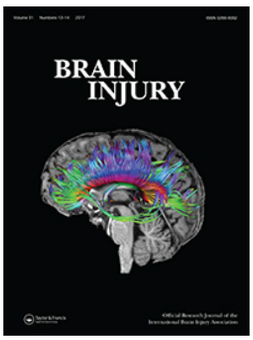

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Temporal profile of care following mild traumatic brain injury: predictors of hospital admission, follow-up referral and six-month outcome

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Temporal profile of care following mild traumatic brain injury: predictors of hospital admission, follow-up referral and six-month outcome

John K. Yue [a,b], Ethan A. Winkler[a,b], Sourabh Sharma[a,b], Mary J. Vassar[a,b], Jonathan J. Ratcliff[c], Frederick K. Korley[d], Seth A. Seabury[e], Adam R. Ferguson[a,b], Hester F. Lingsma[f], Hansen Deng Predictors of mTBI admission, referral and outcome[a,b], Sacha Meeuws[g], Opeolu M. Adeoye[h], Jonathan W. Rick[a,b], Caitlin K. Robinson[a,b], Siena M. Duarte[a,b], Esther L. Yuh[b,i], Pratik Mukherjee[b,i], Sureyya S. Dikmen[j], Thomas W. McAllister[k], Ramon Diaz-Arrastia[l,m], Alex B. Valadka[n], Wayne A. Gordon[o], David O. Okonkwo[p], and Geoffrey T. Manley[a,b], and the TRACK-TBI Investigators

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ABSTRACT

Objective: To investigate the clinical management and medical follow-up of patients with mild traumatic brain injury (mTBI) presenting to emergency departments (EDs). *Methods*: Overall, 168 adult patients with mTBI from the prospective, multicentre Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) Pilot study with Glasgow Coma Scale (GCS) 13–15, no polytrauma and alive at six months were included. Predictors for hospital admission, three-month follow-up referral and six-month functional disability (Glasgow Outcome Scale-Extended (GOSE) ≤ 6) were analysed using multivariable regression. *Results*: Overall, 48% were admitted to hospital, 22% received three-month referral and 27% reported six-month functional disability. Intracranial pathology on ED head computed tomography (multivariable odds ratio (OR) = 81.08, 95% confidence interval (CI) [10.28–639.36]) and amnesia (>30-minutes: OR = 5.27 [1.75–15.87]; unknown duration: OR = 4.43 [1.26–15.62]) predicted hospital admission. Older age (per-year OR = 1.03 [1.01–1.05]) predicted three-month referral, while part-time/unemployment predicted lack of referral (OR = 0.17 [0.06–0.50]). GCS < 15 (OR = 2.46 [1.05–5.78]) and prior history of seizures (OR = 3.62 [1.21–10.89]) predicted six-month functional disability, while increased education (per-year OR = 0.86 [0.76–0.97]) was protective. *Conclusions*: Clinical factors modulate triage to admission, while demographic/socioeconomic elements modulate follow-up care acquisition; six-month functional disability associates with both clinical and demographic/socioeconomic variables. Improving triage to acute and outpatient care requires further investigation to optimize resource allocation and outcome after mTBI.

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Introduction

Traumatic brain injury (TBI) constitutes a significant public health burden and is estimated to be responsible for more than 2 million emergency department (ED) visits and over 52 000 deaths in USA per year with a combined impact of 2.5 million persons [1,2]. The annual burden of TBI is estimated at $60 billion USA dollars – likely an underestimate due to insufficient awareness and reporting [3]. TBI is often crudely classified into mild, moderate and severe based on the Glasgow Coma Scale (GCS) (mild (GCS 13–15), moderate (GCS 9–12) and severe (GCS 3–8)) in the ED [4]. The current American Congress of Rehabilitation Medicine (ACRM) definition of mild traumatic brain injury (mTBI) include loss of consciousness (LOC) of ≤30 minutes, post-traumatic amnesia (PTA) of ≤24 hours and/or alteration of consciousness and focal neurological deficits that may or may not be transient following external impact to the head [5]; mTBI constitutes approximately 80% of all TBIs [6,7].

Considerable heterogeneity exists in the clinical trajectory of mTBI [8,9], and there is paucity of evidence-based data to guide the management of these patients. Importantly, there is limited data to guide clinicians in determining which patients with mTBI need hospital admission. Furthermore, although

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The TRACK-TBI Investigators are listed in the Appendix in alphabetical order by last name.

most of the patients with mTBI have complete resolution of their symptoms within three months, a significant fraction suffers persistent TBI-related symptoms and disability [10]. There is evidence that functional impairment extends past the subacute phase after mTBI. Between 10 and 34% of patients with mTBI experience physical, cognitive and mental health impairment beyond three months post injury [1,11–14]. In one of the largest mTBI analyses to date, 23% of 2784 patients with mTBI remained functionally impaired at six months as measured by the Glasgow Outcome Scale-Extended (GOSE) score of ≤6 [15]. Predictors for functional impairment included age, injury severity and CT abnormalities, but did not include access to follow-up care.

