Seizure After Cardiopulmonary bypass Surgery: A Retrospective Study

Jean Hee Kim

Seoul Saint Mary's Hospital <https://orcid.org/0000-0002-1488-5335>

Jinhee Jang

Seoul Saint Mary's Hospital

Hwan Wook Kim

Seoul Saint Mary's Hospital

Woojun Kim (✉ wjkim@catholic.ac.kr)

Seoul Saint Mary's Hospital

Research article

Keywords: cardiopulmonary bypass, postoperative seizure, epilepsy, nonconvulsive status epilepticus, status epilepticus

Posted Date: February 9th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-191702/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Abstract

Background: We are to investigate prognostic factors of seizure after cardiopulmonary bypass surgery based on the incidence, the operation parameters, and the outcomes of seizure.

Methods: Consecutive patients presented a seizure after a cardiac or aortic surgery using a cardiopulmonary bypass (CPB) during the admission between January 2006 and January 2019 were retrospectively enrolled. Patients with a previous seizure history were excluded. The medical records were reviewed on the demographics, associated medical conditions, laboratory, electroencephalography (EEG), and imaging findings, cardiopulmonary bypass parameters, types of seizure, and prognosis.

Results: Among the 488 patients who received cardiopulmonary surgery using CPB, 29 patients were diagnosed with seizure during admission. There were nine cases of aortic valve replacement, six of mitral valve replacement, four of aorta graft, two of patent ductus arteriosus closure, coronary artery bypass graft, tricuspid annuloplasty, and tumor resection for each. The average durations of the operation and of cardiopulmonary bypass were 278 ± 119 and 108 ± 55 minutes, respectively. The average aortic cross clamping time was 72 ± 41 minutes. The median detection time of a seizure was 34.38 ± 83.37 hours after surgery. Twenty-three patients (79.3%) did not show recovery of mental status after surgery until the seizure was detected. Seventeen patients were diagnosed with status epilepticus, and two of them had nonconvulsive status epilepticus. Nine showed repetitive seizures and three presented a single seizure. EEG analysis showed five cases of spike-and-wave, four of periodic discharges, four of rhythmic delta, and one of burst suppression. From the image studies, sixteen patients showed stroke, two revealed posterior reversible encephalopathy syndrome, and two showed seizure related changes. Nine (31.0%) expired in 25 ± 27 postoperative day. For the survived patients, the average duration of ICU admission was 9 ± 7 days.

Conclusions: Due to its difficulty of detecting preclinical seizure after the surgery, evaluation including performance of EEG in early postoperative phase should be considered.

Background

Cardiopulmonary bypass (CPB)s is an extracorporeal circulation assisting the operation on cardiac and great vessels, which has brought radical changes in cardiac surgery.(1) However, the cardiopulmonary bypass use has been reported to be associated with perioperative morbidity and mortality.(1)

Although rare complication of the operation, the incidence of seizure after cardiac surgery is within the range of 0.5–7.6%.(2) Unlike postoperative stroke that has been clarified on the etiology in a certain degree, the causes of the postoperative seizure are variable. Literatures on the factors associated with postoperative seizure report the multivariate regression analysis on the predictive factors such as age, gender, associated disease, duration of the procedure, and medications used.(2–4)

As the postoperative seizure worsens the prognosis of the surgical outcome, it is important to thoroughly analyze various factors associated with the seizure outcome. However, detecting the seizure is problematic especially in obtunded patients, it should be realized that the postoperative seizure could have been underestimated in the publications.(5)

We are to explore our experience of patients presenting the first seizure after cardiac or aortic surgery using CPB based on the incidence, the operation parameters, and the outcomes of seizure.

Methods

Subjects and study protocol

Consecutive patients who presented a seizure after a cardiopulmonary surgery using a CPB during the admission at Seoul St. Mary's Hospital between January 1, 2006 and January 31, 2019 were identified. Patients with previous seizure history or non-epileptic myoclonus were excluded.

The medical records were reviewed on the following data: sex, age, underlying disease, and diagnosis at discharge. We reported laboratory values of complete blood count including hemoglobin, hematocrit, white blood cell count, and platelet count. Serum aspartate transaminase (AST), serum alanine transferase (ALT), blood urea nitrogen, and serum creatinine level were measured with admission.

