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# Symptoms at 2 Months after Mild TBI: are they Related to Brain Injury? The Results of a Cluster Analysis

**Torgeir Hellstrom[1], Eirik Vikane[2], Jan Sture Skouen[2], Erik Bautz-Holter[1,3], Aasmund Roe[3] and Cecilie Roe[1,3]**

[1]*Department of Physical Medicine and Rehabilitation, Oslo University Hospital HF, Oslo, Norway*
[2]*Department of Physical Medicine and Rehabilitation, Haukeland University Hospital, Bergen, Norway*
[3]*Faculty of Medicine, University of Oslo, Oslo, Norway*

## Abstract

**Objective**: This study sought to explore whether subgroups of patients with mild TBI could be identified by their symptom profile according to cluster analysis. We also investigated whether these clusters are uniquely associated with structural brain damage as well as their relationship to anxiety and depression, other health complaints, functioning and participation in work.

**Methods:** This was a prospective cohort study of patients with mild TBI who were registered at baseline and 6-8 weeks after injury.

**Results:** A total of 270 patients were included. K-mean cluster analyses were conducted to describe groups of subjects with similar profiles of responses to the Rivermead Post Concussion Symptoms Questionnaire (RPQ). The four-cluster solution revealed one cluster with a low level of symptoms (low), one with a generally high symptom level (high), one cluster characterised by a high level of symptoms regarding cognitive functions (cognitive) and one cluster with somatic and frustration dominating symptoms (somatic). No significant differences in symptom level (mean score on RPQ) were revealed between subjects with and without radiological findings on brain scans (p=0.34). The "high" cluster group scored significantly higher than clusters 1, 2 and 3 in terms of both depression and anxiety but significantly lower on the GOSE. Cluster 2 scored significantly lower for health complaints in comparison to the other clusters.

**Conclusion:** Subgroups of patients with mild TBI could be identified according to their symptom profile using cluster analysis. Patients with minor symptoms had a reduced risk for a positive finding on CT or MRI, whereas the high symptom level group struggled to return to work and demonstrated high levels of anxiety, depression and disability.

**Keywords:** Mild traumatic brain injury; Symptom profile; Cluster analysis; Radiological findings

## Introduction

Traumatic brain injury (TBI) is defined as brain injury caused by external trauma ranging from very severe injuries that can cause death and severe disability to minor but frequent injuries [1]. The exact incidence of mild TBI is difficult to assess even when applying standardised definitions [2] due to differences in health care organisations, referral practices and transport distances. Accordingly, the prevalence of disability after mild TBI is also debated [3-5]. Nevertheless, mild injuries are recognised as a major burden for society due to their frequency and the persistence of subjective symptoms, which result in limitations and restrictions for activities and participation, particularly those related to work [6,7]. Even when assessing the incidence of hospital-treated TBI in a neurosurgical department, 86% of all cases classified were defined as mild TBI [8], with the dominating long-term burden considered post-concussion symptoms [4]. Post-concussion syndrome has been described as 'the cluster of signs and symptoms that can be seen after TBI of any severity' [9-11], and this syndrome typically includes one or more difficulties related to the somatic, cognitive and emotional domains. The severity of the injury as well as the localisation of the brain lesions may influence the development of post-concussion syndrome [3]. However, similar symptoms are also frequently reported by individuals with chronic pain or non-brain-related trauma as well as by healthy individuals [12,13]. Therefore, the specificity, sensitivity and predictive value of these symptoms are debated [14], and there appears to be no relationship between symptoms and more objective structural changes or neurological deficits [13,15,16]. However, several instruments have been developed to detect post-concussion symptoms [17]. The Rivermead Post Concussion Symptoms Questionnaire (RPQ) [18] is one of the instruments most frequently used to measure the change in symptoms from the preinjury level. Although the RPQ has been documented to predict functional outcome and disability [19], the ability of subjects to correctly remember their preinjury symptom level has been questioned [15], and the results of the RPQ for TBI patients can overlap with those of healthy subjects [16]. Furthermore, somatic and cognitive effects of TBI, including inattention, sleep disturbance and fatigue, can significantly overlap with the clinical symptoms of depression. Psychiatric syndromes are also present at an elevated rate following TBI, and TBI patients have been shown to be particularly susceptible to depression and anxiety [20]. The existence of common symptoms across different diagnostic entities is a general challenge in medicine, and great effort has been made to develop diagnostic approaches to overcome this problem [21]. By recognising the discriminative value of both the presence and absence of symptoms and the different levels of such symptoms, cluster analyses have advanced the field of diagnostic assessment [22]. With cluster analysis, subgroups of patients with specific symptom profiles are identified and further validated regarding the diagnostic or prognostic validity.

