Does lower extremity fracture fixation technique influence neurologic outcomes in patients with traumatic brain injury? The EAST Brain vs. Bone multicenter trial

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OBJECTIVE: This study aimed to determine whether lower extremity fracture fixation technique and timing (≤24 vs. >24 hours) impact neurologic outcomes in TBI patients.

METHODS: A prospective observational study was conducted across 30 trauma centers. Inclusion criteria were age 18 years and older, head Abbreviated Injury Scale (AIS) score of >2, and a diaphyseal femur or tibia fracture requiring external fixation (Ex-Fix), intramedullary nailing (IMN), or open reduction and internal fixation (ORIF). The analysis was conducted using analysis of variamce, Kruskal-Wallis, and multivariable regression models. Neurologic outcomes were measured by discharge Ranchos Los Amigos Revised Scale (RLAS-R).

RESULTS: Of the 520 patients enrolled, 358 underwent Ex-Fix, IMN, or ORIF as definitive management. Head AIS was similar among cohorts. The Ex-Fix group experienced more severe lower extremity injuries (AIS score, 4–5) compared with the IMN group (16% vs. 3%, $p = 0.01$) but not the ORIF group (16% vs. 6%, $p = 0.1$). Time to operative intervention varied between the cohorts with the longest time to intervention for the IMN group (median hours: Ex-Fix, 15 [8–24] vs. ORIF, 26 [12–85] vs. IMN, 31 [12–70]; $p < 0.001$). The discharge RLAS-R score distribution was similar across the groups. After adjusting for confounders, neither method nor timing of lower extremity fixation influenced the discharge RLAS-R. Instead, increasing age and head AIS score were

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associated with a lower discharge RLAS-R score (odds ratio [OR], 1.02; 95% confidence interval [CI], 1.002–1.03 and OR, 2.37; 95% CI, 1.75–3.22), and a higher Glasgow Coma Scale motor score on admission (OR, 0.84; 95% CI, 0.73–0.97) was associated with higher RLAS-R score at discharge.

CONCLUSION: Neurologic outcomes in TBI are impacted by severity of the head injury and not the fracture fixation technique or timing. Therefore, the strategy of definitive fixation of lower extremity fractures should be dictated by patient physiology and the anatomy of the injured extremity and not by the concern for worsening neurologic outcomes in TBI patients. (*J Trauma Acute Care Surg.* 2023;95: 516–523. Copyright © 2023 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Prognostic and Epidemiological; Level III.

KEY WORDS: Traumatic brain injury; long-bone fractures; neurologic outcomes.

Traumatic brain injury (TBI) is a major public health problem that results in more than 1.2 million annual emergency department visits and hospitalizations in the United States and is associated with 50,000 deaths and 80,000 cases of long-term disability.[1,2] Traumatic brain injury frequently occurs in the setting of multiple injuries and accounts for one third of the multiple injury patient's mortality.[3]

One of the most common concomitant injuries that accompany TBI is long bone fractures, which often require prompt surgical intervention.[4] Although intramedullary nailing (IMN) has become the criterion standard for femur and tibia fracture fixation, as it allows for stable fixation and faster time to fracture union, it is associated with devascularization of the cortex, increased intramedullary pressure, and marrow embolization that is thought to potentiate neurological injury.[5] An alternative fixation method is open reduction and internal fixation (ORIF), which is less likely to be associated with marrow embolization but is associated with perioperative complications that include bleeding, malunion, and postoperative soft tissue infections.[6–9] While some groups advocate for immediate definitive fixation with IMN or ORIF, others support the concept of damage-control orthopedics using external fixation (Ex-Fix), for temporary stabilization, to mitigate the secondary brain insult and potential worsening of neurologic outcomes associated with early definitive fixation.[10]

Early definitive fracture fixation, within 24 hours of injury, has been shown to be associated with shorter hospital and intensive care unit (ICU) length of stay (LOS) and decreased pulmonary complications including pneumonia and acute respiratory distress syndrome.[11,12] Nevertheless, proponents of damage-control orthopedics suggest that early definitive stabilization is detrimental in the multiple injury patient with concomitant head, chest, and abdominal injury because of increased blood loss, surgical stress, pulmonary and neurologic complications, and an increased mortality.[13,14] As a result, severely injured patients with TBI and associated lower extremity fractures represent a highly challenging patient population.

