

# The Association Between the Postconcussion Symptoms and Clinical Outcomes for Patients With Mild Traumatic Brain Injury

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**Background:** Postconcussion symptoms (PCS) (such as dizziness, headache, irritability, fatigue, and impaired memory) are common in patients who sustain a mild traumatic brain injury (mTBI). However, few studies have systematically investigated the association between PCS and clinical outcomes in mTBI patients. Therefore, the present study attempted to examine PCS during the disease course and to determine whether PCS adversely affect outcome.

**Methods:** This was a prospective, cohort and controlled study of 115 mTBI patients. The PCS checklist was used to

identify PCS and the Glasgow Outcome Scale and the Glasgow Outcome Scale-Extended were used to investigate clinical outcomes. All patients were evaluated four times: at 1 week, 2 weeks, 4 weeks, and 8 weeks after the injury.

**Results:** Physical symptoms such as dizziness and headache were prominent in the early after injury stage (1 and 2 weeks). On the other hand, the psychosocial symptoms, such as depression and irritability, were significant at the late after injury stage (4 and 8 weeks). Dizziness adversely affected clinical outcome at both

the early and late stages of the disease, whereas the impact of intracranial lesions and depression on outcome was greatest early and late, respectively.

**Conclusions:** The results show that PCS during the disease course and the relationship between PCS and clinical outcome can be systematically evaluated. In fact, different postconcussion symptom domains should be monitored while the disease is progressing.

**Key Words:** Mild traumatic brain injury, Postconcussion symptoms, Outcomes, Glasgow Outcome Scale-Extended.

*J Trauma.* 2007;62:657–663.

Traumatic brain injury (TBI) is a significant public health problem with an annual incidence of 1.5 to 2 million people in the United States, of which an estimated 70,000 to 90,000 cases result in remarkable functional impairments.<sup>1</sup> Some western studies<sup>2,3</sup> concluded that mild TBI (mTBI) accounts for 90% of TBIs whereas there were 77% to 82% TBIs classified as mild severity group in Taiwanese literature.<sup>4,5</sup> In Taiwan, the incidence rate of mTBI in 2004 was 728 people per 100,000, which meant more than 160,000 people had suffered from this problem.<sup>6</sup> Several studies<sup>7–9</sup> further evidenced that lost productive work time after mTBI may be the largest component of economic costs of brain trauma.

The postconcussion symptoms (PCS) are common complaints after mTBI. Rutherford<sup>10</sup> reported that the most common acute complaints were physical problems (headache and dizziness) that occurred early, whereas the most common chronic ones were psychosocial difficulties (depression and

memory impairment) that occurred late in the illness. Although most mTBI patients recover quickly, usually within 3 months after injury, many studies<sup>11–15</sup> have identified a small proportion of patients who continue to have difficulties more than 1 year after head trauma. In fact, the persistent cognitive and emotional disturbances are often considered potential risk factors for lifetime disability.<sup>16–18</sup>

Surprisingly, few researchers have explored the relationship between PCS and clinical outcome. Moreover, their studies had some methodological drawbacks. Most were cross-sectional studies. Thus, although Chamelian and Feinstein<sup>19</sup> found that dizziness was an adverse predictor of patients' clinical outcomes at 6 months after mTBI, their study failed to distinguish between early and late PCS owing to its cross-sectional nature. Moreover, though commonly used to assess clinical outcomes of severe TBI patients, the Glasgow Outcome Scale (GOS)<sup>20</sup> might not be suitable for mTBI patients. In fact, the GOS was shown clinically to be constrained by a significant ceiling effect and thus was unable to effectively differentiate between PCS and clinical outcomes.

The present study tried to resolve these methodological problems. First, the authors regularly followed mTBI patients immediately after injury to 2 months after injury. In addition, we used the Glasgow Outcome Scale-Extended (GOSE)<sup>21,22</sup> to place greater emphasis on assessment of the TBI patients' social and family relationships, which are possible predictors of patient prognosis. Hence, the purpose of the study was to explore the relationship of PCS and clinical outcome systematically. Two sets of hypotheses needed to be tested. First, in our mTBI patients, the specific PCS would manifest differently

Submitted for publication July 12, 2005.

Accepted for publication December 15, 2005.

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Supported in part by the National Health Research Institute (NHRI-EX94-9106PN), Taiwan, Republic of China.