Early and consistent specialist follow-up beginning at 7–10 days post mTBI and throughout the recovery period appears to reduce the burden of both work/social function impairment and post-concussive symptoms measured at six months [16]. However, there is limited evidence for guiding clinicians in selecting patients with mTBI that will benefit the most from close outpatient follow-up. In a study examining TBI management in EDs using a national database, 38% of patients diagnosed with mTBI were discharged without TBI-specific follow-up recommendations [16,17]. The American College of Emergency Physicians (ACEP) and Centres for Disease Control (CDC) recommends discharging patients with mTBI with a normal neurological examination and a negative head CT scan [18,19]; however, ACEP does not have recommendations regarding hospital admissions in patients with mTBI with abnormal head CT scans (the so-called 'complicated' mTBI patient) or outpatient referrals for those likely to have persistent symptoms [20–22]. Therefore, developing evidence-based guidance for medical decision making during the ED management of mTBI is an important unmet clinical need. Whether such guidelines need to emphasize clinical and/or demographic factors similar to existing guidelines for other phases of TBI care remains to be determined, and hence, further characterization of current practice and referral patterns in the context of long-term outcomes following mTBI are greatly needed. Improved understanding of the profile of individuals vulnerable to poorer outcomes specifically following mTBI will aid in the formation of guidelines to prevent insufficient resource allocation and optimize their trajectory of care.

For these reasons, we sought to elucidate factors influencing hospital admission and outpatient referral for mTBI. Specifically, we estimated the frequency, and identified the clinical and demographic factors associated with: (1) hospital admission; (2) participation in TBI-related outpatient care within three months of injury and (3) functional disability at six months, among patients admitted to ED with mTBI.

Methods

Study design

We utilized data from the Transforming Research and Clinical Knowledge in TBI Pilot (TRACK-TBI Pilot) study, a multicentre prospective observational study conducted at three Level I trauma centres in the United States – San Francisco General Hospital (SFGH), University of Pittsburgh Medical Centre (UPMC) and University Medical Centre Brackenridge (UMCB) in Austin, Texas [23]. Inclusion criteria for TRACK-TBI Pilot were adult patients presenting to a Level I trauma centre with external force trauma to the head and clinically indicated head CT scan within 24 hours of injury. Of note, U.S. trauma centres are classified by the American College of Surgeons using standard criteria, which include the extent of 24-hour in-house specialists, the annual volume of patients, availability of substance abuse screening and injury prevention programs and ongoing research, teaching and training programs; specifically, a Level I trauma centre must admit at least 1200 trauma patients yearly or have 240 admissions with an Injury Severity Score (ISS) ≥15 indicating multisystem trauma [24]. Exclusion criteria were pregnancy, comorbid life-threatening disease, incarceration, on psychiatric hold and non-English speakers due to limitations in participation with outcome assessments. The present study was designed to characterize the temporal profile of health care acquisition and subsequent functional disability following an isolated mTBI through three different time periods—within 24 hours of injury, three months after the injury and six months after the injury. Therefore, we examined the subset of patients with a GCS ≥13, Marshall CT Score of 1–2, no polytrauma as defined by an Abbreviated Injury Scale (AIS) score >1 in any extracranial body region [25–27] and alive at six months (Figure 1).

Patients who were eligible were enrolled through convenience sampling at all three sites – which may be defined as non-randomized enrolment in which those who present to the ED and meet inclusion criteria are offered enrolment into the study. Institutional review board approval was obtained at all participating sites. Informed consent was obtained prior to subject enrolment in the study. For patients unable to provide consent

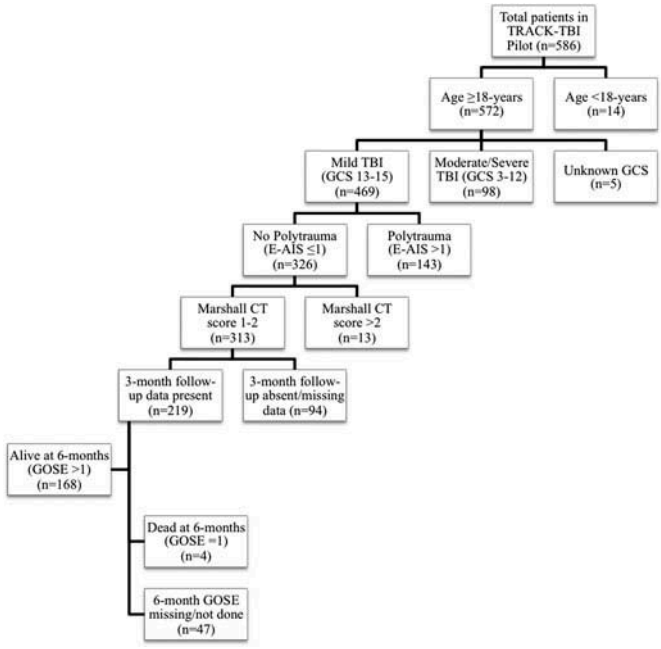

Figure 1. Flowchart of included patients. CT = computed tomography; E-AIS = extracranial Abbreviated Injury Scale score; GCS = Glasgow Coma Scale; GOSE = Glasgow Outcome Scale – Extended; TRACK-TBI Pilot = Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot Study.

due to their injury, consent was obtained from their legally authorized representative (LAR). Patients were then re-consented, if cognitively able at later inpatient and/or outpatient follow-up assessments for continued participation in the study.

