Prognostic nutritional index and mortality in children and adolescents underwent cardiac surgery

Bruna de Melo Silva [1]
https://orcid.org/0000-0003-0970-8884

Christyann Lima Campos Batista [2]
https://orcid.org/0000-0001-5431-5620

Bruna Renata Fernandes Pires [3]
https://orcid.org/0000-0001-8278-6518

Eliete Costa Oliveira [4]
https://orcid.org/0000-0002-4596-0895

Tatiana Abreu Barros [5]
https://orcid.org/0000-0002-8075-9265

José de Ribamar Medeiros Lima Júnior [6]
https://orcid.org/0000-0001-9172-3682

Juliana Moreira da Silva Cruvel [7]
https://orcid.org/0000-0003-1087-7095

[1-7] Hospital Universitário. Universidade Federal do Maranhão. R. Barão de Itapari, 227. Centro. São Luís, MA, Brazil. 65.020-070. Email: bruna_rah@hotmail.com

Abstract

Objectives: to analyze the prognostic nutritional index and factors associated with mortality in children and adolescents with heart disease who underwent cardiac surgery.

Methods: this is a longitudinal, retrospective study that included 98 children and adolescents with heart disease from 0 to 14 years old, and assessed the prognostic nutritional index and nutritional status, through the body mass index for age, weight for height, weight for age and height for age. Multiple logistic regression analysis was performed.

Results: malnutrition was present in 27 patients, 68 were categorized as having a low prognostic nutritional index and 16 died. In the adjusted analysis, malnutrition (OR=4.11; CI95%=1.26-13.40; p=0.019), the low body mass index for age (OR=4.14; CI95%=1.26-13.61; p=0.019), low weight for height (OR=4.15; CI95%=1.29-13.35; p=0.017) and low weight for age (OR=5.20; CI95%=1.39-19.43; p=0.014) were associated with mortality.

Conclusions: malnutrition, low body mass index for age, weight for height and weight for age had shown a significant association with mortality. Despite being an easily applicable indicator of nutritional status, the findings suggest no association between the prognostic nutritional index and mortality in patients with congenital heart disease after cardiac surgery.

Key words *Nutritional status, Infant mortality, Cardiovascular diseases, Cardiac surgical procedures*

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Introduction

Malnutrition is a frequent phenomenon in children and adolescents with cardiovascular disease, and the main responsible factor is the inefficient usage of nutrients, due to the increase of energetic expenditure by virtue of clinical conditions, which are inherent to cardiac alterations.[1] Accordingly, they represent a major cause of recurrent hospitalizations and are associated with high rates of mortality.[2]

Around 80% of children with cardiovascular diseases need surgical intervention, whether corrective or palliative.[3] The evolution of surgical techniques enabled higher rate of survival, whereas the presence of malnutrition in these patients increases the risk of complications in the postoperative period due to higher metabolic demand.[4]

Nutritional status represents an important role in the incidence of morbidity and mortality in the postoperative period.[5] In this way, it is necessary to promote actions related to nutritional assessment even in the postoperative period. Nutritional assessment may establish and even prevent risk situations after surgery, observing that inadequate nutritional status in the period that antecedes it is frequently worsened in the postoperative period.[3,6]

The determination of nutritional status is complex, once many indexes are necessary to perform a complete and accurate description, such as food intake, anthropometric data and biochemical parameters.[6] Various tools were created in order to assess nutritional status.[7] Onodera *et al*.[8] suggested the use of the Prognostic Nutritional Index (PNI) to assess the nutritional status of patients with many diseases.[6,9] It is an indicator that quantifies nutritional and immunological aspects from serum albumin and Total Lymphocyte Count (TLC)[8] and it has been largely used to assess the risk of surgical morbimortality.[5]

PNI seems to be an easily applicable tool; objective, fast and easy to obtaindata, although little evidence in pediatrics reports the usage of this indicator.[6,10] In one of them, the PNI was evaluated as predictor of worsening of kidney function in children with chronic kidney disease.[6]

There is only one study carried out with children that underwent cardiac surgery, however, the rate of mortality outcome was not analyzed and only patients under 18 years of age were included.[10] Due to the gap in literature, the aim of this study was to analyze the PNI and factors associated with mortality in children and adolescents that underwent cardiac surgery.