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DOI: 10.1097/01.ta.0000203577.68764.b8

**Table 1** Demographical Data of mTBI Patients

	Number of Participants	Male (%)	Age	Education	GCS Score	Intracranial Lesions (%)
mTBI patients	115	44	36.70 ± 16.70*	12.30 ± 3.60*	14.95 ± 0.22*	20
Healthy participants	40	53	34.85 ± 13.40*	13.75 ± 2.11*	—	—

\* Mean ± SD.

mTBI, mild traumatic brain injury; GCS, Glasgow Coma Scale.

between the earlier and later after injury stages. Second, the clinical outcomes of the earlier and later after injury stages would be adversely affected by specific PCS, respectively.

## METHODS

### Participants

During a period of 15 months (January 2004 to March 2005), 130 mTBI patients were followed up in the clinic. Fifteen patients were excluded and 115 patients with mTBI participated in this study. The diagnosis of mTBI was made in a Level 1 trauma center by a neurosurgeon and was based on the guidelines of mTBI management proposed by Servadei et al.<sup>23</sup> Accordingly, patients with the following criteria were included in the present study: (1) initial GCS score of 14/15 and (2) initial loss of consciousness of less than 30 minutes. The demographic data of the patients are shown in Table 1. As a control group, we recruited healthy volunteers with no history of significant brain injury or neurologic disorders and with a mean age similar to that of the patients (34.85 years ± 13.40,  $t [153] = -0.63$ ,  $p > 0.05$ ).

The recruitment and follow-up of the mTBI patients discharged from the emergency room or hospital took place in a specific neurosurgery clinic. All patients with a history of suspected psychiatric problems, cerebrovascular insults, or other major medical illnesses (e.g. brain tumors, thyroid dysfunction, etc.) were excluded.

### Measurement of the PCS

The description of PCS in our study matched that described in the International Classification of Diseases (ICD-10) clinical diagnosis of PCS (code F07.2).<sup>24</sup> The symptoms included headache, dizziness, fatigue, irritability, insomnia, difficulty with concentration or memory, emotional lability, alcohol abuse, and stress intolerance. Accordingly, the authors designed a PCS screening instrument, known as the Checklist of Postconcussion Symptoms (CPCS), for clinical use. This instrument was used to assess the severity of 16 commonly reported PCS, including headache, dizziness, fatigue, nausea, vomiting, poor vision, tinnitus, loss of energy, depression, irritability, insomnia, anxiety, attention deficits, memory impairments, psychomotor slowing, and other disturbances. All participants were asked, "Did any of the following symptoms reduce your ability to work or make you sick in the past week?" If patients manifested any symptoms in the scale, an examiner (a clinical neuropsychologist)

scored "1" for each item they reported. The sum of those checked items represented the total PCS score for that patient.

### Measurement of the Clinical Outcomes

Many past studies have reported that mTBI patients manifest many cognitive and emotional disturbances though their GOS-evaluated outcomes are still favorable. Hence, the GOSE, which uses an eight-point ordinal scale and a semi-structured interview, was developed to evaluate patients' clinical outcomes. The GOS and the GOSE are shown in Table 2. The main difference between the GOS and the GOSE is that the latter also assesses patients' social activities and family relationships. Moreover, the examiner had to evaluate patients' before and after injury conditions to make an intrapersonal comparison.

### Procedures

When the patients were discharged from the emergency department or the hospital, they were prospectively evaluated using the CPCS, GOS, and GOSE at 1 week, 2 weeks, 1 month, and 2 months after injury. Because some patients did not need to be followed up continuously, the authors conducted their after-injury evaluations by telephone. The study protocol was approved by the institutional review boards of participating institutions, and the patients gave informed consent after the study requirements were explained.