Operation notes were retrieved for information regarding on the operation title, the anesthetic time, and the cardiopulmonary parameters like cardiopulmonary bypass time, aortic cross clamping time, and activated clotting time. Use of antifibrinolytic drugs for each surgery were identified. Anesthetic agents that may affect seizure were stopped as the operation ends.

Initial seizure detection time was defined as the initial documented time reported by a nursing or medical staff. The time of consultation to be filled out by the attending physician was determined as the initial seizure detection time for any patients who presented prolonged unexplained decreased mental state without a convulsive movement and who had been through the neurology consultation, that made a diagnosis of a non-convulsive seizure fulfilling the criteria and confirmed by the electroencephalogram (EEG) study.(6)

All patients were recommended to conduct either a computerized tomography (CT) scan and/or a magnetic resonance imaging (MRI) and were reviewed by a neuroradiologist (JHJ).

For the prognosis of the seizure after a cardiac pulmonary bypass surgery, the duration of the hospitalized day in the intensive care unit (ICU) for the survived patients and the number of death in the study population were counted.

Seizure classification

As its nature of the retrospective data, the seizure classification was determined based on the documented consultation notes written by a neurologist. The initial manifestations of the seizure are used to categorize the seizure broadly as focal and generalized.(7) Two or more seizures within 24 hours with definite termination of the first episode and full recovery of the initial mental state were defined as an acute repetitive seizures (cluster seizures).(2) The definition of status epilepticus accepted following criteria of “ ≥ 5 min of (a) continuous seizure or (b) two or more discrete seizures between which there is incomplete recovery of consciousness.”(8) Non-convulsive status epilepticus is defined as an altered mental status or behavior from baseline and seizure activity on the EEG lasting for more than 30 minutes. (9)

EEG recordings and analyses

A standard EEG recordings were obtained using the international 10–20 system for electrode placement with duration of 30 minutes. The EEG patterns were classified according to the American Clinical Neurophysiology Society’s Standardized Critical Care EEG Terminology: 2012 version.(10) Prevalent pattern of EEG is classified into periodic discharges, rhythmic delta activity, spike-and-wave or sharp-and-wave, burst suppression, and EEG seizure, which was evaluated by a neurologist (JHK or WK).

Table 1
Characteristics of patients with seizure after cardiopulmonary surgery using
cardiopulmonary bypass

Total no. of patients	29
Female : Male	13 : 16
Mean age	62 ± 14 years
Operation title	
Aortic valve replacement	9
Mitral valve replacement	6
Aortic artery graft	4
Patent ductus arteriosus closure	2
Coronary artery bypass graft	2
Tricuspid annuloplasty	2
Tumor resection	2 (1 myxoma, 1 papillary fibroelastoma)
Others	1 for each title: - Graft replacement of thoracoabdominal aorta - Pulmonary artery embolectomy - Thoracic aorta aneurysm resection - Tricuspid valve replacement - Mitral valve plasty - Aneurysm repair - Atrial septal defect closure - Angiectomy
Operation emergency	
Emergency operation	6 (20.7%)
Urgent operation	13 (44.8%)
Elective operation	10 (34.5%)
Operation parameters	
Operation time	278 ± 119 min
Cardiopulmonary bypass time	108 ± 55 min

Total no. of patients	29
Aortic cross clamping time	72 ± 41 min
Activated clotting time	180 ± 122 min

Ethical approval

The Institutional Review Board of the institution approved this study. The need for an informed consent was waived as there is no study intervention toward the patient and due to its nature of the retrospective study.

Results

Among the 488 patients who received cardiopulmonary surgery using CPB, 29 patients (5.9%) presented seizure during the admission period. There were thirteen female and sixteen male patients. The mean age of the patients was 62 ± 14 years. Demographics, clinical data, and the initial laboratory results on the detection date of the seizure for the 29 patients are summarized in Table 1.

As of the operation, there were nine cases of aortic valve replacement, six of mitral valve replacement, and four of aorta graft operation. There were two cases of patent ductus arteriosus closure, coronary artery bypass graft, tricuspid annuloplasty, and tumor resection for each. After the pathologic evaluation, the tumors were confirmed to be a myxoma and a papillary fibroelastoma, respectively. Six patients had two separate disease entities operated on the day of the surgery: 2 cases of aortic valve replacement with pulmonary artery embolectomy or aortic artery graft, 3 cases of mitral valve replacement with tricuspid annuloplasty (2 cases) or patent ductus arteriosus closure, and 1 case of aortic valve replacement and mitral valve replacement. Six of the cases required emergency operation that require an immediate surgery. Thirteen cases were found to be an urgent surgery, defined as a surgery required to be done within few days depending on the medical condition which is less urgent than the emergency operation. There were ten cases of elective operation. The mean durations of the operation and of cardiopulmonary bypass were 278 ± 119 and 114 ± 60 minutes, respectively. The mean aortic cross clamping time was 70 ± 43 minutes. The mean activated clotting time was 180 ± 122 minutes. Tranexamic acid, an antifibrinolytic drug, was used for twenty two patients (76%).

