Prevalence and characteristics of Postoperative Cognitive Dysfunction (POCD) in on-pump cardiac surgery patients at Dr. Kariadi General Hospital Semarang

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ABSTRACT

Background: Postoperative Cognitive Dysfunction or POCD is a reversible decline in the cognitive function of patients after surgery. The risk factors for POCD are age, comorbidities, duration of CPB, intraoperative hypoperfusion, duration of ventilator use, and postoperative sedation are risk factors of POCD. This study aims to determine the prevalence and characteristics of postoperative cognitive dysfunction (POCD) in patients who undergo on-pump cardiac surgery at Dr. Kariadi General Hospital.

Methods: This study's population was all patients undergoing on-pump cardiac surgery at Dr. RSUP Kariadi in July-December 2021. The study subject was 97 patients, obtained by total sampling technique. The study subjects were examined for cognitive function with MoCA-INA one day before surgery and the third day after surgery. Data were analyzed using SPSS version 23 for Windows.

Results: There were 68 (70.1%) patients who experienced POCD and 29 (29.9%) patients who did not experience POCD. The median age of patients with POCD is 50 (18-68) years and 36 (18-63) years for patients without POCD. Based on MAP during CPB, patients with POCD had a median of 64 (51-80) minutes. In patients with POCD, the median length of CPB was 53 (22-92) minutes, and the median length of the aortic cross-clamp clamp was 35 (11-69) minutes.

Conclusion: We found a high prevalence of POCD patients after on-pump cardiac surgery, as many as 70.1% at Dr. Kariadi General Hospital.

Keywords: POCD, MoCA-INA, On-Pump Cardiac Surgery.


INTRODUCTION

Postoperative cognitive dysfunction (POCD) is a reversible decline in patients' cognitive function after surgery.1 Cognitive decline after surgery is 80%, which can cause increased mortality. Morbidity creates problems in social and economic aspects, marked by prolonged hospitalization, increased costs, and decreased quality of life of patients.2,3 POCD is a cognitive function disorder characterized by disturbances in memory, concentration, and information processing that often occurs after major surgery. The prevalence of POCD is reported to be higher in patients after cardiac surgery procedures, assuming this condition arises due to physiological disturbances due to cardiac-pulmonary bypass (CPB).

However, recent studies have reported that POCD can occur in cardiac surgery with or without CPB.4 Although the pathological pathway of POCD is not known with certainty. There are 3 possible causes. First is inadequate brain perfusion. Second, systemic inflammatory reactions of the body and microemboli.5 Risk factors such as age, hypertension, diabetes, duration of CPB use, intraoperative hypoperfusion, hypothermia, decreased hematocrit, prolonged use of ventilation, and postoperative sedation have been found to influence the occurrence of POCD.4 Sonearto et al. reported that elderly patients (>65 years) had an increased risk of developing POCD after cardiac surgery. Lucy et al. reported that 52% of patients experienced cognitive decline following elective surgery.5 This study aims to determine the prevalences and characteristics of POCD in pump cardiac surgery patients at Dr. Kariadi General Hospital Semarang.

METHODS

The research was conducted in Dr. Kariadi General Hospital, Semarang, Indonesia. The research was carried out during the period from July-December 2021. This is a descriptive study of patients undergoing pump cardiac surgery.

The data were obtained from 146 study subjects who met the inclusion and exclusion criteria. The inclusion criteria were patients undergoing elective on-pump cardiac surgery, aged >18 years, and willing to participate in the study.
The exclusion criteria in this study were patients with a history of cerebrovascular accident (CVA) based on anamnesis and medical records, history of illiteracy, visual and hearing impairment, history of cardiovascular surgery, history of preoperative cognitive impairment based on MoCA-INA score <26, requiring transfusion preoperatively with renal impairment (serum creatinine > 2 mg/dl) and patients on prolonged ventilator usage (3 days of mechanical ventilators usage).

In this study, patients with impaired renal function who had serum creatinine > 2 mg/dl became the exclusion criteria for this research sample. In this study, post-preoperative transfusion became the exclusion criteria because accumulating evidence showed that increased inflammatory response significantly impacts the risk of POCD. The sampling technique was obtained by non-random consecutive sampling with the number of samples based on the patient’s arrival at Dr. RSUP Kariadi Semarang in July – December 2021 period. The research was carried out at Dr. Kariadi General Hospital Semarang after obtaining ethical approval from the Health and Medical Research Ethics Committee of Dr. Kariadi Semarang.

