Cranial Vault Fractures in Civilian Head Injury: Clinical and Radiologic Predictors of Seizures and the Fracture Seizure Index: A Prospective Single-Center Observational Cohort Study

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Abstract

Study Objectives To determine the risk factors of posttraumatic seizures (PTS) among patients with civilian head injury and skull vault fractures.

Methods A 5-year prospective cohort study of patients with skull fractures presenting to our center from March 2013 to February 2017.

Results Of 637 patients with traumatic brain injury (TBI), 135 (21.2%) patients sustained calvarial fractures, 91 (72%) were from road traffic accidents (RTAs), and most were young adult males (M:F = 11.6, mean age = 29.1 ± 2.3 years, 95% CL). Linear fractures in 69 patients and depressed fractures in 50 (39.7%) were the common fracture types. Seventy-seven (61.1%) patients had cerebral contusions, 31 (24.6%) had extradural hematoma (EDH), and 21 (16.7%) patients had Glasgow coma scale (GCS) ≤ 8. Twenty-five (18.5%) patients suffered early PTS, and five had late PTS. Among nonfracture patients (n = 361), 31 (8.6%) had seizures. Seizures occurred more in the fracture subgroup (χ^2 = 10.1, p < 0.05, df = 1) and earlier (χ^2 = 5.9, p = 0.027, df = 1). Fractures and seizures followed a similar trend in occurrence. Among patients with vault fractures, severe head injury, contusions, and intracranial hematoma, the relative risk and odds for early seizures followed a trend predicted by a statistical index—the fracture seizure index (FSI). Late PTS did not show a statistical relationship with early PTS (χ^2 = 2.98, df = 1, p > 0.05).

Conclusion GCS score ≤8, depressed fracture and multifocal cerebral contusions are predictors of early PTS. Seizure risk associated with fractures and other lesions can be predicted by the FSI.

Keywords
- posttraumatic seizures
- skull fracture
- fracture seizure index

Introduction

Skull fracture (SF) is a known clinical manifestation of the mechanical deformations accompanying head injury (HI). Its occurrence indicates a substantial and potentially harmful energy transfer to the skull as well as the underlying intracranial structures.[1,2] Although SFs may occur with no accompanying neurologic injury,[3] and conversely, significant injury to the brain and its coverings sometimes with fatal outcome have been reported without SFs[3–5]; however, SFs occurring in association with life-threatening conditions including intracranial hematoma, parenchyma contusions seizures, cerebral edema, subarachnoid hemorrhage, and hydrocephalus are a frequently reported experience among patients with craniocerebral trauma.[3,4] The frequency of association between cranial vault fractures and these lesions generally and seizures specifically

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is variable judging from previously reported studies.[5–7] This study evaluates and scores the association between seizures, calvarial fractures, and acute traumatic intracranial lesions through an index—fracture seizure index (FSI)—in an attempt to predict the risk of seizures in HI patients with cranial vault fractures. FSI may provide a guide for decisions on seizure prophylaxis in HI patients with cranial vault fractures.

Aims/Objectives

To study SFs and associated lesions, determine the predictors of posttraumatic seizures (PTS) in HI patients with skull vault fractures over a 5-year period from March 2012 to February 2017.

Materials/Methods

A prospective observational cohort study of patients with head trauma and calvarial fracture was presented to the University of Nigeria, Teaching Hospital Enugu, from March 2012 to February 2016.

- *Inclusion criteria*: Patients with history of trauma and HI with computed tomographic (CT) evidence of calvarial fractures were enrolled into the study.
- *Exclusion criteria*: Patients with skull base fractures, history of seizures, or previous admissions for HI. Enrolled patients were evaluated on the basis of age, sex, etiology of HI, level of consciousness (assessed using the Glasgow coma scale [GCS] score), occurrence of seizures and seizure type, electroencephalogram (EEG) reports, and neuroimaging findings on CT scan. Data acquisition and analysis were performed using Statistical Package for the Social Sciences (SPSS; IBM Inc.) version 21. The seizure risk for fractures and associated conditions as well as statistical associations were evaluated using risk ratio estimation, chi-square test, and confidence limits where appropriate and p values were set at the 95% level of confidence. For each associated lesion, a seizure index—SI (x)—was calculated using the relative risk of seizure occurrence associated with the lesion. The fracture seizure index–FSI (T)—the overall risk of seizure in patients with calvarial fracture and associated conditions was estimated by a summation of the relative risk (risk ratio) of seizure occurrence among the associated lesions.

