Phys Med Rehabil Clin N Am* 2011;22:683–700.
- [16] Dikmen S, McLean A, Temkin N. Neuropsychological and psychosocial consequences of minor head injury. *J Neurol Neurosurg Psychiatry* 1986;49:1227–32.
- [17] Stulemeijer M, van der Werf S, Borm GF, Vos PE. Early prediction of favourable recovery 6 months after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2008;79:936–42.
- [18] Jacobs B, Beems T, Stulemeijer M, van Vugt AB, van der Vliet TM, Borm GF, et al. Outcome prediction in mild traumatic brain injury: age and clinical variables are stronger predictors than CT abnormalities. *J Neurotrauma* 2010;27:655–68.
- [19] Vos PE, Jacobs B, Andriessen TM, Lamers KJ, Borm GF, et al. GFAP and S100B are biomarkers of traumatic brain injury: an observational cohort study. *Neurology* 2010;75:1786–93.
- [20] Haagsma JA, Scholten AC, Andriessen TM, Vos PE, Van Beeck EF, et al. Impact of depression and post-traumatic stress disorder on functional outcome and health-related quality of life of patients with mild traumatic brain injury. *J Neurotrauma* 2015;32:853–62.
- [21] Greenspan L, McLellan BA, Greig H. Abbreviated injury scale and injury severity score: a scoring chart. *J Trauma* 1985;25:60–4.
- [22] Baker SP, O'Neill B, Haddon Jr. W, Long WB. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974;14:187–96.
- [23] Copes WS, Champion HR, Sacco WJ, Lawnick MM, Keast SL, Bain LW. The injury severity score revisited. *J Trauma* 1988;28:69–77.
- [24] King NS, Crawford S, Wenden FJ, Moss NE, Wade DT. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *J Neurol* 1995;242:587–92.
- [25] World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: WHO; 1993.
- [26] Ware JE, Snow KK, Kosinski M, Gandek B. New England medical center, H. And health, I. Boston: SF-36 health survey : manual and interpretation guide. Health Institute, New England Medical Center; 1993.

- [27] Guilfoyle MR, Seeley HM, Corteen E, Harkin C, Richards H, Menon DK, et al. Assessing quality of life after traumatic brain injury: examination of the short form 36 health survey. *J Neurotrauma* 2010;27:2173–81.
- [28] Diaz AP, Schwarzbald ML, Thais ME, Hohl A, Bertotti MM, Schmoeller R, et al. Psychiatric disorders and health-related quality of life after severe traumatic brain injury: a prospective study. *J Neurotrauma* 2012;29:1029–37.
- [29] Polinder S, Haagsma JA, van Klaveren D, Steyerberg EW, et al. Health-related quality of life after TBI: a systematic review of study design, instruments, measurement properties, and outcome. *Popul Health Metr* 2015;13:4.
- [30] Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R, Sprangers MA, te Velde A, Verrips E. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998;51:1055–68.
- [31] Ware JE. New england medical center, H. And health, L. Boston: SF-36 physical and mental health summary scales : a user's manual. Health Institute, New England Medical Center; 1994.
- [32] Seattle Quality of Life Group. Information sheet on the perceived quality of life scale (PQoL). Washington: University of Washington, Department of Health Services; 2008.
- [33] Dikmen SS, Machamer JE, Powell JM, Temkin NR. Outcome 3 to 5 years after moderate to severe traumatic brain injury. *Arch Phys Med Rehabil* 2003;84:1449–57.
- [34] Patrick DL, Kinne S, Engelberg RA, Pearlman RA. Functional status and perceived quality of life in adults with and without chronic conditions. *J Clin Epidemiol* 2000;53:779–85.
- [35] Cicerone KD, Azulay J. Perceived self-efficacy and life satisfaction after traumatic brain injury. *J Head Trauma Rehabil* 2007;22:257–66.
- [36] Cohen J. Set correlation and contingency tables. *Appl Psychol Meas* 1988;12:425–34.
- [37] Scholten AC, Haagsma JA, Steyerberg EW, van Beeck EF, Polinder S. Assessment of pre-injury health-related quality of life: a systematic review. *Popul Health Metr* 2017;15:10.
- [38] von Steinbuechel N, Covic A, Polinder S, Kohlmann T, Cepulyte U, Poinstingl H, et al. Assessment of health-related quality of life after TBI: comparison of a disease-specific (QOLIBRI) with a generic (SF-36) instrument. *Behav Neurol* 2016;2016:7928014.
- [39] Iverson GL, Brooks BL, Ashton VL, Lange RT. Interview versus questionnaire symptom reporting in people with the postconcussion syndrome. *J Head Trauma Rehabil* 2010;25:23–30.
- [40] Stulemeijer M, van der Werf SP, Jacobs B, Biert J, van Vugt AB, Brauer JM, Vos PE. Impact of additional extracranial injuries on outcome after mild traumatic brain injury. *J Neurotrauma* 2006;23:1561–9.