After obtaining approval from the Institutional Ethical Committee, patients were recruited for the study based on the inclusion criteria. Informed consent was obtained and the patients were subjected to a history of the medical record. The first data collection was done by history taking and medical records to obtain preoperative data (age, hypertension, diabetes mellitus, and ejection fraction). The second data was obtained from intraoperative medical records and perfusion to obtain intraoperative data (length of CPB, duration of Cross Clamps, Hb, and MAP levels). The third data was obtained by looking at postoperative medical records in the ICU to obtain postoperative data such as ventilator usage duration and sedation usage. MoCA-INA assessed preoperative cognitive function, and patients with MoCA-INA scores <26 were excluded. The patient’s cognitive function will be assessed again with MoCA-INA on the third postoperative day in the ICU, HCU, or ordinary ward.

This study used descriptive statistical analysis to describe the data on the prevalence and the characteristics of POCD patients. Data analysis was carried out by the Statistical Package for the Social Sciences 23.0 software (SPSS Inc.) - IBM SPSS Statistics.

RESULTS
There were 146 patients undergoing on-pump cardiac surgery at Dr. Kariadi General Hospital Semarang in July–December 2021, consisting of 33 pediatric and 113 adult patients. A total of 97 patients met the inclusion criteria, with 8 patients dying, 3 patients undergoing reoperation, and 5 patients undergoing prolonged ventilation therefore excluded from the study.

Characteristics and clinical features of the study subjects are presented in Table 1, where out of 97 research subjects, 68 patients experienced POCD, and 29 patients did not experience POCD. Based on gender, 51 patients were male (52.6%), with 42 (82.4%) having POCD and 46 women (47.4%) with 28 (56.5%) having POCD. There were 44 patients (45.4%) who had no comorbidity, with 27 patients (61.4%) having POCD, 1 patient (1.03%) had comorbidity of diabetes mellitus and hypertension, suffering from POCD (100%), 42 patients (43.3%) had hypertension as the comorbidity with 31 patients having POCD (73.8%), 10 patients (10.3%) having both comorbidities of diabetes mellitus and hypertension with 9 patients having POCD (90%), and 3 patients (3.1 %) were obesity with 2 people (66.7%) having POCD.

A total of 27 patients (27.8%) underwent Table 1. Characteristics and clinical features of the study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N=97)</th>
<th>POCD (N=68)</th>
<th>Without POCD (N=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects, n (%)</td>
<td>97 (100.0)</td>
<td>68 (70.1)</td>
<td>29 (29.9)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>51 (52.6)</td>
<td>42 (82.4)</td>
<td>9 (17.6)</td>
</tr>
<tr>
<td>Female</td>
<td>46 (47.4)</td>
<td>28 (56.5)</td>
<td>20 (43.5)</td>
</tr>
<tr>
<td>Comorbidity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No comorbidity</td>
<td>44 (45.4)</td>
<td>27 (61.4)</td>
<td>17 (38.6)</td>
</tr>
<tr>
<td>Diabetes Mellitus (DM)</td>
<td>1 (1.03)</td>
<td>1 (100.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hypertension (HT)</td>
<td>42 (43.3)</td>
<td>31 (73.8)</td>
<td>11 (26.2)</td>
</tr>
<tr>
<td>DM + HT</td>
<td>10 (10.3)</td>
<td>9 (90.0)</td>
<td>1 (10.0)</td>
</tr>
<tr>
<td>Surgery Type, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>27 (27.8)</td>
<td>25 (92.6)</td>
<td>2 (7.4)</td>
</tr>
<tr>
<td>Valve Surgery</td>
<td>70 (72.2)</td>
<td>43 (61.4)</td>
<td>27 (38.6)</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (3.1)</td>
<td>2 (66.7)</td>
<td>1 (33.0)</td>
</tr>
<tr>
<td>No</td>
<td>94 (96.9)</td>
<td>66 (70.2)</td>
<td>28 (29.8)</td>
</tr>
<tr>
<td>Ejection Fraction (EF), n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 50%</td>
<td>67 (69.1)</td>
<td>44 (65.7)</td>
<td>23 (34.3)</td>
</tr>
<tr>
<td>&lt; 50%</td>
<td>30 (30.9)</td>
<td>24 (80.0)</td>
<td>6 (20.0)</td>
</tr>
</tbody>
</table>

