narra j

Original Article

Neutrophil-to-lymphocyte ratio as a predictor of low cardiac output syndrome after open heart surgery in children with congenital heart disease

Dewi S. Laila[1,2*], Andri Perdana[3], Ruth K. Permatasari[4], Muzal Kadim[5], Najib Advani[5], Bambang Supriyatno[5], Novie A. Chozie[5] and Mulyadi M. Djer[5]

[1]Department of Pediatrics, Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia; [2]Department of Pediatrics, Arifin Achmad General Hospital, Pekanbaru, Indonesia; [3]Department of Pathology Clinic, General Hospital of South Tapanuli, Sipirok, Indonesia; [4]Department of Pediatrics, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia; [5]Department of Pediatric, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

*Corresponding author: dewishandilaila@lecturer.unri.ac.id

Abstract

Neutrophil-to-lymphocyte ratio (NLR) as a predictor in determining low cardiac output syndrome (LCOS) has not been widely reported. The aim of this study was to explore the role of pre-surgery, 0-, 4-, and 8-hour post-surgery NLR as predictors of LCOS incidence after open heart surgery in children with congenital heart disease (CHD). This study used a prognostic test with a prospective cohort design and was conducted from December 2020 until June 2021 at the cardiac intensive care unit (CICU) of Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia. The subject consisted of children aged one month to 18 years who underwent open heart surgery using a cardiopulmonary bypass (CPB) machine. A receiver operating characteristic curve was applied to identify the predictive performance of NLR for poor outcomes (LCOS incidence). Out of 90 patients included in the study, 25 (27.8%) of them developed LCOS between 3 to 53 hours post-surgery. All NLR values (pre-surgery and 0-, 4-, and 8-hours post-surgery) were associated with the incidence of LCOS. Pre-surgery NLR (cut-off value ≥0.88) had a fair predictive value (area under curve (AUC) 70; 95%CI: 57–83) for predicting LCOS incidence with sensitivity and specificity of 64% and 64.62%, respectively. NLR 0-hour post-surgery (cut-off value ≥4.73) had a good predictive value (AUC 81; 95%CI: 69–94) for predicting LCOS incidence, with 80% sensitivity and 80% specificity. NLR 4- and 8-hours post-surgery had very good predictive values (AUC 97%; 95%CI: 92–100 and 98; 95%CI: 94–100, respectively), with cut-off values ≥6.19 and ≥6.78, had the same 92% sensitivity and the same 96% sensitivity. The presence of LCOS was associated with mortality (odds ratio of 5.11 with 95%CI: 3.09–8.46). This study highlights that pre-surgery, 0-, 4-, and 8-hours post-surgery NLR can be predictors of LCOS after open heart surgery in children with CHD.

Keywords: Cardiopulmonary bypass, low cardiac output syndrome, lymphocyte, neutrophil, neutrophil-lymphocyte ratio

Introduction

Congenital heart disease (CHD) is the most common congenital abnormality found in infants and children, found 8–10 per 1000 live births [1]. The clinical manifestations depend on the severity of the disease, ranging from asymptomatic to symptoms of heart failure in neonates [2].

Received: March 7, 2024 - Accepted: May 11, 2024 - Published online: June 6, 2024

Treatment for CHD could be surgery (palliative surgery or definitive surgery) and non-surgery (medicamentosa and cardiology intervention) [2,3]. Surgery is the conventional method that has been used to correct structural abnormalities in CHD [1,3]. The most common treatment for CHD is surgery using a cardiopulmonary bypass (CPB) [1,3,4]. However, children who undergo heart surgery using a CPB machine can experience systemic inflammation [5]. Children who had cardiac surgery using CPB machine had low cardiac output syndrome (LCOS) and increased risk of death [6,7]. This is because the use of a CPB machine will cause changes in the production of inflammatory mediators and cause significant systemic effects such as mild edema, myocardial dysfunction, and severe multiple organ failure [8].

