RESEARCH

Lower Preoperative and Postoperative Hemoglobin Levels in Patients with Postoperative Cognitive Dysfunction Compared to Those Without Postoperative Cognitive Dysfunction Following Heart Valve Replacement

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ABSTRACT

Background: Postoperative cognitive dysfunction (POCD) is a prevalent complication that occurs after surgery, impacting cognitive function. Cognitive performance may be hindered by anemia, as it reduces the delivery of oxygen to the brain and leads to tissue hypoxia, affecting metabolism and ultimately diminishing cognitive function.

Objective: The objective of this study is to examine the potential correlation between hemoglobin levels and the occurrence of POCD in individuals undergoing heart valve replacement surgery.

Methods: This retrospective cohort study included all individuals aged 20 years and above who underwent heart valve replacement surgery from July to December 2021. Hemoglobin levels were assessed both before and after the surgical procedure, and cognitive function was evaluated using the Indonesian-adapted Montreal Cognitive Assessment (MOCA-INA) on the third day after the operation. Statistical analysis involved the use of either Student's t-test or the Mann–Whitney nonparametric test.

Results: A total of 70 participants were included in the study from July to December 2021. The majority of the participants were female (57.1%), and a significant proportion were below 60 years old (81.4%). The average preoperative hemoglobin levels were higher (13.30 g/dL) than the average postoperative hemoglobin levels (10.78 g/dL). In terms of cognitive function, 61.4% of participants experienced postoperative cognitive dysfunction (POCD), with a higher mean MoCA-INA score before surgery (28.41) than after surgery (22.37), along

with a delta Hb of -0.27. Furthermore, postoperative hemoglobin levels were significantly lower in POCD patients than preoperatively (p = 0.003).
Conclusion: The occurrence of postoperative cognitive dysfunction (POCD) was linked to the hemoglobin levels after heart valve replacement.

Keywords: disorders of cognition; dysfunction in cognitive processes; levels of haemoglobin; replacement of heart valves; surgical procedure on the heart

INTRODUCTION

Postoperative cognitive dysfunction (POCD) is a frequent complication after surgery, impacting various cognitive functions such as attention, memory, executive function, and information processing speed.[1] Although reversible, it can become permanent in individuals aged 65 years and older, leading to increased clinical interest due to its significant impact on quality of life, heightened risk of disability, and elevated mortality rates.[2] The International Study of POCD reveals an incidence of 25.8% in the first week and 9.9% at 3 months postoperatively for older patients undergoing noncardiac surgery, with a higher incidence of 40% for those undergoing cardiac surgery, particularly heart valve replacement.[2–5]

The exact pathophysiology of POCD following cardiac surgery remains incompletely understood, attributed to multifactorial causes involving various surgical, patient, and anesthetic factors.[6,7] Preoperative anemia, often present in surgical candidates with chronic diseases, is a common occurrence, and several studies establish correlations between lower preoperative hemoglobin levels and adverse postoperative cerebral outcomes.[8] Research in Indonesia by Soenarto et al. emphasizes the significant role of hemoglobin levels in POCD development, while studies in China by Huang et al. and by Shayan et al. demonstrate associations between preoperative hemoglobin levels, anemia, and POCD occurrence.[9,10]

Although the specific mechanism of POCD induced by anemia remains unclear, evidence suggests that anemia may compromise cognitive function by reducing brain oxygen delivery and altering brain metabolism. Hypoxia-induced impairment of neuronal protein synthesis and synaptic plasticity, crucial for learning, may contribute to cognitive deficits. Despite its impact on increasing postoperative complications, hospitalization costs, and resource consumption, POCD remains inadequately studied in Indonesia, particularly after heart surgery procedures. This study aims to investigate the potential association between hemoglobin levels and POCD following heart valve replacement.[11,12]

METHOD

This retrospective cohort study involved individuals aged 20 years and older who underwent heart valve replacement surgery between July and December 2021. The study population comprised adult patients scheduled for heart valve replacement at RSUP Dr. Kariadi. Cognitive functions were assessed using the Indonesian version of the Montreal Cognitive Assessment (MoCA-INA), a validated and reliable tool.[13] We opted for MoCA-INA over MMSE due to its superior ability to detect mild cognitive impairment. MoCA-INA has a total score of 30, encompassing various cognitive domains, including memory, attention, executive function, language, visuospatial skills, calculation, concentration,

abstraction, and orientation. Cognitive function was evaluated with MoCA-INA before surgery, and a score below 26 was considered indicative of cognitive impairment.[14] Exclusion criteria encompassed a history of cognitive disturbance, cerebrovascular accidents within 1 year before surgery, psychiatric disorders, neurodegenerative diseases, prolonged ventilator usage, and mortality. A total of 70 patients were included in this study.

