

# Functional outcome at one year following moderate to severe traumatic brain injury: A prospective study in Malaysia

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## Abstract

**Background & Objective:** Traumatic brain injury (TBI) is a leading cause of disability among young adult population. Those with more severe TBI continue to experience long term disability. This research aimed to describe the functional outcome of moderate to severe TBI patients at one year post-injury in a Malaysian setting. **Methods:** This was a prospective cohort study conducted at University Malaya Medical Centre (UMMC) involving 100 patients who were admitted with moderate to severe TBI. The functional outcome was assessed at one year post injury using Glasgow Outcome Scale-Extended (GOSE). Factors associated with good outcome were analysed via regression analysis. **Results:** The mean age of the study participants was 39.4 ( $\pm$  17.6). Majority of participants were male, less than 40 years old and involved in a motor vehicle accident. Good outcome (GOSE score of 7 & 8) at one year was reported in 25% of the patients. Factors significantly affecting functional outcome were age, premorbid marital status, education level, presence of concomitant extremity fractures and early inpatient rehabilitation ( $p < 0.05$ ). After adjusting for the confounding factors, absence of concomitant extremity fractures was found to be a significant predictor for good functional outcome at one year (OR 9.26, 95% CI 1.86 - 46.12,  $p = 0.007$ )

**Conclusion:** Good functional outcome at one year following moderate to severe TBI in our population is lower than other studies worldwide. However, factors influencing good outcome at one year is comparable to other developed countries. Early management of concomitant extremity fractures may allow patients to participate in early inpatient rehabilitation for a better outcome.

**Keywords:** Glasgow Outcome Scale-Extended, injury, outcome, trauma, road safety, rehabilitation

## INTRODUCTION

Trauma is one of the top five leading causes of deaths and hospitalizations in Malaysia.<sup>1</sup> Among the trauma cases, 80% are caused by road traffic accidents with 70% of them contributed by motorcycle crash. Since head and neck injuries constituted 85% of injury sustained<sup>2</sup>, traumatic brain injury (TBI) is one of the inevitable major complications that occurs among the trauma survivors. TBI is the most common cause for significant disability and morbidity after trauma.<sup>3</sup> Those with moderate and severe injuries usually suffer greater impact when compared to those with mild TBI.

Demographic profiles have been shown to affect outcome, for example, age was documented

to be an independent factor affecting outcome in TBI.<sup>4</sup> Having a lower premorbid education level was associated with poorer outcomes<sup>5</sup>, whereas role of ethnicity is not clearly defined. Other factors not directly associated with TBI complications such as the presence of extracranial injuries has been previously documented to affect functional outcome too. Those with extracranial injuries resumed work less frequently and have more limitation in physical functioning at 6 months post injury.<sup>6-8</sup> A previous Malaysian study on TBI population reported concomitant extremity injuries to be significantly associated with poorer outcome at 18 months post injury regardless of TBI severity.<sup>9</sup>

Although factors associated with long term

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outcome after TBI are known, most reports are derived from developed countries with established acute post injury rehabilitation care. There are limited studies looking at long term functional outcome among adult TBI patients in Southeast Asia including Malaysia.<sup>9-13</sup> The different cultural background and post injury rehabilitation services may play a role in the final outcome despite the similar acute injury factors with developed countries. Rehabilitation services after TBI in Malaysia are also limited to big centres and most centres do not have a dedicated inpatient rehabilitation service. In view of this background, the present study aimed to describe the functional outcome of moderate to severe TBI patients at one year; as well as to determine the association between patients' functional outcome with premorbid sociodemographic factors, presence of concomitant extremity fractures and early inpatient rehabilitation.

## METHODS

This was a prospective study conducted at University Malaya Medical Centre (UMMC) which is a tertiary referral centre located in Kuala Lumpur, Malaysia. The study population consists of patients who suffered moderate to severe TBI and admitted to UMMC from June to December 2016. Patients were selected using universal sampling method from the neurosurgical wards. Inclusion criteria for the study were patients aged 18 years and above at the time of injury, diagnosed with moderate and severe TBI at the Trauma and Emergency Department, UMMC and availability of a carer or legal guardian for patients who were unable to give consent. Patients who were younger than 18 years old, foreigners, suffered concomitant brain pathology such as brain tumour or metastases, previous history of TBI or medical illnesses which caused significant physical, cognitive or behavioural disabilities were excluded from the study.

