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Post-critical care mortality of patients admitted to an Intensive Care Unit with seizures: a population based study

We read with interest the article published earlier this year exploring the in-hospital outcomes of patients admitted to critical care in status epilepticus [1]. It prompted us to consider our own hospital mortality for seizures, and the longer term outcomes for this patient group. Generalised, convulsive status epilepticus represents the most commonly encountered subtype of status epilepticus (SE) in clinical practice [2]. Due to the nature of treatment related to SE, admission to a critical care environment is often required, particularly following failure of intravenously administered anti-epileptic drugs. Two population-based registry studies have provided data on intensive care unit (ICU) outcomes for SE. A hospital mortality of 5% with an ICU mortality of 1.7% was identified for SE in Australia and New Zealand [3], with similar findings in a European cohort [4]. We sought to assess ICU and longer-term mortality in those admitted to ICU with seizures. We examined 10 years of prospectively collected data in Scotland (Scottish Intensive Care Society Audit Group Dataset) between 2005 and 2014, across all public ICUs. This dataset was linked to the Scottish death records dataset. Patients over the age of 16 years, who required multiple organ support or invasive respiratory support were included (Level Three patients) [5]. All data were anonymised and were part of routinely collected data across Scotland. As a result, ethics committee approval was sought and waived. Approvals were obtained from SICSAG as well as the Scottish National Data Governance Body (Privacy Board Committee, Information Services Division) and the NHS Greater Glasgow and Clyde Caldicott Guardian.

Baseline characteristics of the study population are presented in **Table One**. Proportions were compared using a Kruskal-Wallis or chi-squared tests. A p value <0.05 was considered statistically significant.

To assess the impact of seizures on long-term outcomes, Cox Proportional Hazard modelling was used. This analysis was performed on patients who left the ICU alive. Results are expressed with

Hazard Ratios (HR) and a corresponding 95% confidence interval. Statistical analysis was performed using R (version 3.5.3) software (The R Foundation for Statistical Computing, Vienna, Austria).

Over the 10-year study period, 73,484 patients were admitted to Scottish ICUs and included in this dataset (**Table One**). Of these patients, 2,201 had a primary Acute Physiology and Chronic Health Evaluation (APACHE) III diagnosis of seizures, comprising 3% of the population. The ICU mortality for this group was 5.7% compared with 21.9% for the rest of the population. A Cox proportional hazards analysis (with the outcome of interest being risk of death at 3 years) was performed using an unadjusted/adjusted modelling strategy. Several factors increased mortality hazard within this timeframe but the variable of interest in this context was seizures. A diagnosis of seizures increased mortality hazard at 3 years by 17% (HR 1.17, 95% CI 1.07-1.28), compared with the non-seizure population (reference level).

This population based study has demonstrated that, while the ICU and hospital mortality for this group of patients is low, their long term outcomes appear to be poorer than the general population, despite being a younger and less severely sick group. We hypothesise several reasons for this, including lifestyle factors such as alcohol misuse, which are often associated with seizures and also carry excess long-term mortality from critical illness [6]. Such an association has been found in other population-based studies [7]. This study has several strengths including the use of complete, nationally-linked data. However, limitations include the lack of information on the aetiology of the seizures. Although 90% of patients required to be mechanical lung ventilation on ICU admission and were therefore likely admitted because of SE, this information was unavailable. Furthermore, we do not know the ultimate cause of death.

In conclusion, more research is required to explore targeted interventions addressing holistic health needs in order to help reduce the long-term mortality seen in this vulnerable group.

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Table 1. Baseline patient characteristics of those with and those without a diagnosis of seizures on admission to ICU.

Values are median (IQR [range]) or number (proportion).

	Seizure n=2201	Non seizure n=71283	p- value
Age, Years	50 (39-63 [17-91])	61 (48-72{17-102])	<0.001
Sex; male	1330(60.4)	41409(58.1)	0.029
ICU Length of Stay, Days	1.98 (1.04-3.96[0.02-184.88])	2.68 (1.08-6.46[0.00-497.02])	<0.001
Hospital LOS, Days	8 (3-20[0-455])	14 (5-31[0-3664])	<0.001
APACHE II	17 (11-23 [1-46])	19 (14-25 [1-57])	<0.001
Proportion Ventilated (%)	2036 (92.5)	59985(84.2)	<0.001
CPR before ICU admission (%)	47 (2.14)	5712 (8.01)	<0.001
ICU mortality (%)	126 (5.7)	15586 (21.9)	<0.001
Hospital mortality (%)	238 (10.8)	19949 (28)	<0.001
One year mortality (%)	481 (21.9)	25719 (36.1)	<0.001
Three year mortality (%)	660 (30)	29935 (42)	<0.001