Table 2. The comparison of POCD and Non-POCD patients’ characteristic data

<table>
<thead>
<tr>
<th>Variable</th>
<th>POCD (N=68)</th>
<th>Without POCD (N=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (min-max)</td>
<td>50.0 (18.0-68.0)</td>
<td>36.0 (18 – 63)</td>
</tr>
<tr>
<td>MAP during CPB (mmHg), median (min-max)</td>
<td>64.0 (51.0-80.0)</td>
<td>64.0 (58 – 89)</td>
</tr>
<tr>
<td>Duration of CPB (minutes), median (min-max)</td>
<td>52.0 (22.0-92.0)</td>
<td>3.20 (22 – 83)</td>
</tr>
<tr>
<td>Duration of AOx clamp (minutes), median (min-max)</td>
<td>35.0 (11.0-69.0)</td>
<td>21.0 (11 – 69)</td>
</tr>
<tr>
<td>Delta score of Hb post-surgery (g/dL) (mean±SD)</td>
<td>-3.00±1.95</td>
<td>-2.5 ±(1,26)</td>
</tr>
<tr>
<td>Duration of the ventilator (hours), median (min-max)</td>
<td>18.5 (10.0-48.0)</td>
<td>20.0 (15 – 48)</td>
</tr>
<tr>
<td>Duration of sedation (hours), median (min-max)</td>
<td>16.0 (7.0-45.0)</td>
<td>16.0 (12 – 45)</td>
</tr>
</tbody>
</table>
a type of CABG surgery, of which 25 patients (92.6%) had POCD. There were 70 patients (72.2%) who underwent valve surgery, with 43 people (61.4%) having POCD. Based on the ejection fraction (EF) data, 67 patients (69.1%) had EF 50% with 44 patients (65.7%) experiencing POCD, and 30 patients (30.9%) had EF <50% with 24 patients (80%) had POCD. The comparison of POCD and Non-POCD patients’ characteristic data is presented in Table 2.

The median age of subjects with POCD is 50 (min-max: 18-68) years, and subjects without POCD have a median age of 36 (8-63) years. Based on MAP during CPB, subjects with POCD had a median of 64 (51-80) minutes. In patients with POCD, the median length of CPB was 53 (22-92) minutes, and the median length of AOx clamp was 35 (11-69) minutes. The mean post-op Hb delta value in subjects with POCD was -3.00 (±1.95; 95% CI -3.48 to -2.53) g/dL, with a ventilator duration of 18.5 (min-max: 10-48) hours and a sedation length of 16 (min-max: 7-45) hours.

**DISCUSSION**

Postoperative cognitive dysfunction (POCD) is a reversible decline in patients’ cognitive function after surgery. In cardiac surgery, cognitive decline is suspected of having occurred since the introduction of the cardiac pulmonary bypass (CPB) machine. Results showed that there were 68 (70.1%) of 97 patients had POCD, which was indicated by the postoperative MoCA-INA score <26, and 29 patients (29.8%) did not experience POCD based on the MoCA-INA score ≥26. There were different results from the past study of Soenarto et al., which reported that 40.7% of 54 study subjects had decreased cognitive function and Nurcahyo et al. reported that 68.4% of valvular heart surgery patients had POCD, which may be due to cognitive decline screening instruments and different examination times.

This study classified POCD risk factors into preoperative, intraoperative, and postoperative. The preoperative risk factors include age, gender, body mass index (BMI), comorbidities, and ejection fraction (EF). Based on age, it was found that the study subjects with POCD were older than those without POCD, which is similar to a previous study that reported an increase in the prevalence of POCD with increasing age, with age being a factor associated with the incidence of postoperative POCD. Aging process can induce degenerative processes in the brain that can lead to the appearance of POCD over a more extended period. In addition, the incidence of POCD in old age may be due to alterations in vascular regulation or comorbidities, which can trigger systemic inflammation and neural involvement that predisposes to POCD.

Results showed that most patients who experienced POCD were male, which is in line with several previous studies which showed that male respondents mainly experienced the incidence of POCD. This condition is probably due to the role of the hormone estrogen in maintaining brain homeostasis, and estradiol hormone is known to have greater left prefrontal cortex activity, which is a verbal processing area compared to progesterone.

Comorbidity histories such as diabetes mellitus and hypertension were found in subjects with POCD, with these results in line with previous studies that reported the effect of comorbidities on POCD. Hypertension and Diabetes Mellitus cause impairment of brain autoregulation, increase oxidative stress, and increase the risk of developing vascular encephalopathy, which causes brain damage and impaired cognitive function in patients. The value of ejection fraction is a parameter of ventricular function assessment by echocardiography; 44 patients with POCD had EF of 50%, and 24 patients had EF <50%. These results are in line with several studies that have reported an association between low ejection fraction and impaired cognitive function, where cerebral hypoperfusion can cause POCD.

Mean arterial pressure (MAP), duration of use of CPB, duration of aortic cross-clamp (AOx), and delta hemoglobin were grouped as risk factors for intraoperative POCD. This study found that the median MAP in subjects with POCD was 64 (min-max: 51-80) mmHg and 64 (min-max: 58-89) mmHg in subjects without POCD. It is known that the MAP condition at the time of CPB must be maintained because the condition of brain hypoperfusion that occurs when the MAP is low can result in an increased risk of developing POCD. This finding is different from the study by Gold et al., who reported that a high MAP (80-110 mmHg) during CPB was associated with a low incidence of stroke. Kaibi et al. reported that keeping MAP values low did not reduce the incidence of POCD.