After the initial patient selection, informed consent was taken for study enrolment. Demographic data obtained during the first encounter consists of age, gender, ethnicity, preinjury relationship status, premorbid education level and premorbid employment status. Relationship status at injury was defined as married, single or divorced. Premorbid education level was defined as either primary education, secondary education or tertiary education. Employment status was classified as working; both full time or part time, not employed or studying at the time of injury. Injury details such as

mechanism of injury, initial Glasgow Coma Scale (GCS), duration of loss of consciousness (LOC), presence and duration of post traumatic amnesia (PTA), presence of concomitant long bone fracture at TBI onset and early inpatient rehabilitation were obtained from patients' medical notes or e-documents. Details involving initial GCS, duration of LOC and duration of PTA were used to confirm the severity of TBI diagnosed at the Trauma & Emergency Department. Initial GCS score was defined as the lowest pre-intubation GCS after resuscitation. Criteria for moderate TBI were: patients presented with initial GCS of 9 to 12, PTA duration of 1 hour to 24 hours after injury and LOC duration of 30 to 60 minutes. As for severe TBI, the criteria were: patients presented with initial GCS of 8 or less, duration of PTA of more than 24 hours and duration of LOC of more than one hour. Early inpatient rehabilitation was defined as receiving an active inpatient rehabilitation service in the rehabilitation ward within the first 3 months post TBI.

All patients were then followed up at one year post injury to assess their functional status using Glasgow Outcome Scale-Extended (GOSE)<sup>14</sup> via face to face interview. GOSE consists of 8 categories which are: death (category 1), vegetative state (category 2), lower severe disability (category 3), upper severe disability (category 4), lower moderate disability (category 5), upper moderate disability (category 6), lower good recovery (category 7) and upper good recovery (category 8). The lowest outcome category is category 1.

A structured GOSE interview form which covers aspects of physical, cognitive, psychosocial, relationship and work function of a patient was used to guide the scoring.<sup>15</sup> There is no standardized cut-off point depicting good versus poor outcome based on the 8 categories in GOSE. For this study, we divide the functional outcomes using similar approaches as in previous studies for ease of bivariate and multivariate analyses.<sup>6,16</sup> The functional outcome was divided into 2; either good or poor outcome. Good outcome consists of upper and lower good recovery which is category 7 and 8 in the GOSE scale. For poor outcome, it consists of category 1 to 6 in the GOSE scale. Permission to conduct the study was obtained from the UMMC Ethics Committee.

### *Statistical analysis*

Descriptive analysis using mean and standard deviation were used for continuous variables

while for categorical variables, frequencies and percentages were obtained. Chi-square test was used to investigate association between functional outcome and premorbid sociodemographic data, concurrent long bone fracture and early inpatient rehabilitation. After the initial analysis, multiple logistic regression analysis was used to determine which independent variables that best determined the outcome groups on the GOSE. Only variables that are significantly related to GOSE in the association study were entered into the regression analysis. A p value of less than 0.05 was considered statistically significant. All statistical analysis was performed using SPSS version 23.

## RESULTS

A total of 156 patients with moderate to severe TBI from June to December 2016 were screened. From the total patients screened, 130 patients agreed to participate. At one year follow-up,

30 patients were either uncontactable or lost to follow up resulting in a final study population of 100 patients. Table 1 shows the characteristics of the 100 patients who completed one year follow up after moderate to severe TBI.

The mean age of the study population was 39.4 ( $\pm$  17.6) years old. Slightly more than half of patients were younger than 40 years old. In terms of gender distribution, 87% of patients were males, which reflects the distribution of TBI victims in Malaysia and worldwide. Malay ethnicity constituted 43% of the study population. Most patients in this study population received either primary or secondary education and were employed at the time of injury. Motor vehicle accident was the most common aetiology of injury (77%).

