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Risk assessment of in-hospital mortality of patients with epilepsy: A large cohort study

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ABSTRACT

Purpose: This study aimed to explore the mortality risks of hospitalized patients with epilepsy (PWE).
Methods: Our data source was extracted from discharge abstracts in a hospital medical database. Various clinical variables, including demographical characteristics, natural features of epilepsy, and comprehensive set of comorbidities, were screened to investigate the risk. Comorbidities were defined using a validated ICD-10-based classification. The distributions of comorbid conditions and demographics were presented. In-hospital mortality rates of groups with epilepsy and without epilepsy were compared. Logistic regression was applied to explore the important predictors of in-hospital mortality.
Results: A cohort of 11,422 PWE (male: 58.5%, mean age: 40.2 years) was recruited for the study. The most common comorbidities were cerebrovascular disease, hypertension, and peripheral vascular disease, which accounted for 23.5%, 18.8%, and 8.0% of the study cohort, respectively. In-hospital mortality rates were 2.9% and 1.1% in the epilepsy and nonepilepsy cohort, respectively. Male patients exhibited an increased risk of death (odds ratio (OR) = 1.2; 95% confidence interval (CI) = 1.0–1.6). Patients aged over 65 years were more likely to die than those below 18 years (OR = 18.2; 95% CI = 8.8–31.0). Patients with comorbidities, including central nervous system (CNS) infections, renal disease, traumatic brain and head injuries, anoxic brain injury, metastatic cancer, pulmonary circulation disorders, encephalopathy, solid tumor without metastasis, cardiac arrhythmias, and diabetes without complication, had a higher risk of in-hospital death than patients without comorbidities (OR = 6.1, 5.2, 5.1, 4.4, 3.7, 2.5, 2.4, 2.0, 1.5, 1.4, respectively; 95% CI = 4.1–9.1, 3.8–7.0, 2.8–9.5, 2.4–8.3, 2.2–6.3, 1.5–4.3, 1.4–4.2, 1.1–3.7, 1.1–2.1, 1.0–1.9, respectively).
Conclusion: The in-hospital mortality of PWE increased remarkably with age, and this parameter was predominant in male patients. Central nervous system infection, renal disease, traumatic brain and head injuries, anoxic brain injury, metastatic cancer, pulmonary circulation disorders, encephalopathy, solid tumor without metastasis, cardiac arrhythmias, and diabetes without complication were the most important comorbidities associated with in-hospital death.

1. Introduction

Epilepsy, a spectrum disorder, is a common chronic neurological disorder affecting more than 70 million people worldwide [1]. Epidemiologic findings confirm that people with epilepsy (PWE) are at a higher risk of morbidity and mortality than the general population [2]. Mortality is the most severe consequence among PWE. As a considerable public health problem, epilepsy-related death, particularly sudden unexpected death in epilepsy, has been extensively studied [3]. In previous studies on mortality risk, the demographic information and nature of epilepsy are commonly involved. However, few studies cover a broad range of comorbidities in assessing the risk of death. The reported rates of at least one medical comorbidity range from 26.8% to 84%, which are higher than those of psychiatric comorbidity from 5.9% to 64.1% in PWE [4]. Considering the high prevalence of comorbidity in epilepsy, we should examine many underlying risk factors, including demographical, clinical characteristics, and broad range of comorbidities, to explore the risk of death in PWE. After Quan's ICD-10 coding algorithms for comorbidity, which were developed on the basis of the Charlson and Elixhauser comorbidity index [5], were introduced, almost all organ system comorbidities can be categorized well. Consequently, two studies on mortality-related comorbidity successfully used Quan's index to estimate the prognostic survival rates in public administrative and clinical cohorts [6,7].

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The present study aimed to identify the risks of in-hospital death in epilepsy in a large hospitalized cohort. To enhance the understanding of risks, we included a comprehensive spectrum of medical comorbidities. In general, highlighting the key risk factors of in-hospital mortality leads to early prognostic prediction and helps formulate treatment strategies for improved epilepsy management in hospitals.

2. Methods

2.1. Study population and data collection

The Institutional Ethics Committee of Sichuan Academy of Medical Sciences and Sichuan Provincial People's Hospital provided ethical approval for data use.

The study population was formed by inpatients who were admitted to Sichuan Provincial People's Hospital, which is one of the largest tertiary hospitals in Chengdu, China, with 3277 beds for clinical use, from January 1, 2007 to July 31, 2017. The patients were from different medical departments except outpatient clinic divisions. Patients discharged to another institution or discharged against medical advice were excluded. All inpatients from different age groups who were confirmed with epilepsy were recruited. The administrative data were validated sufficient for reasonably and accurately identifying patients who have ever had epilepsy [8]. The ICD-10 CA codes G40–G41 were utilized to find epilepsy in the diagnosis field of the discharge abstract record. A complementary text-based retrieval was used to include missed epilepsy cases when necessary. Those with seizures/status epilepticus (SE) without an established epilepsy diagnosis and those with reflex epilepsy were excluded. First discharge records were used to collect information regarding patients with multiple admissions.