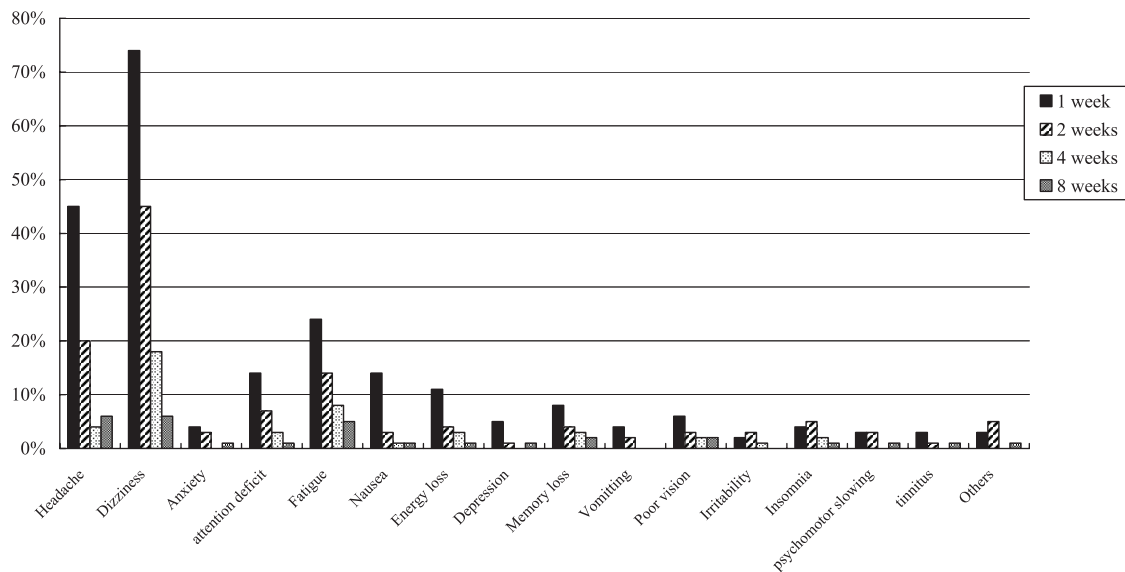
### Data Analysis

The one-way analysis of variance (ANOVA) and a post hoc analysis using Scheffe's procedure, Spearman's correlation,  $\chi^2$  test, and logistic regression were used to evaluate differences between groups. Statistical significance was defined as a probability value of less than 0.05. Commercially

**Table 2** The GOS and the GOSE

Score	GOS	GOSE	Score
1	Death	Death	1
2	Vegetative status	Vegetative status	2
3	Severe disability	Lower severe disability	3
		Upper severe disability	4
4	Moderate disability	Lower moderate disability	5
		Upper moderate disability	6
5	Good recovery	Lower good recovery	7
		Upper good recovery	8

GOS, Glasgow Outcome Scale; GOSE, Glasgow Outcome Scale-Extended.



**Fig. 1.** The frequency of individual postconcussion symptoms after mTBI within 2 months after injury (1 week, 2 weeks, 4 weeks, and 8 weeks).

available software (version 11.0; SPSS, Inc.; Chicago, Ill) was employed.

## RESULTS

### Do Our mTBI Patients Have PCS?

Most of our mTBI patients (85%) had at least one postconcussion symptom. As shown in Figure 1 and Table 3, a variety of symptoms appeared 1 week after injury including dizziness (in 74% of the patients), headache (45%), fatigue (24%), attentional deficits (14%), and nausea (14%). At 2 weeks after injury, 55% of the patients still had a least one PC symptom: dizziness (45%), headache (20%), or fatigue (14%). Less than 7% of the patients reported other PCS, such as nausea, attention deficit, and depression.

At the 4- and 8-week postinjury evaluations, 23% and 13%, respectively, had at least one symptom. Moreover, most

symptoms (except dizziness in 18% of patients) were diminished at 4 weeks after injury. At the 8-week postinjury evaluation, 94% of the patients had no postconcussion symptom.

### Did the PCS Adversely Affect Clinical Outcome?

#### One Week After Injury

To analyze the relationship between PCS and clinical outcome, patients were divided into two groups: those with a GOSE score of 8 (the “good recovery” group) and those with a GOSE score of less than 8 (the “poor recovery” group). All patients had favorable clinical outcomes based on GOS score (GOS = 5).

As shown in Table 4, one-way ANOVA found a significant main effect of groups on PCS scores, and a post hoc analysis using Scheffe’s procedure found a significant main effect of groups on the total PCS scores ( $F = 16.99, p < 0.001$ ). In fact,

**Table 3** The Postconcussion Symptoms Within 2 Months

	1 wk	2 wk	4 wk	8 wk	Control
Headache	45	20	4	6	13
Dizziness	74	45	18	6	8
Anxiety	4	3	0	1	5
Attention deficits	14	7	3	1	8
Fatigue	24	14	8	5	8
Disgusting	14	3	1	1	0
Loss of energy	11	4	3	1	5
Depression	5	1	0	1	3
Memory loss	8	4	3	2	5
Vomiting	4	2	0	0	0
Poor vision	6	3	2	2	3
Irritability	2	3	1	0	5
Insomnia	4	5	2	1	3
Slow response	3	3	0	1	0
Tinnitus	3	1	0	1	5
Others	3	5	0	1	5

Values are presented as percentages.

