

Recurrent Seizures Following Cardiac Surgery: Risk Factors and Outcomes in a Historical Cohort Study

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Objectives: To determine the risk factors for and outcomes after recurrent seizures (RS) in patients following cardiac surgery.

Design: A historical cohort study.

Setting: A single-center university teaching hospital.

Participants: Cardiac surgery patients from April 2003 to September 2010 experiencing postoperative seizures.

Interventions: None.

Measurements and Main Results: Patients were divided into an isolated seizure group and an RS group. Risk factors for RS were determined using logistic regression. Intermediate-term follow-up was conducted by phone. Of 7,280 consecutive patients undergoing cardiac surgery, 61 (0.8%) experienced postoperative seizure and 36 (59%) of those experienced at least 1 recurrence. Of these, 32 (89%) experienced RS within 24 hours of the first seizure, and 29 (81%) had grand mal seizures. Preoperative creatinine ≥ 120 $\mu\text{mol/L}$ ($p = 0.02$), time until first seizure occurred (≤ 4

hours; $p = 0.01$), and procedures involving the thoracic aorta were associated with RS ($R^2 = 0.53$, $p < 0.05$). Patients with RS had longer intensive care unit stays (5.3 v 2.9 days, $p = 0.03$) and longer mechanical ventilation duration (53.3 v 15.0 hours, $p = 0.01$). At a median follow-up of 21 months for the RS group and 16 months for the isolated seizure group, restrictions, anticonvulsant use, morbidity, and mortality were similar between patients with isolated versus recurrent seizures.

Conclusions: Higher preoperative creatinine, thoracic aortic surgery, and early seizure onset were associated with RS after cardiac surgery. When compared to isolated seizures, recurrence per se was not associated with significantly increased long-term morbidity or mortality.

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POSTOPERATIVE SEIZURES, although relatively uncommon, are a well-documented complication of cardiac surgery. The incidence of seizures after cardiac surgery varies between 0.5 and 7.6%.¹ When seizures occur, recurrence rates of 40% to 66% have been reported.^{2–5} Seizures may be caused by thromboembolic ischemic stroke, cerebral air embolism, medication toxicity related to antibiotics, or other perioperative drugs such as tranexamic acid (TXA).^{6–8} The authors previously reported that administration of TXA, preoperative cardiac arrest, Acute Physiology and Chronic Health Evaluation (APACHE) II scores > 20 , previous cardiac surgery, open-chamber procedure, cardiopulmonary bypass (CPB) time > 150 minutes, and preoperative neurologic disease are all independent risk factors for seizures after cardiac surgery.⁴ Importantly, approximately 60% of patients in that study had more than 1 seizure during their postcardiac surgery hospital stay, thereby defining recurrent seizure (RS).

In the general non-surgical population, RS often is related to factors such as a history of epilepsy, subtherapeutic anticonvulsant levels, alcohol withdrawal, and structural brain abnormalities.^{9,10} However, associated risk factors and outcomes for RS after cardiac surgery are not known. Knowing these risk factors could influence in-hospital clinical decision making and

impact a patient's quality of life regarding return-to-normal activity and the possibility of long-term anticonvulsant therapy.

The purpose of this historical cohort study was to create an exploratory predictive model for seizure recurrence after cardiac surgery as well as to compare the outcomes for these patients compared to those with isolated seizure.

METHODS

The local Research Ethics Board approved this study (January 2010) and waived the requirement for patient consent for the historical cohort component of the study. For follow-up, informed consent was obtained from patients prior to the telephone interview.

This report represents a subset of patients from a previously published single-center historical cohort study performed on all patients who underwent cardiac surgery at the authors' institution between April 1, 2003 and September 30, 2010 who had postoperative seizures.⁴ In the original study, the impact of TXA and other risk factors were compared between patients who did and did not experience postoperative seizure. For this present study, patients from the previous cohort who experienced post-cardiac surgery seizures were divided into 2 groups: those who had one postoperative isolated seizure and those who experienced RS (ie, more than one postoperative seizure while in the hospital). The reason for this division was to specifically explore the significance of recurrent seizures as compared to isolated seizures.

Data collected from the authors' cardiac surgery, perfusion service, and intensive care unit (ICU) databases included information on all consecutive cardiac surgery cases performed at their institution. The perfusion service database collects intraoperative variables, and the cardiac surgery and ICU databases collect demographic and comorbidity variables (including postoperative complications), ventilation time, and lengths of ICU and hospital stays. A concurrent pharmacy database maintains information related to the inventory of

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drugs dispensed to various clinical services, including anesthesia for cardiac surgery.⁴

A seizure was defined as a physician-documented event such as rhythmic tonic-clonic motion of localized body parts consistent with a focal seizure, or of all four limbs with a decreased level of consciousness consistent with a grand mal seizure that required prescribed intervention. Nonconvulsive seizures were diagnosed in patients with a persistent decrease in the level of consciousness and confirmed seizure activity on serial electroencephalography (EEG).