Given the potential risk of adverse neurologic sequela in the setting of concomitant long bone fractures and in moving toward identifying treatment strategies in the TBI patient with multiple injuries that improve outcomes,[15] the objectives of this study were to (1) determine the association between type of fracture fixation technique and neurologic outcomes in TBI patients presenting with a concomitant lower extremity long bone fracture and (2) determine the association between timing of fracture fixation (≤24 hours from injury) and neurologic outcomes in TBI patients presenting with a concomitant lower extremity long bone fracture. We hypothesized that fracture fixation with IMN would be associated with worse neurologic outcomes at discharge when compared with ORIF and Ex-Fix treatment strategies. Furthermore, definitive repair ≤24 hours from injury would be associated with worse neurologic outcomes.

PATIENTS AND METHODS

Study Population

The prospective, multicenter, observational Brain vs. Bone trial was approved by the Eastern Association for the Surgery of Trauma Multi-Institutional Trials Committee. Data were collected from March 2019 to March 2022 at 30 trauma centers (28 Level 1 and 2 Level 2) in the United States and Israel (Table 1). All collaborating centers obtained individual local institutional review board approval before participation, and a waiver of informed consent was granted because of the observational nature of the study. Data were abstracted from the medical records and institutional trauma registries and entered into the online data collection portal resource maintained by the American Association for the Surgery of Trauma. The STrengthening the Reporting of OBservational studies in Epidemiology guideline was used to ensure proper reporting of methods, results, and discussion (Supplemental Digital Content, Supplementary Data 1, http://links.lww.com/TA/D131)

Participants

Inclusion criteria were patients 18 years or older who presented with any TBI (mild to severe), a motor Glasgow Coma Scale (mGCS) score of <6 within 24 hours of admission if endotracheally intubated, a head Abbreviated Injury Scale (AIS) score of >2, and a diaphyseal femur or tibia fracture requiring operative fixation. Exclusion criteria were determination of nonsurvivability on admission, incarcerated, and pregnant patients. Patients who were initially managed with Ex-Fix that was subsequently converted to IMN or ORIF, before discharge, were excluded from this analysis. In addition, patients with multiple lower extremity fractures repaired with more than one of the fixation techniques at different time periods during the hospital stay were excluded (Fig. 1).

Covariates

Data on patient demographics, comorbidities, clinical and injury-related characteristics, hospital course, operative interventions, and outcomes were collected and analyzed. Mild, moderate, and severe TBI were defined as the admission Glasgow Coma Scale (GCS) of 13 to 15, 9 to 12, and <9, respectively. Admission mGCS was defined as the highest postresuscitation mGCS value. Type of long bone fracture fixation included Ex-Fix, IMN,

TABLE 1. Characteristics of Participating Trauma Centers (n = 30)

Geographic location, n (%)	
Northeast	8 (26.7)
Southeast	9 (30)
West	2 (6.7)
Midwest	3 (10)
Southwest	7 (23.3)
International	1 (3.3)
Designation level, n (%)	
1+	28 (93.3)
2	2 (6.7)
Trauma admissions per year, mean (SD)	3,345 (1415)

or ORIF only. Injury Severity Score (ISS) was classified as follows: <9, mild injury; 9 to 15, moderate injury; 16 to 24, severe injury; and ≥25, profound/critical injury. Intraoperative hypotension was defined as a systolic blood pressure <100 mm Hg. Intraoperative hypoxia was defined as oxygen saturation <90% by pulse oximetry.

Outcomes

The Ranchos Los Amigos Revised Scale (RLAS-R)[16] is a standardized and validated medical scale used to describe the neurologic and behavioral patterns found in TBI during the initial assessment and the recovery period. Ranchos Los Amigos Revised Scale takes into account patient's state of consciousness and reliance on assistance to carry out neurologic and physical function. The scale consists of 10 levels, with level 1 representing the lowest level of function and level 10 representing the highest level of function. Ranchos Los Amigos Revised Scale score was classified as follows: 1 to 5 (lower score), less purposeful neurologic and behavioral responses, and 6 to 10 (higher score), more purposeful neurologic and behavioral responses. The RLAS-R assessment is typically performed at the bedside by a trained physical or occupational therapist. Ranchos Los Amigos Revised Scale has been shown to have an interrater reliability rate of 0.87 to 0.94.[17] Worse neurologic outcomes were defined as a RLAS-R score of (1–5) at discharge.