**Table 4** The Total PCS Between Good and Poor Recovery Groups

	Good Recovery (GOSE Score = 8)		Poor Recovery (GOSE Score <8)		Control		
	N	M	N	M	N	M	F
1 wk	59	1.66 <sup>†</sup>	56	2.86 <sup>‡§</sup>	40	0.73	16.99*
2 wk	87	0.79	28	2.64 <sup>‡§</sup>	40	0.73	16.95*
4 wk	101	0.27	14	1.57 <sup>‡</sup>	40	0.73	7.88*
8 wk	112	0.23	3	2.33 <sup>‡</sup>	40	0.73	5.97*

\* $p < 0.01$ .

<sup>†</sup> There are significantly more total PCS of the good recovery group than that of the control group.

<sup>‡</sup> There are significantly more total PCS of the poor recovery group than that of the control group.

<sup>§</sup> There are significantly more total PCS of the poor recovery group than that of the good recovery group.

PCS, postconcussion symptoms; N, number of patients; M, mean.

**Table 5** The Headache and Dizziness Among Good Recovery, Poor Recovery, and Control Groups

	Headache		Dizziness	
	N (%)	Odds Ratio	N (%)	Odds Ratio
1 week				
Control (N = 40)	5 (13%)		3 (8%)	
Good recovery (N = 59)	20 (34%)	3.59*	34 (58%)	16.77*
Poor recovery (N = 56)	32 (57%)	9.32*	51 (91%)	125.78*
2 weeks				
Control (N = 40)	5 (13%)		3 (8%)	
Good recovery (N = 87)	11 (13%)	1.01	28 (32%)	5.85*
Poor recovery (N = 28)	12 (43%)	5.25	24 (86%)	73.99*
4 weeks				
Control (N = 40)	5 (13%)		3 (8%)	
Good recovery (N = 101)	3 (3%)	0.21	11 (11%)	1.51
Poor recovery (N = 14)	2 (14%)	1.17	10 (71%)	30.83*
8 weeks				
Control (N = 40)	5 (13%)		3 (8%)	
Good recovery (N = 112)	6 (5%)	0.40	6 (5%)	0.70
Poor recovery (N = 3)	1 (33%)	3.50	1 (33%)	6.17*

\* $p < 0.01$ .

significantly more total PCS presented in both the good and the poor recovery groups than in the control group, and presented in the poor recovery group than in the good recovery group. Meanwhile, the Spearman's correlation study revealed that mTBI patients with more PCS had poorer outcomes, as measured by the GOSE ( $r = -0.40$ ,  $p < 0.01$ ). As for the impacts of individual PCS on clinical outcome,  $\chi^2$  analysis showed that headache ( $\chi^2 = 6.27$ ,  $p < 0.01$ ), dizziness ( $\chi^2 = 16.67$ ,  $p < 0.001$ ), and nausea ( $\chi^2 = 5.14$ ,  $p < 0.05$ ) were strongly associated with GOSE rating. Moreover, the logistic regression analysis (Table 5) revealed much more headache and dizziness in the poor and good recovery groups than in the control. Therefore, intracranial lesions had an adverse impact on GOSE score ( $\phi = -0.25$ ,  $p < 0.01$ ).

### Two Weeks After Injury

As shown in Table 4, although 76% of the mTBI patients recovered well, one-way ANOVA revealed a significant main effect of groups on PCS, and a post hoc analysis with Scheffe's procedure showed that significantly more PCS were present in the poor recovery group than the control group ( $F = 16.95$ ,  $p < 0.001$ ). Furthermore, Spearman's correlation study showed that mTBI patients with more PCS had poorer outcomes, as measured by the GOSE ( $r = -0.48$ ,  $p < 0.05$ ). As for the impacts of individual PCS on clinical outcome,  $\chi^2$  analysis indicated that headache ( $\chi^2 = 12.09$ ,  $p < 0.01$ ) and dizziness

( $\chi^2 = 24.50$ ,  $p < 0.001$ ) individually were still markedly associated with GOSE score. Logistic regression analysis (Table 5) found significantly more dizziness in the good and poor recovery groups than in the control. In addition, anxiety ( $\chi^2 = 5.77$ ,  $p < 0.05$ ), fatigue ( $\chi^2 = 10.27$ ,  $p < 0.01$ ), loss of energy ( $\chi^2 = 16.24$ ,  $p < 0.001$ ), and irritability ( $\chi^2 = 12.88$ ,  $p < 0.001$ ) were all markedly associated with GOSE rating. As found at 1 week after injury, the intracranial lesions had a negative effect on GOSE score ( $\phi = -0.41$ ,  $p < 0.05$ ).