LCOS is a condition where cardiac output decreases due to myocardial dysfunction after cardiac surgery. LCOS is the most frequent complication after cardiac surgery, with an incidence of 25% [9]. A study in Cipto Mangunkusumo Hospital, Jakarta, Indonesia in 2017, the incidence of LCOS was found 45% [10]. LCOS most often occurs 6–18 hours after cardiac surgery with CPB machine [11]. This makes strategic actions in preventing and treating LCOS very important [11].

In recent years, the neutrophil-to-lymphocyte ratio (NLR) has become an inflammatory marker that has the potential to be used in various conditions, one of which is cardiovascular disorders [12,13]. NLR is a potential marker of inflammation to determine the presence of inflammation [12,13]. NLR was chosen because it is considered superior, frequently used, easy to calculate, and cheaper than other inflammatory markers [14]. However, until now, the use of NLR as a predictor in determining LCOS has not been widely reported. The aim of this study was to determine if the high NLR values of pre-surgery, 0-, 4-, and 8-hours post-surgery could be used as a predictor of the incidence of LCOS after open heart surgery in children with CHD.

Method

Study design and setting

A prospective cohort study was conducted from December 2020 until June 2021 at the Cardiac Intensive Care Unit (CICU) of Dr. Cipto Mangunkusumo, Jakarta, Indonesia. Dr. Cipto Mangunkusumo Hospital is the main national referral center hospital in Indonesia. The population of this study was pediatric patients aged one month to 18 years who had open heart surgery using a CPB machine. The NLR was measured serially and the presence of the LCOS was assessed till 18 hours post-surgery.

Patients and sampling method

The subjects consisted of children aged one month to 18 years who underwent open heart surgery using a CPB machine and had parental consent. Patients who had chronic diseases (such as rheumatic heart disease, systemic lupus erythematous, and diabetic mellitus) before the study or were hospitalized for other diseases while undergoing open heart surgery were excluded from this study. This study used the total sampling during the period of December 2020 and June 2021 with a minimum sample size of 69 children.

Study variables

The independent variable was NLR of pre- and post-surgery. NLR was measured using standard laboratory examination by comparison of two combinations of independent marker for inflammation: neutrophils and lymphocytes. Pre-surgery NLR was measured within 24 hours before surgery, while post-surgery NLR was measured at 0, 4, and 8 hours after the patient after surgery.

The dependent variable was the presence of LCOS after cardiac surgery and was assessed based on the combination of clinical symptoms, hemodynamics, and laboratory: decreased perfusion, tachycardia, oliguria (urine output <1 mL/kg body weight/hour), lactate levels >3 mmol/L, decreased mixed venous saturation (<70%), and cardiac index (3.5 L/min/m^2). Cardiac index measurement was conducted using echocardiography by a pediatric cardiologist or intensivist on duty after open heart surgery. The measurement was carried out once within a period of 18 hours. LCOS confirmed by the doctor in charge.

Laila et al. Narra J 2024; 4 (2): e736 - http://doi.org/10.52225/narra.v4i2.736

In addition, baseline demographic and clinical characteristics were collected, including gender, age, weight, and height. Nutritional status was divided into wasting, normal weight, severe wasting, and overweight measured by weight for height z score. The main diagnostic was divided into two groups: acyanotic and cyanotic CHD, and the surgery procedure was classified into two groups: definitive and palliative. Surgery risk was assessed and categorized using the risk adjustment for congenital heart disease 1 (RACHS-1), which estimated the risk of mortality in children aged <18 years undergoing cardiac surgery. RACHS-1 was divided into five groups; the higher the score, the higher the mortality rate.

Study procedure

All patients who met the inclusion and exclusion criteria were recruited. Then, an initial screening was carried out, including history taking, physical examination, laboratory examination, radiology and echocardiography. The definite diagnosis of each patient was confirmed with cardiac catheterization and cardiac CT scans. A laboratory examination was carried out to assess pre-surgery NLR within 24 hours before open heart surgery. After the patient underwent open heart surgery, laboratory tests were carried out to assess post-surgery NLR at 0, 4, and 8 hours after surgery. During 0–18 hours after surgery, patients were monitored for the time when clinical signs of LCOS occurred based on the LCOS criteria. The echocardiography examination was conducted transthoracic with an echocardiography (GE Vivid E95 Ultrasound).

