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Comparisons of the mortality and clinical presentations of status epilepticus in private practice community and university hospital settings in Richmond, Virginia

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ABSTRACT

We prospectively compared the clinical course of 119 patients treated for status epilepticus (SE) in private practice community hospitals and 344 SE patients treated in the VCU university hospitals in Richmond, Virginia USA over a 2-year period to test the hypothesis that SE presents with the same mortality and clinical patterns in both clinical settings. Of the patients reviewed, the major etiologies for SE were cerebrovascular disease, decreased anti-epileptic drug levels in epileptic patients, anoxia–hypoxia, and remote symptomatic. The other etiologies included were alcohol related, trauma, central nervous system infections, tumors, systemic infection, metabolic disorders, idiopathic, and hemorrhage. These observations provide the first direct prospective comparison of SE present in university and private practice community hospital settings in the same geographic area. Mortality was the highest in the elderly population while the pediatric population had low mortality in both clinical settings. Etiology risk factors for outcome were similar for both the populations. The data also suggest that the higher degree of illness severity in university hospitals may be associated with a higher incidence of SE, but not with mortality or a different clinical presentation of the condition. The results of this study demonstrate that SE has the same mortality and is present in an essentially identical manner in university and private practice community hospitals and underscores the fact that mortality in SE is not just associated with tertiary care hospitals and the importance of recognizing the severity of SE in the private practice setting.

1. Introduction

Status epilepticus (SE) is a major medical and neurological emergency that requires immediate treatment to avoid significant morbidity and mortality. Status epilepticus has been estimated to affect as many as 200,000 people in the United States annually and causes as many as 55,000 deaths per year.[1,2] Despite significant improvements in the diagnosis and treatment of SE over the past 30 years, SE in adults is still associated with a significant morbidity and mortality.[1–4] The economic burden of SE is also high with SE patients having 30–60% higher reimbursements than patients admitted for other acute health problems including acute myocardial infarction or congestive heart failure.[5] Thus, understanding the prognosis and clinical presentation of SE is of considerable importance in improving the evaluation and treatment of this major neurological condition.

The varied clinical presentations of SE make it difficult to study.[2,6] Individuals with epilepsy comprise a large group at risk to develop SE; however, a large proportion of SE cases occurs in the context of an acute medical or neurological illness.[2,4,6,7] All of the major adult clinical studies on SE have been obtained from large tertiary care university and medical school affiliated hospital-based populations.[7–16] Thus, the natural clinical presentation and mortality associated with SE in a community private practice setting is completely unknown. Since private practice hospitals make up the largest group of patients it is essential to determine whether SE has the same high mortality in the private practice hospital setting that represents the largest patient hospital population. It is especially important to target educational programs and treatment protocols on SE at private practicing neurologists and intensive care physicians if SE presents with a high mortality in this setting. Despite the importance of evaluating the mortality and clinical presentation of SE in the private practice setting, this population of SE patients has not been evaluated. It has been assumed that SE in the private practice setting is less severe

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and may not be associated with a high mortality. Thus, it is essential to study SE in the private practice setting to address this important issue and determine the natural presentation of SE in a private practice setting and compare it to the tertiary university studies.

The present study was initiated to utilize the Richmond SE database to test the hypothesis that SE manifests the same high mortality in the private practice community hospital setting as observed in the tertiary care hospital studies. Our findings provide the first prospective study of SE in both a tertiary care academic medical center and in community private practice hospitals in Richmond, VA over a 2-year time period. Thus, the results from this study will provide important data to test the hypothesis that the presentation of SE in the private practice community setting has the same mortality and clinical presentation as in a major tertiary care center. The data demonstrate that SE has the same mortality and is present in an essentially identical manner in both tertiary care and private practice hospital settings.

2. Materials and methods

Patients presenting to private practice community and university hospitals in the greater Richmond metropolitan area were prospectively collected over the same 2-year time period from 1988–1990 by the same team of investigators. This data base represents a unique resource to test the hypothesis presented in this study and to our knowledge is the only data base in the United States that can compare a large number of SE cases in private practice and tertiary care hospitals in the same data set, studied with the same team of investigators and over the same time period. We used this unique data set to conduct this study and directly compare the mortality and clinical presentation of SE in the private practice and university care settings. The Institutional Review Board for the Protection of Human Subjects approved all data collection and handling in this study.