Hemoglobin levels were assessed both prior to and following heart valve replacement using the Automatic Blood Cell Analyzer. Analysis of hemoglobin was conducted using this automated tool. Postoperative cognitive dysfunction (POCD) was defined as a transient reduction in cognitive function associated with the surgical procedure. The Indonesian version of the Montreal Cognitive Assessment (MoCA-INA) was employed for cognitive evaluation, administered before the surgery and on the third day post-surgery. Cognitive impairment was identified by a MoCA-INA score below 26. The postoperative scores were then utilized to classify each patient into either the POCD or non-POCD groups.

We adhered to our institutional guidelines in employing a standard anesthesia protocol. Premedication involved administering 0.07 mg/kg midazolam. Anesthesia induction utilized inhaled sevoflurane at a Minimal Alveolar Concentration (MAC) of 1.0, supplemented with intravenous injections of fentanyl (4 mcg/kg) and rocuronium (1.2 mg/kg). Maintenance included inhaled sevoflurane at 1.0 MAC, intravenous administration of 1 mcg/kg fentanyl every 30 minutes, and 0.1 mg/kg rocuronium every 45 minutes. Mean arterial pressure was maintained within the range of 55–70 mm Hg during cardiopulmonary bypass (CPB). Heparin (300 IU/kg) was administered to maintain an activated clotting time exceeding 400 seconds. Additionally, all patients received a 0.02 mg/kg morphine infusion for 48 hours postoperatively.

Statistical analysis was carried out using the Statistical Package for the Social Sciences software (SPSS Inc.). The study aimed for a statistical power requiring a total of 70 patients, and indeed, 70 patients were included in the analysis. Descriptive analysis utilized the univariate method, presenting categorical variables as frequency and percentage, and numerical variables as frequency, median, minimum, maximum, mean, and standard deviation. The Kolmogorov-Smirnov test was employed to assess the data distribution. The difference between hemoglobin levels and postoperative cognitive dysfunction (POCD) before and after surgery was determined using either Student's t-test or the Mann–Whitney nonparametric test. Results were deemed significant if $P < 0.05$.

The protocols associated with this research underwent scrutiny and approval from the Health Research Ethics Committee of RSUP Dr. Kariadi, identified by the ethical approval number No.608/EC/KEPK-RSDK/2020. Before undergoing surgery, all patients provided their consent by signing an informed consent form.

RESULTS

Seventy patients were included in the study between July and December 2021. A significant proportion of the participants were female (57.1%), and the majority were below 60 years of age (81.4%). Among the participants, 42.9% had comorbidities, with hypertension (36%) being the most prevalent. The majority of patients exhibited a mean arterial pressure

of less than 65 mmHg (61.4%), and a considerable number had an ejection fraction greater than 50 (77.1%). The categorical attributes of the patients are detailed in Table 1.

In this investigation, the average age and body mass index (BMI) of the participants were 38.5 years and 20.60 kg/m2, respectively. The average preoperative hemoglobin levels were higher (13.30 g/dL) than the mean postoperative hemoglobin levels (10.78 g/dL), and the distribution of hemoglobin values followed a normal pattern. Concerning cognitive function, the mean MoCA-INA score before surgery was higher (28.41) than the mean MoCA-INA score after surgery (22.37, with a delta Hb of -0.27), and the distribution of MoCA-INA scores was not normal. The average duration of surgery was 128.42 minutes, and the anesthesia duration was 322.35 minutes. The numerical characteristics of the patients are detailed in Table 2.

The findings of this investigation revealed that 43 patients (61.4%) experienced the development of postoperative cognitive dysfunction (POCD). The distribution of preoperative hemoglobin ($p = 0.542$) and postoperative hemoglobin ($p = 0.157$) was similar between individuals with impaired and normal cognitive function. However, in POCD patients, the hemoglobin level before surgery was significantly lower compared to the hemoglobin level after surgery ($p = 0.003$). The association between hemoglobin and POCD is presented in Table 3.