Statistical analysis

We first described baseline characteristics and outcomes using mean, median, or proportion as appropriate. Kolmogorov-Smirnov test was used to assess the normality of data distribution. The NLR cut point value was determined pre-surgery and 0, 4, and 8 hours after surgery based on the receiver operating characteristic (ROC) curve. Then, the Chi-squared test was used to determine the association between the cut-off NLR value and the incidence of LCOS. The associations between some post-surgery variables and the incidence of LCOS were determined by Wilcoxon test, Mann-Whitney test, or Chi-squared test. Statistical analysis was conducted using SPSS version 22 (IBM, New York, USA).

Results

Patients' characteristics

There were 112 patients who underwent open heart surgery with CPB machines during the study period, of which 90 patients met the inclusion criteria. Most patients were male, and the median age was 28 months (**Table 1**). More than half of the patients were malnourished (62.2%). The most common congenital heart disease was tetralogy of Fallot (47.8%) and followed by ventricular septal defect (VSD) (27.8%). LCOS was diagnosed in 25 (27.8%) patients. The risk of surgery was also assessed using risk adjustment for congenital heart surgery 1 (RACHS-1) and the vast majority (88.9%) of the patients were category 2 (**Table 1**).

Table 1. Characteristics of patients included in the study

Characteristics	Total	LCOS (+)	LCOS (-)
	n=90	n=25	n=65
Gender, n (%)			
Male	51 (56.7)	18 (72.0)	33 (50.8)
Female	39 (43.3)	7 (28.0)	32 (49.2)
Median age, months (range)	28 (14–51)	33 (14–73)	28 (12–49)
Median weight, kg (range)	10 (8–10)	9 (8–17)	10 (8–13)
Median height, cm (range)	83 (70–100)	79 (65–108)	85 (75–100)
Nutritional status, n (%)			
Wasting	56 (62.2)	14 (56.0)	42 (64.6)
Normoweight	25 (27.8)	8 (32.0)	17 (26.2)
Severe wasting	8 (8.9)	2 (8.0)	6 (9.2)
Overweight	1 (1.1)	1 (4.0)	0 (0.0)
Main diagnosis, n (%)			
Acyanotic			
Ventricular septal defect (VSD)	25 (27.8)	2 (8.0)	23 (35.4)