3. Data collection

Data on each case was entered into the Virginia Commonwealth University (VCU) SE database for analysis. Utilizing the same data collection criteria and research staff to obtain information from both private practice community and university hospital settings greatly improved the reliability and uniformity of the data. The private practice neurologists reported SE cases to the VCU SE Research Project by direct contact, or by utilizing a well publicized referral phone number staffed 24 h a day, 7 days a week. Within 8 h of notification, a member of the SE team reviewed the hospital record and extracted the appropriate study intake information. The SE research team determined if each case met the definition of SE for inclusion in the study then reviewed intake data weekly. Onset of SE was based upon observations from witnesses or paramedics in non-hospital initiated SE, and observations by nurses or physicians for hospital initiated SE. Of the cases reported to the SE team in a prospective manner, approximately 86% met the definitional criteria for SE and the remaining 14% had to be excluded because the diagnosis could not be established with certainty. All patient records were kept completely confidential by the SE data management team. Medical records for included cases were reviewed in detail following discharge or death. A standardized data form entry system was completed on each patient including the following information: demographic data, detailed seizure history, electrophysiology data, and previous medical or neurological history, immediate precipitating etiology of SE, laboratory studies, hospital course, and outcome. A careful time line of each SE event was compiled to evaluate the duration of SE and the time to recovery or mortality. Outcome was evaluated as alive or dead within 30 days after the cessation of SE.

4. Definitions

4.1. Status epilepticus

The SE research team to determine if each case fulfilled the International Classification of Epileptic Seizures definitional criteria for SE[17] reviewed the charts and case histories of the identified patients. SE was defined as continuous or intermittent seizure activity without regaining consciousness lasting for 30 min or longer. Seizure duration was defined as the time from the onset of SE until both clinical and electrographic evidence demonstrated that seizure activity had subsided. SE seizure types were defined as partial or generalized SE based on standard International Classification of Seizure Types and Types of Status Epilepticus.[7,10,17–19]

4.2. Etiology

Etiologies of SE were defined as the immediate precipitating cause of SE employing established procedures.[4,7] Medical conditions that were not directly the cause of SE or previous medical conditions or that were not related to the initiation of SE were not considered acute etiologies. Occasionally, SE was caused by more than one etiology. Unknown SE represented patients that had no identifiable immediate precipitating cause for SE. A large percentage of these idiopathic cases were found to have remote symptomatic etiologies that were defined as previous episode of cerebral vascular disease or other neurological injuries as described.[20] These previous conditions were not acute at the initiation of SE. Alcohol withdrawal SE was defined as SE caused by a documented withdrawal of alcohol. Decreased anti-epileptic drug withdrawal was defined as a case of documented cessation or decrease of anticonvulsant medication in a patient with epilepsy leading to the initiation of seizures and SE. Systemic infections were defined as a systemic infection without any evidence of a central nervous system infection or meningitis. The idiopathic etiology represented cases where no remote or precipitating event was identifiable as a cause of SE. Anoxia, hypoxia, hemorrhage, cerebral vascular accidents (CVA), tumor, metabolic conditions, and trauma were defined as a precipitating cause of SE using standard clinical definitions for these precipitating events.[7,21]

4.3. Age

The pediatric population included patients between 1 month and 15 years of age. The adult group included patients aged 16 years and older.

5. Results

The results in this study are directed at testing the hypothesis that SE presents with the same mortality and clinical patterns in both clinical settings. It is important to directly evaluate the mortality and clinical presentation of SE in the private practice setting and compare it to tertiary care studies to determine if SE is associated with the high mortality. The evaluation of this study will provide the first evidence to test this hypothesis.