The median detection time of a seizure was 34.38 ± 83.37 hours after the surgery. Twenty three patients (79.3%) did not show recovery of mental status after surgery until the seizure was detected. Seventeen patients (58.6%) were diagnosed with status epilepticus, and two of them had non-convulsive status epilepticus. Nine (31.0%) showed repetitive seizures and three (10.3%) presented a single seizure.

EEG analysis showed five cases of rhythmic spike-and-wave activity, four of periodic discharges, four of rhythmic delta activity, and one of burst suppression. Out of 25 patients who had been through the brain image study, thirteen patients (44.8%) conducted both brain CT and brain MRI and eleven patients (37.9%) went through brain MRI only. Only one patient performed brain CT only. Four patients (13.8%) did

not go through an image study due to unstable condition. Either brain CT or MRI, sixteen patients (66.7%) appeared acute stroke, while two patients (6.9%) revealed posterior reversible encephalopathy syndrome (PRES). There were two patients with seizure related changes and three with old lesions in the brain MRI whether symptomatic or not. Two patients did not show any change in the image.

Nine (31.0%) of the patients expired during admission in median 25 ± 27 postoperative day. Six patients expired within thirty days after the operation. As of the cause of the mortality, four patients died from sepsis, and two patients died from cardiovascular cause such as low cardiac output syndrome and myocardial infarction. One patient expired from acute respiratory distress syndrome. Causes of death were uncertain for remaining 2 patients. For the survived 20 patients (69.0%), the average duration of ICU admission was 9 ± 7 days.

Discussion

In this study, patients who presented the first seizure in their lives after the cardiac or aortic surgery are described on the factors associated with the seizure. We focused on the patients who received surgery using CPB, in purpose of recruiting subjects who received major cardiac or aortic surgery, which has higher potential risk of complications. The incidence of the seizure in this study is within the range of the reported seizure after adult cardiac surgery which was 0.5–7.6%.⁽²⁾ More than half of the operations are related to the cardiac valve related, especially the aortic valve replacement. It shows higher proportion compared to the previous study, which reported 15.7% for aortic valve procedure and 9.2% for mitral valve procedure.⁽⁴⁾ The urgency of the operation in the current study has been evenly distributed.

In a study on the operation parameters, CPB time and aortic cross-clamp time were reviewed. CPB time longer than 150 minutes was recognized as a significant factor associated with post cardiac surgery seizure.⁽⁴⁾ While the CPB is an unavoidable procedure in the major cardiac or aortic surgery, it has been known that the longer the CPB use, the higher incidence of complications including the neurologic complications due to its systematic inflammatory response.⁽¹⁾ In support of the systemic inflammatory response after CPB utilization, the association between the elevated cytokine level and the duration of the CPB has been reported.^(1, 11, 12)

While the cross-clamp time did not gain significance in the mentioned study above, another study on the association with the seizure within 24 hour after the operation revealed that the aortic cross-clamping time as a significant univariate association with the seizure.⁽³⁾ It has been discovered that the myocardial ischemic time is prolonged as the aortic cross-clamping time delayed.⁽¹³⁾ This prolongation leads to the release of myocardial enzymes, which exacerbated the complication of the surgery.⁽¹³⁾ A study on the prognostic impact of prolonged cross-clamping time in coronary artery bypass grafting, the adjusted analysis revealed that the aortic cross-clamping time longer than 75 minutes was an independent predictor of mortality and other adverse effects.⁽¹³⁾ This duration is similar to the average aortic cross-clamping time of the current study.