Laila et al. Narra J 2024; 4 (2): e736 - http://doi.org/10.52225/narra.v4i2.736

Characteristics	Total n=90	LCOS (+) n=25	LCOS (-) n=65
Atrioventricular septal defect (AVSD)	4 (4.4)	1 (4.0)	3 (4.6)
Atrial septal defect (ASD)	3 (3.3)	0 (0.0)	3 (4.6)
Complete atrioventricular septal defect (CAVSD)	2 (2.2)	0 (0.0)	2 (3.1)
Partial anomalous pulmonary venous drainage (PAPVD)	2 (2.2)	0 (0.0)	2 (3.1)
Interrupted aortic arch (IAA)	1 (1.1)	1 (4.0)	0 (0.0)
Cyanotic			
Tetralogy of Fallot (TF)	43 (47.8)	18 (72.0)	25 (38.5)
Double outlet right ventricle (DORV)	2 (2.2)	1 (4.0)	1 (1.5)
Pulmonary artery with intact ventricular septum (PA IVS)	2 (2.2)	1 (4.0)	1 (1.5)
Transposition of great arteries with intact ventricular septum (TGA IVS)	2 (2.2)	1 (4.0)	1 (1.5)
Transposition of great arteries with ventricular septal defect (TGA VSD)	2 (2.2)	0 (0.0)	2 (3.1)
Pulmonary artery with ventricular septal defect (PA VSD)	1 (1.1)	0 (0.0)	1 (1.5)
Truncus arteriosus with ventricular septal defect (TA VSD)	1 (1.1)	0 (0.0)	1 (1.5)
Other diagnosis, n (%)			
No other disease	74 (82.2)	22 (88.0)	52 (80.0)
Pulmonary hypertension (PH)	9 (10)	1 (4.0)	8 (12.3)
Down syndrome	4 (4.4)	0 (0.0)	4 (8.2)
Congenital hypothyroid	1 (1.1)	0 (0.0)	1 (1.5)
Anal atresia	1 (1.1)	1 (4.0)	0 (0.0)
Klinefelter syndrome	1 (1.1)	1 (4.0)	0 (0.0)
Surgery procedure, n (%)			
Definitive			
Tetralogy of Fallot repair	42 (46.7)	18 (72.0)	24 (36.9)
VSD closure	26 (28.9)	3 (12.0)	23 (35.4)
ASD closure	3 (3.3)	0 (0.0)	3 (4.6)
AVSD repair	3 (3.3)	1 (4.0)	2 (3.1)
Arterial switch operation	2 (2.2)	1 (4.0)	1 (1.5)
CAVSD repair	2 (2.2)	0 (0.0)	2 (3.1)
PAPVD repair	2 (2.2)	0 (0.0)	2 (3.1)
Rastelli	1 (1.1)	1 (4.0)	0 (0.0)
Interrupted aortic arch (IAA) repair	1 (1.1)	1 (4.0)	0 (0.0)
Palliative			
Bidirectional cavopulmonary shunt (BCPS)	7 (7.8)	0 (0.0)	7 (10.8)
Blalock-Taussig (BT) shunt	1 (1.1)	0 (0.0)	1 (1.5)
Risk adjustment for congenital heart surgery (RACHS)-1 risk score			
1	6 (6.7)	2 (8.0)	4 (6.2)
2	80 (88.9)	22 (88.0)	58 (89.2)
3	3 (3.3)	0 (0.0)	3 (4.6)
4	1 (1.1)	1 (4.0)	0 (0.0)
5	0 (0.0)	0 (0.0)	0 (0.0)

LCOS: low cardiac output syndrome

LCOS incidence and associated factors

Out of all patients who developed LCOS, most of them experienced LCOS after four hours post-surgery, where the median time to LCOS occurrence was seven hours and ranged between three hours to 53 hours. Our data indicated that CPB usage time and NLR values were associated with the incidence of LCOS (**Table 2**). The mortality rate of those with and without LCOS was 44% and 1.5%, respectively, and the incidence of LCOS was associated with mortality (**Table 2**). Those who had LCOS were likely to die approximately five times compared to those without LCOS.

Table 2. Factors associated with the incidence of low cardiac output syndrome (LCOS) among children with open heart surgery using cardiopulmonary bypass (CPB) machine

Outcome	LCOS (+) n=25	LCOS (-) n=65	*p*-value
Surgical procedure time, minutes (range)	260 (193–324)	200 (178–240)	0.060[a]
CPB usage time, minute (range)	139 (97–181)	74 (54–98)	<0.001[a]
Aorta cross clamp time, minutes (range)	41 (29.50–68.50)	35 (29–51)	0.118[a]
Length of ventilator use, hours (range)	39 (16–104.75)	21 (17–61)	0.120[a]

Outcome	LCOS (+)	LCOS (-)	*p*-value
	n=25	n=65	
Length of stay in CICU, days (range)	3 (1–9)	2 (1–4)	0.250[a]
Length of hospital stay, days (range)	10 (5–15)	9 (6–15)	0.814[a]
Neutrophil-to-lymphocyte ratio value (range)			
Pre-surgery	1.17 (0.24–9.21)	0.70 (0.18–1.85)	<0.001[b]
0-h post-surgery	6.53 (1.89–15.40)	3.69 (0.74–8.70)	<0.001[b]
4-h post-surgery	13.56 (4.17–20.63)	3.95 (0.72–4.70)	<0.001[b]
8-h post-surgery	13.56 (4.17–20.63)	3.91 (0.47–9.61)	<0.001[b]
Mortality, n (%)			
Yes	11 (44.0)	1 (1.5)	<0.001[c]
No	14 (56.0)	64 (98.5)	