5.1. Clinical presentation

SE was a common neurological condition presenting in both university and private practice community hospitals. The combined total population in this study was composed of 59% white

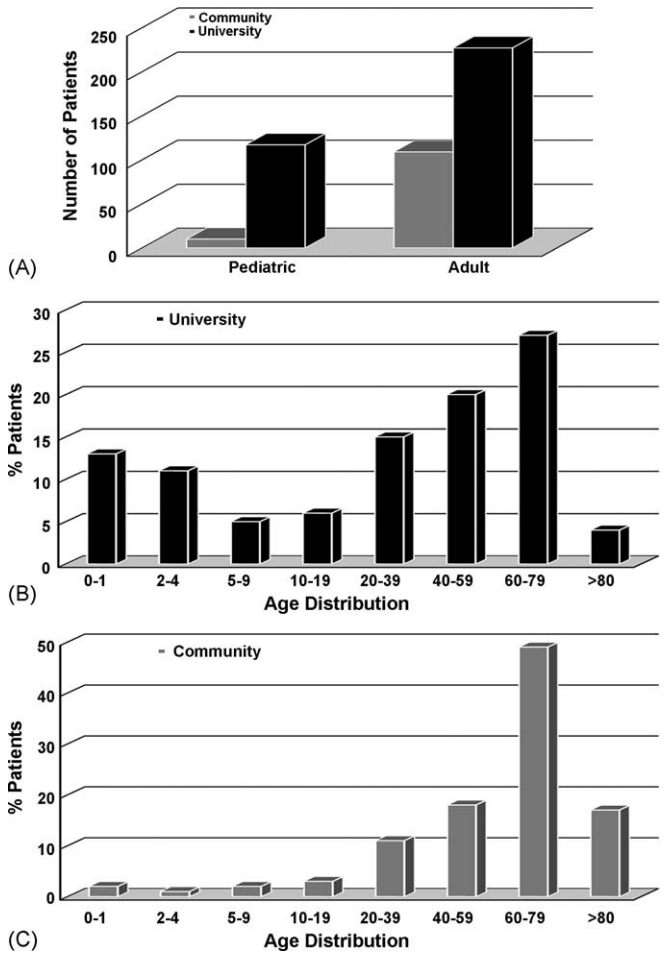

Fig. 1. Number of pediatric and adult patients and their age distribution present with SE in private practice community and university hospital. (A) 344 patients presented with SE at the university hospital while 119 SE patients presented at private practice community hospitals. The pediatric SE population was higher at the university hospital. (B and C) Both hospital settings had similar age distributions for patients from infancy to elderly. The highest number of patients occurred in the elderly (60–79) age group in both populations.

and 41% non-white patients. The mortalities for males and females were not significantly different in the two populations and the Caucasian versus non-Caucasian populations had no significant differences in mortality between the private practice community and university populations. The overall mortality of SE in the adult population was 29%. The number of patients with SE was higher in the adult population (Fig. 1).

Fig. 1A presents the number of adult and pediatric patients present in both hospital settings. The numbers of cases in the university hospital was higher (344 patients) than in the combined population in the private practice community hospitals (119) over the 2-year time period. In addition, the majority of pediatric SE cases in Richmond were treated at the university hospital. This in part was a reflection of fact that the majority of acutely ill pediatric cases were taken by EMS to the university hospital for treatment. Despite the differences in the number of SE cases in the two hospital settings, both the private practice community and university hospital studies exceeded 100 patients, allowing for adequate comparison of the two populations.

The age distribution of SE from infancy to the elderly for university and private practice community hospitals is shown in Fig. 1B and C. Both populations had a similar age distribution, with the highest number of SE patients occurring in the elderly population. The private practice community hospital population manifested a higher overall percentage of patients in the elderly population. This in part may reflect the fact that the majority of pediatric cases were treated at the university hospital (Fig. 1A) and that the younger adults with more serious medical and surgical conditions presented to the tertiary care center. However, the age distributions were very similar for both clinical settings and demonstrate the significant presentation of SE in elderly patients in both populations.

5.2. Mortality due to SE

Mortality during and after SE for university and private practice community hospitals is shown in Fig. 2A. The overall mortality in the private practice community population was 31% and 27% in the university population. There was no statistically significant difference in mortality between university and private practice community hospitals. Thus, despite the tertiary care setting of the university hospitals, the mortalities for SE in these two populations were the same. In addition, the majority of mortality from SE occurred after cessation of SE in both populations.