***Corresponding author:** Torgeir Hellstrom, Depertment of Physical Medicine and Rehabilitation, Oslo University Hospital HF, Pb 4956 Nydalen, 0424 Oslo, Norway, Tel: + 47 22119721; Fax: + 47 23027455; E-mail: torgeir.hellstrom@ous-hf.no

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These strategies have thus far primarily been applied in TBI research to identify different psychological profiles of patients [23,24]. Using the postal questionnaire, Bohnen et al. identified a three-factor model of residual subjective and psychological complaints in mild TBI patients [25]. Axelrod et al. have evaluated the latent factor structure of the RPQ and found that these factors are best described as clusters of psychological, somatic, cognitive and infrequent complaints [26]. Cicerone and Kalmar identified four meaningful clusters of self-reported symptoms using the Post Mild Traumatic Brain Injury Symptom Checklist; in this analysis, patient symptom clusters were largely unrelated to neurological or neuropsychological functioning, although the study included only a small number of patients 50 [27]. Lippa et al. found no differences in the severity or profiles of post-concussion symptoms after blast and nonblast TBI [28]. However the association with structural brain damage was not explored, and the identification of patient clusters with symptom profiles associated with structural brain damage in mild TBI would likely facilitate the diagnostic process [29]. In addition, the relationship between important outcomes such as functional level and participation in work may contribute to the prognostic evaluation, and strong relationships for clusters related to general health complaints may indicate nonspecific symptom profiles.

The aim of this study was to explore whether subgroups of patients with mild TBI could be identified according to their symptom profile using cluster analysis. In addition, we sought to explore whether these clusters could be uniquely associated with structural brain damage and assessed their relationships with anxiety and depression, other health complaints, functioning and participation in work.

## Material and Methods

### Design

This was a prospective cohort study of patients with mild TBI who were registered at baseline and 6-8 weeks after injury.

### Patients

The patients were admitted consecutively to the Department of Neurosurgery at Haukeland University Hospital (HUH) and Oslo University Hospital (OUH) with mild TBI during the period from January 2009 to November 2011. The study inclusion criteria consisted of patients aged 16-55 years, hospitalisation with a GCS between 13 and 15 within 30 minutes after trauma, loss of consciousness lasting fewer than 30 minutes and posttraumatic amnesia lasting fewer than 24 hours.

A total of 843 patients fulfilled the inclusion criteria. Of these, 185 were excluded due to substance abuse, somatic diseases, psychiatric disease and language difficulties (non-native Norwegian speakers). In addition, 269 patients were not willing to participate or did not attend the clinic 6-8 weeks post-injury, 110 patients did not meet the symptom criteria at 6-8 weeks, and we were unable to find the home address for 9 patients. In all, 270 patients were included, consisting of 169 from HUH and 101 from OUH. No statistically significant differences in demographics and injury-related variables between the two patient groups were found. The study was approved by the Norwegian Regional Committee for Medical Research Ethics. We also obtained written informed consent from all participants. The study was registered in Clinical Trials on the 24th of February, 2009, under NCT00869154.

### Data collection

**Demographic data:** Demographic data of the participants were assessed at baseline as well as at 6-8 weeks post-injury. The demographic characteristics covered age at onset and gender. Education level was categorised as 0-9 (below upper secondary level), 10-12 (upper secondary education) or above 13 (tertiary education). Employment status was categorised as full time or part time, unemployed or on social benefits, on sick leave, student status or not in regular work.

**Computed tomography (CT) brain scans:** Computed tomography (CT) brain scans were administered to all participants within 24 hours of injury.

