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Differentiation of psychogenic nonepileptic attacks from status epilepticus among patients intubated for convulsive activity

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ABSTRACT

Background and objective: Patients with psychogenic nonepileptic attacks (PNEA) sometimes receive aggressive treatment leading to intubation. This study aimed to identify patient characteristics that can help differentiate PNEA from status epilepticus (SE).
Methods: We retrospectively identified patients with a final diagnosis of PNEA or SE, who were intubated for emergent convulsive symptoms and underwent continuous electroencephalography (cEEG) between 2012 and 2017. Patients who had acute brain injury or progressive brain disease as the cause of SE were excluded. We compared clinical features and laboratory values between the two groups, and identified risk factors for PNEA-related convulsive activity.
Results: Over a six-year period, 24 of 148 consecutive patients (16%) intubated for convulsive activity had a final diagnosis of PNEA rather than SE. Compared to patients intubated for SE, intubated PNEA patients more likely were <50 years of age, female, white, had a history of a psychiatric disorder, had no history of an intracranial abnormality, and had a maximum systolic blood pressure <140 mm Hg (all $P < 0.001$). Patients with 0–2 of these six risk factors had a 0% (0/88) likelihood of having PNEA, those with 3–4 had a 15% (6/39) chance of having PNEA, and those with 5–6 had an 86% (18/21) chance of having PNEA. Sensitivity for PNEA among those with 5–6 risk factors was 75% (95% CI: 53–89%) and specificity was 98% (95% CI: 93–99%).
Conclusions: In the absence of a clear precipitating brain injury, approximately one in six patients intubated for emergent convulsive symptoms had PNEA rather than SE. Although PNEA cannot be diagnosed only by the presence of these risk factors, these simple characteristics could raise clinical suspicion for PNEA in the appropriate setting. Urgent neurological consultation may prevent unnecessary intubation of this at-risk patient population.

1. Introduction

Psychogenic nonepileptic attacks (PNEA) are defined as paroxysmal movements or abnormal behaviors that resemble epileptic seizures that are not accompanied by epileptiform activity on electroencephalography (EEG), and are caused by psychogenic factors [1,2]. In order to definitely diagnose PNEA, video-continuous EEG (cEEG) is required to confirm that paroxysmal movements or abnormal behaviors are occurring without accompanying epileptiform activity, as no individual clinical signs alone can distinguish PNEA from epileptic seizure [2,3]. Prolonged episodes of PNEA are sometimes mistaken for and inappropriately treated as status epilepticus (SE), leading to aggressive antiepileptic treatment and endotracheal intubation, which can be fatal [4–6]. In most circumstances, these treatments are given to patients in the emergency department (ED) prior to EEG monitoring. In this study, we aimed to identify patient characteristics and clinical features that can help differentiate PNEA from SE.

2. Methods

This study was approved by the Henry Ford Institutional Review Board. As the study was retrospective and posed no significant

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risks, the requirement for written informed consent was waived. The data that support the findings of this study will be made available by the corresponding author upon reasonable request.

2.1. Study population

We retrospectively reviewed our electronic medical record (www.EPIC.com) for all adult patients (age ≥ 18 years) who underwent video-cEEG monitoring at Henry Ford Hospital from January 2012 to October 2017. Patients who had a discharge diagnosis of "nonepileptic" or "psychogenic" seizures or spells, "pseudoseizures," "seizure", or "status epilepticus" were identified. In all cases, the diagnoses of PNEA and status epilepticus were reconfirmed by retrospective chart review. The diagnosis of PNEA was confirmed if the patient had characteristic clinical signs of PNEA witnessed by the attending neurologist during admission, supported by video-cEEG demonstrating no epileptiform activity during convulsive activity when available [2]. The diagnosis of genetic or localization-related epilepsy as the cause of SE was documented by an attending neurologist in all cases, again using video-cEEG to support the diagnosis. Only patients who were intubated due to PNEA or SE in the ED or on the hospital floor were included in the analysis. Patients with multiple intubations for convulsive symptoms during the study period were included, but we analyzed only the first admission. We excluded patients who had an uncertain cause of their convulsive activity (epileptic seizure versus PNEA); patients who had a new diagnosis of acute brain injury or a progressive brain disease as a cause of SE, including acute stroke, traumatic brain injury, central nervous system infection, hypertensive encephalopathy, metabolic encephalopathy, hypoxic ischemic encephalopathy, drug withdrawal or intoxication, or brain tumor; patients who were admitted directly to the epilepsy monitoring unit (EMU) or admitted for titration of antiepileptic drugs or epilepsy surgery; and those who were intubated due to causes other than severe convulsive activity.