The majority of patients in both populations died at some time interval following the control and successful treatment of SE. The definition of mortality in this study was death during or up to 30

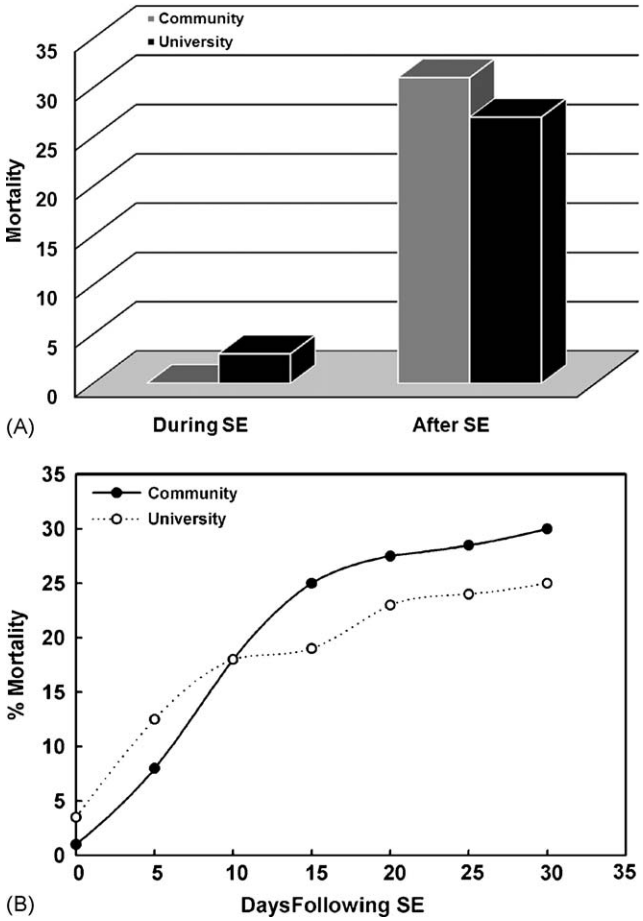

Fig. 2. Mortality during and after SE for private practice community and university hospitals. (A) Overall mortality 31% and 27% in the private practice community and university hospital populations, respectively, which were not significantly different from each other. The majority of mortality from SE occurred after SE in both populations. (B) Mortality curves for patients with SE in the private practice community and university populations. Percent mortality from the cessation of SE following successful treatment to 30 days after SE was plotted. Mortality time curves were almost identical for both the populations with the majority of deaths occurring in the first 2-week after SE. Twenty days after SE the mortality rates leveled off, indicating that the majority of SE related deaths had reached a plateau.

days after SE. Treatment of SE was essentially the same in both clinical settings. Both private practice community and university SE treatment protocols were well developed and were essentially identical due to a coordinated effort in the Richmond private practice community to provide the best possible care for SE through physician and hospital staff education programs.

Fig. 2B presents the percent mortality from the cessation of SE following successful treatment to 30 days after SE for the private practice community and university populations. Both populations demonstrated essentially identical mortality time curves with the majority of deaths occurring in the first 2 weeks after SE. Twenty days after SE the mortality rates leveled off, indicating that the majority of SE related deaths had reached a plateau.

5.3. Age distribution of mortality

Fig. 3 shows the age distribution of mortality for university and private practice community hospitals. The highest mortality in both populations was seen in the elderly. Elderly patients (60 years or older) with SE had mortality rates that exceeded 40% in both populations. The low number of pediatric patients and the level of medical severity of the pediatric cases in the private practice community hospitals accounted in part for the absence of deaths in the private practice community pediatric population. The overall university mortality for the pediatric population was less than 5%. This data demonstrates that the elderly patients in both clinical populations were the highest at risk groups to develop mortality from SE.