Table 2 shows the distribution of patients in the GOSE outcome categories of our study population. More than two-thirds of our patients

**Table 1: Socio-demographic and clinical background information of the participants**

| Patient characteristics                | Total number (n=100) | Percentage (%) |
|--|----------------------|----------------|
| <b>Gender</b>                          |                      |                |
| Male                                   | 87                   | 87%            |
| Female                                 | 13                   | 13%            |
| <b>Age group</b>                       |                      |                |
| Less than 40 years old                 | 57                   | 57%            |
| 40 years old and above                 | 43                   | 43%            |
| <b>Ethnicity</b>                       |                      |                |
| Malay                                  | 43                   | 43%            |
| Chinese                                | 29                   | 29%            |
| Indian                                 | 28                   | 28%            |
| <b>Premorbid marital status</b>        |                      |                |
| Single/Widowed                         | 50                   | 50%            |
| Married                                | 50                   | 50%            |
| <b>Premorbid education level</b>       |                      |                |
| Primary/Secondary level                | 77                   | 77%            |
| Tertiary level                         | 23                   | 23%            |
| <b>Premorbid employment</b>            |                      |                |
| Employed                               | 73                   | 73%            |
| Unemployed/Student                     | 27                   | 27%            |
| <b>Aetiology of injury</b>             |                      |                |
| MVA                                    | 77                   | 77%            |
| Fall/Assault                           | 23                   | 23%            |
| <b>Concomitant extremity fractures</b> |                      |                |
| Yes                                    | 31                   | 31%            |
| No                                     | 69                   | 69%            |
| <b>Early inpatient rehabilitation</b>  |                      |                |
| Yes                                    | 38                   | 38%            |
| No                                     | 62                   | 62%            |

**Table 2: Functional outcome at one year post injury based on the Glasgow Outcome Scale-Extended (GOSE)**

| Outcome variable (GOSE)            | Number (n=100) | Percentage based on category (%) |
|------------------------------------|----------------|----------------------------------|
| <b>Good Outcome (category 7-8)</b> | <b>25</b>      | <b>100%</b>                      |
| 7 – Lower Good Recovery            | 19             | 76%                              |
| 8 – Upper Good Recovery            | 6              | 24%                              |
| <b>Poor Outcome (category 1-6)</b> | <b>75</b>      | <b>100%</b>                      |
| 1 – Dead                           | 2              | 2.7%                             |
| 2 – Vegetative state               | -              | -                                |
| 3 – Lower Severe Disability        | 16             | 21.3%                            |
| 4 – Upper Severe Disability        | 21             | 28%                              |
| 5 – Lower Moderate Disability      | 17             | 22.7%                            |
| 6 – Upper Moderate Disability      | 19             | 25.3%                            |

(75%) reported to have poor outcome. Patients with poor outcome almost evenly spread in categories 3 to 6, but mostly reported to have upper severe disability. As for patients with good outcome, majority of them were in category 7 (lower good recovery) at one year post injury.

#### *Factors influencing functional outcome at one year*

From the univariate analysis, five factors were found to be significantly affecting the functional outcome at one year (Table 3). Patients aged less than 40 years old, those who were single or widowed, completed tertiary education, absence of concomitant extremity fractures and received early inpatient rehabilitation within 3 months of injury were shown to have significant association with good functional outcome at one year.

In Table 4, TBI patients in the younger age group of less than 40 years old showed a 3.1 times higher chance of a good outcome at one year post injury. Those who were single or widowed had 2.7 times higher chance of a good outcome at one year and those who completed their education up to tertiary level before the injury has 5.4 times higher likelihood of a good outcome. Patients who do not have concomitant extremity fractures showed 7.2 times higher chance of a good outcome while those receiving early inpatient rehabilitation within 3 months of injury had 2.7 times higher chance of a good outcome at one year. Duration of inpatient rehabilitation (more than 4 weeks versus less than 4 weeks) was also tested but did not show any significant association with good functional outcome at one year (p value = 0.175).