$$\mathrm{FSI}(T) = \sum fx$$

where fx = relative risk or risk ratio (rr) of each associated lesion. Overall risk was graded as low risk (low), moderate risk (intermediate), and high risk (major). Risk of seizures based on FSI was used to design a simple guide for seizure prophylaxis in head-injured patients with calvarial fractures and seizures.

Ethical approval: Informed consent was obtained from every prospective patient or caregiver in the case of a patient(s) incapable of providing consent. Ethical approval for this study was obtained from the institutional review board (IRB) of the hospital.

Results

A total of 637 patients with HI were studied over a 5-year period, 135 (21.2%) of them sustained calvarial fractures, and 91 (71.4%) of fractures resulted from road traffic accidents (RTAs) (►**Table 1**). The age range was 5 months to 65 years (►**Table 2**). There was a strong male predilection, M:F = 11.6:1 (124 males and 11 females) among the fracture subgroup compared with the nonfracture group 2.6:1 (361 males and 141 females) ($\chi^2 = 13.0$, $p < 0.05$, df = 1). Cranial CT scans showed 69 (54.8%) patients with linear fractures, 50 (39.7%) with depressed fractures, 7 (5.6%) with elevated fractures, and 8 (5.9%) patients with more than one fracture type. Among those with fractures, 77 (61.1%) had cerebral contusions, 11 (8.7%) intracerebral hematoma, 12 (9.5%) subdural hematoma, and 31 (24.6%) had extradural hematoma (EDH). Sixty-nine (51.1%) patients with fracture had mild HI, 45 (33.3%) sustained moderate HI, whereas 21 (15.6%) sustained severe HI GCS ≤8. Thirty (22.2%) patients had PTS, 25 (18.5%) suffered PTS, and 5 (3.7) had late PTS. Among nonfracture patients (361), 31 (8.6%) suffered seizures, 27 of them were early PTS and 4 were late PTS. Seizures occurred significantly more in the fracture subgroup ($\chi^2 = 10.1$, $p < 0.05$, df = 1, hazard ratio [HR] = 2.58).

The mean injury-to-ictus interval in the fracture group was 1.94 ± 0.90 days (95% confidence interval [CI]) for early

Table 1 Etiology

Etiology	Frequency (%)
Road traffic accident	97 (71.4)
Motorcycle	63 (46.8)
Motor vehicle Tricycle	32 (23.8) 2 (0.8)
Assault	26 (19.0)
Machete cuts	19 (13.5)
Gunshot	4 (3.2)
Other	3 (2.4)
Fall from height	11 (8.7)
Other (recreational)	1 (0.8)
Total	135 (100)

Table 2 Age distribution (years)

Age groups (y)	Frequency	Percentage	Cumulative percentage
0–10	13	9.6	9.6
11–20	18	13.3	22.9
21–30	45	33.3	56.2
31–40	41	30.4	86.6
41–50	8	6.0	92.6
51–60	4	3.0	95.6
61–70	6	4.4	100.0
Total	135	100.0	

Mean age: 29.1 ± 2.3 years; 95% CL range: 5 months to 65 years.