[a] Analyzed using Mann-Whitney test
[b] Analyzed using Wilcoxon test
[c] Analyzed using Chi-squared test, with relative risk 5.11 and 95% confidence interval 3.09–8.46

Role of NLR for predicting LCOS

Before carrying out the sensitivity test, the optimal cut points for NLR pre-surgery, 0-, 4-, and 8-hours post-surgery were determined using ROC and AUC. The cut point was used to divide the NLR into two groups (**Table 3**). Our analysis indicated that all NLR values (pre-surgery and 0-, 4-, and 8-hours post-surgery) were associated with the incidence of LCOS after open heart surgery using CPB (**Table 3**). Pre-surgery NLR ≥0.88 was associated with the risk of post-surgery LCOS by 2.32 times compared with NLR <0.88 (p=0.027) (**Table 3**). NLR at 0-hour post-surgery ≥4.73 was associated with the risk of developing post-surgery LCOS by 6.9 times compared to the NLR <4.73 (p<0.0001). NLR at 4-hour post-surgery ≥6.19 was associated with the risk of developing post-surgery LCOS by 29.9 times compared to the NLR <6.19 (p<0.0001). NLR at 8-hour post-surgery was ≥6.78 associated with the risk of developing post-surgery LCOS as much as 29.9 times compared to NLR <6.78 (p<0.0001) (**Table 3**).

Table 3. Relationship between neutrophil-to-lymphocyte ratio (NLR) and incidence of low cardiac output syndrome (LCOS) among children with open heart surgery using cardiopulmonary bypass (CPB) machine

Variable	LCOS n (%)	Non-LCOS n (%)	Relative risk (CI 95%)	*p*-value [a]
Pre-surgery NLR				
≥0.88	16 (41.0)	23 (59.0)	2.32 (1.15–4.69)	0.027
<0.88	9 (17.6)	42 (82.4)		
0-h post-surgery NLR				
≥4.73	20 (60.6)	13 (39.4)	6.90 (2.86–16.67)	<0.0001
<4.73	5 (8.8)	52 (91.2)		
4-h post-surgery NLR				
≥6.19	23 (92.0)	2 (8.0)	29.90 (7.60–117.58)	<0.0001
<6.19	2 (3.1)	63 (96.9)		
8-h post-surgery NLR				
≥6.78	23 (92.0)	2 (8.0)	29.90 (7.60–117.58)	<0.0001
<6.78	2 (3.1)	63 (96.9)		

[a] Analyzed using Chi-squared test

Using the same cut-off points, our analyses indicated that all NLR values (pre-surgery and 0-, 4-, and 8-hours post-surgery) had predictive values to predict the incidence of LCOS with NLR of 4- and 8-hours post-surgery had the same performance (**Table 4**). They had AUC 97%; 95%CI: 92–100 and 98; 95%CI: 94–100, respectively, with the same 92% sensitivity and the same 96% sensitivity (**Table 4**).

Table 4. Performance characteristics of neutrophil-to-lymphocyte ratio (NLR) in predicting low cardiac output syndrome (LCOS) among children with open heart surgery using cardiopulmonary bypass (CPB) machine

Variable	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Likelihood ratio	Area under the curve (CI 95%)
Pre-surgery NLR	64.00	64.62	41.03	82.35	1.81	70 (57–83)
0-h post-surgery NLR	80.00	80.00	60.61	91.23	4.00	81 (69–94)

Variable	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Likelihood ratio	Area under the curve (CI 95%)
4-h post-surgery NLR	92.00	96.92	92.00	96.92	29.90	97 (92–100)
8-h post-surgery NLR	92.00	96.92	92.00	96.92	29.90	98 (94–100)

On the ROC curve, the NLR values at four hours and eight hours post-surgery have better predictive power in predicting the incidence of LCOS compared to pre-surgery and 0-hour post-surgery NLR (**Figure 1**).