2.2. Data collection

Relevant clinical data were abstracted and recorded in a Research Electronic Data Capture (REDCap) database (www.project-redcap.org) [7]. Clinical data that we collected included demographics; diagnosis of epilepsy, and PNEA prior to admission; prior history of psychiatric disorders and remote intracranial abnormalities including ischemic stroke, intracerebral hemorrhage, cerebral aneurysm, cerebral arteriovenous malformation, and traumatic brain injury; prior history of intellectual disability or developmental delay; source of hospital admission; location of convulsive events; duration of convulsive symptoms; clinical signs of epilepsy-related seizures categorized as (a) generalized tonic-clonic seizure (GTC), (b) focal motor seizure with retained awareness, (c) focal motor seizure with impaired awareness or nonconvulsive seizure (subtle or unresponsiveness without prominent motor activity); Glasgow Coma Scale (GCS) score on hospital admission; coma on hospital admission (defined as GCS score ≤ 8); highest and lowest vital signs before intubation, if data for times of intubation and vital sign measurement were available; highest and lowest vital signs on the first day of admission, if data for times of intubation and vital sign measurement were not available; the first laboratory parameters on day 1 of admission; and antiepileptic (AEDs) and continuous infusion antiepileptic (cIV-AEDs) drugs and dosages administered during the index convulsive event. We did not have access to data regarding the use of benzodiazepines or other AEDs in the prehospital setting. Data on benzodiazepines given during the event included only bolus intravenous or intramuscular administration of lorazepam, diazepam, or midazolam. Dosage of benzodiazepines was calculated as diazepam equivalents, with 5 mg of diazepam being equivalent to 1 mg of lorazepam and 2 mg of midazolam (dosage of continuous infusion midazolam was not included) [8,9]. Continuous infusion of midazolam, propofol, pentobarbital, and ketamine was classified as cIV-AEDs.

2.3. Outcome assessment

Outcome assessments included inhospital mortality; GCS at hospital discharge; and intensive care unit (ICU) and hospital length of stay. Inhospital complications included hypotension requiring vasopressors, nosocomial infections, deep vein thrombosis (DVT), arrhythmia, decubitus ulcer, and rhabdomyolysis, defined as creatine phosphokinase ≥1000 IU/L or more than 5 times of upper limit of normal [10]. We also recorded rehospitalization within 30 days of discharge at any EPIC Care Everywhere Network hospital in Southeast Michigan, which includes the 5-hospital Henry Ford Health System.

2.4. Statistical analysis

To identify predictors of PNEA among patients with severe convulsive activity requiring intubation, we compared clinical features, laboratory values, and treatments between patients who were intubated for PNEA as opposed to SE. For practical use, we analyzed only clinical data that can be assessed immediately in the ED before intubation. Continuous data were described using means, standard deviations, medians, and interquartile range as appropriate, while categorical data were described using counts and column percentages. Univariate two-group comparisons were carried out using independent t-tests for normally distributed continuous variables, Mann–Whitney U tests for non-normally distributed continuous variables, Pearson's chi-square tests for categorical variables with expected cell counts >5, and Fisher's exact tests for categorical variables with expected cell counts <5. Odds ratios and 95% confidence intervals (95% CI) for each individual variable were calculated. Multivariable analysis was not performed due to the small sample size. Sensitivity, specificity, and positive and negative predictive values for PNEA depending on the number of risk factors present were calculated. All analyses were performed using PASW Statistics version 18 [11]. Statistical significance was set at $P < 0.05$.