seizures and 21.0 ± 3.5 days for late PTS, whereas among the nonfracture group, 3.1 ± 1.7 days (95% CI) were for early seizures and 19 ± 2.7 days for late seizures. Early seizures also occurred significantly earlier in the fracture group (χ^2 = 5.9, p = 0.027, df = 1). However, there was no statistical difference between mean injury to ictus interval for late seizures among the fracture and no fracture subgroups (χ^2 = 1.66, p > 0.05, df = 1). Early seizures were generalized in 13, focal in 7, and secondarily generalized in 5 patients, whereas late seizures in the fracture subgroup were focal in 3 and secondarily generalized in 2 patients respectively. Among patients with fracture and early seizures, 11 (47.8%) had GCS score ≤8 (odds ratio [OR] = 4.9, rr for seizure risk = 8), 12 (52%) had depressed SFs (OR = 3.2, rr = 4.1), and 14 (60.9%) sustained multifocal cerebral contusions (OR = 3.5, rr = 5.2). The occurrence of late PTS did not show a statistical relationship with early PTS in both the fracture (χ^2 = 2.98, DF = 1, p > 0.05) and nonfracture subgroups (χ^2 = 1.17, df = 1, p > 0.05). The statistical association between calvarial fractures, seizures, and acute traumatic lesions are depicted in ►**Tables 3** and **4** For associated lesions, an SI (x) was estimated, and FSI$^{(T)}$ as summation of seizure risk is depicted in ►**Table 3**. Based on FSI, we propose a seizure prophylaxis guide for patients with skull vault fractures—low risk-watchful surveillance, no seizure prophylaxis.

Moderate risk: seizure prophylaxis for 1 week.

High risk: seizure prophylaxis for 2 weeks.

Discussion

From this series, the incidence of skull vault fractures is 21.2%. A similar incidence of 21.2% was previously reported by authors from another region of Nigeria.[8] The incidence of SFs varies with the severity of HI as well as age group among other factors.[9,10] The distribution of fracture type shows that linear and depressed fractures are more common in 54.8 and 39.7% cohorts, respectively.

Some 6% of the patients with HI present with more than one fracture type. Among patients with vault fractures, a mean age at presentation of 29.1 ± 2.3 years clearly illustrates its high occurrence among young adult patients and shares some similarity with the demographic profile for closed HI in the setting and globally.[8,10,11] The authors also found a greater male predilection for PTS among our cohorts with vault fracture (M:F = 11.6), when compared with the nonfracture subgroup (M:F = 2.6). In a longitudinal prospective observational study from the Indian subcontinent, Thapa et al found a higher association between female sex and PTS. However, their findings did not specifically describe the sex demographics of HI in patients with vault fractures.[12] The authors' suspicion of a causal association between fractures and early seizures derives from the following findings.

First, vault fractures and early PTS share a similar trend over the study period (►**Fig. 1**), and this relationship was confirmed by a HR of 2.58. A more frequent occurrence of early PTS in the fracture subgroup is also suggestive of some causal association (χ^2= 10.1, p < 0.05, df = 1). Further, there was a significant temporal association between early seizures (χ^2 = 5.9, p < 0.05, df = 1) and fractures, and this association was absent in patients with late seizures.

These may all suggest a likely role for vault fractures in the etiology of early seizures. Yeh et al, in a retrospective population-based study, found an adjusted HR of developing epilepsy of 10.5 among TBI patients with SFs generally.[13] About four decades ago, among 1,000 patients with nonmissile depressed fractures, Jennett et al found a 10% and 15% early and late seizure incidence rates.[14] We believe the considerable difference between Jennet's series and early and late seizure

Table 3 Fracture seizure index, associated lesions, and seizure prophylaxis guide

A. Lesion	Seizure risk (rr)	SI (x)
No fracture or associated lesions	0.97	1.0
Linear fracture	2.2	2.0
Hemorrhages or focal contusion	3.1	3.0
Depressed fracture	4.0	4.0
Multifocal contusions	5.4	5.0
Severe head injury	8.3	8.0
B. Seizure risk	$\mathrm{FSI}(T) = \sum fx$	
Low	0–2	
Intermediate	3–5	
High risk	> 5	
C. Seizure prophylaxis based on FSI	**Risk**	Total $\mathrm{FSI}(T) = \sum fx$
Not advisable	Low	0–2
Advised for 1 wk	Intermediate	3–5
Advised for 2 wk	High	> 5

Abbreviations: FSI, fracture seizure index; rr, or risk ratio; SI, seizure index.