As the current study is focused on patients with isolated, non-polytraumatic mTBI, we performed analyses in our primary patient population (GCS 13–15, no polytrauma, Marshall CT score 1–2) (Figure 1) to determine the similarities between patients who were included at three months (e.g. those with complete three-month follow-up care data, n = 219) versus patients who were excluded due to missing data (n = 94) (Table, Supplemental Digital Content 1), as well as between patients who were alive at six months with complete GOSE data (e.g. final patient sample, n = 168) versus patients who died (n = 4) or were lost to follow-up at six months (n = 47) (Table, Supplemental Digital Content 2). In both analyses, no statistically significant differences were observed between the included and excluded patient groups.

Assessments and outcomes

A full demographic and clinical history was obtained according to the National Institutes of Health (NIH) and National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements (CDEs), version 1 [28–31]. Three endpoints were assessed – hospital admission at the time of acute mTBI, outpatient follow-up care for mTBI symptoms at three months and functional disability at six months post mTBI. Hospital admission was captured at baseline. At three months, all patients were queried by telephone regarding whether they received follow-up outpatient therapy (physical, cognitive and/or psychological/psychiatric) specifically due to sequelae from their head injury after discharge from the ED or hospital. Per the TRACK-TBI Pilot research protocol all patients were assessed for orientation prior to participating follow-up phone calls and assessments. At six months, the GOSE was utilized to assess functional outcome [32]. The GOSE is an eight-point ordinal scale (1-Dead, 2-Vegetative State, 3-Lower Severe Disability, 4-Upper Severe Disability, 5-Lower Moderate Disability, 6-Upper Moderate Disability, 7-Lower Good Recovery and 8-Upper Good Recovery) providing an overall measure of functional disability based on information obtained through a structured interview focused on cognition, independence, employability and social/community participation and has been widely employed as the standard outcome measure in a number of TBI and mTBI trials [33–36]. Dichotomization of the GOSE to favourable vs. unfavourable outcome can be performed and adjusted to increase the sensitivity for the subgroup of interest [33]. For patients with TBI with good prognosis, e.g. mTBI, 'Good Recovery' (GOSE of 7–8) is considered to be a favourable outcome [33], where GOSE ≤6 qualified for, at minimum, moderate disability [15,32]. Accordingly, six-month outcome in the current analysis was dichotomized to GOSE ≤6 vs. GOSE 7–8.

Statistical analysis

Demographic and clinical characteristics are reported using mean and standard deviation (SD) for continuous variables and proportions for categorical variables. Predictors were selected based on existing literature relevant to mTBI [15,37]. Binary logistic regression models were constructed for each of the three endpoints (acute hospital admission, three-month outpatient follow-up and six-month functional disability) with demographic and clinical variables as predictors. Univariate predictors with $p < 0.10$ were entered onto the respective multivariable logistic regression model for each assessed endpoint. All multivariable models conformed to tests for goodness-of-fit (Hosmer–Lemeshow goodness-of-fit chi-squared statistic, $p > 0.05$) and multicollinearity ($r < 0.7$). To prevent overfitting, we adhered to the rule of 10 for multiple regression analysis (hospital admission: n = 80/168, six multivariable predictors; three-month follow-up: n = 37/168, three multivariable predictors; six-month GOSE ≤6: n = 46/168, four multivariable predictors) [38]. Significance was assessed at $\alpha = 0.05$. All analyses were performed using Statistical Package for the Social Sciences (SPSS), v. 22 (IBM Corporation, Chicago, IL).

Results

Descriptive statistics

Demographic and clinical descriptors are summarized in Table 1.

Of 168 patients included in the analysis, the mean age was 44.5 (SD 18) and 68% were male. Mean education level was 14.2 years (SD 3.1). Patients were predominantly of Caucasian race

Table 1. Descriptive statistics for 168 patients following mTBI.

Variable	Statistic
Age (y)	44.5 (18.0)
Sex	
Male	115 (68.5%)
Female	53 (31.5%)
Education (y)	14.2 (3.1)
Race	
Caucasian	128 (76.2%)
African-American/African	16 (9.5%)
Other races	24 (14.5%)
Employment	
Full time	65 (38.7%)
Part time/unemployed	65 (38.7%)
Not in paid workforce	38 (22.6%)
Prior medical history	
Psychiatric disorder	57 (33.9%)
Prior seizure	18 (10.7%)
Substance use	34 (20.2%)
Anticoagulant use	25 (14.9%)
Mechanism of injury	
Motor vehicle accident	31 (18.5%)
Pedestrian versus auto	23 (13.7%)
Fall	80 (47.6%)
Assault	27 (16.1%)
Other	7 (4.2%)
Loss of consciousness	
<30 minutes	125 (74.4%)
>30 minutes	7 (4.2%)
Unknown	36 (21.4%)
Post-traumatic amnesia	
<30 minutes	112 (66.7%)
>30 minutes	30 (17.9%)
Unknown	26 (15.5%)
GCS <15	38 (22.6%)
CT intracranial pathology	46 (27.4%)

Continuous variables are reported using means and standard deviations. Categorical variables are reported as numerical values and percentages.
CT = computed tomography; GCS = Glasgow Coma Scale; mTBI = mild traumatic brain injury.