**Magnetic resonance imaging (MRI) brain scans:** Magnetic resonance imaging (MRI) brain scans were performed using a system with a 1.5 Tesla MRI unit (Siemens or Phillips). Conventional scanning sequences consisted of sagittal T1, axial T2, coronal FLAIR (Fluid Attenuated Inversion Recovery) and DWI (diffusion-weighted imaging) components. Intracranial pathology on brain scans was defined as the presence of oedema, contusion, epidural haematoma, subdural haematoma, subarachnoid haemorrhage or diffuse axonal injury. Some patients also underwent X-ray, CT or MRI of the cervical spine. Scans of the cervical spine were defined as positive according to the trauma description.

**The diagnosis and injury mechanism:** The diagnosis and injury mechanism were reviewed using medical records and the International Classification of Diseases and Related Health Problems, 10th edition (ICD-10). The ICD-10 codes S06.0-S06.9 were used to classify intracranial injuries. The external cause of the injury was classified as related to a transport accident, fall (irrespective of height), violence or other cause.

**Symptoms at admission and clinical findings:** Symptoms at admission and clinical findings were abstracted from the medical records and included headache, neck pain and physical examination factors. Hyperreflexia, increased muscle tone and a positive Babinski test were taken as signs of injury to the central nervous system (CNS), whereas hyporeflexia and decreased muscle tone were taken as signs of injury to the peripheral nervous system (PNS).

### Measures

**The Glasgow coma scale score (GCS):** The Glasgow coma scale score (GCS) assesses the level of consciousness after TBI based on eye, verbal and motor responses [30]. This scale provides a score ranging from 3-15. Head injury was classified as mild if the GCS score at admission ranged from 13-15. The GCS was assessed within the first 24 hours, and the lowest GCS score within the first 24 hours is presented.

**Post-traumatic amnesia (PTA):** Post-traumatic amnesia (PTA) was measured by asking the patients to recall events retrospectively and was also abstracted from the medical records. PTA was dichotomised into less than 1 hour and between 1 and 24 hours. A duration of less than 24 hours was used as a measure of mild brain injury.

*The RPQ* consists of 16 items, which represent the most frequently reported symptoms after mild TBI. This instrument covers the cognitive, emotional and physical domains and has been shown to be valid for diagnosing PCS [31]. For this questionnaire, patients are asked to rate the degree for which each item has become more of a problem during the previous 24 hours compared to before the TBI. The responses are then rated on a 5-point Likert scale as follows: 0=not experienced at all; 1=no more of a problem; 2=a mild problem; 3=a moderate problem; and 4=a severe problem. The results of the clinical examination revealed that missing data often indicated that the subjects had no problems with a given item; therefore, such items were substituted with a score of 0. The 16 items of the RPQ are divided into three sub scales, including cognitive (poor memory, poor concentration, taking longer to think), emotional (irritability, depression, frustration, restlessness) and somatic (headache, dizziness, nausea, noise sensitivity, sleep disturbance, fatigue, blurred vision, light sensitivity, double vision) symptoms. The RPQ items are then summed to a total score, excluding ratings of 1 as recommended by King et al. [31]. We also registered patients with at least one cognitive, one emotional and one somatic symptom. A symptom was regarded as a current PCS symptom when it was rated as moderate or severe (scores ≥ 3).

**The Hospital Anxiety and Depression Scale (HAD):** The Hospital Anxiety and Depression Scale (HAD) is a 14-item scale used as a measure of anxiety and depression [32]. The scores for each item range from 0-3, and those for each subscale of anxiety and depression range from 0-21, with scores of 0-7 representing normal levels, 8-10 representing mild symptoms, 11-14 representing moderate symptoms, and 15-21 representing severe symptoms.

**The Subjective Health Complaints (SHC) inventory:** The Subjective Health Complaints (SHC) inventory proposes 29 questions concerning the severity of subjective and psychological health complaints during the last 30 days, and the responses are rated on a 4-point scale from 0=no complaint to 3=severe complaint. The mean number of complaints for each patient and the mean score are reported [33].

**To measure pain, a numeric rating scale**: To measure pain, a numeric rating scale from 0-10 was used to rate headache, neck/shoulder and lower back/leg pain. For the evaluation, the patient places a mark on a line indicating their level of pain; a score of 0 indicates the absence of pain, while 10 represents the strongest possible pain. The level of pain is divided into mild (1-3), moderate (4-6) and severe (7-10) categories.