Tranexamic acid, a synthetic antifibrinolytic agent, reduces blood loss during the surgery, and it has been often used in a cardiac surgery as in this series of patients.(14) Though, its association with seizure has been reported; it crosses blood-brain-barrier easily and acts as a competitive antagonist at the glycine receptor due to its structural similarity with glycine, blocking its inhibitory action.(14, 15)

Image study results could be classified into four groups: acute stroke, PRES, seizure related changes, and previous cerebral lesions. There are multifactorial causes occurred during the surgery, which produce temporary or permanent lesions in the brain. The arterial blood gas or debris produced during the surgery may perform as an emboli which causes reduction in blood flow and local inflammation in air embolic site.(5, 14) Not only the direct embolization and hypoperfusion caused by an the emboli but also hypotension produced in peri-cardiopulmonary bypass may be the cause of the stroke.(14) Following the hypotension period, disruption of the autoregulation of the cerebral perfusion leads to cerebral vasodilatation and vasogenic cerebral edema, resulting in the hyperperfusion exceeding the required flow rate for the cerebral metabolic demand. In addition to the endothelial dysfunction and disruption of the blood brain barrier, PRES occurs.(16–18) Out of five patients who did not show any significant change nor acute lesion in the image, in this study, four patients survived with 11 ± 10 average days of ICU admission. Fifteen patients in cases of abnormalities detected in the brain image survived, the hospitalized days in the ICU was 10 ± 6 days in average. The ICU duration of the two groups were similar in terms of the duration in the ICU.

The median detection time of the seizure in the current study exceeds 24 hours after the surgery. Also, most of the patients (79.3%) presented seizure without recovery of the mental status after surgery. The delay in seizure diagnosis past the 24 hours was studied to be associated with a 75% mortality rate due to prolonged nonconvulsive seizure activity.(15, 19) While only two patients found to be classified as a nonconvulsive status epilepticus, it could be under-recognized considering the subtle presentation of the disease itself. Also, literatures have reported the range of the nonconvulsive status epilepticus to be 8–40% in critically ill patients(15, 19–22), which implies the importance of the earlier suspicion of the possibility of the nonconvulsive seizure in patients who did not regain consciousness after the surgery for the purpose of the more favored prognosis.

Several limitations exist in this study. It was a single-center retrospective study with design of a case series, which limited intervention and statistical analysis on the risk factors of seizures. Furthermore, more than half of the cases failed to go through an image study of the brain due to the critical conditions, and it provided limited radiologic information on the cause or injury after the seizure.

Conclusion

The results of this study provide the characteristics of patients who developed seizure after cardiac or aortic surgery using CPB. Considerable number of patients experienced seizure after the surgery using CPB, and a substantial portion of them were associated with significant acute brain lesion and fatal prognosis. However, the seizures were detected after hours of unconsciousness after surgery in many

patients, possibly due to its difficulty of detecting preclinical seizure in unconscious patients. Evaluations such as EEG should be considered in early postoperative phase in patients with high risk of seizure outcome. A large prospective, randomized, controlled study is warranted to investigate the routine application of the EEG in patients after the cardiopulmonary bypass surgery.

Abbreviations

CPB
Cardiopulmonary bypass
AST
Aspartate transaminase
ALT
Alanine transferase
EEG
Electroencephalography
CT
Computerized tomography
MRI
Magnetic resonance imaging
ICU
Intensive care unit
PRES
posterior reversible encephalopathy syndrome

Declarations

Ethics approval and consent to participate:

The Institutional Review Board of the institution approved this study. The need for an informed consent was waived as there is no study intervention toward the patient and due to its nature of the retrospective study.

Consent for publication:

Not applicable.

Availability of data and materials

Not applicable

Competing interests:

The authors declare that they have no competing interests.

Funding:

None

Authors' contributions:

JHK drafted the manuscript. JHK and WK evaluated electroencephalography.

JHJ reviewed brain image data from computerized tomography and/or magnetic resonance image.

HWK participated in treatment and contributed conceptualization, review, and supervising process.

WK contributed conceptualization, review, and supervising process.

