In-Hospital mortality of Status Epilepticus in China: Results from a nationwide survey

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Abstract

Purpose: We attempted to determine the nationwide in-hospital mortality rate in people with status epilepticus (SE) in China.

Methods: Using the database of the Chinese Hospital Quality Monitoring System (HQMS), we identified people hospitalised from 2013 to 2017 with an ICD-10 code G41 for SE as the primary diagnosis. HQMS was developed by the National Health Commission of the People's Republic of China. Demographics, outcomes at discharge, and financial information were extracted automatically from the medical records.

Results: We identified 29,031 cases with SE as the primary diagnosis from 585 tertiary centres during the five-year period. Among those included, there was a preponderance of men (61%), and the mean age was 40.4 ± 25.2 years (range: 0 – 98). The in-hospital mortality rate was 1.46% over the whole time period, while the overall mortality ranged from 1.80% in 2013 to 1.20% in 2017. The mean cost of treatment was 14517.81 RMB ($ 2147.92) per individual, and the mean duration of hospital stay was 9.25 days.

Conclusion: We provide an overview of mortality related to SE in China as the HQMS database covers a large number of cases of SE in China, making it one of the most efficient tools for mortality investigation. The use of electronic medical records in China creates several challenges and here we discuss lessons learned. The methodology will be improved and will be used in future studies.

Keywords: Seizure, hospitalization, outcome, Chinese Hospital Quality Monitoring System

Introduction

Status Epilepticus (SE), the most extreme outcome of seizures, is an emergency requiring specialised evaluation and appropriate treatment. Without prompt medical intervention, SE can have long-term consequences, including cognitive deterioration, neurological deficits, and in extreme cases, death. In resource-poor settings where medical infrastructure is lacking or deficient, early access to in-patient facilities is critical to the final outcome [1]. A recent meta-analysis suggested that the overall incidence of SE in different populations and regions is around 12.6/100,000 [2]. The reported mortality rates in developing regions showed a huge range, depending on the methodology used. While mature economies report high mortality rates due to SE, there is a lack of corresponding data in most other countries. Previous regional studies in China have suggested some differences in the demographics, incidence, aetiology, and mortality rates for people with SE compared to those in other settings. In this national assessment, we attempted to establish a nationwide baseline level of the incidence of SE in China and to clarify the associated mortality rate.

Methods

Data Source

This retrospective survey used the inpatient medical records database of the Hospital Quality Monitoring System (HQMS) developed by the National Health Commission of the People's Republic of China. Designed to evaluate the status of healthcare all over China, this information system was established in 2013 to monitor the medical records in the hospital information system at each centres [3]. The database includes over 500 tertiary medical centres from 31 jurisdictions across mainland China, including all 22 provinces, 4 municipalities, and 5 autonomous regions, with over 12 million new neurological disorder cases included annually [4]. For neurological disorders, the system monitored 585 centres over the last 5 years. All centres in the monitoring system were required to upload details of all admissions. The information provided a brief review of the medical record, the so-called "front page record," including mandatory information on diagnosis, nosocomial infections, complications, safety, drug use, and outcome evaluation at discharge for each in-patient episode. The diagnosis was coded on the basis of the International Statistical Classification of Diseases and Related Health

Problems 10th Revision, ICD-10. Information on the primary diagnosis and main reasons for admission was mandatory and restricted to one diagnosis, while additional diagnoses was optional. Diagnoses reported in the front page record were made by attending physicians and confirmed after review by a senior physician; the diagnosis of SE was based on the Chinese guidelines [5, 6] which were in accordance with the international definitions.

In the database, the five outcome possible at discharge were 1) resolved, 2) improved, 3) discharged without improvement, 4) deceased, and 5) others. Death reports in the system were checked and found to be consistent with records at the civil registration affairs bureaux.

Inclusion Criteria

Individuals with the primary diagnosis of SE were identified based on the ICD-10 code G41 which includes grand mal status epilepticus (G41.0), petit mal status epilepticus (G41.1), complex partial status epilepticus (G41.2), other status epilepticus (G41.8), and unspecified status epilepticus (G41.9). Discharges between 01/01/2013 and 31/12/2017 with the primary diagnostic code of G41 in the database were included in the study. As data from Tibet was missing from 2013 to 2016, no data from this site was included in the present assessment. For individuals with multiple admissions, only data from the first episode were included.