3. Results

Of 1735 patients who underwent cEEG monitoring at Henry Ford Hospital (HFH) between January 2012 and October 2017, 662 patients had a discharge diagnosis of seizure, status epilepticus, or PNEA. Of these, 493 patients had a discharge diagnosis of epilepsy-related seizures or SE, 144 patients had PNEA as a principal diagnosis, and 25 patients with an uncertain diagnosis of convulsive activity were excluded (Fig. 1). Among the 493 patients with a diagnosis of seizure or SE, we excluded 274 patients who either did not have SE, who had acute brain injury as the cause of SE, or who were admitted directly to the EMU or hospital floor for medication adjustment or planned epilepsy surgery. After excluding patients who met exclusion criteria and who did not require intubation, 148 patients were intubated for severe convulsive symptoms: 24 (16%) for PNEA, and 124 (84%) for SE (Fig. 1). Of the 24 patients intubated for PNEA, 17 patients (71%) had the diagnosis confirmed on subsequent video-EEG monitoring (convulsive symptoms without epileptiform activity), whereas 7 patients (29%) were diagnosed based on history and directly observed clinical signs alone.

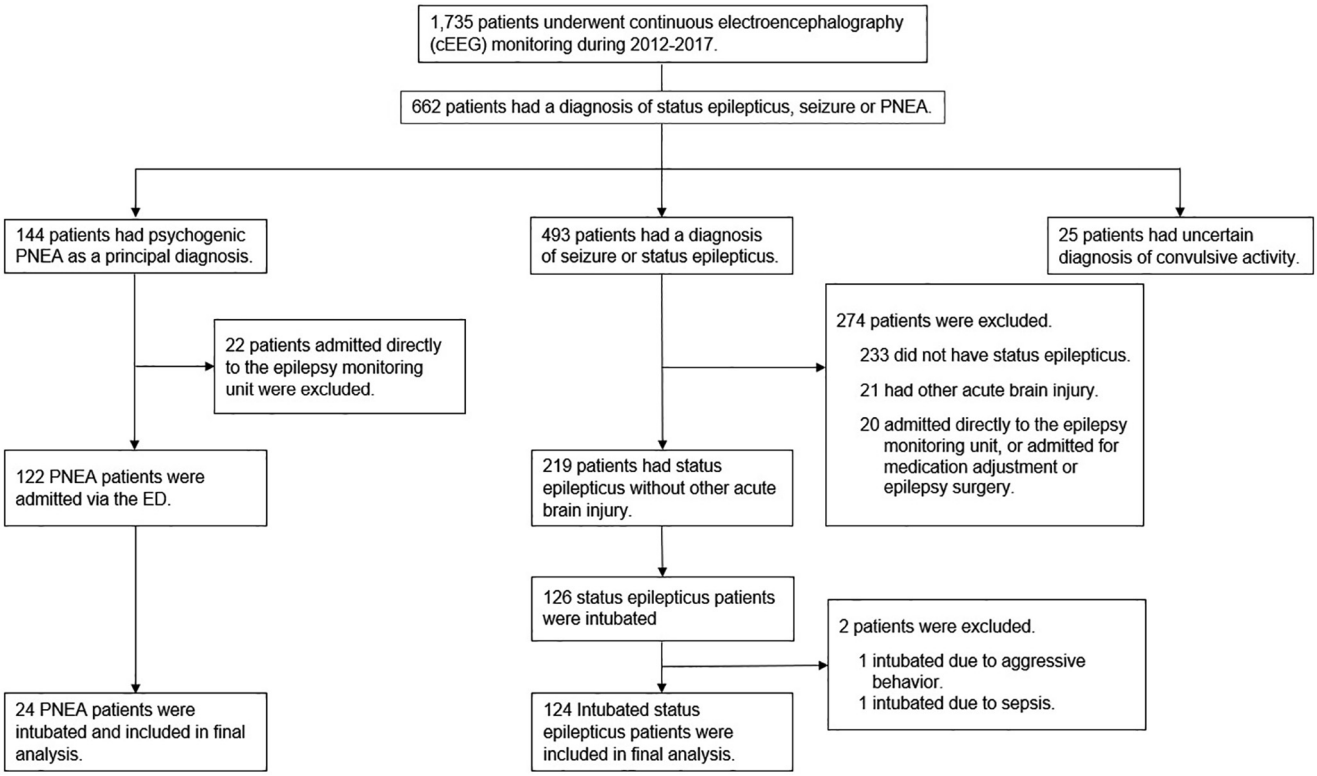

Fig. 1. Study Population.

