The Effect of Pre-existing Seizure Disorders on Mortality and Hospital Length of Stay Following Burn Injury

Kenisha Atwell, MD, Colleen Bartley, MD, Bruce Cairns, MD, and Anthony Charles, MD, MPH

Patients with a seizure disorder have a higher incidence of burn injury; however, there are limited studies that examine the association between pre-existing seizure disorders (PSD) and burn outcomes. This is a retrospective study of admitted burn patients. Variables analyzed include patient demographics, clinical characteristics, associated PSD, hospital length of stay (LOS), and mortality. Multivariate logistic regression was performed to analyze the impact of PSD on burn mortality and LOS. Seven thousand six hundred and forty patients met the inclusion criteria and 1.31% (*n* = 100) patients had a PSD. There was no difference in mortality rate between patients with or without PSD (odds ratio [OR] = 2.28, 95% confidence interval [CI] = 0.87 to 5.93). Multivariate logistic regression showed that patients with PSD had significantly increased odds of longer hospital LOS (OR = 2.85, 95% CI = 1.73 to 4.67). Seizure disorder management is mandatory in reducing burn injury and decreasing the costs associated with increased hospital LOS.

Burn injury ranks fourth worldwide in trauma-related injuries, preceded by traffic accidents, falls, and interpersonal violence.[1] Burn injury account for 180,000 deaths annually and nonfatal burns can cause severe morbidity and disability.[2] In 2016, according to the American Burn Association, 486,000 patients received medical treatment for burn injury and 3400 burn injury deaths occurred.[3] Although burn injury can be attributed to socioeconomic, environmental, and familial factors, many comorbid illnesses, particularly seizure disorders play a role in burn injury incidence.[4,5]

Seizure disorder is considered the fourth most common neurologic disorder following migraine, stroke, and Alzheimer's disease.[6] The yearly incidence rate of seizures in the United States is 150,000 with a higher prevalence in younger children and older adults; and 1 in 26 individuals will develop a seizure disorder during their lifetime.[6,7] Overall, in the United States, seizure disorders affect 3.4 million people.[8] Individuals with a seizure disorder are more likely to die as a result of an accident than nonseizure disorder patients, and a person with a seizure disorder has a 5% chance per year of visiting an emergency department due to a seizure-related injury.[9,10] One study showed that among 344 patients who reported seizures in past 12 months, 24% had a reported head injury, 16% suffered from burn or scald injury, 10% from dental injury, and 6% sustained fractures,[9] and those with a seizure disorder also had a higher frequency of burns than the general population (6.9% vs 3.9%).[11]

It is well established that people with seizure disorders have more hospital admissions than the general population[12] and whether the hospitalization is specific to seizure disorders alone or the associated injuries is not well delineated. Furthermore, it is still unclear as to whether injured patients with seizure disorders have increased hospital stays with the associated cost.

In this regard, we sought to characterize the effect of pre-existing seizure disorders (PSD) in burn-injured patients and burn outcomes, specifically intensive care unit and hospital length of stay (LOS) in addition to burn mortality.

METHODS

This is a retrospective study of all burn patients admitted to the University of North Carolina Jaycee Burn Center from 2002 to 2012. The North Carolina Jaycee Burn Center at UNC was established in 1981 and averages more than 1200 acute admissions per year. The burn center is a single-unit, 36-bed facility that has been verified by the American Burn Association for pediatric and adult care.

The medical records of subjects identified by the UNC Burn database query were reviewed to verify baseline demographic data, injury characteristics, and provide detailed information on medical comorbidities. Pre-existing comorbidities, especially seizure disorders were obtained from medical records and recorded into the burn registry. This information is reported from patient, family, or others that intimately know the patient's history upon admission to the burn center. Injury characteristics of interest included burn etiology, %TBSA burn, presence of inhalation injury, and intubation status on admission to the burn center. Inhalation injury diagnosis was based on history, physical examination, and/or bronchoscopic examination.

Patient characteristics included demographics (sex, age, race), % total body surface area burned (TBSA), burn mechanism (Scald vs Flame), presence of inhalation injury, and

Department of Surgery, University of North Carolina at Chapel Hill, North Carolina Jaycee Burn Center

Funding: This work was supported by the National Institute of Health under award number: 5T32GM008450-23. Research reported in this manuscript was supported by the National Institute of Health under award NIH Grant #5T32GM008450-23.

Conflict of Interest: The authors have no conflict of interest.