Our primary outcome was to determine whether type of fracture fixation technique was associated with a lower RLAS-R (1–5) at discharge. Our secondary outcome was to determine whether timing of fracture fixation, specifically ≤24 hours from injury, was associated with a lower RLAS-R (1–5) at discharge. Additional outcomes assessed included hospital and ICU LOS, in-patient mortality, ventilator days, and discharge disposition.

Statistical Analysis

Categorical variables are presented in terms of frequencies and proportions; comparisons among the three lower extremity fixation groups were made with Pearson's χ^2 statistic and Fisher's exact test when appropriate. Means and SDs are reported for normally distributed continuous measurements, and analysis of variance was used to compare among the three groups. Nonnormal data, such as those representing length of time, were reported as medians and interquartile ranges (25th percentile to 75th percentile) and analyzed using the Kruskal-Wallis test. For all three-way comparisons, a p value of <0.05 was considered statistically significant. Multiple pair-wise

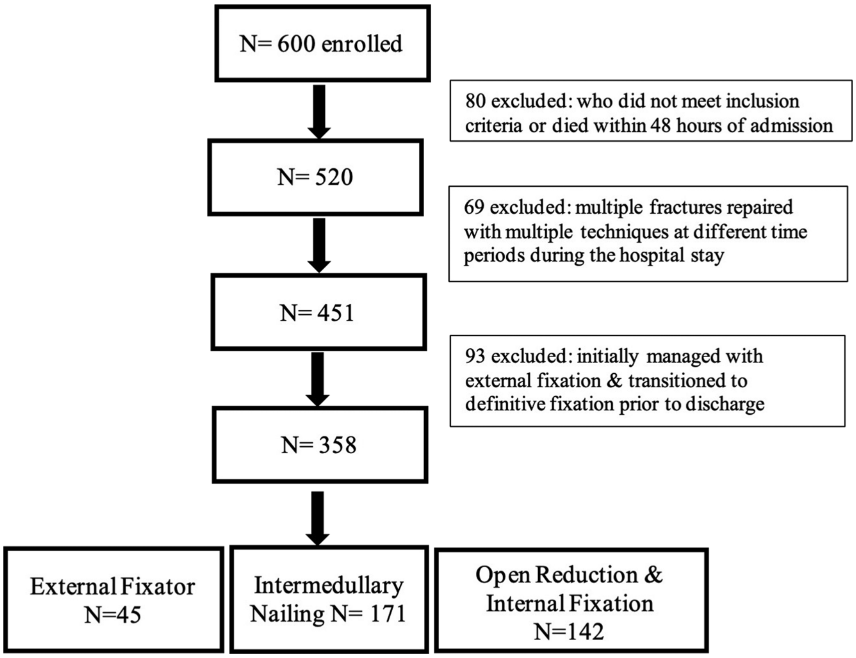

Figure 1. Flow chart of study enrollment, inclusion, and exclusion of patients presenting with a TBI and concomitant diaphyseal lower extremity fracture.

comparisons were carried out using the Bonferroni correction factor, dividing the 0.05 α level by the number of comparisons required. A multivariable generalized linear mixed model was constructed to determine the unadjusted and adjusted effect of the fixation procedures on the binary outcome measure, with trauma facility modeled as a random effect to remove bias and account for facility variation as a sample of the larger population of trauma centers. The regression included patients with data available for all factors entered into the model. Odds ratios (ORs) and their corresponding 95% confidence intervals (95% CIs) were reported for each factor included in the regression models.