Outcome Assessment

In-hospital deaths were the primary observational endpoints, and mortality ratios were estimated reports.

Basic demographic data and cost information were collected as secondary endpoints. The per capita gross domestic product (GDP) was calculated based on the China statistical yearbook 2017 [7]. The financial information was calculated in US dollars based on the exchange rate published by the Organization for Economic Cooperation and Development [8].

Statistical Analysis

We used Microsoft Excel 2017 Software for Mac for the analysis. We used the addresses of the care providers rather than the home addresses of the people with SE for all estimations in this study. Standard deviations are provided when means are estimated.

Results

Overall, we identified 29,031 records with the primary diagnostic code G41. An increasing trend was seen with from 2013 to 2017 with 3277 cases of SE in the first year, 5480 in the second, 6060 in the third year, 7235 in the fourth year and 6979 cases in the last year of the series.

Most individuals were discharged. In 2017, 3530 (50.6%) people with SE were discharged from Neurological care, followed by intensive care units (6%), Departments of Neurosurgery (4.8%) and Emergency Departments (1.9%). Other departments combined reported 2561 discharges (36.7%).

The most common diagnostic code in this population was G41.9 (N = 20205, 69.6%), followed by G41.0 (N = 4960, 17.1%) and G41.8 (N = 1721, 5.9%). Codes G41.1 was used in 8210 cases and G41.2 in 1325 people.

There was a preponderance of men among the people with SE, irrespective of the year of study or department of discharge (N = 18890, 65.1%), with a mean age of 40.45 ± 25.23 years.

Primary Outcome

There were 425 deaths recorded. The overall in-hospital mortality rate was 1.46%. In-hospital mortality rates exhibited a downward trend between 2013 and 2017 from 1.80% in the first year to 1.20% in the last year of the series. The highest in-hospital mortality rates were reported in the Jilin (5.9%), Heilongjiang (4.4%) and Liaoning (2.2%) provinces. Data on the primary outcomes in 30 provinces are summarised in Table 1.

The data also showed that a large number of individuals were discharged without a recorded improvement. These discharges ranged from 8.7% and 9.9% between 2013 and 2017.

Secondary Outcomes

Per capita GDP and the in-hospital costs are shown in Table 1. The mean cost of treatment was 14517.81 ± 24805.24 RMB ($ 2147.92 ± 3669.95) per individual, and the mean duration of hospital stay was 9.25 ±11.40 days. The cost and length of stay remained stable during the five years of the study.

Discussion

We assessed in-hospital mortality associated with SE in China. The HQMS

database covers the discharge records of a large number of health providers across China. The system developed by the National Health Commission, automatically collected data from the front page of the medical records from all discharges. Information from this database was considered reliable for the assessment of in-hospital mortality related to SE. Our finding significantly lower than previously reported is interesting.

Several single-centre studies using different methodologies reported a wide-range of mortality rates associated with SE in the Chinese population, mostly higher than 15%. Latest reported data suggest an overall mortality between 15.40% [9] and 16.9% [10]. The mortality associated with convulsive status epilepticus (CSE) was 16.4% [11], which was comparable to that reported in 2009 [11]. The highest mortality estimation of 18.9% was from a small study of CSE in a neuro-intensive care unit [12]. Several studies have, however, reported lower mortality rates in the Chinese population. Our findings are consistent with those from a retrospective hospital-based study in Jilin province, which reported an overall mortality of 6.7% [13]. In a study from Sichuan, a 1.5% mortality rate in people with non-refractory SE, with an overall mortality of 7.14% in all people with SE [14]. Our current study provides a more accurate estimate and suggests that the previous studies might have overestimated the mortality associated with SE in Chinese people.

Investigations of mortality using national administration data sets have been carried out in other regions, reporting relatively lower results. An US study using the Nationwide Inpatient Sample (NIS) [15], used the ICD-9-CM coding system to search for the primary diagnosis of generalised convulsive SE (345.3); it excluded people with epilepsia partialis continua and psychomotor SE (345.7) as well as those with a clinical diagnosis of syncope (780.2). A recent meta-analysis of mortality over the last 30 years, however, reported a mortality rate of 15.9% [16], which was higher than estimation using the NIS. It was suggested future studies should include people with SE with “subtle status” to avoid the possible underestimation [17].