Address correspondence to Anthony Charles MD, MPH, Department of Surgery, UNC School of Medicine, 4008 Burnett Womack Building, CB 7228, Chapel Hill, North Carolina. Email: anthchar@med.unc.edu

doi:10.1093/jbcr/irz141

Charlson comorbidity index (CCI). Baseline patient and injury characteristics were compared between groups (PSD/NSD) using Analysis of Variance for continuous variables and chi-squared for discrete variables. We employed both univariate and multivariate models to determine the relative influence of PSD after controlling for covariates. To estimate the odds of mortality and odds of increased ICU and Hospital LOS, we used a multivariate logistic regression model controlling for pertinent confounders (age, TBSA, mechanism of injury, presence of inhalation injury, comorbidities using CCI, and PSD status).

All statistical analyses were performed using the Stata IC/15.0 (StataCorp LP, College Station, TX). In all cases, a *P*-value <.05 was considered statistically significant. University of North Carolina Institutional Review Board approved this study.

RESULTS

Seven thousand six hundred and forty adult and pediatric patients were included in the analysis. Sixty-nine percent (n = 5,252) of patient population were male. Mean age was 32 ± 22.4 years. Both flame and scald burns occurred with similar frequency at 46% (n = 3453) and 49% (n = 3678), respectively. Only 7.6% (n = 579) of the patient cohort had evidence of inhalation injury. Overall, mean CCI (mCCI) was 0.38 ± 1. Twenty percent of burn patients had at least one comorbidity. Mean %TBSA of burn was 8.6 ± 12%, with men having a higher surface area of burns (n = 5244) and average TBSA of 9.0, compared to women at 7.7 (n = 2396). Overall survival was 96%, with no difference between male and female survival, 96.4% (n = 5033) and 96% (n = 2251), respectively. Median hospital and ICU LOS was 5 (interquartile range [IQR]: 2 to 11) and 0 (0 to 1) days, respectively (Table 1).

Bivariate analysis was performed to compare patients with PSD to patients with no history of PSD (NSD). Of the population of analyzed, 1.31% (n = 100) had a PSD. Mean age for PSD vs NSD was 46.5 ± 17.1 and 32 ± 22.4, respectively (P < .001). There was no statistically significant difference between the two groups in mean TBSA, race, mechanism for burn injury, inhalation injury, mortality, and median ICU LOS. Although PSD patient had an unadjusted 7% increase in mortality compared to 3.8% in NSD population, the difference was not statistically significant. PSD patients had a higher mean CCI score of 0.71 ± 1.3 compared with NSD patients at 0.38 ± 1.0, P < .002. Males were most affected in patients with PSD vs NSD, P < .001 and minorities had a higher crude incidence of seizures, although the difference was not statistically significant, P = .314. Median hospital LOS was higher in patients with a PSD, 11 days (IQR: 6 to 23), P < .001. There was no difference in median ICU LOS between the two groups or days on mechanical ventilation (Table 1).

Multivariate logistic regression comparing PSD vs NSD patients, after controlling for significant covariates, showed that PSD patients had an almost 3-fold increase in hospital LOS (odds ratio [OR] = 2.85, 95% confidence interval [CI] = 1.73 to 4.67) with no statistically significant differences in ICU LOS and mortality, (OR = 1.15, 95% CI = 0.71 to 1.87) and (OR = 2.28, 95% CI = 0.88 to 5.93), respectively (Table 2).

DISCUSSION

Our results indicate that PSD is not an independent predictor for mortality following burn injury. However, significant increases in hospital LOS in burn patients with PSD were found.

The lack of difference in mortality is not entirely surprising as Boschini et al discovered looking at the role of seizure disorders in a resource poor setting. This is in line with the determinant of mortality in burn patients, which is still dependent of %TBSA, age, and the presence of inhalation

Table 1. Characteristics of burn patients with and without seizure disorder

	All Burns (%) (n = 7640)	Seizure (%) (n = 100)	No Seizure (%) (n = 7540)	P
Mean age, y (SD)	32 (±22.4)	46.5 (±17.1)	32 (±22.4)	<.001
% Mean TBSA (SD)	8.6 (±12)	6.75 (±7.9)	8.6 (±12)	.129
Mean CCI (SD)	0.38 (± 1.0)	0.71 (±1.3)	0.38 (±1.0)	.002
Sex				<.001
Male	5252 (69)	54 (54)	5252 (69)	
Female	2388 (31)	46 (46)	2388 (31)	
Race				.314
White	3895 (51)	44 (44)	3839 (51)	
Non-White	3742 (49)	56 (56)	3698 (49)	
Etiology				.250
Flame/Fire	3453 (46)	36 (37)	3417 (46)	
Scald	3678 (49)	58 (59)	3629 (48)	
Other	450 (6)	4 (4)	446 (6)	
Inhalation injury	579 (7.6)	12 (12)	567 (7.5)	.094
Mortality rate	366 (4)	7 (7)	282 (3.8)	.094
Median ICU LOS (IQR)	0 (0–1)	0 (0–2)	0 (0–1)	.202
Median Hospital LOS (IQR)	5 (2–13)	11 (6–23)	5 (2–13)	<.001

CCI, Charlson comorbidity index; *ICU LOS*, intensive care unit length of stay; *TBSA*, total body surface area.