**The Glasgow Outcome Scale Extended (GOSE):** The Glasgow Outcome Scale Extended (GOSE) is a global assessment of functioning tool for the areas of independence, work, social and leisure activities and participation in social life. The GOSE is an 8-point ordinal scale [34] and the categories are divided into upper and lower levels of good recovery [7,8], moderate disability [5,6], severe disability [3,4], vegetative state [2] and deceased [1].

## Data analysis and statistics

Statistical analyses were performed using SPSS for Windows, version 19 (SPSS Inc., Chicago, IL, USA). Descriptive data are presented as proportions and mean values with standard deviations (SDs). A 5% significance level was used. K-mean cluster analyses were conducted to describe groups of subjects with similar profiles of responses to the RPQ. Two-, three-, four- and five-cluster solutions were explored. Iteration procedures with up to 10 iterations were applied to obtain stable cluster solutions. Euclidean distances between clusters were evaluated and reported. F-statistics were used to evaluate the distance between items and their cluster centres in each solution. Each cluster solution was related to structural changes on CT/MRI, HAD anxiety and depression subscales, general health complaints, GOSE and sick leave. The optimal cluster solution was based on the highest number of clusters while maintaining a minimum cluster distance above 2 and a subject number above 20 in each cluster. Odds ratios were used to assess effect size and describe the strength of the association between subjects with positive radiologic findings on brain scans and the cluster solution.

## Results

A total of 270 patients with a mean age of 33 (SD 12) years were included. The demographic characteristics and injury mechanisms are presented in Table 1.

A GCS of 13 was reported for 5% of patients, 19% had a GCS of 14, and 76% had a GCS of 15. Furthermore, 12% experienced post-traumatic amnesia for between 1 and 24 hours, and the remaining patients experienced post-traumatic amnesia with a duration less than 1 hour. The diagnosed intracranial injuries and clinical and radiological pathology results are presented in Table 2.

## Health status 6-8 weeks post-injury

In total, 32% of patients were employed at the time of injury and reported sickness absences (N=203). Approximately six weeks post-injury, 43% had returned to their daily employment or occupation. For the students and the 7% of patients who were unemployed or on social benefits at the time of injury, it was difficult to determine the actual rate of return to “work” at 6-8 weeks post-injury. Functional recovery ranged from moderate disability to the upper level of good recovery

| Gender | Frequency |
|---|---|
| Male | 62% |
| Female | 38% |
| *Education* | |
| Below 10 years | 10% |
| 10-12 years<br>Above 12 years | 54%<br>36% |
| *Working status* | |
| Employment full time or part time | 75% |
| Students | 18% |
| Unemployed/social benefits | 7% |
| *Injury mechanism* | |
| Falls | 39% |
| Traffic injuries | 30% |
| Violence | 19% |
| Others | 12% |
| *Influence of intoxicant* | |
| Alcohol | 33% |
| Another intoxicant | 2% |

**Table 1:** Demographic characteristics and injury mechanisms (N=270).

| Diagnosis | Frequency |
|---|---|
| S06.0 | 82% |
| S06.2 | 3% |
| S06.3 | 3% |
| S06.4, S06.5, S06.6 | 11% |
| S06.8 | 1% |
| *Symptoms at admission* | |
| Neck pain | 32% |
| Headache | 61% |
| *Clinical findings* | |
| CNS injury | 2% |
| PNS injury | 2% |
| *Radiology (intracranial injury)* | |
| Positive CT scan | 21% |
| Positive MRI given negative CT scan | 6% |
| *Radiology (cervical spine)* | |
| Positive X-ray or MRI | 11% |

**Table 2:** Frequency of ICD 10 diagnosis, symptoms from the head and neck and associated radiological findings as well as clinical signs from the peripheral (PNS) or central nervous system (CNS) (N=270).

according to the GOSE score (Table 3). The mean sum of the RPQ was 16.36 (SD=14.24). Of 270 patients, 192 reported three symptoms or more. Sixty-eight patients (25%) reported at least one moderate or severe cognitive, emotional and somatic symptom. Additionally, 86% of patients reported symptoms (score ≥ 2) related to the 16 items of the RPQ at two months. The mean HAD anxiety score was 5.87 (SD=4.42), the mean HAD depression score was 3.67 (SD=3.78), and the mean total HAD score was 9.54 (SD=7.58). The distribution of these symptoms is illustrated in Table 4.