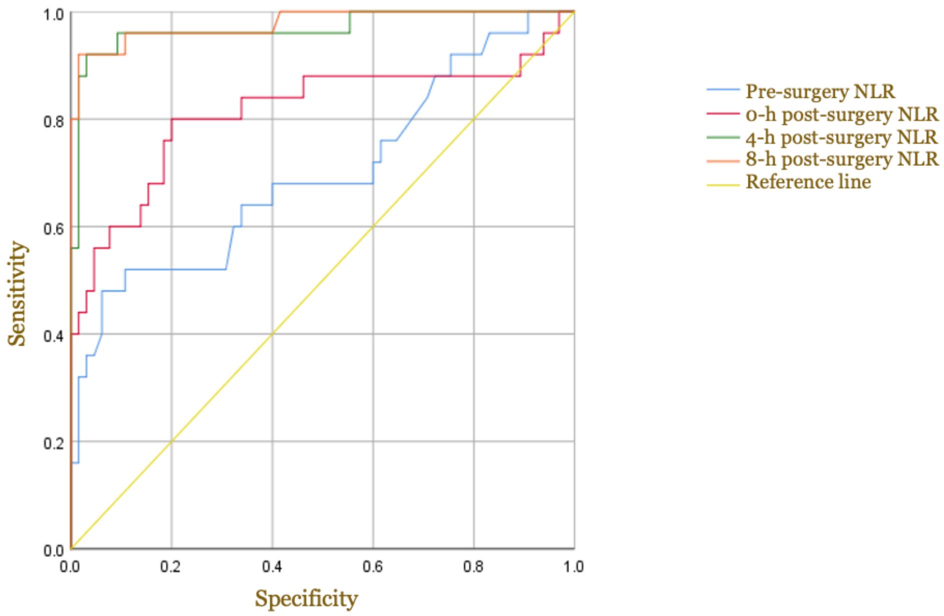

Figure 1. Receiver operating characteristic (ROC) curve of neutrophil-to-lymphocyte ratio (NLR) value in predicting low cardiac output syndrome (LCOS) after open heart surgery using cardiopulmonary bypass (CPB) machine in children.

Discussion

As the most common congenital abnormality found in children, CHD often requires surgical management to correct the structural abnormalities [1,3]. A study found that children who had cardiac surgery with a CPB machine may experience systemic inflammation due to changes in the production of inflammatory mediators [12]. Changes in these inflammatory mediators can cause myocardial dysfunction, which, if not handled properly, can lead to LCOS, which are the most common post-cardiac surgery complications, with an incidence of 25%–45% [6,9,10]. Heart surgery performed at an earlier age can provide opportunities for children with CHD to achieve more ideal weight [15,16]. However, not all babies could have a surgery on early in life, either due to medical or non-medical factors. In our study, the median age of the subjects was 28 months. In a prospective cohort study in 2014 at the same hospital as our study, the median age of the patients was 53 months [17]. A study in California found that both medical and non-medical factors were important in determining why the surgery could not be performed at an earlier age [18].

In our study, the most common diagnosis of CHD was tetralogy of Fallot. A previous study in the same hospital in 2015 found that the most common CHD diagnoses were ventricle septal defect (VSD) (28.7%) and tetralogy of Fallot (24.4%) [17]. The anatomical complexity that occurs in tetralogy of Fallot (TF) requires complicated surgical procedures so that LCOS often becomes a post-surgery complication in this disorder [19].

The diagnosis of LCOS is defined based on clinical manifestations such as tachycardia, oliguria, poor perfusion, or cardiac arrest, with or without decreased oxygen saturation or metabolic acidosis [20]. In this study, the diagnosis of LCOS was based on the combination of clinical manifestation, hemodynamic, and laboratory according to LCOS criteria [21]. The incidence of LCOS in this study was 27.8% and this is lower than in a previous study in China in

2017 [10]. A study in Guatemala found the incidence of LCOS after pediatric cardiac surgery was 4% [22]. Meanwhile, in America, the incidence of LCOS was 25% [9], similar to the incidence of LCOS in our study. Several factors could cause this difference, such as the number and characteristics of patients and the services between centers.