Table 2. Odds of mortality, hospital and ICU LOS in burn seizure patients*

Variables	Adjusted odds ratio, 95% confidence interval	*P*
Mortality	2.28 (0.88–5.93)	.091
Hospital LOS	2.85 (1.73–4.67)	<.001
ICU LOS	1.15 (0.71–1.87)	.563

ICU LOS, intensive care unit length of stay; *TBSA*, total body surface area.
*Controlling for age, %TBSA, mechanism of injury, CCI, and inhalation injury.

injury.[13] Furthermore, seizure disorder was not an important comorbidity in the CCI as it was not included.

Reasons for increased LOS are multifactorial. Delayed presentation is a predicting factor of increased hospital LOS. In one study assessing the management outcome in burn injuries in Tanzania, they found that late presentation following burn injury led to increased hospital LOS and mortality.[14] Patients presented due to burn wound infection and sepsis, which required longer hospital stays.[14] In our study, eight patients presented late following burn injury with average delayed presentation of 8.6 days with average hospital LOS stay of 9.95 days.

Noncompliance to seizure medications is another factor that increases hospital LOS. In our study, 28% of PSD patients were noncompliant with antiepileptic medications. Noncompliance was documented as due to recent dose changes, insurance or fiscal limitations, or forgetfulness. Patients who are noncompliant with their seizure medications have longer hospital stays and repeated emergency department and physician office visits.[15] Davis et al showed that nonadherence with antiepileptic drugs was associated with an 11% increased likelihood of inpatient hospitalization and a 48% increase in emergency room admissions.[16]

Degree or depth of burn injury is a third factor that increases hospital LOS. In our seizure patients, 10% suffered third-degree burns, and 95% underwent some type of surgical debridement for burns ranging from superficial to third degree. The complexity in burn management may account for the initial hospital admission and eventual prolong hospital LOS due to the need for surgical debridement and burn care. Rimmer et al in their retrospective study, showed that 72% of burns in epileptic patients were full-thickness burns, compared to 68% of the general population.[17] Another study assessing large volume small TBSA full-thickness burns at a regional hospital in South Africa found that PSD patients had prolonged hospital stay due to the need for and delay in surgical treatment.[18]

The reoccurrence of seizures in patients with PSD while admitted for burn care may also explain increases in hospital LOS. One study assessing the frequency of seizures in hospitalized patients with PSD showed that 5.4% of their patient group experienced inpatient seizures while hospitalized.[19] Inpatient seizures often required further workup for diagnosis and management depending on the seizure type and characteristics.[20] In our study, 10% of seizures reoccurred which led to required inpatient EEG monitoring to determine type of seizure and to guide management in some patients. In a clinical review evaluating the utility of a seizure care pathway to improve therapeutic guidance and minimizing LOS, researchers found that patients who had EEG performed waited a median of 5 days which contributed significantly to increase LOS.[20]

In patients with seizure disorder, comorbid conditions are more common, and patients are often hospitalized for unrelated illnesses compared to the general population,[21] which could account for the increase in hospital and ICU LOS. The CCI was higher in our PSD cohort. Bone health and fractures due to chronic antiepileptic medication use, stroke, depression, migraine, and ADHD are common seizure disorder comorbid conditions.[22] A large percentage of individuals with seizure disorders have at least one medical and psychiatric comorbidity, respectively.[22] Comorbidities influence hospital LOS, surgical outcomes, and development of complications and functional status.[23]

Factors that increase hospital LOS have direct influence on medical costs. In 2016, there were 35.7 million hospital stays in the United States, and the cost of these stays was over $417 billion with a mean cost per stay of $11,700.[24] A systematic review of individuals with seizure disorders showed a total direct healthcare costs that ranged from $10,192 to $47,862 with a lifetime cost of 11.1 billion.[25,26] Seizure disorder patients experience higher out of pocket costs and productivity losses compared to nonseizure disorder patients.

LIMITATIONS

The limitations of this study are those inherent to any study with a retrospective methodology. In addition, we could not confirm whether the burn injury was seizure related in all cases. Furthermore, we do not have serum levels for the antiseizure medications for the patients to help determine if seizures were the proximate cause of the burn injury. We also could not capture hospital acquired infections in the database that may be the cause of prolonged hospital LOS. In addition, as a burn center, we could not capture all seizure-related burns that were managed by smaller units or as outpatients or those that died prior to presentation to the hospital.