RESULTS

Demographics and Injury Characteristics

Of the 520 subjects enrolled in the Brain vs. Bone study, 358 (69%) underwent Ex-Fix, IMN, or ORIF only as the primary management strategy during index hospitalization. Of those, 45 patients (12.7%) underwent Ex-Fix, 171 (48.7%) underwent IMN, and 142 (39.6%) underwent ORIF for the treatment of their femur and tibia fractures. Demographics and injury characteristics of the entire cohort are presented in Table 2. Mechanism of injury, head AIS, ISS, and GCS score were similar among the three groups. The most common mechanisms of injury were motor vehicle and motorcycle collisions, and pedestrian struck events. Patients were critically injured with an ISS of >25 in greater than 50% of patients in all three groups (Table 2).

While the median age of the cohort was 38 years (IQR, 26–56 years), pair-wise comparisons revealed that the Ex-Fix group was slightly older than the IMN group (48 ± 19 vs. 40 ± 18 years old, $p = 0.02$). The Ex-Fix group experienced more severe lower extremity injuries (AIS score, 4–5) when compared with the IMN group (16% vs. 3%, $p = 0.01$) but not when compared with the ORIF group (16% vs. 6%, $p = 0.1$). On the other hand, lower extremity injury severity (AIS score, 4–5) was similar between the IMN and ORIF group (3% vs. 6%, $p = 0.94$). Finally, the Ex-Fix patients were more likely to present with an mGCS of 1 to 3 on admission when compared with the ORIF group (58% vs. 26%, $p = 0.004$) but not when compared with the IMN group (57% vs. 40%, $p = 0.1$). Similarly, the IMN group was more likely to present with a mGCS of 1 to 3 on admission when compared with the ORIF group (40% vs. 26%, $p = 0.02$) (Table 2).

TBI and Lower Extremity Fracture Characteristics and Intraoperative Management

Traumatic brain injury characteristics and treatments were similar across all three groups (Table 3). Patients undergoing Ex-Fix were more likely to undergo operative intervention within ≤24 hours from time of injury (71% vs. 46% vs. 45%, $p = 0.006$). Time to operative intervention varied between the cohorts with the longest time to intervention for the IMN group (median hours: Ex-Fix group, 15 [8–24] vs. ORIF group, 26 [12–85] vs. IMN group, 31 [12–70]; $p < 0.001$). Intraoperative parameters were similar across all groups with the exception of a lower estimated blood loss, median (interquartile range) in milliliters, in the Ex-Fix group (70 [50–200]) when compared with the IMN (175 [80–300]) and ORIF group (150 [50–300]), with $p = 0.01$ (Table 3).

TABLE 2. Demographics and Injury Severity in Patients Presenting With a TBI and Concomitant Lower Extremity Fracture (n = 358)

	Ex-Fix (n = 45)	IMN (n = 171)	ORIF (n = 142)	*p*
Male, n (%)	34 (75.6)	40 (23.4)	101 (71)	0.5
Age, mean (SD), y	48 (19)	40 (18)	44 (19)	0.02*
Race, n (%)				0.4
White	31 (69)	93 (54)	88 (62)	
Black	8 (18)	43 (25)	30 (21)	
Other	6 (13)	35 (21)	24 (17)	
MOI, n (%)				0.6
MCC	10 (22)	31 (18)	20 (14)	
MVC	18 (40)	67 (39)	49 (36)	
Peds struck	11 (24)	46 (27)	44 (40)	
Other	6 (13)	27 (16)	29 (20)	
AIS, n (%)				
Head				
2–3	24 (58)	96 (56)	90 (64)	0.4
4–5	18 (42)	74 (44)	51 (36)	
Lower extremity				
2–3	37 (84)	165 (96.4)	131 (94)	0.0167*
4–5	7 (16)	5 (3)	8 (6)	
6	0	1 (0.6)	0	
Thoracic				
2–3	26 (79)	76 (70)	59 (71)	0.82
4–5	5 (15)	23 (21)	15 (18)	
Abdominal				
2–3	17 (65)	43 (66)	43 (67)	0.83
4–5	5 (19)	12 (19)	8 (13)	
ISS, n (%)				0.053
<16	4 (9)	6 (4)	11 (8)	
16–24	7 (16)	50 (29)	49 (35)	
>25	33 (75)	115 (67)	81 (58)	
GCS, n (%)				0.2
3–8	25 (56)	95 (56)	64 (45)	
9–12	10 (22)	32 (20)	29 (20)	
13–15	10 (22)	41 (24)	49 (35)	
GCS motor, n (%)				0.0019*
1–3	26 (58)	69 (40)	37 (26)	
4–5	10 (22)	58 (34)	64 (45)	
6	9 (20)	44 (26)	41 (29)	
Intubated				
In the field	14 (31)	64 (37)	41 (29)	0.26
In the trauma bay	23 (51)	74 (43)	68 (48)	0.55

*Pair-wise comparisons performed, with results and corresponding *p* values detailed in the text.