(76%). Thirty-nine per cent of patients were employed full-time pre-injury, 18% were part-time, 20% were unemployed and 23% were not in the paid workforce (retired, student or disabled). Self-reported medical or psychiatric disorders were present in 54% of patients. The most common mechanism of injury was fall, followed by motor vehicle accident, assault, pedestrian versus auto and other. ED GCS was primarily 15. The majority of patients had LOC and/or PTA <30 minutes, and no patients had LOC or PTA >24 hours. Twenty-seven per cent of patients showed intracranial pathology on initial head CT.

Temporal profile of care acquisition and outcome following mTBI

In the studied population, 48% of patients with mTBI were admitted to the hospital for acute inpatient care following injury. Twenty-two per cent of patients were referred to and seen in outpatient clinic for mTBI within three months of injury. At six months post injury, 27% of patients demonstrated persistent functional disability as assessed by GOSE ≤6 (GOSE 3: 0.6%, GOSE 5: 11.3%, GOSE 6: 15.5%). The remaining 73% of patients had good recovery as evidenced by a GOSE 7 (36.3%) or 8 (36.3%).

The distribution of GOSE scores for patients admitted to the hospital ($n = 80$) was 1, 10, 14, 40 and 35% for GOSE 3, 5, 6, 7 and 8 respectively. Comparatively, the GOSE distribution for non-admitted patients was 0, 13, 17, 33 and 38%, respectively ($p = 0.686$).

Hospital admission

Having identified the proportion of patients who were hospitalized, received outpatient services and/or demonstrated persistent disability, we next sought to identify the predictors governing decision making at each phase of care.

Overall, 98% (45 of 46) of patients with positive intracranial pathology on ED head CT were admitted compared with 29% (35 of 122) of patients with negative head CT (univariate OR 111.86, 95% CI [14.84–843.29], $p < 0.001$). Notably, the 35 patients who had a negative head CT and were admitted included 4 of 4 patients with isolated skull fractures, 4 of 9 patients on anticoagulants, 10 of 19 patients with PTA >30 minutes, 6 of 13 patients with unknown duration of PTA and 10 of 23 patients who were not in the paid workforce. Accordingly, patients with PTA >30 minutes (OR 4.20, 95% CI [1.76–10.04], $p = 0.001$) and patients who were unable to recall duration or presence of PTA (OR 4.89, 95% CI [1.89–12.62], $p = 0.001$) demonstrated greater likelihood of admission compared to patients with <30 minutes of amnesia (Table 2). Older age (per-year OR 1.02, 95% CI [1.01–1.04], $p = 0.013$), employment (categorical $p = 0.038$; not in paid workforce vs. full-time: OR 2.39, 95% CI [1.04–5.47], $p = 0.04$) and history of anticoagulant medications (OR 5.53, 95% CI [1.97–15.57], $p = 0.001$) were associated with increased odds of hospital admission. History of prior seizure (but not seizures on presentation) was associated with decreased odds of hospital admission (Table 2).

On multivariable analysis, intracranial pathology on CT remained the driver of hospital admission (OR 81.08, 95% CI

Table 2. Predictors of acute hospital admission after mTBI.

Predictor	Univariate OR [95% CI]	Sig. (*p*)	Multivariable OR [95% CI]	Sig. (*p*)
Age (y)	1.02 [1.01–1.04]	0.013	1.01 [0.98–1.04]	0.523
Sex		0.800		
Male	Reference	–		
Female	1.09 [0.57–2.09]			
Education (y)	0.99 [0.90–1.09]	0.797		
Employment		0.038		0.211
Full time	Reference	–	Reference	–
Part time/unemployed	0.83 [0.41–1.66]	0.594	1.18 [0.45–3.11]	0.733
Not in paid workforce	2.39 [1.04–5.47]	0.040	2.83 [0.86–9.35]	0.088
Prior medical history				
Psychiatric disorder	0.99 [0.52–1.87]	0.963		
Prior seizure	0.28 [0.09–0.88]	0.030	0.30 [0.06–1.38]	0.122
Substance use	0.62 [0.29–1.34]	0.222		
Anticoagulant use	5.53 [1.97–15.57]	0.001	2.20 [0.45–10.71]	0.327
Mechanism of injury		0.555		
Motor vehicle accident	Reference	–		
Pedestrian versus auto	0.50 [0.17–1.52]	0.221		
Fall	1.04 [0.45–2.38]	0.933		
Assault	0.65 [0.23–1.83]	0.409		
Other	0.70 [0.13–3.68]	0.676		
Loss of consciousness		0.131		
<30 minutes	Reference	–		
>30 minutes	3.29 [0.61–17.59]	0.164		
Unknown	1.84 [0.87–3.90]	0.111		
Post-traumatic amnesia		<0.001		0.003
<30 minutes	Reference	–	Reference	–
>30 minutes	4.20 [1.76–10.04]	0.001	5.27 [1.75–15.87]	0.003
Unknown	4.89 [1.89–12.62]	0.001	4.43 [1.26–15.62]	0.021
GCS <15	1.71 [0.82–3.55]	0.152		
CT intracranial pathology	111.86 [14.84–843.29]	<0.001	81.08 [10.28–639.36]	<0.001

Logistic regression using the presence or absence of acute hospital admission as the response variable. Univariate predictors with $p < 0.10$ were entered onto the multivariable model.