We monitored the hemodynamic function of subjects who experienced LCOS at the time the diagnosis was made and found an increase in lactate values, a decrease in chloride, hemodynamic disturbances and the occurrence of metabolic acidosis. This is supported by the study in Australia that found hemodynamic disturbances could occur in LCOS without any other clear cause, which was confirmed by appropriate supporting examinations [11]. A study in India in 2010 stated that metabolic acidosis that occurs after open heart surgery is a sign that cardiac output has decreased [23].

A cohort study in the United States of 47 children who underwent cardiac surgery from July 2015 to January 2016 showed that pre-surgery NLR values were associated with the incidence of post-surgery LCOS, but post-surgery NLR values were not associated with post-surgery LCOS events [24]. Furthermore, this study suggested that an increase in pre-surgery NLR was associated with moderate or severe LCOS incidence in the first 12 hours post-surgery [24]. In our study, 4- and 8-hour post-surgery NLR had the highest sensitivity and specificity, with a cut-off NLR >6.19 and >6.78 associated with the risk of developing LCOS as much as 29.90 times. Since the NLR value is easy to determine, it has the potential to predict a poor outcome after open cardiac surgery with a CPB machine.

This study has some limitations. This study was only conducted in one center in Indonesia, so it is necessary to carry out multicenter studies from hospitals that provide pediatric cardiac surgery services to obtain better research results. Our study only examined one inflammatory marker, NLR, and did not compare with other inflammatory markers. By comparing various post-surgical inflammatory markers, it is hoped that it will be able to provide better performance in predicting LCOS, thus providing a better impact in the management of pediatric patients with CHD who will undergo surgery.

Conclusions

Our study indicated that the incidence of LCOS post-open cardiac surgery with a CPB machine was high and its incidence was associated with 5-fold mortality. NLR pre-surgery as well as 0-, 4- and 8-hours post-surgery had good predictive performance to predict the incidence of LCOS; therefore, it could be used to predict LCOS in the clinical setting. This could have a significant impact on the management of pediatric patients with CHD who will undergo open heart surgery, in particular, as a strategy for preventing the incidence of LCOS.

Ethics approval

Permission from research subjects or parents is stated in filling out the informed consent and if approved, they will be included in the research and receive ethical approval from the Ethics Committee of the Faculty of Medicine, University of Indonesia/RSUPN Dr. Cipto Mangunkusumo, Jakarta (KET-1424/UN2.F1/ETIK/PPM.00.02/2020)

Acknowledgments

The authors would like to thank all the staff at the Department of Pediatrics, University of Indonesia and thank to all the patients included in the study.

Competing interests

All the authors declare that there are no conflicts of interest.

Funding

This study received no external funding.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

How to cite

Laila DS, Perdana A, Permatasari RK, *et al*. Neutrophil-to-lymphocyte ratio as a predictor of low cardiac output syndrome after open heart surgery in children with congenital heart disease. Narra J 2024; 4 (2): e736 - http://doi.org/10.52225/narra.v4i2.736.