3.1. Baseline characteristics

Patients who were intubated for PNEA as opposed to SE were younger and more likely to be female and white (Table 1). Prior history of PNEA and psychiatric disorder documented in the medical record were more frequent in those intubated for PNEA, whereas a prior history of intracranial abnormality or epilepsy was more common in patients intubated for SE (Table 1). More patients with PNEA than SE were transferred from an outside hospital, and the majority of intubations (96% and 84% respectively) occurred in the ED. The duration of convulsive symptoms with PNEA was shorter compared with that of SE (20 vs 88 minutes, $P < 0.001$). In patients with SE, 57% had generalized tonic-clonic SE, 13% had focal motor SE with impaired consciousness, 3% had nonconvulsive SE without prominent motor activity, 2% had focal motor SE with retained awareness, and 25% did not have clinical signs of seizure described in the medical record. Among patients with PNEA, 79% had convulsion resembling generalized tonic-clonic seizures, and 21% did not have convulsive symptoms documented. Compared with SE patients, PNEA patients were more likely to have GCS of 15 (71% vs 11%, $P < 0.001$) and less likely to be in coma (GCS score ≤ 8, 8% vs 52%, $P < 0.001$) on hospital admission (Table 1).

3.2. Vital signs and laboratory parameters

Regarding the most extreme vital signs prior to intubation, patients who were intubated for PNEA had significantly lower median maximum and minimum recorded systolic blood pressures compared with those who were intubated for SE (Table 1). Regarding all vital signs on the day of intubation, patients who were intubated for PNEA had lower maximum systolic blood pressure (SBP) and maximum heart rate than those who were intubated for SE (Supplemental Table 1). Other highest and lowest vital signs were not significantly different between the two groups. Patients with PNEA also had lower median CPK levels on day 1 of admission than those with SE (97 vs 265 IU/L, $P < 0.001$) (Table1). Other admission laboratory parameters are reported in Supplementary Table 2; patients with SE had slightly higher blood glucose, serum creatinine, and anion gap values than those with PNEA.

3.3. Antiepileptic treatment

Antiepileptic treatment was not different between the two groups (Supplemental Table 3). The median number of AEDs used during the convulsive event was 2 in both groups; benzodiazepine was the most common AEDs used in both groups (96% and 91% of patients with PNEA and SE, respectively), followed by levetiracetam, phenytoin, lacosamide, sodium valproate, and phenobarbital. Median dosage of benzodiazepine used during the event was 30 mg of diazepam equivalent in both groups. Continuous infusion antiepileptic were used in 52% and 61% of patients with PNEA and SE, respectively; propofol and midazolam are most commonly used cIV-AEDs in both groups (Supplemental Table 3).

3.4. Outcomes

Mortality was 6% in patients intubated for SE, while none of the patients intubated for PNEA died ($P = 0.599$). Compared with patients with PNEA, those who were intubated for SE had longer median ICU (4 vs 2 days, $P < 0.001$) and hospital length of stay (9 vs 3 days, $P < 0.001$), were less likely to have GCS score of 15 at discharge (61% vs 100%, $P < 0.001$), and had more inhospital complications (52% vs 17%, $P = 0.002$), primarily hospital acquired infections (24% vs 4%, $P = 0.027$; Table 2).

Table 1
Patient Characteristics.