MCC, motor cycle collision; MOI, mechanism of injury; MVC, motor vehicle collition; Peds, pedestrian.

Neurologic and Nonneurologic Outcomes

Ranchos Los Amigos Revised Scale distribution, hospital and ICU LOS, and mortality did not differ significantly across the groups (Table 4).

TABLE 3. Lower Extremity Fracture and TBI Characteristics and Management (n = 358)

	Ex-Fix (n = 45)	IMN (n = 171)	ORIF (n = 142)	*p*
Femur fracture morphology, n (%)				
Laterality				
Left	10 (50)	57 (50)	39 (52)	0.98
Right	8 (40)	50 (43)	30 (40)	
Bilateral	2 (10)	8 (7)	6 (8)	
Type				
Closed	10 (50)	99 (86)	62 (83)	0.006
Open	10 (50)	16 (14)	71 (17)	
Displaced	17 (89)	103 (89)	58 (78)	0.09
Nondisplaced	2 (11)	12 (11)	15 (22)	
Tibia fracture morphology, n (%)				
Laterality				
Left	15 (39)	33 (43)	34 (39)	0.04
Right	16 (41)	41 (53)	47 (54)	
Bilateral	8 (21)	3 (4)	6 (7)	
Type				
Closed	18 (46)	49 (64)	65 (75)	0.008
Open	21 (54)	28 (36)	25 (22)	
Displaced	31 (84)	62 (83)	58 (68)	0.04
Nondisplaced	6 (16)	13 (17)	27 (32)	
Multiple fractures, n (%)	8 (18)	18 (11)	15 (11)	0.36
Time to OR, median (IQR), h	15 (8–24)	31 (12–70)	25.5 (12–85)	<0.001
Operating room ≤24 h, n (%)	32 (71)	79 (46)	64 (45)	0.006
Intraoperative parameters				
Transfusions, n (%)	22 (59)	125 (75)	92 (66)	0.07
Hypoxia, n (%)	4 (12)	14 (9)	9 (7)	0.58
Hypotension, n (%)	13 (36)	60 (36)	34 (25)	0.06
Length of procedure, median (IQR)	128 (72–217)	147 (92–240)	160 (93–245)	0.2
Estimated blood loss, median (IQR), mL	70 (50–200)	175 (80–300)	150 (50–300)	0.01
Intracranial lesion, n (%)				
Subdural hematoma	24 (55)	82 (48)	72 (51)	0.73
Epidural hematoma	5 (11)	11 (7)	12 (9)	0.53
Intraventricular hemorrhage	6 (14)	23 (14)	16 (11)	0.83
Subarachnoid hemorrhage	20 (46)	106 (62)	94 (65)	0.07
Intraparenchymal contusion	11 (25)	64 (38)	40 (38)	0.12
Cerebral edema	8 (18)	18 (11)	10 (7)	0.1
Diffuse axonal injury	6 (14)	21 (12)	16 (11)	0.91
Skull fracture	11 (25)	51 (36)	53 (38)	0.3
ICP monitoring, n (%)	10 (22)	34 (20)	22 (15)	0.48
Indication for ICP monitoring, n (%)				
Worsening GCS	5 (50)	10 (24)	8 (36)	0.48
Lesion progression on imaging	4 (40)	17 (50)	11 (50)	0.84
Postoperative	0	4 (12)	1 (5)	0.4
Type of ICP monitor, n (%)				0.056
Bolt	4 (40)	12 (35)	15 (68)	
Intraventricular catheter	2 (20)	13 (38)	6 (27)	
Intraparenchymal catheter	4 (40)	9 (27)	1 (5)	
Neurosurgical intervention, n (%)	2 (4.4)	19 (11.1)	11 (7.8)	0.31

ICP, intracranial pressure.