Methods

This is a longitudinal retrospective study, with quantitative approach. The study population was composed by children and adolescents between 0 to 14 years of age that underwent cardiac surgery from January 2017 to May 2020. The survey was carried out in the University Hospital of the Federal University of Maranhão (HU-UFMA – Portuguese acronym), at Mother and Child Unit, located at the city of São Luís, which provides care exclusively for the Unified Health System (SUS – Portuguese acronym) and represents a structure of reference for pediatric cardiac surgery in the state.

The sample size calculation was performed using Microsoft Office Excel®software, based on the number of patients that underwent cardiac surgery in the Hospital's pediatrics sector, in the period between January 2017 and May 2020. Considering a sampling error of 5% and a 95% confidence interval for heterogeneous samples, it was established as minimum sample 89 patients. Due to the sample size in relation to the population, data collection was performed with all of the patients, posteriorly withdrawing those who match the non-inclusion criteria.

The non-inclusion criteria were: 1. genetic syndromes (Turner syndrome, Down Syndrome, or unknown syndrome); 2. Chronic kidney disease; 3. Hepatic insufficiency. A total of 114 patients underwent surgery in the evaluated period, 98 patients were included (Figure 1).

Data collection was performed in specific charts and forms from the Nutrition Service. Anthropometric data, weight and height, were collected in the admission of patients and biochemical exams, C-Reactive Protein (CRP), albumin and TLC, were collected at the postoperative period.

The explanatory variables were: sex, age (<2 years/≥2 years), (CRP) (<0.5mg/L/≥0.5mg/L), albumin, TLC, types of surgery, types of cardiovascular disease, pulmonary hypertension (yes/no), presence of malnutrition (yes/no), weight for height (W/H), weight for age (W/A), body mass index for age (BMI/A), height for age (H/A) and PNI. The outcome variable: death.

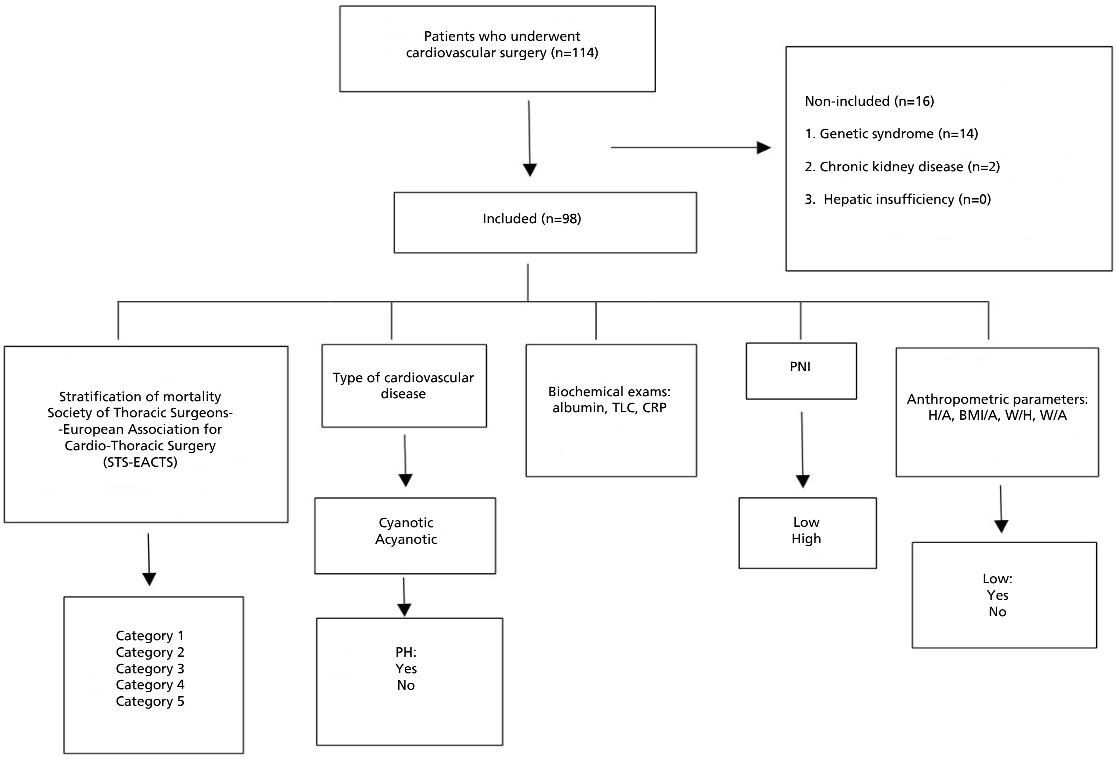
Cardiovascular diseases were categorized as cyanotic and acyanotic. Cardiac surgeries were classified with the STS-EACT (Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery) mortality score, which stratifies mortality according to data from each surgical procedure in five categories.[11]