Characteristics	Intubated PNEA (*N* = 24)	Intubated SE (*N* = 124)	*P* Value
Demographics			
Age, years	36 [27–42]	54 [42–65]	**<0.001**
Female	19 (79)	48 (39)	**<0.001**
Race			**<0.001**
White	20 (91)	35 (29)	
African-American	1 (5)	82 (69)	
Others	0 (0)	2 (2)	
Comorbid diseases			
Prior history of intracranial abnormality	2 (8)	77 (62)	**<0.001**
Intellectual disability/Developmental delay	0 (0)	11 (9)	0.212
Epilepsy	5 (21)	101 (82)	**<0.001**
PNEA	5 (21)	0	**<0.001**
Psychiatric disorders	21 (88)	31 (25)	**<0.001**
Admission sources			**0.039**
Emergency department	4 (17)	55 (44)	
Transferred from other hospital	20 (83)	69 (56)	
Location of convulsive activity			0.200
ED	23 (96)	104 (84)	
Inhospital	1 (4)	20 (16)	
Generalized convulsive symptoms [a]	19 (79)	70 (57)	**0.037**
Duration of convulsive symptoms, minutes [b]	20 [2–45]	88 [54–181]	**<0.001**
GCS on day 1 of admission	15 [13–15]	8 [6–10]	**<0.001**
Patients with GCS of 15 on admission	17 (71)	13 (11)	**<0.001**
Coma (GCS ≤ 8) on admission	2 (8)	64 (52)	**<0.001**
Vital signs documented before intubation			
Maximum temperature, °C [c]	36.6 [36.4–37.0]	36.9 [36.6–37.5]	0.054
Minimum temperature, °C [c]	36.6 [36.4–37.0]	36.8 [36.5–37.2]	0.203
Maximum SBP, mmHg [d]	127 [108–140]	169 [148–206]	**<0.001**
Minimum SBP, mmHg [d]	100 [97–102]	132 [107–149]	**<0.001**
Maximum DBP, mmHg [d]	82 [73–100]	93 [79–112]	0.143
Minimum DBP, mmHg [d]	64 [58–69]	78 [67–91]	**0.014**
Maximum heart rate, beats per minute [e]	110 [98–121]	125 [107–143]	0.061
Minimum heart rate, beats per minute [e]	93 [74–102]	97 [74–114]	0.442
Maximum respiratory rate, per minute [f]	24 [20–30]	24 [20–31]	0.805
Minimum respiratory rate, per minute [f]	15 [12–19]	17 [14–20]	0.378
Maximum SpO2, % [g]	99 [98–100]	100 [98–100]	0.322
Minimum SpO2, % [g]	94 [89–99]	96 [94–99]	0.447
Laboratory parameters on admission [h]			
CPK, IU/L	97 [67–164]	265 [115–607]	**<0.001**
CPK more than 250 IU/L	3 (18)	38 (54)	**0.008**

Data are *n* (% of total available data within each column) or median [IQR].
P values in bold are statistically significant ($P < 0.05$).
PNEA = psychogenic nonepileptic attacks; SE = status epilepticus; EEG = electroencephalogram; ED = emergency department; GTC = generalized tonic clonic seizure; GCS = Glasgow Coma Scale; SBP = Systolic Blood pressure; DBP = Diastolic Blood Pressure; SpO2 = peripheral oxygen saturation; CPK = Creatine Phosphokinase.
[a] Data on clinical signs of convulsive activity were not documented in 5 (21%) patients with intubated PNEA and 31 (25%) patients with intubated status epilepticus.
[b] Data are available for 65 patients (7 with intubated PNEA and 58 with intubated status epilepticus).
[c] Data are available for 82 patients (7 with intubated PNEA and 75 with intubated status epilepticus).
[d] Data are available for 93 patients (11 with intubated PNEA and 82 with intubated status epilepticus).
[e] Data are available for 94 patients (12 with intubated PNEA and 82 with intubated status epilepticus).
[f] Data are available for 89 patients (12 with intubated PNEA and 77 with intubated status epilepticus).
[g] Data are available for 93 patients (12 with intubated PNEA and 81 with intubated status epilepticus).
[h] Data are available for 88 patients (17 with intubated PNEA with and 71 intubated status epilepticus).

3.5. Risk factors for PNEA-related convulsive activity

Risk factors for PNEA that can be assessed immediately before intubation included age < 50 years, female gender, white race, presence of psychiatric disorder, absence of prior intracranial abnormality, and maximum SBP < 140 mmHg (Table 3). The cutoff of <50 years of age was used because this value is close to the median of the SE group, and the SBP cutoff of <140 mmHg was used because this value is close to the 75% percentile in the PNEA group and the 25th percentile in the SE group. Odds ratios for risk factors for PNEA based on these variables are reported in Table 3. Patients with 0–2 of these risk factors had a 0% (0/88) likelihood of having PNEA, those with 3–4 had a 15% (6/39) chance of having PNEA, and those with 5–6 had an 86% (18/21) chance of having PNEA (Table 4). Sensitivity for PNEA among those with 5–6 risk factors was 75.0% (95% CI, 53.0%–89.4%), specificity was 97.6% (95% CI 92.6%–99.4%), positive predictive value was 85.7% (95% CI 62.6%–96.2%), and negative predictive value was 95.3% (95% CI 89.6%–98.1%; Table 4).