CI = confidence interval; CT = computed tomography; GCS = Glasgow Coma Scale; mTBI = mild traumatic brain injury; OR = odds ratio.

[10.28–639.36], $p < 0.001$]. In addition to CT, a PTA >30 minutes (OR 5.27, 95% CI [1.75–15.87], $p = 0.003$) or a period of amnesia that could not be accurately quantified by the patient (OR 4.43, 95% CI [1.26–15.62], $p = 0.021$) persisted as predictors of hospital admission (Table 2). Age, employment, history of seizures and history of anticoagulant use did not survive multivariable analysis. The model conformed to goodness-of-fit (Hosmer–Lemeshow chi-squared statistic 2.734, $p = 0.950$).

Referral to outpatient follow-up care within three months of injury

We next shifted our attention to identify predictors of referral to outpatient follow-up care. Overall, 25% (20 of 80) of hospital admitted patients and 19% (17 of 88) of ED discharge patients received outpatient care for their mTBI within three months of injury ($p = 0.375$).

Univariate predictors for follow-up care consisted only of social and demographic variables (Table 3). Older age (per-year OR 1.02, 95% CI [1.01–1.04], $p = 0.029$) and female gender (OR 2.24, 95% CI [1.06–4.76], $p = 0.035$) were associated with three-month follow-up care. Patients who were employed part-time or unemployed demonstrated lower odds of follow-up care (OR 0.18, 95% CI 0.06–0.50, $p = 0.001$). Surprisingly, inpatient hospitalization, initial CT findings and/or injury characteristics were not significant predictors of referral to three-month follow-up care.

On multivariable analysis (Table 3), employment status remained a significant predictor of outpatient follow-up care ($p = 0.005$). Patients employed part-time or without employment showed decreased likelihood of follow-up care acquisition (OR 0.17, 95% CI [0.06–0.50], $p = 0.001$) compared to patients with full-time employment at baseline. No significant differences were observed between full-time employment and those who were not part of the workforce (retired, student, disabled; OR 0.47, 95% CI [0.17–1.35], $p = 0.163$). Whether this finding reflects differences in insurance status remain unknown, as insurance status was not encoded in TRACK-TBI Pilot. Older age (OR 1.03, 95% CI [1.01–1.05], $p = 0.045$) persisted as a modest multivariable predictor of three-month follow-up referral, while female gender did not. The model conformed to goodness-of-fit (Hosmer–Lemeshow chi-squared statistic 3.639, $p = 0.888$).

Impaired functional outcome at six months following injury

Finally, we sought to identify predictors of six-month functional disability (GOSE ≤6) and determine whether initial injury, inpatient hospitalization or acquisition of follow-up care was associated with outcome following mTBI.

Overall, 25% (20 of 80) of patients admitted to hospital and 30% (26 of 88) of patients not admitted to hospital reported a six-month GOSE ≤6. Inpatient hospitalization did not increase the odds of disability at six months (OR 0.80, 95% CI [0.40–1.57], $p = 0.510$]. Thirty-two per cent (12 of 37) of patients who received three-month follow-up care and 26% (34 of 131) of patients who did not receive three-month follow-up care reported a six-month GOSE ≤6. Acquisition

Table 3. Predictors of 3-month follow-up referral after mTBI.

Predictor	Univariate OR [95% CI]	Sig. (p)	Multivariable OR [95% CI]	Sig. (p)
Age (y)	1.02 [1.00–1.04]	0.029	1.03 [1.01–1.05]	0.045
Gender		0.035		0.120
Male	Reference	–	Reference	–
Female	2.24 [1.06–4.76]		1.90 [0.85–4.25]	
Education (y)	1.01 [0.90–1.14]	0.881		
Employment		0.004		0.005
Full time	Reference	–	Reference	–
Part time/unemployed	0.18 [0.06–0.50]	0.001	0.17 [0.06–0.50]	0.001
Not in paid workforce	0.85 [0.36–2.04]	0.722	0.47 [0.17–1.35]	0.163
Prior medical history				
Psychiatric disorder	1.25 [0.58–2.66]	0.570		
Prior seizure	0.41 [0.09–1.87]	0.251		
Substance use	1.11 [0.46–2.72]	0.813		
Anticoagulant use	1.47 [0.56–3.83]	0.436		
Mechanism of injury		0.516		
Motor vehicle accident	Reference	–		
Pedestrian versus auto	1.83 [0.55–6.08]	0.325		
Fall	0.86 [0.31–2.34]	0.764		
Assault	0.60 [0.15–2.31]	0.455		
Other	1.37 [0.22–8.66]	0.737		
Loss of consciousness		0.598		
<30 minutes	Reference	–		
>30 minutes	–	–		
Unknown	0.61 [0.23–1.59]	0.310		
Post-traumatic amnesia		0.158		
<30 minutes	Reference	–		
>30 minutes	0.72 [0.27–1.93]	0.507		
Unknown	0.24 [0.05–1.07]	0.062		
GCS <15	0.60 [0.23–1.57]	0.295		
CT intracranial pathology	1.16 [0.52–2.59]	0.717		
Hospital admission	0.72 [0.35–1.49]	0.376		

Logistic regression using the presence or absence of follow-up referral as the response variable. Univariate predictors with $p < 0.10$ were entered onto the multivariable model.