The H/A (0 to 14 years), BMI/A (0 to 14 years), W/H (up to 5 years) and W/A (up to 10 years) indicators of every patients were assessed and classified as malnourished (yes/no) using the classification of the recommended indicator for age: W/H in <2 years and BMI/A in ≥2 years.[12] The H/A, BMI/A, W/H and W/A indicators were classified as low (yes/no) and analyzed with the Z-score, considering the < -2 cutoff in the World Health Organization (WHO) 2006/2007 growth curves, using the software WHO Anthro® 3.2.2 and WHO Anthro Plus® 1.0.4.

The PNI was calculated using the following formula: 10x serum albumin value (g/dl) + 0.005 x TLC in the

Figure 1

Flowchart of selection and distribution of population and sample included in the study, São Luís, 2021.



PH = Pulmonary Hypertension; TLC = Total Lymphocyte Count; CRP=C Reactive Protein; PNI = Prognostic Nutritional Index; H/A = Height for Age; BMI/A = Body Mass Index for Age; W/H = Weight for Height; W/A = Weight for Age.

peripheral blood (by mm^3).[8] Based on this index, patients were divided in two groups: high PNI (PNI≥55) and low PNI (PNI<55).[10]

In order to minimize missing data in the database (6%), the multiple imputation strategy was used. Once they are quantitative variables, the chosen method was the Predictive Mean Matching. Multiple imputation was performed using the public domain application Multivariate Imputation by Chained Equations (MICE), operated in the R software.[13]

The descriptive statistics are displayed as± meanstandard deviation or median and interquartile range for numerical variables and as frequency and proportion for categorical variables. The normal distribution of numerical variables was tested with the Saphiro-Wilk test. The variables with normal distribution were described as ± mean standard deviation, theothers as median and interquartile range.

Simple (unadjusted) and multiple (adjusted) logistic regression analyses between were performed between the study variables (sex, age, gestational age, CRP, albumin, TLC, cardiovascular disease, STS-EACTS mortality score, type of cardiovascular disease, PNI classification, malnutrition, low H/A) and the outcome variable (death). Continuous variables without evidence of linearity with death probability were analyzed categorically (age and CRP).

The selection of confounding variables for multiple logistic regression occurred by means of the building of a theoretical model, DAG (Directed Acyclic Graphs) with the DAGitty® software (Figure 2). The results are shown in the form of Odds Ratio (OR) with confidence interval of 95%. STATA® 14.0 software was used in all analyses.

The present study was locally approved by the Research Ethics Committee of the Federal University of Maranhão (opinion nº. 4.240.637, CAAE n° 36433520.1.0000.5086).