4. Discussion

Intubation for PNEA-related convulsive activity is associated with an increased risk of medical complications, prolonged hospital stay, and a high rate of readmission within 30 days [12]. In this single-center study we found over a period of over six years that 16% of patients who were intubated for severe convulsive

Table 2
Outcomes.

Outcome	Intubated PNEA (*N* = 24)	Intubated SE (*N* = 124)	*P* Value
Mortality	0 (0)	7 (6)	0.599
ICU length of stay, days	2 [1–2]	4 [2–10]	**<0.001**
Hospital length of stay, days	3 [2–4]	9 [5–17]	**<0.001**
GCS of 15 at discharge	24 (100)	71 (61)	**<0.001**
Inhospital complications	4 (17)	64 (52)	**0.002**
Hypotension requiring vasopressor	2 (8)	27 (22)	0.166
Hospital acquired infections	1 (4)	30 (24)	**0.027**
HAP/VAP	1 (4)	17 (14)	0.308
Urinary tract infection	0	10 (8)	0.367
Catheter-related bloodstream infection	0	3 (2)	>0.999
Other infection	0	5 (4)	>0.999
Deep vein thrombosis	1 (4)	9 (7)	>0.999
Arrhythmia	0	6 (5)	0.590
Decubitus ulcer	0	2 (2)	>0.999
Rhabdomyolysis	0	13 (11)	0.128
Rehospitalization within 30 days	4 (17)	16 (13)	0.744

Data are *n* (% of total available data within each column) or median [IQR].
P values in bold are statistically significant ($P < 0.05$).
PNEA = psychogenic nonepileptic attacks; SE = status epilepticus; HAP = hospital acquired pneumonia; VAP = ventilator associated pneumonia; GCS = Glasgow Coma Scale.

symptoms (primarily in the ED) had PNEA rather than SE. Age < 50 years, female gender, white race, history of a psychiatric disorder, absence of prior intracranial abnormality, and maximum SBP < 140 mm Hg identify patients with convulsive symptoms resulting from PNEA rather than SE. Patients with convulsive symptoms who had 5 or 6 of these risk factors have an 86% likelihood of having PNEA, with 75% sensitivity and 98% specificity. Although PNEA cannot be diagnosed based solely on the presence of these clinical characteristics, when these risk factors are recognized in patients presenting with convulsive activity, together with appropriate clinical suspicion, clinicians can consider emergent neurological consultation and rapid-response EEG before proceeding with intubation.

The 16% incidence of PNEA among patients intubated for severe convulsive symptoms is comparable with that of patients admitted for inpatient video-EEG monitoring for suspected epilepsy (15–32%) [13,14]. The predominance of younger female patients among those intubated for PNEA in our study is similar to the demographics of PNEA in general, in most [15–18], but not all studies [19]. Although racial disparities have been reported in epilepsy care related to surgical access and medication adherence [20,21], to our knowledge white race has not previously been identified as a risk factor for PNEA. In a study of 80 consecutive PNEA admissions at HFH during the same time period as the present study, 15% were intubated, and white race was over-represented in this group as well [12]. Other risk factors for intubation among hospitalized PNEA patients included prolonged duration of convulsive symptoms, depressed level of consciousness, and overly aggressive treatment with benzodiazepines [12].

Table 4
Observed PNEA Risk based on Number of Risk Factors.