CONCLUSION

Burn injury can contribute to the larger costs already incurred by patients with seizure disorders. As part of a larger burn and injury prevention strategy, seizure management with pharmacotherapy is imperative. Furthermore, within a burn unit, it is important to check the serum levels of seizure medication as appropriate to ensure that therapeutic drug levels are achieved early in the hospital course. In addition, neurology consults to help in management may be initiated. Failure of appropriate management of seizure disorders within a burn unit will increase the cost of care.

REFERENCES

1. WHO | The global burden of disease: 2004 update [Internet]. [cited 28 Apr. 2019]; available from: https://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/
2. Burns [Internet]. [cited 28 Apr. 2019]; available from: https://www.who.int/news-room/fact-sheets/detail/burns

3. Burn Incidence Fact Sheet – American Burn Association [Internet]. [cited 28 Apr. 2019]; available from: https://ameriburn.org/who-we-are/media/burn-incidence-fact-sheet/
4. Edelman LS. Social and economic factors associated with the risk of burn injury. Burns 2007;33:958–65.
5. Park JO, Shin SD, Kim J, Song KJ, Peck MD. Association between socioeconomic status and burn injury severity. Burns 2009;35:482–90.
6. Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders? Neurology 2007;68:326–37.
7. Institute of Medicine (US) Committee on the Public Health Dimensions of the Epilepsies. Epilepsy Across the Spectrum: Promoting Health and Understanding. Washington (DC): National Academies Press (US); 2012.
8. Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy - United States, 2015. MMWR Morb Mortal Wkly Rep 2017;66:821–5.
9. Buck D, Baker GA, Jacoby A, Smith DF, Chadwick DW. Patients' experiences of injury as a result of epilepsy. Epilepsia 1997;38:439–44.
10. Spitz MC. Injuries and death as a consequence of seizures in people with epilepsy. Epilepsia 1998;39:904–7.
11. Téllez-Zenteno JF, Hunter G, Wiebe S. Injuries in people with self-reported epilepsy: a population-based study. Epilepsia 2008;49:954–61.
12. Aldenkamp A, Arends J. The relative influence of epileptic EEG discharges, short nonconvulsive seizures, and type of epilepsy on cognitive function. Epilepsia 2004;45:54–63.
13. Boschini LP, Tyson AF, Samuel JC et al. The role of seizure disorders in burn injury and outcome in Sub-Saharan Africa. J Burn Care Res 2014;35:e406–12.
14. Chalya PL, Mabula JB, Dass RM et al. Pattern of childhood burn injuries and their management outcome at Bugando Medical Centre in Northwestern Tanzania. BMC Res Notes 2011;4:485.
15. Hovinga CA, Asato MR, Manjunath R et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: survey of patients with epilepsy and physicians. Epilepsy Behav 2008;13:316–22.
16. Davis KL, Candrilli SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. Epilepsia 2008;49:446–54.
17. Rimmer RB, Bay RC, Foster KN et al. Thermal injury in patients with seizure disorders: an opportunity for prevention. J Burn Care Res 2007;28:318–23.
18. Allorto NL, Oosthuizen GV, Clarke DL, Muckart DJ. The spectrum and outcome of burns at a regional hospital in South Africa. Burns 2009;35:1004–8.
19. Niesen AD, Jacob AK, Brickson JP et al. Occurrence of seizures in hospitalized patients with a pre-existing seizure disorder. Signa Vitae 2012;7:21–8.
20. Iyer PM, McNamara PH, Fitzgerald M et al. A seizure care pathway in the emergency department: preliminary quality and safety improvements. Epilepsy Res Treat 2012;2012:273175.
21. Nguyen R, Téllez Zenteno JF. Injuries in epilepsy: a review of its prevalence, risk factors, type of injuries and prevention. Neurol Int 2009;1:e20.
22. Seidenberg M, Pulsipher DT, Hermann B. Association of epilepsy and comorbid conditions. Future Neurol 2009;4:663–8.
23. Librero J, Peiró S, Ordiñana R. Chronic comorbidity and outcomes of hospital care: length of stay, mortality, and readmission at 30 and 365 days. J Clin Epidemiol 1999;52:171–9.
24. Freeman WJ, Weiss AJ, Heslin KC. Overview of U.S. hospital stays in 2016: variation by geographic region: statistical brief #246. In: Healthcare cost and utilization project (HCUP) statistical briefs. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006.
25. Begley CE, Durgin TL. The direct cost of epilepsy in the United States: a systematic review of estimates. Epilepsia 2015;56:1376–87.
26. Begley CE, Famulari M, Annegers JF et al. The cost of epilepsy in the United States: an estimate from population-based clinical and survey data. Epilepsia 2000;41:342–51.