A national investigation based on the Thai Universal Coverage Scheme electronic database, covered over 75% of the Thai population and used the ICD-10 code G41. The first analysis using data from 2004 to 2012 showed a mortality rate of 8.4% [18]. The most recent analysis used data from 2005 to 2015 and reported a slight drop in the in-hospital mortality to 7.5% [19]. People with SE treated at primary care centres had poorer outcomes than those treated at tertiary care centres.

In England and Wales, SE-associated mortality rate was evaluated using data from the Office of National Statistics [20]. The study was initially based ICD-10 classification. The findings suggest a continuous downward trend in SE mortality from 8.6% in 2001 to 6.5% in 2013.The decreasing trend was unlikely to be caused by the limitation of the database. Our findings also suggested a downward trend in mortality from 2013-2017. It is possible that the advanced methods of diagnosis and treatment during the studied years contributed to an improvement in the prognosis of SE patients in China.

A recent study from New Zealand showed that the 30-day mortality was 4.6% [21], which was much lower than the reported rates from other developed regions.

Our data suggest that the mortality rate related to SE in China is lower than the previous estimates with a seemingly continuous downward trend. Whether the current results are an underestimation remains a critical question, but we consider the decreasing trend to be reliable as we used the same study method. The clarification of these issues would provide an insight into the value of the current medical study in the administrative database.

Our study addressed the main concern in the US study by including individuals with all types of SE using the ICD-10 diagnostic code, but it still has limitations. Firstly, the current search scheme only allowed for the evaluation of people with the primary diagnosis of SE. Acute symptomatic causes which are frequently identified (up to 61.4%) as the main aetiology of SE [22] were not considered. These mainly include central nervous system infection, stroke or autoimmune encephalitis [9, 13, 22], and apparently serve as the main drivers of SE- related death [23]. The current search strategy is therefore likely to have missed people with severe SE or those who died in whom the direct cause was listed as the primary diagnosis and not as SE. This could be one of the most important reasons for underestimation.

Secondly, this study included only the first admission records of individuals to avoid listing subsequent multiple admissions of the same individual as multiple cases. This strategy was designed to avoid overestimating the total population of people with SE. It could, however, have potentially caused an underestimation since it excluded follow-up information in people with multiple admissions, so the possible death of an individual during a later admission would not have been identified; this could underestimate the poor outcomes in people with multiple admissions.

Thirdly, while the in-hospital mortality rate was low, there was a considerable proportion of people continuing in SE at discharge. While some individuals or their families made the decision to have the person with SE discharged for non-medical reasons or against medical advice, outcomes in these individuals were evaluated as poor, with either ongoing seizures, or other serious complications which required hospitalization. There is limited knowledge on outcomes in these people. It seems that most of them were taken home rather than to another care facility, to so they could die in their own homes. Some people also refuse invasive treatments for cultural or religious reasons. Some also choose to stop treatment for financial reasons when the chances of survival were slim. Since these people represent a group with poor outcome at discharge, the real mortality rate may be underestimated. The previous study of super-refractory SE (SRSE) in mainland China showed that in 4 of 12 people with SRSE, treatment was stopped because of a decision made by the families; all 4 individuals died within 24 hours of discontinuing treatment [12]. The number of deaths in such discharges needs further investigation.

Fourthly, the study pool based on the search strategy was highly selective. We only included people discharged from the tertiary centres monitored by the HQMS system, excluding individuals who were discharged from, or who had died in, primary or secondary health care settings. In China primary and secondary care is rapidly developing, but the capacity of primary healthcare providers remains inadequate [24]. In terms of pre-hospital care, access is also insufficient in vast portions of the country. In a hospital-based stroke registration, 11% of people with ischaemic stroke reached the hospital within 3 h [25]. Due to limited access to immediate treatment, it is possible that people with severe SE never accessed the health care system or left it without getting involved in the in-patient processes, which would also lead to an underestimation of the mortality rate. Additionally, as suggested by an observational study from Switzerland, while CSE is more likely to be recognised and treated, NCSE (non-CSE) is more likely to be missed as a medical emergency, The missed events could be listed as other neurological events such as acute ischemic stroke or intracranial haemorrhage, leading to fatal outcomes due to delayed treatment.