All authors read and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Salis S, Mazzanti VV, Merli G, Salvi L, Tedesco CC, Veglia F, et al. Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2008;22(6):814–22.
2. Sharma V, Katznelson R, Jerath A, Garrido-Olivares L, Carroll J, Rao V, et al. The association between tranexamic acid and convulsive seizures after cardiac surgery: a multivariate analysis in 11 529 patients. *Anaesthesia*. 2014;69(2):124–30.
3. Kalavrouziotis D, Voisine P, Mohammadi S, Dionne S, Dagenais F. High-dose tranexamic acid is an independent predictor of early seizure after cardiopulmonary bypass. *Ann Thorac Surg*. 2012;93(1):148–54.
4. Manji RA, Grocott HP, Leake J, Ariano RE, Manji JS, Menkis AH, et al. Seizures following cardiac surgery: the impact of tranexamic acid and other risk factors. *Can J Anaesth*. 2012;59(1):6–13.
5. Marcuse LV, Bronster DJ, Fields M, Polanco A, Yu T, Chikwe J. Evaluating the obtunded patient after cardiac surgery: the role of continuous electroencephalography. *J Crit Care*. 2014;29(2):316.e1-5.
6. Leitinger M, Beniczky S, Rohrer A, Gardella E, Kalss G, Qerama E, et al. Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus—approach to clinical application. *Epilepsy Behav*. 2015;49:158–63.
7. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017;58(4):522–30.

8. Lowenstein DH, Bleck T, Macdonald RL. It's Time to Revise the Definition of Status Epilepticus. *Epilepsia*. 1999;40(1):120–2.
9. Haffey S, McKernan A, Pang K. Non-convulsive status epilepticus: a profile of patients diagnosed within a tertiary referral centre. *J Neurol Neurosurg Psychiatry*. 2004;75(7):1043–4.
10. Hirsch LJ, LaRoche SM, Gaspard N, Gerard E, Svoronos A, Herman ST, et al. American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology: 2012 version. *J Clin Neurophysiol*. 2013;30(1):1–27.
11. Whitten CW, Hill GE, Ivy R, Greilich PE, Lipton JM. Does the duration of cardiopulmonary bypass or aortic cross-clamp, in the absence of blood and/or blood product administration, influence the IL-6 response to cardiac surgery? *Anesth Analg*. 1998;86(1):28–33.
12. Khabar KS, elBarbary MA, Khouqeer F, Devol E, al-Gain S, al-Halees Z. Circulating endotoxin and cytokines after cardiopulmonary bypass: differential correlation with duration of bypass and systemic inflammatory response/multiple organ dysfunction syndromes. *Clin Immunol Immunopathol*. 1997;85(1):97–103.
13. Ruggieri VG, Bounader K, Verhoye JP, Onorati F, Rubino AS, Gatti G, et al. Prognostic Impact of Prolonged Cross-Clamp Time in Coronary Artery Bypass Grafting. *Heart Lung Circ*. 2018;27(12):1476–82.
14. Brouwer ME, McMeniman WJ. Seizures Following Cardiopulmonary Bypass. *J Extra Corpor Technol*. 2016;48(3):137–40.
15. Patariaia E, Jung R, Aull-Watschinger S, Skhirtladze-Dworschak K, Dworschak M. Seizures After Adult Cardiac Surgery and Interventional Cardiac Procedures. *J Cardiothorac Vasc Anesth*. 2018;32(5):2323–9.
16. Lipsman N, Farb R, Al-Radi OO, Casaubon LK. Status epilepticus due to hyperfusion injury post cardiac surgery. *Can J Neurol Sci*. 2010;37(3):412–5.
17. Chen S, Hu J, Xu L, Brandon D, Yu J, Zhang J. Posterior Reversible Encephalopathy Syndrome After Transplantation: a Review. *Mol Neurobiol*. 2016;53(10):6897–909.
18. Arimura FE, Camargo PC, Costa AN, Teixeira RH, Carraro RM, Afonso JE Jr, et al. Posterior reversible encephalopathy syndrome in lung transplantation: 5 case reports. *Transplant Proc*. 2014;46(6):1845–8.
19. Young GB, Jordan KG, Doig GS. An assessment of nonconvulsive seizures in the intensive care unit using continuous EEG monitoring: an investigation of variables associated with mortality. *Neurology*. 1996;47(1):83–9.
20. Goldstone AB, Bronster DJ, Anyanwu AC, Goldstein MA, Filsoufi F, Adams DH, et al. Predictors and outcomes of seizures after cardiac surgery: a multivariable analysis of 2,578 patients. *Ann Thorac Surg*. 2011;91(2):514–8.
21. Murkin JM, Falter F, Granton J, Young B, Burt C, Chu M. High-dose tranexamic Acid is associated with nonischemic clinical seizures in cardiac surgical patients. *Anesth Analg*. 2010;110(2):350–3.

22. Dham BS, Hunter K, Rincon F. The epidemiology of status epilepticus in the United States. *Neurocrit Care*. 2014;20(3):476–83.