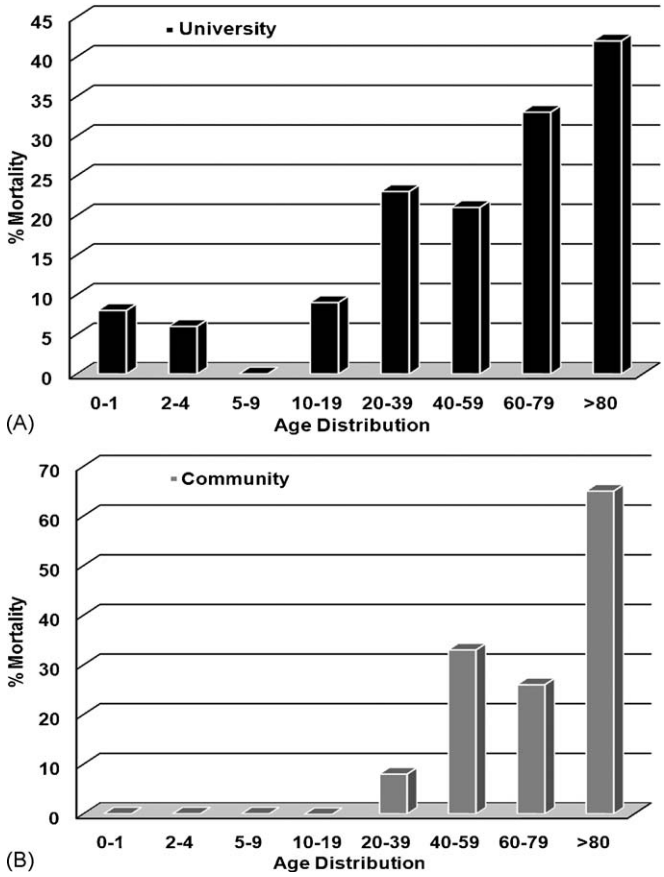

Fig. 3. Age distribution and mortality for private practice community and university hospitals. The data present the number of patients in the database plotted against age groups. The elderly population exhibited the highest mortality (>40%) while the pediatric population had a low level of mortality in both hospital settings. The overall mortality for the pediatric population in the university settings was less than 5%.

5.4. Seizure duration and mortality

Previous studies have indicated that seizure duration significantly affected mortality in adult SE.[4,7,10,18] To determine if there was a difference in mortality between patients with prolonged SE versus non-prolonged SE, the database was divided into patients who seized from 30 to 60 min (non-prolonged SE group) and patients who seized for greater than 60 min (prolonged SE group). The mortality after SE for the prolonged seizure group in the private practice community and university was 37% and 35%, respectively. In the non-prolonged SE group the mortality for the private practice community and university populations was 8% and 7%, respectively. The differences between prolonged versus non-prolonged SE in mortality for the two populations were statistically significant ($p < 0.05$), demonstrating a significant effect of seizure duration in both populations. In addition, in both the university and private practice community populations the non-prolonged and prolonged SE groups had a very similar mortality levels and these levels between the populations for these two seizure durations were not statistically significant (Fig. 4). These results support the previous findings from university studies[4,7,10] that seizure duration plays a significant role in contributing to mortality and to our knowledge provides the first demonstration that the same finding occurs in the private practice community hospital SE population.

5.5. Etiologies of SE

The major etiologies of SE in both clinical settings were very similar with CVA, withdrawal or decrease from antiepileptic drugs, remote symptomatic, alcohol withdrawal, and anoxia and hypoxia being the most common etiologies in adults (Fig. 5). In children infections presented as the major etiology accounting for more than 30% of the cases in both populations (data not shown). Because of the higher complexity of the overall patient cases in the tertiary care center, the university hospital setting had a higher percentage of acutely ill etiologies. The most common etiology in the private practice community population was CVA accounting for 38%. Decreased anti-epileptic drug, anoxia/hypoxia, and unknown were other major etiologies. Remote symptomatic etiologies were also major etiologies in both populations and the majority of remote symptomatic cases were related to a