Additionally, the mean score for self-reported health problems was 16.03 (SD=11.63), and the mean number of health problems for each patient was 9 (range=0 - 29). On a scale of pain intensity, the mean score for headache was 3.44 (SD=2.93), that for neck and shoulder pain was 3.38 (SD=2.92), and that for lower back and leg pain was 2.53 (SD=2.89).

## RPQ and cluster analysis

No significant differences in symptom level (mean RPQ score) were revealed between subjects with and without radiological findings on brain scans (p=0.34). All investigated cluster solutions exhibited one cluster with high symptom levels across all problems. The two-cluster solution only differentiated between high and low symptom levels. In the five-cluster solution, minimal distance was found between two of the cluster centres (0.005). The four-cluster solution revealed one cluster with low symptoms (low), one cluster with a generally high symptom level (high), one cluster characterised by a high level of symptoms regarding cognitive functions (cognitive) and one cluster with dominating somatic and frustration symptoms (somatic) (Table 5). The Euclidean distance was used as the "ordinary" distance between the clusters (Table 6). As a measure of the characteristic for each item on the RPQ, we used the mean square and mean square error, and F-statistics were used to evaluate distance between the items and their cluster centres in each solution (Table 7). The four-cluster solution appeared to better differentiate between subjects with and without positive radiological findings on brain scans, demonstrating an odds ratio of 0.6 for the association between a low symptom profile and a positive radiological finding, as compared to the other clusters ($X^2$=3.20, p=0.07). The profiles in the four-cluster solution also revealed distinct patterns regarding anxiety and depression, general health complaints, functioning and absence related to sickness (Table 8). Clusters 1, 2 and 3 were significantly lower than the "high" cluster group in terms of both depression and anxiety but were significantly higher for the GOSE. Cluster 2 was significantly lower in regards to health complaints compared to the other clusters.

| GOSE score | Frequency |
|---|---|
| Upper good recovery | 26% |
| Lower good recovery | 27% |
| Upper moderate disability | 39% |
| Moderate disability | 8% |

**Table 3:** Percentage of subjects reporting disability and recovery on the Glasgow Outcome Scale (GOSE).

| HAD – anxiety scores | Frequency |
|---|---|
| 0-7 | 68% |
| 8-10 | 16% |
| 11-14 | 12% |
| 15-21 | 4% |
| *HAD – depression scores* | |
| 0-7 | 83% |
| 8-10 | 10% |
| 11-14 | 7% |
| 15-21 | 0% |

**Table 4:** The frequency of subjects reporting normal (0-7), mild (8-11), moderate (11-14) or severe (15-21) symptoms on the anxiety and depression subscale of the Hospital Anxiety and Depression Scale (HAD).

## Discussion

One novel feature of this study was the use of cluster analysis to evaluate symptom profiles of patients with mild TBI. To date, cluster analysis has mainly been applied in TBI research to identify distinct psychological profiles in patients [23,24]. In this study, we defined different clusters of symptoms at the individual level that were associated with brain injury lesions on CT and MRI as well as anxiety, depression and global function. Four distinct subgroups of patients with mild TBI were identified, and these subgroups were characterised as demonstrating high and low levels of symptoms, high scores for cognitive symptoms and an intermediate symptom level related primarily to somatic symptoms. The external validity of these subgroups was supported by the significant differences in anxiety and functional level between the clusters.

In the present study, a significant number of patients reported persistent symptoms 6-8 weeks after injury, although many patients recovered well. Other studies on mild TBI have also reported persistent symptoms 3 months after injury [4,35] and the high number of complaints in the present study is in accordance with the general findings in the previous patient group [36] . Previously, it was shown that patients report more symptoms when a list of symptoms is read to them as compared to when they are asked to state them spontaneously [6]. However, the RPQ may represent the best possible way to overcome this problem, as it was shown to be reliable both when self-administered and clinician administered [31]. In addition, this scale is unbiased for gender and age [37]. Nevertheless, it has been difficult to predict recovery based on individual symptoms, which may be due to large interindividual differences in the severity of intracranial injury in mild TBI [38]. Both a positive correlation [39] and the absence of any correlation [40] between findings on CT and outcome after mild TBI have been reported, and similar results have been demonstrated for MRI [41,42]. However, the general view is that radiological findings represent a poor predictor of functional outcome in mild TBI [36]. Twenty-seven percent of patients in the present study demonstrated intracranial injury, as shown by CT and MRI. Although we found no significant differences in symptom level (mean RPQ score) between subjects with and without imaging abnormalities on CT and MRI, the four-cluster solution seemed to better differentiate subjects with and without positive radiologic findings in comparison to the other cluster solutions. Furthermore, patients with minor symptoms had a reduced risk for a positive finding, indicating that the symptom level may guide the indications for MRI.