### Four Weeks After Injury

At 4 weeks after injury, 88% mTBI patients were recovering well. The one-way ANOVA found a significant main effect of groups on PCS, and a post hoc analysis with Scheffe's procedure found significantly more PCS were present in the poor recovery group than the control group ( $F = 7.88$ ,  $p < 0.01$ ). Furthermore, Spearman's correlation revealed that mTBI patients with more PCS had poorer outcome, as measured by the GOSE ( $r = -0.60$ ,  $p < 0.05$ ). As for the impacts of individual PCS on the clinical outcomes,  $\chi^2$  analysis showed that dizziness ( $\chi^2 = 30.19$ ,  $p < 0.001$ ), fatigue ( $\chi^2 = 4.09$ ,  $p < 0.05$ ), and irritability ( $\chi^2 = 7.28$ ,  $p < 0.01$ ) remained markedly associated with GOSE score. Logistic regression analysis (Table 5) found more dizziness in the poor recovery group than in the control. Attention deficit ( $\chi^2 = 8.56$ ,  $p < 0.01$ ) was significantly associated with GOSE score, and intracranial lesions had an adverse impact on GOSE score ( $\phi = -0.33$ ,  $p < 0.01$ ).

### Eight Weeks After Injury

Most patients (97%) had recovered well by 8 weeks after injury. Moreover, one-way ANOVA revealed a significant main effect on PCS, and a post hoc analysis with Scheffe's procedure showed significantly more PCS were present in the poor recovery group than the control group ( $F = 5.97$ ,  $p < 0.01$ ). The Spearman's correlation showed that mTBI patients with more PCS had poorer outcome, as measured by the GOSE ( $r = -0.26$ ,  $p < 0.01$ ). As for the impacts of individual PCS on the clinical outcomes, the  $\chi^2$  analysis showed that headache ( $\chi^2 = 4.00$ ,  $p < 0.05$ ), dizziness ( $\chi^2 = 4.00$ ,  $p < 0.05$ ), fatigue ( $\chi^2 = 4.92$ ,  $p < 0.05$ ), poor vision ( $\chi^2 = 75.98$ ,  $p < 0.001$ ), nausea ( $\chi^2 = 37.66$ ,  $p < 0.001$ ), and depression ( $\chi^2 = 37.66$ ,  $p < 0.001$ ) were significantly associated with GOSE score. As at 4 weeks after injury, logistic regression analysis revealed the presence of more dizziness in the poor recovery group than the control (Table 5). Surprisingly, intracranial lesions and GOSE score were not associated ( $\phi = -0.06$ ,  $p > 0.05$ ).

## DISCUSSION

### Definition of mTBI

The definition of mTBI is controversial.<sup>25–32</sup> In most studies to date,<sup>33–36</sup> mTBI patients had GCS scores of 13/15. However, Tellier and colleagues<sup>37</sup> suggested that patients who had "mild head injury" were not a homogeneous group.



The studies of Hsiang et al.<sup>38</sup> and Hsiang<sup>39</sup> further supported this point of view. They considered the pathophysiology of mTBI in these patients was heterogeneous and recommended subdivision of head injury patients with GCS scores of 13/15 into a “mild head injury” and “high-risk mild head injury” groups. “Real” mild head injury was defined as GCS score of 15 without any acute positive radiographic findings. In addition, Uchino et al.,<sup>35</sup> while confirming the results of previous studies, favored exclusion of patients with GCS score of 13 from the mild head injury category, because of a high incidence of brain damage on computed tomography scans in those patients. Hence, to avoid the ambiguity associated with heterogeneity of pathophysiology, our study included only mTBI patients with GCS score of 14/15.