Table 1. Categorical Characteristics of Study Participants (N = 70)

Variables	Frequency (n)	Percentage (%)
Age (years)		
≥ 60	13	18,6
< 60	57	81,4
Gender		
Male	30	42,9
Female	40	57,1
Comorbid		
Yes	30	42,9
No	40	57,1
Hypertension		
Yes	36	37,1
No	44	62,9
Diabetes mellitus		
Yes	2	2,9
No	68	97,1
Hypertension + diabetes mellitus		
Yes	1	1,4
No	69	98,6
Dyslipidemia		
Yes	9	12,9
No	61	87,1
Obesity		
Yes	6	8,6
No	64	91,4
Mean Arterial Pressure (mmHg)		
<65	43	61,4
≥65	27	38,6
DAOR		
≥ 60	4	5,7
< 60	66	94,3
Ejection Fraction (%)		
≤ 50	16	22,9
> 50	54	77,1

DAOR: Duration of Aortic Occlusion

Table 2. Numerical Characteristics of the Overall Study Population (N = 70)

Variables	Min	Max	Mean	SD	p*
Age (years)	18	65	38.5	12.37	0.20
Weight (kg)	30	94	51.5	10.50	0.20
Height (cm)	140	180	157.7	7.96	0.20
BMI (kg/m^2)	14.72	29.14	20.60	3.31	0.20
Preoperative					
Hemoglobin (g/dL)	9.20	23.20	13.30	2.02	0.15
Ejection Fraction (%)	24.50	87	59.71	11.44	0.51
Natrium (mEq/L)	128	155	138.17	4.67	0.20
Kalium (mEq/L)	2	5	3.77	0.53	0.00
Chloride (mEq/L)	86	111	102.10	4.99	0.00
MoCA-INA	26	30	28.41	1.37	0.00
Intraoperative					
MAC Sevoflurane	5	10	7.57	2.51	0.00
Natrium (mEq/L)	128	151	136.44	3.10	0.01
Kalium (mEq/L)	2.70	5.80	3.86	0.67	0.00
Heart Rate (bpm)	45	100	67.77	11.98	0.20
Temperature (^{o}C)	34.30	36.20	35.31	0.44	0.03
MAP (mmHg)	52	88	69.65	8.18	0.07
MAP during CPB (mmHg)	51	89	64.21	5.82	0.00
Anesthesia duration (minutes)	250	390	322.35	33.18	0.00
Surgery duration (minutes)	90	180	128.42	24.53	0.00
CPB duration (minutes)	22	92	41.44	15.73	0.00
Cross Clamp duration (minutes)	11	64	29.01	14.57	0.00
Bleeding amount (ml)	200	500	325.92	58.12	0.00
DC shock frequency (times)	0	3	1.57	0.62	0.00
Postoperative					
Hemoglobin (g/dL)	6.80	15.60	10.78	1.60	0.20
Natrium (mEq/L)	127	151	137.05	4.82	0.01
Kalium (mEq/L)	3.40	5.80	4.15	0.39	0.00
Chloride (mEq/L)	86	112	110.54	5.56	0.05
Lactat (mg/dL)	0.59	5.70	2.58	0.97	0.03
Ventilator duration (hours)	10	48	19.31	6.62	0.00
MoCA-INA	13	30	22.37	4.72	0.00
Duration in ICU (days)	3	12	3.52	0.39	0.00
Delta Hemoglobin (g/dL)**	-0,76	0,37	-0.27	0.18	0.20

*p-value obtained from the Kolmogorov-Smirnov normality test
** Delta Hemoglobin (ΔHb) was calculated as postoperative hemoglobin minus preoperative hemoglobin

BMI: Body Mass Index, EF: Ejection fraction, MoCA-INA: Montreal Cognitive Assessment, MAC: Minimal Alveolar Concentration, MAP: Mean Arterial Pressure, CPB: Cardiopulmonary Bypass, DC: Direct-Current, ICU: Intensive Care Unit, Min: minimum, Max: maximum, SD: Standard Deviation

Table 3. Comparison of Hemoglobin Levels Between POCD and Non-POCD Groups

Variables	With POCD (n=43 (61,4%))	Without POCD (n=27 (38,6%))	p
Preoperative Hb	13.48±2.23	13.02±1.64	0.542
Postoperative Hb	10.60±1.74	11.05±1.32	0.157
Delta Hb	-0.31±0.19	-0.19±0.14	0.003*

Hb: Hemoglobin, POCD: Postoperative Cognitive Dysfunction, SD: Standard Deviation

DISCUSSION

Postoperative cognitive dysfunction (POCD) refers to a transient decline in cognitive function associated with surgical procedures, affecting individuals of varying ages but more commonly observed in advanced age. A recent review by Glumac et al. highlighted preoperative risk factors, such as age, gender, educational background, obesity, and metabolic syndrome history.[15] This study found a predominant representation of female patients below 60 years of age, aligning with previous research by Nurcahyo et al., which also reported a higher proportion of female patients with a median age of 44.5 years.[16] The aging process may contribute to degenerative changes in the brain, potentially increasing the long-term risk of POCD following surgery.