Binomial logistic regression was performed to ascertain the effects of age, premorbid

marital status, premorbid education level, concomitant extremity fractures and early inpatient rehabilitation on the likelihood of good or poor functional outcome at one year post injury. The logistic regression model was statistically significant,  $X^2(4) = 23.95$ ,  $p < 0.05$  (via Omnibus Tests of Model Coefficients). The model explained 32% (Nagelkerke R<sup>2</sup>) of the variance in functional outcome and correctly classified 81% of cases. After adjusting for the confounding factors, only absence of concomitant extremity fracture was found to be significant in predicting outcome at one year with 9.2 times likelihood of a good functional outcome. (Table 5)

## DISCUSSION

The interest concerning functional outcome of patients with TBI is increasing, especially in recent years where the level of TBI acute care have improved tremendously. This is one of the few studies to describe the long term functional outcome of moderate to severe adult TBI population and to investigate predictors of functional outcome among persons with TBI in Malaysia. Assessment of functional outcome was performed at one year to allow maximum natural recovery or for recovery to optimize, although functional improvement can continue up to a few years post injury.<sup>17</sup> One year after injury, only 25% of our study population showed good outcome according to GOSE which is lower than most studies in developed countries.<sup>18-21</sup> However, it must be highlighted that not all of the studies used GOSE as their outcome measure. In fact, in some older studies, Glasgow Outcome Scale (GOS) were chosen although it is less sensitive in detecting small but clinically relevant changes in

**Table 3: Demographic and clinical data of study population and its association with good outcome at 1 year post injury according to GOSE**

| Demographic and clinical data                                  | Total number<br>n (%)<br>100 (100%) | GOSE at 1 year                    |                                   | p value<br>(sig. p value < 0.05) |
|--|-------------------------------------|-----------------------------------|-----------------------------------|----------------------------------|
|  |                                     | Good Outcome<br>n (%)<br>25 (25%) | Poor Outcome<br>n (%)<br>75 (75%) |                                  |
| Gender   |                                     |                                   |                                   |                                  |
| Male   | 87 (87%)                            | 23 (26.4%)                        | 64 (73.6%)                        | 0.391                            |
| Female   | 13 (13%)                            | 2 (15.4%)                         | 11 (84.6%)                        |                                  |
| Age group  |                                     |                                   |                                   |                                  |
| Less than 40 years old   | 57 (57%)                            | 19 (33.3%)                        | 38 (66.7%)                        | <b>0.027</b>                     |
| 40 years old and above   | 43 (43%)                            | 6 (13.9%)                         | 37 (86.1%)                        |                                  |
| Ethnicity  |                                     |                                   |                                   |                                  |
| Malay  | 43 (43%)                            | 9 (20.9%)                         | 34 (79.1%)                        | 0.714                            |
| Chinese  | 29 (29%)                            | 8 (27.6%)                         | 21 (72.4%)                        |                                  |
| Indian   | 28 (28%)                            | 8 (28.6%)                         | 20 (71.4%)                        |                                  |
| Premorbid marital status                                       |                                     |                                   |                                   |                                  |
| Single/Widowed   | 50 (50%)                            | 17 (34%)                          | 33 (66%)                          | <b>0.038</b>                     |
| Married  | 50 (50%)                            | 8 (16%)                           | 42 (84%)                          |                                  |
| Premorbid education level                                      |                                     |                                   |                                   |                                  |
| Primary & Secondary  | 77 (77%)                            | 13 (16.9%)                        | 64 (83.1%)                        | <b>0.001</b>                     |
| Tertiary   | 23 (23%)                            | 12 (52.2%)                        | 11 (47.8%)                        |                                  |
| Premorbid employment   |                                     |                                   |                                   |                                  |
| Employed   | 73 (73%)                            | 18 (24.7%)                        | 55 (75.3%)                        | 0.897                            |
| Unemployed/Student   | 27 (27%)                            | 7 (25.9%)                         | 20 (74.1%)                        |                                  |
| Aetiology of injury  |                                     |                                   |                                   |                                  |
| MVA  | 77 (77%)                            | 18 (23.4%)                        | 59 (76.6%)                        | 0.493                            |
| Fall & Assault   | 23 (23%)                            | 7 (30.4%)                         | 16 (69.6%)                        |                                  |
| Severity of injury   |                                     |                                   |                                   |                                  |
| Moderate   | 25 (25%)                            | 8 (32%)                           | 17 (68%)                          | 0.351                            |
| Severe   | 75 (75%)                            | 17 (22.7%)                        | 58 (77.3%)                        |                                  |
| Concomitant extremity fractures                                |                                     |                                   |                                   |                                  |
| Yes  | 31 (31%)                            | 2 (6.5%)                          | 29 (93.5%)                        | <b>0.004</b>                     |
| No   | 69 (69%)                            | 23 (33.3%)                        | 46 (66.7%)                        |                                  |
| Early inpatient rehabilitation within first 3 months of injury |                                     |                                   |                                   |                                  |
| Yes  | 38 (38%)                            | 14 (36.8%)                        | 24 (63.2%)                        | <b>0.032</b>                     |
| No   | 62 (62%)                            | 11 (17.7%)                        | 51 (82.3%)                        |                                  |