Factors Associated With Worse Neurologic Outcomes at Discharge

After adjusting for confounders, neither method nor timing of lower extremity fracture fixation influenced the RLAS-R score at discharge. Instead, increasing age (OR, 1.02; 95% CI, 1.002–1.03) and increasing head AIS (OR, 2.37; 95% CI, 1.75–32.2) were associated with an RLAS-R (1–5) score at discharge. On the other hand, a higher mGCS score on admission (OR,

TABLE 4. Outcomes of Patient Presenting With a TBI and Concomitant Lower Extremity Fracture (n = 358)

	Ex-Fix (n = 45)	IMN (n = 171)	ORIF (n = 142)	*p*
Hospital LOS, median (IQR)	23 (14–38)	18 (10–30)	17 (9–29)	0.19
ICU LOS, median (IQR)	11 (4–18)	9 (4–16)	8 (3–16)	0.36
Ventilator days, median (IQR)	5 (1–13)	5 (1–13)	5 (1–13)	0.91
Mortality, n (%)	8 (18)	12 (7)	11 (8)	0.065
RLAS-R, n (%)				0.96
1–5	13 (29)	52 (30)	44 (31)	
6–10	32 (71)	119 (70)	98 (69)	
Disposition				0.044
Home	8 (22)	42 (27)	23 (18)	
Acute rehab	10 (28)	74 (47)	56 (44)	
Subacute rehab	4 (11)	7 (5)	14 (11)	
Skilled nursing facility	13 (36)	25 (16)	27 (22)	

0.84; 95% CI, 0.73–0.97) was associated with a decreased likelihood of experiencing a lower RLAS-R score at discharge (Table 5).

DISCUSSION

Definitive fracture fixation in the setting of concomitant TBI remains a controversial and multifaceted topic. While numerous studies have focused on the timing of definitive long bone fracture fixation in the setting of a TBI,[7,8,18–26] very few have assessed the effects of fracture fixation method on neurologic outcomes in this patient population.[27] We report that, in patients presenting with mild to severe TBI, neither fracture fixation technique (Ex-Fix vs. IMN vs. ORIF) nor early fixation (≤24 hours of injury) was associated with worse neurologic outcomes at discharge. Instead, increasing patient age and head AIS score and a lower admission mGCS were associated with an increased risk of experiencing a lower RLAS-R score at discharge.

To our knowledge, this study is one of the first to directly compare the three different treatment modalities for diaphyseal femur and tibia fracture fixation and their effect on neurologic outcomes in patients with concomitant TBI. The influence of head injury severity rather than fracture fixation technique may be attributed to the intraoperative mitigation of the complications associated with IMN and ORIF. That is, minimizing intraoperative hypoxia and hypotension; balanced transfusions with red blood cells, fresh frozen plasma, and platelets; prompt correction of coagulopathy; and the use of newer IMN techniques, which have been shown to reduce marrow embolization, such as the Reamer/Irrigator/Aspirator device.[28]

The association between severity of the head injury rather than timing of fracture fixation seen in our cohort is compatible with the current available literature.[20,27,29,30] Poole@ et al.[29] showed that severity of the head injury itself and not timing of fracture fixation (≥24 hours) was associated with a decline in GCS and worse neurologic outcomes at discharge. In a retrospective review of 1,362 patients presenting with a TBI and concomitant lower extremity fractures undergoing IMN at 4 different time intervals (24, 24–48, 48–120, and >120 hours from time of injury) and nonoperative controls, Brundage et al.[20] showed that discharge GCS was associated with head AIS and ISS and not timing of fracture fixation. Kalb et al.[30] retrospectively reviewed patients with a severe TBI and lower extremity fracture and compared outcomes in those undergoing early versus late fracture fixation. Similarly, timing was not associated with lower GCS at discharge or worsening outpatient neurologic outcomes. Perhaps the influence of timing on neurologic outcomes is mitigated by a more regimented preoperative care model[22] owing to the advancements in damage-control resuscitation. Specifically, effective preoperative resuscitation, restrictive use of crystalloids, timely hemodynamic normalization before operative intervention, preoperative monitoring and treatment of elevated intracranial pressure, and the collaborative multidisciplinary critical care model of intensivists, traumatologists, orthopedic surgeons and neurosurgeons may help minimize secondary insult to the brain.