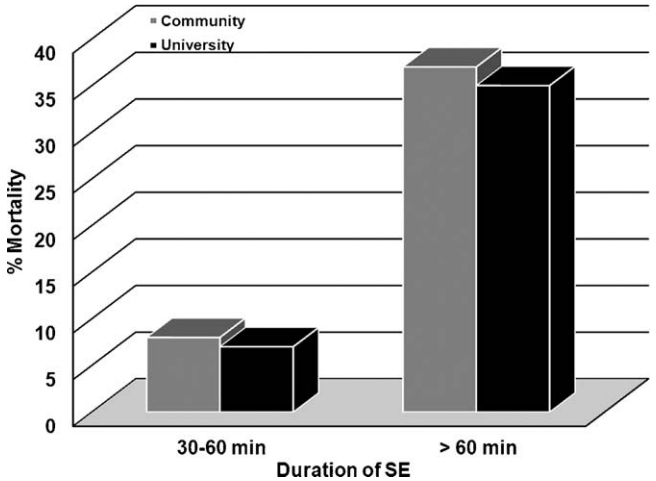

Fig. 4. Seizure duration and mortality outcome for private practice community and university hospitals. The database was divided into patients who seized from 30–60 min (non-prolonged SE) and patients who seized for >60 min (prolonged SE). Mortality for the non-prolonged SE group was 8% and 7%, respectively while the mortality for the prolonged SE group was 37% and 35%, respectively in the private practice community and university hospital settings.

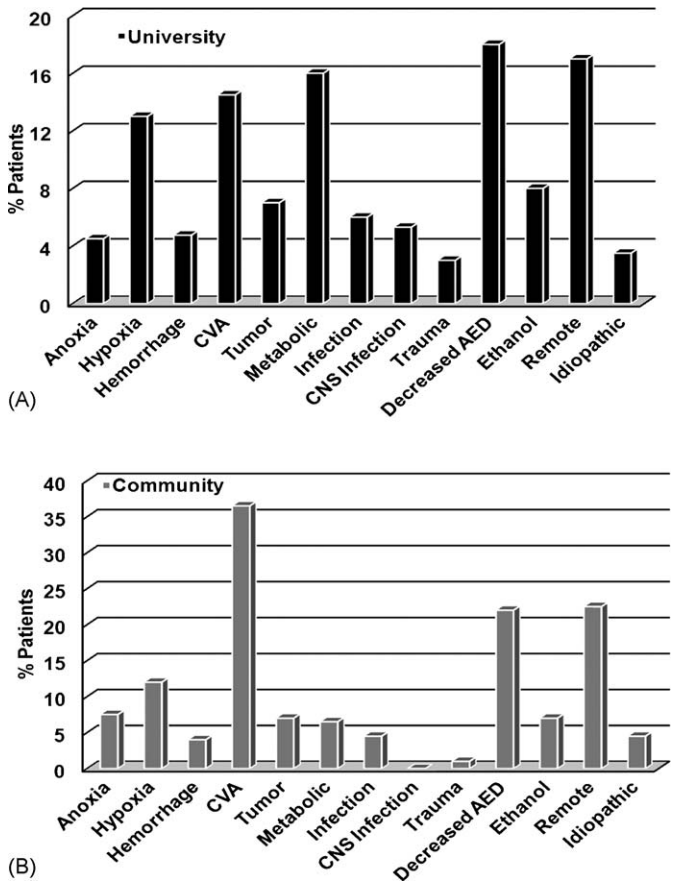

Fig. 5. Adult etiologies for SE in the university and private practice community population. The data represent the number of patients in each category of etiology for the database (multiple etiologies are included for some patients). The major etiologies of SE in both clinical settings were very similar in the two populations.