A telephone interview was conducted more than a year after discharge to ascertain if there had been any hospital readmission, new neurologic diagnoses (eg, RS and stroke), the need for long-term anticonvulsant therapy, and/or any activity restrictions (such as driving) instituted that were related to seizures.

Statistical Analysis

All statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL). Univariate analysis was performed with a Student's 2-sample t-test (for normally distributed data), the Mann-Whitney U test (for non-normally distributed data) and Pearson's chi-square test (for categorical data) in which potential recurrent seizure risk factors and outcomes were compared between groups. Due to a relatively small sample size, the authors opted to create an exploratory (ie, hypothesis-generating) model for risk factors for RS that could serve as a basis for future studies. As such, multivariable logistic regression was performed using clinically relevant variables (that had a univariate p value <0.1) to create a

model with the highest R² value and largest area under the receiver operating curve (ROC). A 2-tailed p value ≤ 0.05 was considered statistically significant.

RESULTS

Sixty-one (0.8%) of 7,280 consecutive patients experienced a postoperative seizure (Fig 1). Of these 61 patients, 36 (59%) had at least 1 RS, 17 patients (28%) experienced more than 1 recurrence, and 3 (8%) had non-convulsive status epilepticus. Of the 36 patients with RS, 32 (89%) experienced RS within 24 hours of the first seizure, and 4 patients (11%) experienced RS >24 hours after the first seizure. Grand mal seizures accounted for the majority of patients with RS (29/36; 81%), and each seizure (except for the 3 patients with nonconvulsive status epilepticus) lasted less than 5 minutes.

A comparative univariate analysis between patients with RS and patients with isolated seizure is outlined in Table 1. Importantly, patients with RS had higher preoperative creatinine levels, higher APACHE II scores, more thoracic aortic and deep hypothermic circulatory arrest (DHCA), more postoperative cerebrovascular accidents (CVA), and a shorter period of time from the end of surgery until the first seizure occurrence (ie, early onset of the first seizure). Of note, patients with isolated seizures and patients with RS had similar doses of TXA given, although the authors did not know the serum (or cerebrospinal fluid levels¹¹) of TXA.

Variables associated with RS that were considered biologically plausible and that had a p value < 0.1 were further examined in the authors' multivariate model. These variables included preoperative creatinine, APACHE II score, open-

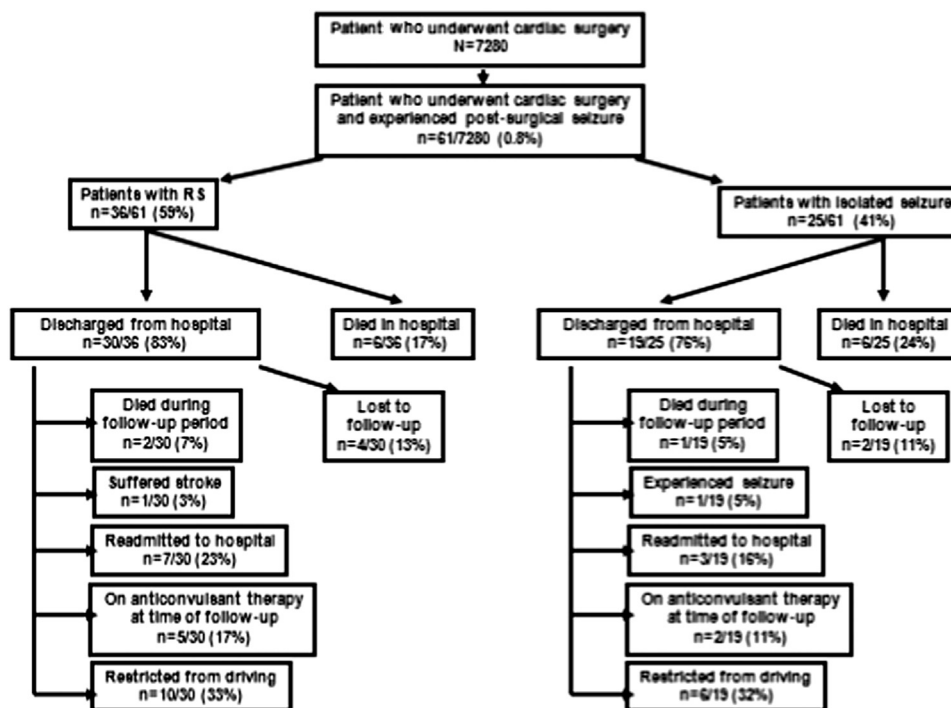


Fig 1. Flow diagram of the historical cohort observed in this study comparing patients with isolated seizures to patients with recurrent seizures (RS). The median follow-up period was 21 (6-30) months for the recurrent seizure group and 16 (11-28) months for the isolated seizure group.

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