**Table 4: Association between premorbid socio-demographic data, concomitant extremity fractures and early inpatient rehabilitation with good functional outcome (based on Glasgow Outcome Scale-Extended categories 7 & 8) at one year post injury**

| Independent variables           | Odds ratio | 95% Confidence Interval |
|---------------------------------|------------|-------------------------|
| Age group                       |            |                         |
| ≥ 40 years old                  | 1          |                         |
| < 40 years old                  | 3.08       | 1.108 – 8.58            |
| Premorbid marital status        |            |                         |
| Married                         | 1          |                         |
| Single/widowed                  | 2.71       | 1.04 – 7.04             |
| Premorbid education level       |            |                         |
| Primary/Secondary               | 1          |                         |
| Tertiary                        | 5.37       | 1.95 – 14.78            |
| Early inpatient rehabilitation  |            |                         |
| No                              | 1          |                         |
| Yes                             | 2.7        | 1.07 – 6.83             |
| Concomitant extremity fractures |            |                         |
| Yes                             | 1          |                         |
| No                              | 7.25       | 1.59 – 33.08            |

outcome as compared to GOSE. Secondly, this study used stricter criteria to document someone as having a good outcome. Level 7 and 8 in the GOSE scale (“good recovery” categories) were chosen as “good outcome”; unlike some other studies which included level 5 and 6 (“moderate disability” categories) as “favourable” outcome. We believe that patients in “good recovery” categories represent the true clinically significant outcome that makes a difference in terms of independency level and caregiver burden.

Outcome studies on patients with TBI have shown that functional status can be predicted by demographic, injury severity, and trauma-related factors.<sup>22-24</sup> Younger age was consistently found to be significantly associated with good functional outcome at one year post injury. When compared to older age group, majority of the younger patients who sustained severe TBI

achieved the greatest improvement in both GOS and Functional Independence Measure (FIM) scores at one year.<sup>25</sup> It has also been shown that increasing age was associated with lower rate of change on functional measures between admission and discharge FIM despite longer rehabilitation length of stay.<sup>26</sup> Older age above 40 years old was also included as a poor predictor of good recovery in the main TBI prediction models.<sup>22,27</sup> In a Norwegian multicentre study, unfavourable outcome (GOSE of lower than category 5) was observed at one year follow-up in 72% of TBI patients of above 65 years old.<sup>28</sup> The cause could be multifactorial; which can be attributed to the consequences of biological ageing as well as high prevalence of comorbidities,<sup>25,29</sup> thus causing the elderly to be more prone to complications.<sup>30</sup>

The association between marital status and good functional outcome was not very clear in

**Table 5: Multiple logistic regression analysis predicting good functional outcome at one year post injury**

| Independent variable                    | Adjusted Odds Ratio | 95% CI       | p value      |
|---|---------------------|--------------|--------------|
| Age                                     | 1.75                | 0.43 – 7.08  | 0.435        |
| Premorbid marital status                | 1.93                | 0.54 – 6.99  | 0.314        |
| Premorbid education level               | 2.88                | 0.76 – 10.96 | 0.122        |
| Absence concomitant extremity fractures | 9.26                | 1.86 – 46.12 | <b>0.007</b> |
| Early inpatient rehabilitation          | 1.66                | 0.47 – 5.89  | 0.434        |

the literature. A study looking at return to work or study outcome showed that single or widowed patients had significantly higher rate of return to work or school after TBI.<sup>31</sup> Another study reported that being married at the time of injury was not associated with good outcome in GOSE score.<sup>16</sup> However, further analysis showed that 76% of the married TBI patients were older than 40 years old, thus the poor outcome may be attributed to the older age of the married population in the study. As for our study, the findings that single patients and those completed higher education level showed more favourable outcome were consistent with the literature, both at short term as well as long term post injury.<sup>6,32</sup> One possible reason for the patients' good outcome is perhaps due to their better premorbid income and financial security that they can afford a better compliance to early rehabilitation treatment, although this association was not tested in this study.