CI = confidence interval; CT = computed tomography; GCS = Glasgow Coma Scale; mTBI = mild traumatic brain injury; OR = odds ratio.

Table 4. Predictors of 6-month functional disability after mTBI.

Predictor	Univariate OR [95% CI]	Sig. (*p*)	Multivariable OR [95% CI]	Sig. (*p*)
Age (y)	1.00 [0.98–1.02]	0.794		
Gender		0.580		
Male	Reference	–		
Female	1.23 [0.60–2.52]			
Education (y)	0.86 [0.76–0.96]	0.010	0.86 [0.76–0.97]	0.017
Employment		0.554		
Full time	Reference	–		
Part time/unemployed	1.09 [0.49–2.39]	0.840		
Not in paid workforce	1.59 [0.66–3.83]	0.298		
Prior medical history				
Psychiatric disorder	2.59 [1.29–5.22]	0.008	2.15 [0.98–4.72]	0.055
Prior seizure	5.16 [1.86–14.32]	0.002	3.62 [1.21–10.89]	0.022
substance use	2.62 [1.19–5.76]	0.016	1.64 [0.68–3.93]	0.268
Anticoagulant use	0.81 [0.30–2.18]	0.682		
Mechanism of injury		0.134		
Motor vehicle accident	Reference	–		
Pedestrian versus auto	1.16 [0.31–4.39]	0.830		
Fall	1.39 [0.50–3.87]	0.530		
Assault	3.87 [1.20–12.44]	0.023		
Other	1.67 [0.26–10.77]	0.592		
Loss of consciousness		0.531		
<30 minutes	Reference	–		
>30 minutes	0.47 [0.05–4.01]	0.486		
Unknown	1.39 [0.63–3.10]	0.415		
Post-traumatic amnesia		0.939		
<30 minutes	Reference	–		
>30 minutes	1.17 [0.48–2.84]	0.726		
Unknown	1.01 [0.39–2.64]	0.989		
GCS <15	2.08 [0.97–4.48]	0.060	2.46 [1.05–5.78]	0.039
CT Intracranial pathology	0.91 [0.42–1.97]	0.817		
Hospital admission	0.80 [0.40–1.57]	0.510		
Outpatient referral	1.37 [0.62–3.02]	0.436		

Logistic regression using the presence or absence of 6-month GOSE ≤6 as the response variable. Univariate predictors with $p < 0.10$ were entered onto the multivariable model.

CI = confidence interval; CT = computed tomography; GCS = Glasgow Coma Scale; GOSE = Glasgow Outcome Scale Extended; mTBI = mild traumatic brain injury; OR = odds ratio.

of follow-up care at three months did not decrease the odds of disability at six months (OR 1.37, 95% CI [0.62–3.02], p = 0.436) (Table 4).

Education and past medical history showed statistically significant associations with six-month functional disability (Table 4). Specifically, patients with more years of education demonstrated lower propensity for functional disability as assessed by GOSE (per-year OR 0.86, 95% CI [0.76–0.96], p = 0.01). Conversely, prior history of seizure (OR 5.16, 95% CI [1.86–14.32], p = 0.002), psychiatric disorders (OR 2.59, 95% CI [1.29–5.22], p = 0.008) and substance use (OR 2.62, 95% CI [1.19–5.76], p = 0.016) were associated with greater likelihood of functional disability. A non-significant trend was observed for ED GCS <15 (OR 2.08, 95% CI 0.97–4.48, p = 0.06).

On multivariable analysis (Table 4), higher education years remained a predictor of decreased likelihood of six-month functional disability (OR 0.86, 95% CI [0.76–0.97], p = 0.017); conversely, history of prior seizure (OR 3.62, 95% CI [1.21–10.89], p = 0.022) and GCS <15 (OR 2.46, 95% CI [1.05–5.78], p = 0.039) maintained their association with a greater likelihood of disability. A history of psychiatric disorders demonstrated a non-significant statistical trend (OR 2.15, 95% CI [0.98–4.72], p = 0.055) for six-month disability, while substance use did not survive multivariable analysis. The model conformed to goodness-of-fit (Hosmer and Lemeshow chi-squared statistic 5.627, p = 0.689).

Discussion

In the present study, we sought to characterize clinical decision making at various phases of mTBI care, which included initial hospitalization and use of outpatient services within three months post injury as well as extended outcome following mTBI in the absence of systemic injuries. We found that while half of patients with mTBI were admitted to the hospital for acute management, less than a quarter of patients were successfully referred to and/or acquired outpatient care irrespective of their admission status. At six months, 27% of patients were functionally disabled on the GOSE outcome measure – defined as reductions in work capacity and/or social interaction to the point of noticeable impairment, along with marked psychological/mood disturbance. Regression analysis of predictors of inpatient admission and outpatient follow-up services found a divergence in clinical care and/or decision-making. Surprisingly, neither inpatient hospitalization nor outpatient follow-up care acquisition predicted six-month functional disability; the rates of hospital admission (43–50%) and outpatient follow-up care (21–26%) were similar in the disabled vs. the non-disabled. The lack of overt association between admission, subacute care and chronic disability is difficult to interpret in a non-randomized study, but underscores the multidimensional nature of mTBI recovery. In order to understand this better, more data are needed to evaluate the decision-making criteria for referral as well as the barriers to acquiring follow-up care after mTBI. Additional information is also needed regarding the nature and quality of outpatient care received.