Additionally, 42.9% of patients in this study had comorbidities, with hypertension being the most prevalent (36%). A meta-analysis by Feinkohl et al. reported a statistically significant 27% increase in the risk of POCD associated with hypertension.[17] Hypertensive patients face a heightened risk of reduced cerebral perfusion during perioperative hypotension due to altered cerebrovascular autoregulation, potentially leading to cognitive dysfunction post-cardiac surgery.[18]

The mean preoperative hemoglobin levels in this study were higher (13.30 g/dL) than the mean postoperative levels (10.78 g/dL), consistent with findings by Soenarto et al. and Nurchayo et al., emphasizing a decline in hemoglobin levels after cardiac surgery.[19] Lower hemoglobin levels may impact neuropsychological performance by diminishing brain oxygen levels or reducing the threshold for transient ischemia, influencing subsequent cognition.[10]

Cognitive function was assessed using the Montreal Cognitive Assessment adapted for the Indonesian population (MoCA-INA), with a score below 26 on the third day post-surgery indicating POCD.[20] While comprehensive psychometric batteries are standard for POCD diagnosis, the use of MoCA-INA was pragmatic in this study due to limited resources. The mean MoCA-INA score before surgery (28.41) was higher than the mean score after surgery (22.37), aligning with results from Arifin et al., suggesting a decline in cognitive performance post-surgery.[16]

The study highlighted intraoperative risk factors for POCD, including hypoxemia, hypotension, thrombus, and emboli. A longer operation time and complex surgical strategy may contribute to endotoxin release and increased risk of brain emboli.[21] The duration and depth of anesthesia also influence cerebral oxygenation, potentially contributing to POCD. The study's mean surgery duration was 128.42 minutes, differing from Nurcahyo et al.'s findings, potentially attributable to the smaller sample size in this study.[2]

The investigation revealed a significant association between lower preoperative hemoglobin levels and POCD ($p = 0.003$), in line with Arbi's findings. Anemia-related hypoxia may trigger cellular and molecular changes in the brain, impacting protein synthesis and synaptic plasticity essential for learning.[22] Cerebrovascular responses to hypoxemia, particularly in the context of anemia, may contribute to cerebral hypoxia and compromise regional cerebrovascular reserve.[23]

However, due to the retrospective observational design of this study, a causal relationship between hemoglobin levels and postoperative cognitive dysfunction cannot be established. Lower hemoglobin levels may reflect reduced cerebral oxygen reserve or serve as a marker of underlying systemic conditions, such as inflammation or impaired physiological reserve, which could increase vulnerability to perioperative cerebral hypoxia and subsequent cognitive impairment. Therefore, the observed association should be interpreted cautiously as a predisposing factor rather than a direct cause of POCD.[10,22,23]

Hypoxia-induced impairment in protein synthesis and synaptic plasticity may affect working memory and learning, crucial for cognitive functions primarily affected by POCD. This study provides support for a potential connection between hemoglobin levels and the occurrence of POCD.[24–26]

Despite these insights, the study has limitations, including the absence of a neuropsychological test battery, a short-term evaluation of hemoglobin and cognitive function, and the need for larger sample sizes and long-term follow-up studies to enhance our understanding of the relationship between hemoglobin levels and cognitive function after heart valve replacement surgery.[27–29]

CONCLUSION

Postoperative cognitive dysfunction (POCD) arising from heart valve surgery is a critical concern that demands careful attention from healthcare practitioners. In patients with POCD, the hemoglobin levels post-surgery exhibited a noteworthy reduction compared to the pre-surgery levels, indicating a significant association between hemoglobin values and the occurrence of POCD following heart valve replacement. However, the intricate pathogenesis and multifaceted risk factors associated with POCD necessitate additional research, including an exploration of long-term cognitive outcomes.

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