References

1. Djer MM. Penanganan penyakit jantung bawaan tanpa operasi (kardiologi intervensi). Jakarta: Sagung Seto; 2014.
2. Djer MM, Madiyono B. Tatalaksana penyakit jantung bawaan. Sari Pediatri 2016;2(3):155-162.
3. Jonas RA. Congenital heart surgery in developing countries. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2008;11(1):3-6.
4. Gazit AZ, Huddleston CB, Checchia PA, *et al.* Care of the pediatric cardiac surgery patient-part 1. Curr Probl Surg 2010;47(3):185-250.
5. Ascenzi JA, Kane PL. Update on complications of pediatric cardiac surgery. Crit Care Nurs Clin North Am 2007;19(4):361-369.
6. Maganti M, Badiwala M, Sheikh A, *et al.* Predictors of low cardiac output syndrome after isolated mitral valve surgery. J Thorac Cardiovasc Surg 2010;140(4):790-796.
7. Huber JN, Hilkin BM, Hook JS, *et al.* Neutrophil phenotype correlates with postoperative inflammatory outcomes in infants undergoing cardiopulmonary bypass. Pediatr Crit Care Med 2017;18(12):1145-1152.
8. Allan CK, Newburger JW, McGrath E, *et al.* The relationship between inflammatory activation and clinical outcome after infant cardiopulmonary bypass. Anesth Analg 2010;111(5):1244-1251.
9. Bhat T, Teli S, Rijal J, *et al.* Neutrophil to lymphocyte ratio and cardiovascular diseases: A review. Expert Rev Cardiovasc Ther 2013;11(1):55-59.
10. Xu H, Sun Y, Zhang S. The relationship between neutrophil to lymphocyte ratio and clinical outcome in pediatric patients after cardiopulmonary bypass surgery: A retrospective study. Front Pediatr 2019;7:308.
11. Moursy EY, Megallaa MH, Mouftah RF, *et al.* Relationship between neutrophil-lymphocyte ratio and microvascular complications in Egyptian patients with type 2 diabetes. Am J Intern Med 2015;3(6):250-255.
12. Hoffman TM, Wernovsky G, Atz AM, *et al.* Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. Circulation 2003;107(7):996-1002.
13. Kusumajaya R, Advani N, Yanuarso PB, *et al.* Biomarkers in low cardiac output syndrome after open cardiac surgery in children. Paediatr Indones 2021;61(4):223-228.
14. Fakhri D, Busro PW, Rahmat B, *et al.* Risk factors of sepsis after open congenital cardiac surgery in infants: A pilot study. Med J Indones 2016;25(3):182-189.
15. Knirsch W, Zingg W, Bernet V, *et al.* Determinants of body weight gain and association with neurodevelopmental outcome in infants operated for congenital heart disease. Interact Cardiovasc Thorac Surg 2010;10(3):377-382.
16. Murni I, Djer M, Yanuarso P, *et al.* Outcome of pediatric cardiac surgery and predictors of major complication in a developing country. Ann Pediatr Cardiol 2019;12(1):38.
17. Chang RKR, Chen AY, Klitzner TS. Factors associated with age at operation for children with congenital heart disease. Pediatrics 2000;105(5):1073-1081.
18. Athanasiadis DI, Mylonas KS, Kasparian K, *et al.* Surgical outcomes in syndromic tetralogy of fallot: A systematic review and evidence quality assessment. Pediatr Cardiol 2019;40(6):1105-1112.
19. Hoffman TM, Wernovsky G, Atz AM, *et al.* Prophylactic intravenous use of milrinone after cardiac operation in pediatrics (PRIMACORP) study. Prophylactic intravenous use of milrinone after cardiac operation in pediatrics. Am Heart J 2002;143(1):15-21.
20. Rotta AT, Laussen PC, Wessel DL. Critical care after surgery for congenital heart disease. In: Fuhrman BP, Zimmerman J, Carcillo JA, Clark RS, Rotta AT, Tobias JD, Relvas MS, Thompson AE, eds. Pediatric Critical Care. 4th ed. Elsevier; 2011.
21. Leon-Wyss JR, Veshti A, Veras O, *et al.* Pediatric cardiac surgery: a challenge and outcome analysis of the guatemala effort. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2009;12(1):8-11.

22. Jones B, Hayden M, Fraser JF, *et al*. Low cardiac output syndrome in children. Curr Anaesth Crit Care 2005;16(6):347-358.
23. Kumar G, Iyer PU. Management of perioperative low cardiac output state without extracorporeal life support: What is feasible? Ann Pediatr Cardiol 2010;3(2):147-158.