The median results of the duration of CPB use showed that patients with POCD had a longer median value of CPB use. This condition is associated with the potential to increase the pro-inflammatory response due to blood exposure to the surface of the CPB circuit. This inflammation will cause endothelial dysfunction and leakage of the blood-brain barrier, thereby triggering an inflammatory process in the brain and the appearance of cognitive impairment.

Xu et al. reported that the duration of CPB usage correlated with POCD, with the incidence of patients with POCD prolonging the duration of CPB usage. In contrast to Sonearto et al., who reported that the cross-clamp duration was not a significant risk factor for POCD, and Nurcahyo et al. found that patients who did not have POCD had a longer median cross-clamp duration than patients who had POCD.

The hemoglobin delta found in patients with POCD was -3.00 g/dL (±SB 1.95; 95% CI -3.22 to -2.50) compared to -2.5 g/dL (±SB 1.95; 95% CI -3.00 to -2.04) in patients without POCD. Low Hemoglobin levels can increase the risk of cognitive decline due to inadequate blood oxygenation in the brain. Hemodilution conditions such as a hematocrit of 15%-15% intraoperatively or a decrease of ≥12% from baseline can result in POCD. Expanded infarct area due to small embolic lesions from hypoperfusion or embolization correlates with POCD as
a clinical symptom. Sun et al. reported that a decrease in intraoperative Hb levels was a risk factor for POCD on the second postoperative day. Del Felice et al. recommended that the Hb value during CPB should not be below 9.4 mg/dL and should not be lower than 9.2 mg/dL at the end of CPB to avoid the risk of brain dysfunction.

The risk factors for postoperative POCD include ventilator usage duration and sedation usage duration. This study found that the median length of ventilator use in patients with POCD was shorter (18.5 hours) than in patients without POCD (20 hours). The study by Mu et al. showed that patients with a duration of ventilator use of 14.9 hours (12.2 – 18.0 hours) had POCD, but it did not differ significantly. Other studies have shown that 80% of delirium in patients on mechanical ventilation is caused by damage to the hippocampus. Decreased ventilation causes brain damage which is thought to be due to hypoxic ischemia, systemic inflammation that causes increased levels of brain proinflammatory cytokines and changes in neurotransmission in the brain. Prolonged mechanical ventilation after surgery will exacerbate cognitive decline due to hippocampal regulation of proinflammatory IL-1, IL-6, and TNF. The median length of sedation in patients with POCD is 16 (min-max: 7-45 hours), with propofol, midazolam, and dexmedetomidine being the most widely used opiates in clinical practice. Previous studies have found that sedation with propofol and dexmedetomidine is thought to reduce the incidence of delirium, and the use of midazolam in patients undergoing surgery may increase the risk of delirium and POCD.

This study conducted a cognitive examination only on the third postoperative day. So, it is necessary to do further research to conduct cognitive examinations on the seventh day, one month, three months, and up to a year after surgery.

CONCLUSION
Coronary artery bypass graft (CABG) on-pump at RSUP Dr. Kariadi General Hospital Semarang. Based on the results of the study, it was found that there was an incidence of 70.1% of the incidence of Postoperative Cognitive Dysfunction (POCD) after on-pump heart surgery, 61.4% incidence of POCD after on-pump valve heart surgery, 92.6% incidence of POCD after heart surgery. Characteristics of on-pump heart surgery patients who experienced POCD at Dr. Kariadi General Hospital Semarang are 50 years old, more males than females, the majority have comorbid DM and HT, ejection fraction <50%, MAP during CPB 64mmHg, CPB duration 52 minutes, aortic cross-clamp duration 35 minutes, delta Hb post op - 3.00, the length of the ventilator is 18.5 hours, and the duration of sedation is 16 hours.

ACKNOWLEDGMENTS
Nothing.

CONFLICT OF INTEREST
There is no conflict of interest in this manuscript.

ETHICAL CONSIDERATION
This research was approved by the Health and Medical Research Ethics Committee of Dr. Kariadi General Hospital, Central Java, Semarang, Indonesia, with the number: 860/EC/KEPK-RSDK/2021.

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AUTHOR CONTRIBUTION
All authors contributed to this study’s conception and design, data analysis and interpretation, article drafting, critical revision, final approval of the article, and publication.

REFERENCES
cognitive dysfunction in older people. Exp Gerontol. 2020;130:110791.