The mean total HAD scores indicate overall mild symptoms of anxiety and depression, although the subscore was higher for anxiety than for depression, which is in agreement with previous studies [4]. The cognitive cluster was significantly lower than the "high" cluster group in terms of both depression and anxiety. This finding may be related to self-awareness difficulties [43] or the increased importance of emotional symptoms in the "high cluster group" as a result of other preinjury and injury factors.

There were no significant differences between the "cognitive" cluster and the "somatic" and "high symptom level" clusters regarding general health complaints, which indicated a general overlap between

| Symptom | Cluster 1 (Cognitive N=42) | Cluster 2 (Low N=129) | Cluster 3 (Somatic N=57) | Cluster 4 (High N=42) |
|---|---|---|---|---|
| Headache | 2 | 1 | 2 | 3 |
| Dizziness | 2 | 0 | 1 | 2 |
| Nausea | 1 | 0 | 1 | 1 |
| Noise sensitivity | 1 | 0 | 0 | 3 |
| Sleeping problems | 2 | 0 | 2 | 3 |
| Fatigue | 3 | 1 | 2 | 4 |
| Irritability | 1 | 0 | 1 | 3 |
| Depression | 1 | 0 | 1 | 3 |
| Frustration | 2 | 0 | 2 | 3 |
| Forgetting | 3 | 0 | 1 | 3 |
| Problems with concentration | 3 | 0 | 1 | 3 |
| Take longer to think | 3 | 0 | 1 | 3 |
| Blurred vision | 1 | 0 | 0 | 2 |
| Light sensitivity | 1 | 0 | 0 | 2 |
| Diplopia | 0 | 0 | 0 | 1 |
| Restless | 1 | 0 | 1 | 2 |

**Table 5:** The mean score for each item in the RPQ of the subjects assigned to each of the four clusters.

| Cluster | Cluster1 (Cognitive N=42) | Cluster 2 (Low N=129) | Cluster 3 (Somatic N=57) | Cluster 4 (High N=42) |
|---|---|---|---|---|
| 1 | | 5.94 | 3.47 | 4.74 |
| 2 | 5.94 | | 4.33 | 9.41 |
| 3 | 3.47 | 4.33 | | 5.80 |
| 4 | 4.74 | 9.41 | 5.80 | |

**Table 6:** Euclidean distance between the final cluster centres.

| Symptom | Cluster | | Error | | F | Sig. |
|---|---|---|---|---|---|---|
| | Mean Square | df | Mean Square | df | | |
| Headache | 81.52 | 3 | 1.32 | 266 | 61.64 | .00 |
| Dizziness | 52.04 | 3 | 1.16 | 266 | 44.85 | .00 |
| Nausea | 20.06 | 3 | .89 | 266 | 22.51 | .00 |
| Noise sensitivity | 67.89 | 3 | .99 | 266 | 68.46 | .00 |
| Sleeping problems | 113.71 | 3 | 1.13 | 266 | 100.47 | .00 |
| Fatigue | 109.76 | 3 | 1.05 | 266 | 104.53 | .00 |
| Irritability | 76.71 | 3 | 1.03 | 266 | 74.24 | .00 |
| Depression | 61.60 | 3 | .98 | 266 | 63.19 | .00 |
| Frustration | 107.54 | 3 | .90 | 266 | 118.91 | .00 |
| Forgetting | 104.26 | 3 | .97 | 266 | 108.05 | .00 |
| Problems with concentration | 124.71 | 3 | .82 | 266 | 151.55 | .00 |
| Take longer to think | 113.82 | 3 | .75 | 266 | 150.88 | .00 |
| Blurred vision | 50.54 | 3 | .92 | 266 | 55.12 | .00 |
| Light sensitivity | 38.53 | 3 | .97 | 266 | 39.78 | .00 |
| Diplopia | 9.22 | 3 | .58 | 266 | 16.01 | .00 |
| Restless | 51.02 | 3 | .94 | 266 | 54.49 | .00 |