Multivariable predictors of hospital admission in the current sample of patients with mTBI included intracranial pathology on initial head CT and extended or unknown duration of amnesia. Head CT is a known predictor of hospital admission, with a sensitivity of 100% in detecting intracranial injury independent of all other risk factors [39]. Large studies have reported >98% admission rates for patients with complicated mTBI [40], a number identical to the current analysis. Historically, 8–31% of mTBI is complicated [34,41]; the 27% observed in our sample can be expected from a clinical trial targeting the enrolment of patients with TBI at three urban Level I trauma centres – sites to which more severe and complex injuries are triaged [42]. While a hospitalization rate of 48% may appear elevated for mTBI, it may be related to several factors unique to the current population including a higher incidence of complicated mTBI, as well as CT-negative patients with skull fractures, anticoagulation and/or extended durations of amnesia, corroborating prior literature [43–46]. Notably, patients unable to quantify their period of amnesia showed a similar increase in likelihood of admission as patients with verified greater than 30 minutes of amnesia. As specified by the ACEP/CDC guidelines for CT following acute mTBI, it is possible that PTA of >30 minutes is a general marker of admission practices independent of other risk factors [18,19]. Whether the 'unknown duration' equates to true amnesia rather than acute disorientation and/or unavailable date at the time of injury remains indeterminate as this coding was not specified in version 1 of the NIH NINDS TBI CDEs. This suggests that further refinement of standard variable definitions is needed to better characterize the reasons for unknown PTA.

In our study, 22% of patients obtained outpatient follow-up at three months post injury. While this may seem adequate and/or high following mTBI as the majority of patients are expected to recover without residual deficits, there is a growing body of literature suggesting that up to half of patients with mTBI may suffer posttraumatic and/or postconcussional symptoms at one year post injury [47–49]. In a large Level II randomized-controlled trial (RCT), patients with PTA <7 days who received specialist intervention had significantly less social disability and fewer postconcussional symptoms at six months compared to those who did not [16]. Currently, the European Federation of Neurological Societies Grade C guidelines recommend that all patients with mTBI admitted to hospital receive outpatient follow-up at least once in the outpatient clinic within two weeks of discharge [45]. With a hospitalization rate of 48%, the follow-up rates of the current study fall short of guideline recommendations. In a recent study of 462 non-hospitalized patients with mTBI, the rate of outpatient follow-up was 25%, with patients scoring higher on anxiety and/or depression scales at two weeks showing higher risk of follow-up [36]. Thus, it is important to improve not only the characterization of the 22% of patients with mTBI who successfully reach follow-up, but also the reasons why follow-up was not obtained in the remaining 78% of patients.

Hospital admission was not found to predict referral of care in our mTBI cohort. Multivariable predictors of follow-up care consisted only of age and baseline employment status (full-time vs. part-time/unemployed). No significant differences in three-month follow-up care were observed between patients employed full-time and those not part of the workforce (e.g. the retired, students and disabled), implicating insurance status as a potential determinant of follow-up care utilization. Uninsured patient status has been shown to be an independent negative predictor of trauma outcomes [50,51]. Referral to care without adequate financial means of care acquisition is an important factor in the persistent lack of continuity of care in certain subpopulations of patients with mTBI – the young, unemployed and uninsured. While the lack of insurance status in our study is a significant limitation, our analysis shows that older age and baseline full-time employment are predictors of increased follow-up care, and successfully obtaining follow-up care is dependent on demographic and socioeconomic factors. It is likely that a majority of patients with mTBI will improve with or without follow-up during the natural course of recovery. Conversely, there likely exists a significant subpopulation of patients with mTBI who are either unaware of their deficits and/or without the means of returning to care, who are at high risk of nonimprovement or further decline.

In prognosticating six-month functional disability, a combination of socioeconomic (lower education), medical history (baseline psychiatric disorder, substance use, seizure history, anticoagulant use) and injury severity factors (GCS <15) showed univariate effects, which is consistent with prior literature [37,42]. The multivariable predictors – education, prior seizure and GCS <15 – demonstrate that a combined profile of socioeconomic, past medical history and clinical information is important in delineating the subgroup of patients at risk for persistent functional deficits. Notably, prior seizure as a risk factor for six-month disability highlights the need for thorough evaluation of baseline comorbidities even in mTBI [52,53]. As an indicator of reduced work capacity and/or significantly disrupted social relationships – neither of which constitute expected outcomes after mTBI – the dichotomized GOSE (≤6) has utility and can target the subgroup of patients with more severe persistent morbidity. Similar to prior literature [54], nearly 30% of patients with mTBI in our study reported GOSE ≤6. The six-month disability rates of 32 and 26% in those with and without three-month follow-up care is higher than expected, but not exceedingly so – de Koning and colleagues show that even in nonhospitalized patients with mTBI, the incidence of GOSE ≤7 is 36% [36]. It should be noted that our population has a large (54%) or pre-existing medical and/or psychiatric problems, which is likely reflective of the subpopulation most vulnerable to TBI in urban Level I trauma centres.