Before screening and data extraction were performed, the diagnostic accuracy of the discharge abstracts was assessed. In brief, we selected all patients with epilepsies and conditions resembling seizures (e.g., migraine, transient cerebral ischemia, syncope, psychogenic seizures, and acute anxiety attack) in the fiscal year 2012 (January to March) and divided them into two groups (286 patients with epilepsy and 548 inpatients with conditions resembling seizures). We then chose 30% of the 286 patients with epilepsy and 15% of the 548 inpatients with conditions resembling seizures to set up the candidates for diagnostic accuracy estimation. The epilepsy diagnostic criteria were based on the 1981 or 2005 classifications [9,10]. Two experts on epilepsy were involved in independently reading all the medical charts and reviewing all notes, including physician history, physical examination, laboratory tests, imaging reports (if available), and other pertinent investigations. Later, the two reviewers reached a consensus and indicated the presence or absence/suspected (suspected epilepsy refers to those not fully satisfying the diagnostic criteria of epilepsy) of epilepsy. Finally, a sensitivity of 91.7% (95% CI: 83.0%–96.3%), a specificity of 94.0% (95% CI: 86.0%–97.8%), a positive predictive value of 93.9% (95% CI: 85.7%–97.7%), and a negative predictive value of 91.9% (95% CI: 83.4%–96.4%) were obtained for diagnostic accuracy. However, the classification of epilepsy was not considered in the present study. In addition, the misclassification of epilepsy was not considered in the percent agreement.

2.2. Comorbidity classification

Comorbid conditions were defined using the clinical diagnosis at discharge. Comorbidity coding algorithms were referenced through the commonly used comorbidity measurement tools developed by Charlson [11] and Elixhauser [12]. Considering that ICD-10 coding uses a new alphanumeric system that allows the explicit coding of clinical diagnosis, we preferred Quan's coding algorithms [5] and the slightly modified version of St. Germaine-Smith [6]. In our study, a comprehensive set of 33 comorbidities recommended by St. Germaine-Smith was included [6]: congestive heart failure, peripheral vascular disease, chronic pulmonary disease, renal disease, mild liver disease, moderate or severe liver disease, diabetes with complications, diabetes without complications, peptic ulcer disease (excluding bleeding), myocardial infarction, valvular disease, metastatic cancer, brain tumor, solid tumor without metastasis, rheumatoid arthritis/collagen vascular disease, paraplegia and hemiplegia, cerebrovascular disease, aspiration pneumonia, dementia, pulmonary circulation disorders, cardiac arrhythmias, hypertension, traumatic brain and head injuries, multiple sclerosis, cerebral palsy, anoxic brain injury, encephalopathy, alcohol abuse, drug abuse, psychoses, depression, fracture, and central nervous system (CNS) infections.

2.3. Data processing and statistical analysis

Matlab (R2009b) was used to process the large discharge abstract data. In detail, each patient diagnosis was programmed for automatic assignment to a comorbidity category by matching the ICD-10 code of the diagnosis with the code of the comorbidity category. Statistical analysis was conducted with SPSS 17.0 (Chicago, IL, U.S.A.), and a 5% level of significance was assumed. A sex- and age-matched nonepilepsy cohort with the same sample size was randomly selected from the hospital database. The in-hospital mortality rates and associated comorbidities of the epilepsy and nonepilepsy cohorts were compared. Descriptive statistics was performed to describe the baseline demographic information and prevalence of the comorbidities. Logistic regression was conducted to examine the contribution of the predictive variables in in-hospital mortality. In the model, the independent variables contained all 33 comorbidities. In addition to in-hospital SE, age (<18, 18–34, 35–64, and ≥65 years), gender, emergency admission, and surgery performed in hospitals were considered independent variables. In-hospital death was set as a dependent variable. Stepwise selection was carried out to develop a parsimonious model with prespecified selection criteria to emphasize the predictive variables associated with the hospitalized mortality of PWE. The predictive variables with $p < 0.1$ were included in the model, and the variables with $p > 0.05$ were retained.

3. Results

3.1. Baseline demographics

A cohort of 11,422 PWE (58.5% male) from over 730,000 admissions (from November 1, 2006 to July 31, 2017) in Sichuan Provincial People's Hospital satisfied our inclusion criteria. The temporal trends of patient acquisition in this cohort were as follows: 385 (2007), 407 (2008), 529 (2009), 811 (2010), 1009 (2011), 1103 (2012), 1197 (2013), 1392 (2014), 1730 (2015), 1863 (2016), and 996 (January to July 2017). The mean patient age was 40.2 years, with a standard deviation (SD) of 25.9 years. The prevalence by age distribution was as follows: 2884 patients (25.2%) were younger than 18 years, 2488 patients (21.8%) were 18–34 years, 3500 patients (30.6%) were 35–64 years, and 2550 patients (22.3%) were 65 years or older. The median length of stay was six days (interquartile range: 1–14 days). A total of 9101 (79.7%) inpatients, with previously identified epilepsy, were hospitalized for other diseases.

3.2. Prevalence of comorbidities

Table 1 shows that the most common comorbidities were cerebrovascular disease, hypertension, and peripheral vascular disease, which account for 23.5%, 18.8%, and 8.0% of the study cohort, respectively. By contrast, several comorbidities, such as drug abuse, multiple sclerosis, peptic ulcer disease (excluding bleeding), alcohol abuse, cerebral palsy, and psychoses were uncommon.