A meta-analysis study concluded that early intensive rehabilitation treatment in a rehabilitation facility promote functional recovery of patients with moderate to severe TBI.<sup>33</sup> Our study showed 37% of TBI patients who received early inpatient rehabilitation within the first 12 weeks of injury achieved good outcome as compared to 17% who didn't receive early inpatient rehabilitation. This benefit is more pronounced when rehabilitation was started immediately after discharged from the acute surgical care.<sup>18,34-36</sup> Husam *et al.*<sup>36</sup> concluded that increasing time from injury to rehabilitation admission was associated with lower functional score at discharge from rehabilitation. Andelic *et al.*<sup>37</sup> compared the functional outcome at one year between severe TBI patients who received continuous chain of treatment from acute wards directly into rehabilitation unit and another group of patients who only received inpatient rehabilitation care after a waiting period at a local hospital or nursing home. They found that 26% from the first group achieved good recovery as measured by GOSE compared to only 7% from the second group.

The time taken from onset of injury to inpatient rehabilitation can be variable due to different brain injury severity and its associated complications during the acute care. In the context of TBI rehabilitation service in UMMC, most patients were referred early for rehabilitation assessment even when patients were still in the Intensive Care Unit (ICU). However, some of the patients could not be transferred to the rehabilitation ward earlier due to ongoing active medical complications such as pneumonia or refusal from family to extend

hospital stay due to financial constraints. The inpatient TBI rehabilitation program at UMMC is designated for adult individuals with TBI who can benefit from an intensive, outcome-oriented program. It is located in the rehabilitation ward with the capacity of 25 beds. The goal for this inpatient rehabilitation program is to maximize recovery of the individual's physical, cognitive, behavioral, and functional abilities that facilitate independence. The treatment team consists of rehabilitation physicians, nurses, occupational and physical therapists, speech and language pathologists, and medical social worker.

Most studies in the literature found that presence of concomitant extracranial injuries contributed to greater morbidity and poorer functional outcome.<sup>38,39</sup> The severity of concomitant extracranial injuries also plays a role to the final outcome. A previous study conducted by Leong *et al.*<sup>9</sup> on TBI patients in the same centre found that the more severe the extremity injuries are, the worse the functional outcome was at 18 months. Complications from long bone extremity fractures contributed to majority of complaints by the patients. Thus, we focused on investigating the association between concomitant extremity fractures with functional outcome in this study.

Extremity fractures were present in 31% of the TBI patients in this study and 87% of them were victims of motor vehicle accidents (MVA). In terms of injury sustained, a slightly higher proportion of fractures involving upper limb was reported as compared to lower limb (19% versus 12%). Extremity fractures sustained from a high impact trauma due to MVA mostly needed a longer duration to heal. Among those with extremity fractures in this study, 58% had surgical fixation done. The longer duration of non-weight bearing status after lower limb fracture may have caused a delay to start an intensive rehabilitation program. In addition, the complications of fractures such as restricted range of movement, pain or limb length discrepancy, coupled with complications of severe TBI such as poor cognition, coordination, and balance, may have further limit a better functional gain at one year.

One of the limitations of this study was the universal sampling method that was used as it may not capture all TBI patients who were admitted to other wards other than the neurosurgical ward. Besides that, TBI was a complex condition which involved cognitive, behavioural and psychological impact that was not further explored in this study. However, this study provides the evident that TBI patients with severe injuries can benefit from an

early inpatient rehabilitation referral and treatment in a dedicated environment to improve their long term functional and independence.

In conclusion, good functional outcome at one year following moderate to severe TBI in a Malaysian population is slightly lower than other Western studies. However, the factors associated with good outcome such as patients' premorbid status (age, marital status and education level), absence of concomitant extremity fractures and early inpatient rehabilitation are comparable to other studies worldwide. Early inpatient rehabilitation should be provided when available as it can improve the functional outcome. Since concomitant extremity fractures significantly influenced the outcome post TBI, it is very important to treat the fractures early and aggressively so that patients can start intensive rehabilitation earlier.

## DISCLOSURE

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Conflicts of interest: None

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