Fifthly, the search strategy used was based on the ICD-10 diagnostic code. The terminology does not correlate with the definitions and classification of SE in the current guidelines. Thus, we failed to distinguish between individuals

with tonic-clonic SE and other sub-types. For the same reason, it was also difficult to differentiate between refractory and SRSE.

Lastly, this was an observational study as no controls were available. Other factors, such as economic burden and poor access to health care, could also have led to a lower estimation of in-hospital mortality.

Our study reported an important increase in the number of people with SE discharged. This increase is less likely to be caused by an increase in incidence or change in the admission thresholds. The reports from the China Statistical Yearbook showed that the number of beds per hospital in China had been increasing from 457.86 in 2013 to 612.05 in 2017 to catch up with the treatment gap [26]. According to the HQMS database, the average number of discharges per month from Neurology Departments also increased [27]. A similar trend was also observed in discharges with stroke in the HQMS database. These increases could possibly be due to the increased number of beds in hospitals participating in the monitoring system.

We are currently performing a second analysis using an adjusted method, searching for individuals by all listed diagnoses and not just the primary diagnosis. We have also started a multicentre follow-up observational study to investigate the 30- and 90-day mortality following discharge from hospital.

This report using the nationwide health care data on neurological disorders in China provides a few lessons in the methodology and application of big data in medicine.

Conclusion

Despite the limitations, this study of mortality of SE in China shows that the overall mortality rate from 2013 to 2017 was 1.46% with a seemingly declining trend. With the largest number of studied hospitals and people with SE, HQMS is one of the most efficient tools for investigating SE-associated mortality in China. Given that the use of electronic medical records in China faces various challenges, we have provided explanations and discussed the lessons learned from the first attempt. We will continue to improve the methodology in future studies.

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Disclosures

The authors have no conflicts of interest.

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Table 1. Outcome evaluation and economic features in Status Epilepticus at discharge

Administrative Districts	Per Capita GDP (USD)	Number of people Discharged (N)	In-hospital mortality rate （%）	In-hospital Cost （Mean±SD，USD）
Beijing	19091.82	578	1.56	6263.31 ± 5074.86
Shanghai	18743.5	467	3.21	3236.44 ± 6490.18
Tianjin	17626.01	148	3.38	2217.44 ± 3647.76
Jiangsu	15823.27	2853	0.46	2276.25 ± 3054.65
Zhejiang	13539.26	738	0.68	3199.17 ± 4477.60
Fujian	12174.3	841	0.95	1979.53 ± 3524.29
Guangdong	11882.86	2214	1.67	2177.41 ± 4368.43
Shandong	10739.84	1067	1.22	1626.68 ± 2198.32
Neimenggu	9416.56	345	1.74	2102.75 ± 2527.68
Chongqing	9346.03	620	0.81	2026.07 ± 3751.16
Hubei	8893.62	2620	2.48	1938.45 ± 2838.23
Shaanxi	8448.37	731	1.37	1553.68 ± 2263.71
Jilin	8137.86	518	4.63	2485.24 ± 3668.71
Liaoning	7927.26	494	3.24	2231.3 ± 3950.37
Ningxia	7470.35	138	0.72	2176.28 ± 3091.12
Hunan	7311.91	306	0.98	2731.27 ± 4843.57
Hainan	7129.99	689	0.58	2647.2 ± 4816.24
Henan	6895.73	2589	0.58	1576.89 ± 2183.04

Hebei	6692.48	711	1.13	3156.63 ± 7285.15
Sichuan	6590.29	2988	1.67	1583.09 ± 2390.43
Xinjiang	6584.85	476	1.47	2050.97 ± 4318.78
Qinghai	6494.08	109	3.67	2907.18 ± 3015.74
Jiangxi	6404.05	1531	1.11	2117.62 ± 3950.37
Anhui	6390.63	1477	1.62	1850.65 ± 3202.50
Heilongjiang	6209.59	451	4.43	2597.91 ± 3586.19
Shanxi	6205.95	902	0.89	2048.67 ± 3051.03
Guangxi	5610.1	523	2.68	2485.04 ± 5303.28
Guizhou	5411.61	241	1.24	1723.16 ± 3685.66
Yunnan	5046.64	1268	0.71	1720.71 ± 2554/58
Gansu	4202.96	398	1.76	951.08 ± 1906.70
Total	9564.14	29031	1.46	2147.92 ± 3669.95