Table 4 Markers and associations of posttraumatic seizure

	Seizure	No seizure	Total	Significance	Relative risk
Sex					
Male	21 (15.5%)	103 (76.3%)	124 (91.8%)	$\chi^2 = 3.303$, $p = 0.069$	
Female	4 (3%)	7 (5.2%)	11 (8.2%)		
Total	25 (18.5%)	110 (81.5%)	135 (100%)		
Type of fracture					
Depressed	17 (13.8%)	38 (30.9%)	55 (44.7%)	$\chi^2 = 6.682$, $p = 0.009$	4.0
Linear	8 (6.5%)	60 (48.8%)	68 (55.3%)	$\chi^2 = 0.755$ $p = 0.873$	2.2
Total	25 (20.3%)	98 (79.7%)	123 (100%)		
Cerebral contusions					
Present	25 (18.5%)	66 (48.9%)	91 (69.5%)	$\chi^2 = 6.59$, $p = 0.033$	
Absent	3 (2%)	37 (28.5%)	40 (30.5%)		5.2
Total	27 (20.4%)	103 (78.5%)	131 (100%)		
Admission GCS					
3–8	11 (8.1%)	10 (7.4%)	27 (20.0%)	$\chi^2 = 10.48$, $p = 0.001$	8.3
9–12	10 (7.4%)	35 (25.9)	108 (80.0%)		2.3
13–15	9 (6.7%)	60 (44.5%)			0.7
Total	30 (22.2%)	105 (77.8%)	135 (100%)		
Intracranial hemorrhages					
Present	16	25	41		3.1
Absent	16	78	94	$\chi^2 = 5.982$, $p = 0.014$	
Total	32	103	135		

Abbreviation: GCS, Glasgow coma scale.

rates of 18.5% and 3.7%, respectively, from this study is a result of dissimilar study populations as well as times of study.[14] We opine that a clear elucidation of the association between vault fractures and PTS will provide a sound scientific basis for recommendations on the management of fracture-associated PTS based on scientific evidence. This is the basis of our study. In a previous population-based study, Annegers and Coan[7] attributed a moderate risk of seizure occurrence to HI patients with associated SFs (relative risk: 2.9); however, they related seizure risk neither to fracture characteristics nor to other associated lesions in their statistical analysis.

We wish to state that our study is not the first to evaluate the statistical relationship between PTS, SFs, acute traumatic mass lesions, and HI severity.[15] Some other authors have also previously published mathematical methods for predicting seizure occurrence after HI.[15–17] However, these models were mainly for penetrating HI and also were used to evaluate war injuries—study population with disparate epidemiologic and etiopathogenic characteristics when compared with our civilian and peace time cohorts. This study, however, is the first attempt at defining seizure risk among patients with civilian HI, vault fractures, and associated lesions using a predictable scientific profile based on relative risk estimation (►**Tables 3** and **4**). We are unable to explain a direct pathophysiologic link between seizure occurrence and vault fractures in the absence of cortical injury, presence of an intact dura, and underanged cerebral cortical homeostasis and biochemical milieu. However, we hold the opinion that abnormal energy transfer to underlying cortical regions from a fracture-genic mechanical skull deformation may provide the pathophysiologic substrate for seizure induction by increasing neuronal excitability in an incompressible brain. This view is supported by evidence from an experimental HI model.[18] The phenomenon of fracture-associated seizure disorder occurs without prejudice to the seizure-inducing potentials of other associated lesions such as contusions, intracranial hematoma, and cerebral edema. ►**Table 3** shows the seizure risk indices of the different lesions as well as the FSI, a summation of seizure risk. From this study, FSI values 0 to 2 suggest low seizure risk. This subgroup includes patients with either linear fractures alone or no fractures at all as well as patients with no associated lesions or severe HI.

We do not advocate seizure prophylaxis in this category. However, we advocate watchful surveillance and EEG for those with linear fractures. Those with intermediate or moderate risk for seizures have FSI values 3 to 5. This class corresponds to patients with depressed fractures, multifocal