The relationship between age and adverse neurologic outcomes is well-documented.[31] In support, this study found that increasing age was associated with an increased likelihood of experiencing worse neurologic outcomes at discharge. Prior studies have found an inflection point around the fourth or fifth decade of life, at which unfavorable outcomes tend to increase steeply in a linear and continuous manner in TBI patients.[31,32] This in part is due to the physiological, morphological, and inflammatory response changes in the aging brain that begin in the fifth decade of life, altering the brain's ability to recover after injury.[33–35]

The association between mGCS score and a decreased R-RLAS at discharge identified in our study is not surprising. The motor component of the GCS score has been shown to contain all the prognostic information within the total GCS score in the setting of a TBI.[36] In addition, the mGCS score is the most easily and consistently assessable component even in patients where the full GCS score is difficult or impossible to obtain.[37] As a result, the International Mission for Prognosis and Analysis

TABLE 5. Factors Associated With Decreased RLAS at Discharge (n = 352)

	Lower RLAS-R (1–5) at Discharge (n = 109)		
	Adjusted OR	95% CI	*p*
Age	1.02	(1.002–1.03)	0.03
Sex	0.76	(0.42–1.41)	
Head AIS	2.37	(1.75–3.22)	<0.001
LE AIS	0.87	(0.55–1.35)	
Admission GCS motor score	0.84	(0.73–0.97)	0.02
Operating room ≤24 h	0.86	(0.50–1.49)	
Fracture fixation type			
Ex-fix	0.93	(0.40–2.19)	
IMN	0.89	(0.49–1.62)	
ORIF	1.20	(0.63–2.26)	
Ex-fix vs. IMN	1.03	(0.43–2.49)	
Ex-fix vs. ORIF	0.85	(0.34–2.13)	
IMN vs. ORIF	0.82	(0.46–1.48)	

LE, lower extremity.

of Clinical Trials in TBI (IMPACT)[38] developed a prognostic model for TBI, in collaboration with the CRASH (Corticosteroid Randomization After Significant Head Injury)[39] group, based on several clinical and radiological factors including mGCS. These trials demonstrated that mGCS was a strong predictor of 6-month mortality and functional outcomes.[40] Therefore, the admission mGCS score was incorporated as a variable in the IMPACT prognostic calculator and is now supported further by this current study as an important marker of neurological outcomes that providers should be aware of and incorporate into prognostic discussions.

Limitations

The results of this study should be interpreted within the context of its limitations. First, by design, a prospective observational study inherently prohibits inferences related to causal relationships or temporal associations. Second, the study lacks clinical information regarding intracranial and cerebral perfusion pressure changes and treatments in patients who received intracranial pressure monitoring in the perioperative period. Third, the variability in practice and surgical management at the participating institutions determining the type of fracture fixation a patient underwent (Ex-Fix vs. IMN vs. ORIF) introduces potential selection bias. Fourth, the lack of clinical information such as blood alcohol level, toxicology screening, baseline dementia, stroke, and history of prior TBI introduces both information bias and residual confounders. Also, while this was a multicenter study, the overall power may be insufficient to overcome a Type II error for a small but significant difference between the cohorts. Finally, given that the study population was managed in primarily large volume Level 1 trauma centers, the results might not be generalizable to all trauma centers with differing resource profiles.

CONCLUSION

Neurologic outcomes in the multiple injury patient, presenting with a TBI and concomitant lower extremity fractures, are impacted by severity of the head injury itself and not the fracture fixation technique or timing. Therefore, management of the lower extremity fractures in the setting of a TBI should be tailored to the patient's physiology and fracture anatomy and may not need to be delayed or modified due to concern for worsening neurologic outcomes in this patient population.

AUTHORSHIP

M.G., J.K., and D.S. contributed in the study design. M.G. and D.S. contributed in the data collection, data interpretation, literature review, manuscript revision, and final approval. J.K. contributed in the data analysis. The Brain vs. Bone Study Group contributed in the data collection and critical review of the manuscript.

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DISCLOSURE

The authors declare no conflicts of interest.

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