### The PCS in mTBI Patients

The prospective design of our study permitted us to show significant association between PCS and disease course. Unlike past studies,<sup>10,13</sup> which reported headache as the most common symptom after mTBI, our study found dizziness was the most prominent and persistent. In contrast to most past studies, which were cross-sectional, our prospective cohort study revealed symptom prevalence at different stages after mTBI. Even so, most of the other PCS had lessened by 2 weeks after injury. In fact, the results of some past cross-sectional studies support this result. For instance, Dikmen and colleagues<sup>11</sup> found that very few minor head injury patients reported PCS after 1 month. Recent studies<sup>40,41</sup> agreed and showed that symptoms usually disappeared by 3 months after injury. However, symptoms can persist from months to years after injury and may even be permanent, causing disability in some individuals. When this cluster of PCS is persistent in nature, it is often called persistent PCS (PPCS).<sup>42</sup> In our study, there were only three patients with PPCS at 8 weeks after injury.

Some researchers explored whether PCS is specific to mTBI or simply a nonspecific symptom cluster. Iverson<sup>43</sup> examined the prevalence of postconcussion-like symptoms in a sample of healthy individuals. Participants completed the British Columbia Postconcussion Symptom Inventory-Short Form (BC-PSI-Sf), a test designed to measure both the frequency and intensity of ICD-10 criteria for PCS, and the Beck Depression Inventory (2nd edition). Specific endorsement rates of postconcussion-like symptoms ranged from 35.9% to 75.7% for any experience of the symptoms in the past 2 weeks. In our study, less than 15% of the healthy participants complained of PCS. Moreover, there was significantly more headache and dizziness in mTBI patients than in the control group (Table 5).

### The Outcome of mTBI

In the literature, the GOS remains the most widely used outcome measure of head injury severity.<sup>44,45</sup> However, past researchers<sup>22,46–48</sup> showed that the GOSE could better differentiate levels of recovery in mild-to-moderate TBI patients when combined with a structured interview. Levin et al.<sup>48</sup>

reported that the validity of GOSE exceeded that of GOS in mild-to-moderate TBI. In fact, the GOSE was more sensitive to change than the GOS at the 3-month and 6-month assessments. In our study, GOS scores did not change significantly (all patients appeared to be fully recovered) between evaluations, whereas a number of patients did not achieve optimal recovery as measured by the GOSE. Therefore, our findings support the conclusion that the GOSE is the better of the two methods for measuring the clinical outcomes in mild-to-moderate TBI patients.

### PCS Adversely Affected Clinical Outcome in mTBI Patients

Regardless of the stage after head trauma, the PCS reported by mTBI patients had a significant negative influence on clinical outcome. Unfortunately, few studies have directly investigated the association between PCS and clinical outcome. Haboubi et al.<sup>15</sup> showed a significant number of 1,255 patients with minor head injury still complained at 2 weeks after injury of some PCS, which might contribute to a delay in return to work. In addition, Chamelian and Feinstein<sup>19</sup> compared clinical outcomes in mild-to-moderate TBI patients with and without dizziness. Their results showed that the presence of dizziness at 6 months after injury was an adverse prognostic indicator. In fact, our results provide further evidence that dizziness is the most persistent symptom adversely affecting clinical outcome as well as disease course. Moreover, we found that emotional disturbances, such as irritability and depression, might be adverse factors for clinical prognosis at 4 weeks after injury. Some researchers<sup>16,49,50</sup> reported depressive symptoms in 25% of patients 1 year after mTBI. The negative impact of emotional and cognitive difficulties on clinical outcomes has also been reported. Rutherford<sup>10</sup> proposed that the emotional and cognitive problems were late PCS that might negatively influence clinical outcome. Notably, Jorge et al.<sup>51</sup> showed that depression after mTBI adversely affected clinical outcome. Moreover, recently, Wilson et al.<sup>52</sup> concluded from a study of 135 TBI patients that there was a significant negative correlation between outcome and depression at 6 months after injury. In addition, our study confirmed that latent PCS, such as depression and irritability, adversely affect clinical outcome, even 8 weeks after injury.

### CONCLUSION

A significant number of PCS follow (at 1–8 weeks) mTBI. However, most of them are diminished by 4 weeks post-mTBI. In addition, the PCS adversely influenced mTBI outcome. Physical symptoms had more adverse impact on outcome at early mTBI stages (1 and 2 weeks), whereas emotional disturbances had more adverse impacts at later stages (4 and 8 weeks). Therefore, it is vital to help the patient to understand and face the difficulties posed by PCS. Moreover, progress of the disease should be monitored by monitoring different PCS domains.

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