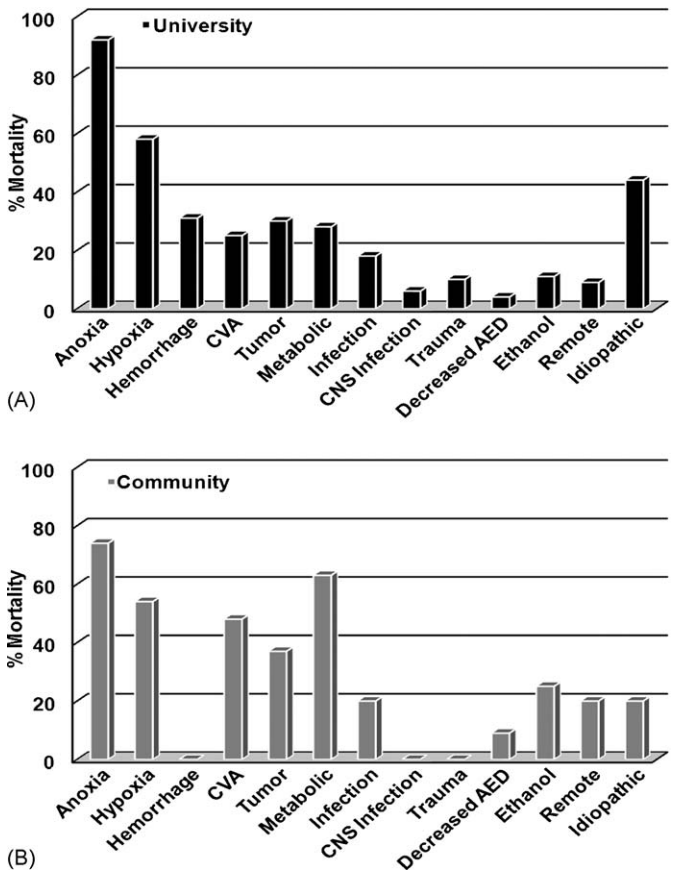

Fig. 6. Etiologies of adult patients with SE and mortality in the university and private practice community population. The data give the number of patients in each category of etiology for the database (multiple etiologies are included for some patients). The mortalities for each of the major etiologies were very similar in the two populations.

previous CVA as described.[20] These cases had no acute precipitating cause of SE, but had a documented CVA or neurological insult in the past that probably contributed to the initiation of SE. Other minor etiologies in both populations included hemorrhage, and tumors. Metabolic disorders, systemic infections and alcohol related SE, central nervous system infections and trauma represented a larger percentage of the patients in the university population. Over 32% of the SE patients had a previous seizure history. However, the majority of patients (68%) had no previous history of seizures.

5.6. Etiology and mortality in SE

It was important to evaluate the mortality for each etiology for both populations. The mortality of SE for each etiology for university and private practice community hospital populations is presented in Fig. 6. The mortalities for each of the major etiologies were very similar in the two populations. Mortalities greater than 40% were observed for anoxia and hypoxia in both populations. CVA in the private practice community study had mortality greater than 40% and in the university setting the mortality for CVA was 25%. Etiologies of tumor, metabolic disorders, and infections also had significant mortality in both populations. Decreased anti-epileptic drug, alcohol related and remote symptomatic were associated with a mortality of less than 20%. Although no mortality was observed in the hemorrhage, CNS infection or trauma categories in the private practice community population this may be the result of the smaller number of patients representing these categories in this population compared to the university series. Anoxia/hypoxia and CVA etiologies demonstrated a statistically significant association with increased mortality. These results indicate that specific etiologies of SE are associated with higher mortality rates as described previously.[2,4,7,10]

6. Discussion

To our knowledge this study provides the first direct prospective evaluation of SE by a coordinated research team evaluating the presentation of SE in a tertiary referral university hospital and the surrounding private practice community hospitals in a defined geographic area, Richmond, VA. Evaluating the presentation of SE in the private practice setting is a major advance in our understanding of this condition in all hospital settings and tests the hypothesis that SE has the same mortality and clinical presentation in tertiary care and private practice settings. The results demonstrated that both university and private practice community hospital populations manifested essentially identical mortality patterns and clinical presentation of SE. This was an important finding in this study and demonstrates that the significant mortality of SE described in university hospital settings is not merely a factor of the high severity of illness associated with tertiary referral centers. Both small and large private practice community hospital populations in Richmond, VA were included in this study and the mortality between these populations was not significantly different from the VCU university tertiary care facility. This finding with a large prospective sample size for SE patients indicates that the presentation of SE in these different health care

environments does not influence the mortality of this condition. This further underscores the importance of developing prognostic indicators for outcome and novel treatment methods for SE to improve outcome in all clinical settings.