The distribution of six-month GOSE did not differ between admitted and non-admitted patients, which may suggest that patients who are admitted (e.g. those with intracranial injury, skull fracture, anticoagulant use, prolonged or unknown PTA) receive the care they need to minimize their morbidity, and patients who are not admitted are at less risk of functional deficits measured by the GOSE. The same can be applied to three-month follow-up: while receiving follow-up care did not influence odds of six-month disability, patients who receive outpatient follow-up likely are in need of and benefit from care, to the extent that their six-month outcome is commensurate with those who, in general, had less severe injuries.

There has been an increased focus on implementation of medical research into clinical practice in the form of evidenced-based clinical practice guidelines [55,56]. However, such guidelines for outpatient follow-up and/or care following mTBI have yet to be established. In other settings, e.g., post-traumatic stress disorder following acute trauma, have successfully utilized data from the electronic medical record to predict outcomes and create clinical practice guidelines [57]. A similar approach incorporating demographics, medical comorbidities, employment and insurance status, in addition to the known predictive injury characteristics [15] should be evaluated as next steps for triage and referral guidelines specific to mTBI. Whether the predictors identified in the present manuscript may be independently replicated and serve as a starting place for the development of such guidelines remains to be seen.

Limitations

Although we have begun to bridge the information gap in mTBI between acute care discharge, access to outpatient care and outcome, the current study has several limitations. The number of patients (n = 168) is modest, and our study is restricted to patients with mTBI who presented to the ED at three Level I trauma centres. The large proportion of patients with prior comorbidities is likely in part related to the health risks associated with urban and low-income settings, which may affect acute prognosis and/or access to follow-up care. Patients treated at Level I trauma centres are associated with more severe injuries and complications, often due to transport and triage protocols for patients suffering trauma, which may have influenced the proportion of patients reporting six-month functional disability. While there is general agreement on the improvement of survival for patients treated at trauma centres [58–60], positive outcomes following TBI may also be moderated by living in a rural area where patients are more willing to seek social support, thus advancing perception of quality of life [61]. Our sampling bias limits the generalizability of our results in other settings, e.g. Level II trauma centres, community-based hospitals and/or non-hospital based TBI care and future investigations employing randomization strategies with sufficient sample sizes are necessary to delineate recovery profiles of subpopulations with and without comorbidities following mTBI across these settings. Secondly, different recovery profiles can arise from referral to different outpatient services after mTBI, and further research is needed to characterize the types and durations of outpatient services received in order to standardize and optimize recommended outpatient therapies following mTBI. Third, we were unable to include intoxication as a risk factor for admission and poor outcome [62,63], as only 41% of the current sample had a blood alcohol level drawn in the ED – a shortcoming of current clinical standards of care even at Level trauma centres. Fourth, our present analysis did not evaluate detailed imaging parameters as predictors of admission, referral and outcome, and complementary investigations with such a focus may lead to a better understanding of unique injury signatures with prognostic significance. Fifth, only patients with six-month GOSE data were included, and thus, the results may lack generalizability to patients who were lost to follow-up. Sixth, certain CDEs lack sufficient granularity, and the inclusion of unknowns may have skewed the present analyses. We also lacked the baseline health economic and insurance data from these patients with mTBI, which were unavailable in NIH NINDS CDE, version 1. These, along with granular demographic and injury history; duration of outpatient therapy; reasons for seeking/not seeking care and two-week, three-month, six-month and one-year outcomes including the GOSE with a comprehensive battery of measures in accordance to the NIH NINDS CDE, version 2 [64], are currently being collected from patients with TBI in the ongoing 12-center Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study (tracktbi.ucsf.edu; enrolling 2014–2018) and the Collaborative European NeuroTrauma Effectiveness Research in TBI (CENTER-TBI; center-tbi.eu) study [65] – data sources that can be utilized to fully characterize the unknowns present in the current analysis. Seventh, due to the limitation of a smaller sample, we were limited in the number of predictors that could be suitably included without overfitting the regression model. It is our hope that in future, larger validation studies, a greater number of predictors can be in included to delineate the nuances of admission, referral and outcome.

Conclusions

The temporal profile of the pathway of care after mTBI care requires further characterization. We demonstrate that clinical factors influence triage to admission, demographic and socioeconomic factors modulate medical follow-up and a convergence of initial injury characteristics, medical history and socioeconomic factors influences long-term outcome. Therefore, a careful consideration of demographic/socioeconomic, past medical history and injury characteristics are required in different phases of mTBI care – often in the context of one another. The source of the divergence of predictors for various phases of mTBI care is unclear. Further clarification is needed to develop evidence-based clinical practice guidelines to optimize continuity, triage and resource allocation for care of those inflicted with mild head trauma.

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Declaration of Interest

The authors report no other declarations of interest.

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