**Table 7:** Mean square distance with the mean square error from the cluster centre for each item in the Rivermead Post Concussion Symptoms Questionnaire.

| Measures | Cluster1 (Cognitive) N=42 (31) | Cluster 2 (Low) N=129 (97) | Cluster 3 (Somatic) N=57 (44) | Cluster 4 (High) N=42 (31) | p-value |
|---|---|---|---|---|---|
| HAD anxiety | 7.33 (3.06) | 3.06 (2.92) | 8.08 (3.75) | 10.42 (3.81) | <0.001* |
| HAD depression | 5.26 (3.69) | 1.66 (2.31) | 1.66 (2.31) | 8.00 (3.83) | <0.001* |
| Health comp. | 17.88 (9.17) | 9.11 (7.12) | 19.25 (7.88) | 31.12 (13.16) | <0.001** |
| GOSE | 6.22 (0.65) | 7.23 (0.73) | 6.35 (0.83) | 5.95 (0.70) | <0.001* |
| Sickness absc. | 53 % | 26 % | 56% | 48% | 0.001 |

* All clusters different except for 3 and 1
**Cluster 2 differed from 1, 3 and 4

**Table 8:** The mean score (and SD) for the anxiety and depression subscale of the Hospital Anxiety and Depression Scale, the Subjective Health Complaints inventory, the Glasgow Outcome Scale Extended (GOSE) score and the percentage of subjects reporting sickness-related absence for the four cluster solutions. The number of patients in each cluster is shown. Students and pupils were not included in the analysis of sickness absence, and the number of subjects for this analysis is shown in parentheses.

the symptoms in the RPQ and other symptoms [44]. Although there were no significant differences, the "high level cluster" demonstrated more health complaints than the other clusters, and factors such as premorbid characteristics, injury factors, and personal factors may explain this high level of symptoms. The impact of these factors on recovery is well known [45], although how these factors may be effectively modified through the rehabilitation process remains largely unexplored.

In agreement with other studies, the majority of patients showed a favourable functional outcome, as measured by GOSE levels 6-8 [6]. Even with a GOSE score of 6-8, cognitive, somatic and emotional problems were present, and a low RPQ level was associated with significantly better recovery. The poorest recovery was identified in the "high symptom level" group, although the burden of symptoms in this group may be flawed by preinjury factors [46].

The magnitude of sick leave reported in the present study at two months of follow up is comparable to that reported in other studies on mild TBI and return to work [47]. Patients often find their symptoms debilitating enough to be unable to return to work regardless of whether the symptoms are cognitive or somatic. However, the "low-cluster" group demonstrated fewer problems related to returning to work and therefore likely consisted of patients with a successful recovery who did not require follow-up. The cognitive group was characterised by high sickness absence and primarily cognitive symptoms, which suggests that rehabilitation for these patients should be cognitively oriented. Given that TBI affects primarily young individuals in their most productive years, it is crucial that rehabilitation includes efforts to return these patients to work successfully [48].

One limitation of the present study was that symptoms were self-reported. Additionally, there was a lack of valid, premorbid data. A further limitation was that this study was conducted in trauma centres, which may introduce bias towards the more severe end of the MTBI spectrum. However, 76% of patients were classified with a GCS of 15, and 82% were diagnosed as S06.0. These results were limited to adults who were employed at the time of the injury because this was a return-to-work study. In addition, the participants were assessed at two different University hospitals. However, no statistically significant differences in demographics and injury-related variables between the two patients groups were found. Although this study had several limitations, one strength was the relatively high number of participants (N=270) in the representative cohort of adults aged 16-55 years.

## Conclusion

Subgroups of patients with mild TBI can be identified according to their symptom profile using cluster analysis. Patients with minor symptoms had a reduced risk for a positive finding on CT or MRI, whereas the high symptom level group struggled to return to work and demonstrated high levels of anxiety, depression and disability.

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