Number of risk factors	Total patients, *n* (%)	PNEA, *n*	PNEA risk, %
0	17 (11.5)	0	0.0
1	40 (27.0)	0	0.0
2	31 (20.9)	0	0.0
3	24 (16.2)	2	8.3
4	15 (10.1)	4	26.7
5	16 (10.8)	14	87.5
6	5 (3.4)	4	80.0

For patients with 5–6 risk factors, sensitivity for PNEA was 75.0% (95% CI, 53.0%–89.4%), specificity was 97.6% (95% CI 92.6%–99.4%), positive predictive value was 85.7% (95% CI 62.6%–96.2%), and negative predictive value was 95.3% (95% CI 89.6%–98.1%).

A prior history of psychiatric illness was identified as a risk factor for PNEA among intubated patients with convulsive activity, which parallels the high frequency of mental health disorders among PNEA patients in general [19,22–24]. Chronic intracranial abnormalities (such as stroke or traumatic brain injury) consistent with localization-related epilepsy identified patients in our study who were more likely to have SE than PNEA. Of the vital sign data that we recorded, lower maximum SBP prior to intubation best differentiated PNEA from SE (Table 1); similar trends in DBP and heart rate were also observed (Table 1 and Supplemental Table 1). Increases in blood pressure and heart rate in patients with SE are well-known to be caused by sympathetic hyperactivity and surges in catecholamine levels [25–27]. Increases in SBP also occur during episodes of PNEA [28,29], but our findings indicate that the magnitude of this hypertensive response is not as extreme as that seen in SE. Seventy-five percent of PNEA patients had a maximal SBP prior to intubation below the cut-point of <140 mm Hg, whereas 75% of SE patients had a maximal SBP above this value.

Elevated serum creatine phosphokinase (CPK), a result of myocyte breakdown and rhabdomyolysis, is a common systemic complication of convulsive SE [30]. A prior study comparing 9 patients with prolonged episodes of PNEA and 10 patients with refractory generalized convulsive SE also found that CPK was lower in patients with PNEA than in those with SE, consistent with our finding [31].

Most episodes of PNEA in our study lasted longer than 5 minutes, resembling not a brief epileptic seizure, but status epilepticus, which requires aggressive treatment that can lead to complications. While the frequency of inhospital complications was lower in PNEA than in SE patients, 17% had complications possibly

Table 3
Odds Ratios for Risk Factors for PNEA-Related Convulsive Activity.

Risk Factor[a]	Intubated PNEA (*N* = 24)	Intubated SE (*N* = 124)	Odds ratio (95%CI)	*P* Value
Age < 50 years	22 (92)	49 (40)	16.8 (3.8–74.8)	<0.001
Female	19 (79)	48 (39)	6.0 (2.1–17.2)	<0.001
White [b]	20 (91)	35 (29)	24.0 (5.3–108.2)	<0.001
Prior history of psychiatric disorders	21 (88)	31 (25)	21.0 (5.9–75.2)	<0.001
Absence of prior intracranial abnormality	22 (92)	47 (38)	18.0 (4.1–80.1)	<0.001
Maximum SBP < 140 mmHg [c]	12 (67)	18 (16)	10.6 (3.5–31.8)	<0.001

Data are *n* (% of total available data within each column).
PNEA = psychogenic nonepileptic attacks; SE = status epilepticus; SBP = systolic blood pressure; GCS = Glasgow Coma Scale; CPK = Creatine phosphokinase.
[a] Only factors that can be assessed immediately before intubation were included.
[b] Data are available for 22 of 24 intubated PNEA and 119 of 124 intubated status epilepticus patients.
[c] Data are available for 18 of 24 intubated PNEA and 113 of 124 intubated status epilepticus patients.

related to unnecessary intubation including hypotension requiring vasopressors, nosocomial infections, and deep vein thrombosis (Table 2). This finding supports the result of a prior study showing that prolonged episodes of PNEA are associated with a higher healthcare utilization and costs [32], and emphasizes the importance of early diagnosis of PNEA. Although some semiological features may help distinguish PNEA from SE, no single clinical sign can be relied on as a perfect diagnostic discriminator [2,3]. The clinical diagnosis of PNEA requires that the events be observed by an experienced neurologist in conjunction with evaluation of the overall clinical picture [3,33]. Since our goal was to identify features that can be quickly and easily assessed by non-neurologists, we did not include clinical motor phenomena as predictive factors.