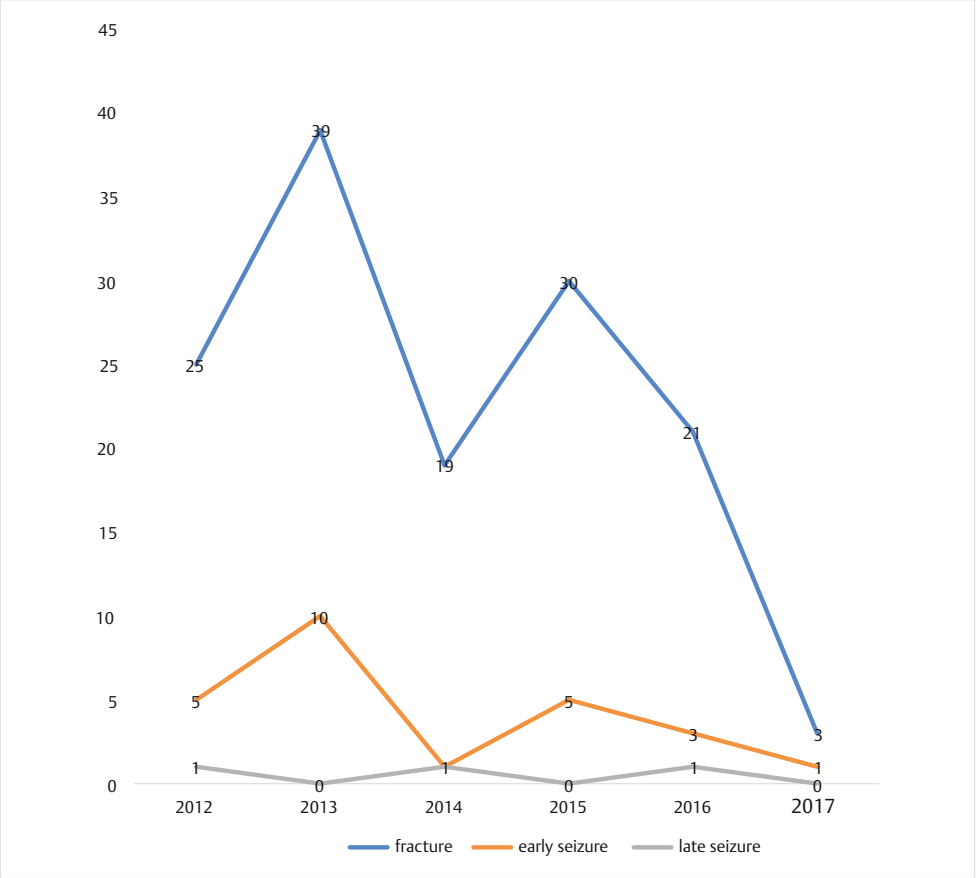

Fig. 1 Line graph showing the profile of fractures and seizures over the study period. *HR = 2.58 for early seizures.*

contusions, and intracranial hemorrhages. For the moderate seizure risk group, we advocate EEG as well as the current practice of seizure prophylaxis for 1 week. Those with FSI > 5 have the highest seizure risk. This subcategory includes severe HI patients and shows that the risk of seizures is highest among them if they sustain fractures as well.

We advocate EEG and seizure prophylaxis for 2 weeks in this category to cover for the critical period of altered neuroexcitability and trauma-induced neuroinflammation that has been reported to persist till the second week in patients with severe HI.[19] In the estimation of FSI, the concept of risk summation for multiple lesions applies. For instance, in a patient with multifocal contusions with SI (*x*) = 5 and associated depressed fracture with SI (*x*) = 4, the FSI (*fx*) is 9.0, a value within the high seizure risk category. We are currently applying this protocol to our patients with HI and vault fractures to evaluate its usefulness in reducing the current (22.2%) incidence of seizures and hope to publish the results in a future paper. We also hope that this study will trigger more clinical inquiry from other authors aimed at verifying the scientific and clinical utility of FSI. This study did not consider the impact of surgical treatment of SFs in the risk or outcome evaluation because fracture treatment has not been shown to alter the natural history of PTS.[20] Our study has some limitations including the noninclusion of some other likely risk factors for PTS such as genetic predisposition.[21] We also believe that seizure risk determination in children with HI may require a modified FSI or different schema altogether because of the influence of age on both the rate of occurrence and type of PTS based on a previously reported study.[22]

Conclusion

Our study suggests that vault fractures may have a causal association with early PTS. Occurrence of early PTS bears a predictable relationship with vault fractures and associated lesions defined by the FSI. We believe decisions on prophylaxis for early seizures in HI patients with vault fractures can be guided by FSI-based risk estimation.

Conflict of Interest
None.

Funding
None.

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