Although the data demonstrate that SE has essentially the same mortality and clinical features in the private practice community and university populations, there are several minor differences in the presentation of SE in these populations. Cerebrovascular accidents were the most common cause of SE in the private practice community, representing 38% of the cases. Cerebrovascular accidents were found to represent 25% of the cases in the VCU hospital setting and have been reported to comprise 10–25% of the cases of SE presenting in tertiary care facilities in several large series.[7–16] The increased percentage of CVA related SE cases in the private practice community hospital setting may indicate the patient care demographics of the Greater Richmond Metropolitan Area or may reflect the presentation of SE in non-tertiary care facilities. Cerebrovascular disease is cared for in private practice community hospitals with an equal or greater percentage than in the university setting in Richmond, VA. However, alcohol and drug related etiologies of SE were clearly more centralized in the tertiary care university facilities, as demonstrated by comparing the lower percentage of these etiologies in the private practice community population compared with the VCU population and with previous studies from VCU and other university-based series.[1,2,4,6,7,10]

The private practice community population also represented a large number of cases diagnosed with anoxia/hypoxia. Cardiac arrest is the most common etiology of these etiologies and is present similarly in both hospital settings. It is also clear from these results that SE associated with anoxia/hypoxia, CVA, tumors, metabolic disorders and generalized infections were associated with a high mortality in both studies despite the increased percentage of these cases in the university population. Decreased anti-epileptic drugs had a lower mortality rate in both series and accounted for a similar percentage of SE cases in both populations. Alcohol related etiologies also had a similar mortality and overall percent of SE cases in both populations. These results confirm the lower mortality rates observed with alcohol related and decreased anti-epileptic drugs etiologies seen in other larger university series.[7–16] The lack of mortality seen with hemorrhage, CNS infection, and trauma in the private practice community setting most likely represents the smaller number of patients seen in the private practice setting with these serious neurological problems. Many of these cases were referred to the VCU tertiary care facility in Richmond. However, these differences may reflect other differences in the severity or presentation of these cases in the different populations and larger studies are needed to evaluate these differences more definitively.

Clinical SE series that contain a high percentage of anti-epileptic drug or alcohol withdrawal etiologies of SE have a lower overall mortality rate.[1,2,4,6,7,10] Three series in the literature[6,11,22] have indicated a lower mortality associated with SE in adults. Their series also had a large percentage of patients with alcohol related and anticonvulsant withdrawal etiologies. The VCU retrospective series demonstrated a lower total percentage of patients with alcohol withdrawal and decreased anti-epileptic medications.[4,7] This was also shown in private practice community setting. The CVA and anoxia/hypoxia represented over 55% of the patients in the private practice population. Decreased anti-epileptic medications and alcohol withdrawal represented only 25% of the patients. Thus, the overall mortality of 32% seen in private practice community setting is consistent with our previous observations and others.[6] The mortality associated with SE for each etiology in the private practice setting was similar to the mortalities observed in our large university studies[4,7] and those of other investigators.[2,4,6,7]

Age was shown to be an important factor contributing to mortality in association with SE in both populations. A significant increase in mortality was demonstrated with advancing age. Patients beyond 60 years of age have a dramatically higher increase in mortality than younger patients. In addition, the number of patients experiencing SE also was significantly increased in the later decades. These findings are consistent with previous studies.[1,2,4,6,7,10,14] SE clearly is a significant condition for the older population and further study of this condition in the later years is an important aspect of aging research.

This study provided direct evidence that the mortality and clinical presentation of SE in university and private practice community hospitals were essentially identical. Mortality, age distribution, etiologies were nearly identical in the two populations. In addition, this study directly tested the proposed hypothesis and demonstrated that the significant morbidity and mortality observed in the large academic medical centers are not primarily the result of the tertiary care patient population, but rather are mainly determined by the underlying pathophysiology of SE. private practice community hospitals need to initiate SE protocols and treatment education programs for SE with the same vigor as academic medical centers to achieve favorable outcomes for SE. To our knowledge this study provides the first direct prospective comparison of SE present in university and private practice hospital settings in the same geographic area. Mortality was the highest in the elderly population in both study groups. The pediatric population in both clinical settings had a very low mortality. Etiology risk factors for outcome were similar for both populations. The higher degree of illness severity observed in university hospitals may be associated with a higher incidence of SE. Further studies are needed to evaluate the epidemiology of SE in university and private practice community hospitals to address these issues.

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