To date, literature regarding the differentiation of convulsive PNEA from SE in the emergency setting is limited. In this study, we identified risk factors that can be readily assessed shortly after ED arrival that may help identify patients with a high likelihood of PNEA among those presenting with emergent convulsive symptoms. Though longer duration of convulsive activity, lower admission GCS score, and higher serum CPK also helped to differentiate SE from PNEA, these data were typically recorded after intubation in the medical record. However, a normal GCS score and CPK level can help identify possible PNEA patients among those who have already been intubated. A prior history of PNEA or epilepsy may also help differentiate PNEA from SE, but these diagnoses frequently coexist: approximately 20% of patients with PNEA in our study also had a prior history of epilepsy.

GCS scores in our study were obtained on hospital admission, not ED arrival, primarily because the GCS is difficult to assess in the presence of ongoing convulsive activity. Many more patients intubated for PNEA had a normal GCS score of 15 on hospital admission than did those intubated for status epilepticus (71% vs 11%, Table 1). This might be explained by the fact that postictal alterations of consciousness did not occur in the patients who had PNEA-related convulsive activity, unlike those who had status epilepticus.

A strength of this study includes the fact that we selected patients from a cEEG database and only included patients whose diagnoses were confirmed by an attending neurologist; we did not include convulsive events with uncertain diagnosis. Our study also has limitations. First, we studied patients admitted to a single tertiary referral center in the Midwest United States, which may limit generalizability. In particular, the over-representation of white race among PNEA patients may be unique to this region. Second, we cannot be certain that all convulsive symptoms in the ED were nonepileptic among those with a final diagnosis of PNEA, since 21% had a concurrent diagnosis of epilepsy, and 29% did not experience convulsive symptoms on video-EEG, with the diagnosis based on history and clinical signs alone. Third, since we only analyzed patients who underwent video-cEEG, we may have excluded some patients intubated for convulsive symptoms during the 6-year study period who did not undergo monitoring. Fourth, vital sign data documented before intubation were unavailable in some cases because the precise times of intubation and vital sign measurement were not available, since many of our patients were transferred from referring hospitals. For this reason, we also analyzed highest and lowest vital sign data on the entire first day of admission. Finally, although the number of positive risk factors indicating the probability of PNEA may be helpful in clinical practice, the probabilities are based on small numbers of patients. Because of the small sample size, the 95% CI for odds ratios of those risk factors are wide, and we could not perform multivariable analysis to identify independent predictors of PNEA. Prospective validation is needed to determine if the PNEA risk factors that we have identified are broadly applicable across populations.

In conclusion, PNEA in patients presenting with emergent convulsive symptoms is not uncommon and can be predicted with a high degree of certainty based on the presence of specific demographic, past medical, and physiologic risk factors that can be assessed prior to making the decision to intubate. In addition to clinical judgement, these risk factors could raise clinical suspicion for PNEA. Since the outcome of convulsive PNEA is typically benign and complications are increased with intubation [12], we recommend urgent neurological evaluation of at-risk patients and generation of a management plan that avoids over-sedation and unnecessary intubation if at all possible.

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Conflict of interest disclosures

S.A.M. has received consulting fees from UCB Pharma. No other disclosures were reported.

Ethics approval

This study was approved by the Henry Ford Institutional Review Board (IRB No. 11654).

Consent to participate

As the study was retrospective and posed no significant risks, the requirement for written informed consent was waived.

Consent for publication

This manuscript complies with all instructions for authors. All authors have met authorship requirements and approved the submitted manuscript. This manuscript has not been published elsewhere and is not under consideration by another journal. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed.

Availability of data and material

The data that support the findings of this study will be made available by the corresponding author upon reasonable request.

Authors' contributions

TV had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of data analysis, performed data collection, analysis and interpretation, drafted and revised the manuscript. NP performed data collection, analysis and interpretation, assisted in drafting and revised the manuscript. GO, RGK, JM, and GB assisted in data interpretation and critically reviewed the manuscript. SAM designed the study and data analysis, performed data review and interpretation, drafted and revised the manuscript. All authors have read and approved the final manuscript, and agree to be accountable for all aspects of the work. TV takes responsibility for the paper as a whole.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2020.107679.

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