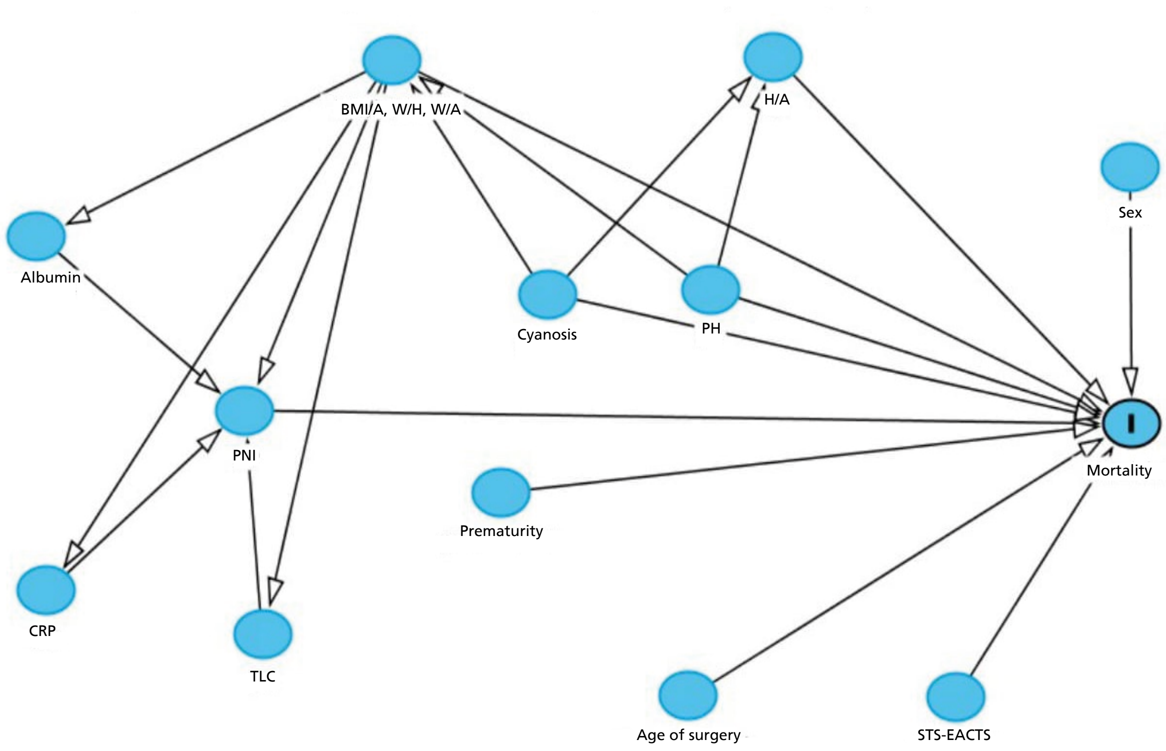
Results

The clinical and demographic characteristics of patients with cardiovascular diseases are shown in Table 1. Of the 98 participants, most were men (57.1%), half had less than 2 years of age and the most prevalent cardiovascular disease was interatrial communication (33.7%). Of the performed surgeries, 39.2% were classified in category 1 of the STS-EACTS score and there were no surgery classified in category 5.

Regarding the nutritional status in the postoperative period of patients, 69.4% were categorized as having low PNI. Malnutrition was observed in 27.5% of patients, and when assessed by the indicators, 34.7% had low H/A;

Figure 2

Selection of adjust variable with the DAG (Directed Acyclic Graphs).



I = Outcome; CRP=C Reactive Protein; TLC = Total Lymphocyte Count; PNI = Prognostic Nutritional Index; STS-EACTS = Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; BMI/A = Body Mass Index for Age; W/H = Weight for Height; W/A = Weight for Age; PH = Pulmonary Hypertension.

31.6% low BMI/A; 31% low W/H; 43% low W/A. 16.3% of patients died after cardiovascular surgery (Table 1).

In the non-adjusted analysis, age, the STS-EACTS mortality score, cyanotic heart disease, malnutrition, low BMI/A, W/H and W/A shown association with mortality (Table 2).

Patients with age higher than 2 years shown a decrease of 73% in chances of death (OR=0.27; CI95%=0.08-0.92; *p*=0.036%. The association between STS-EACTS mortality score and death outcome was significant only in category 4, that is, surgeries belonging to this category shown higher chances of leading patients to death. (OR= .25; CI95%=1.07-16.84; *p*=0.039). Likewise, cyanotic cardiovascular diseases increased chances of death up to 5 times (OR=5.01; CI95%=1.57-15.95; *p*=0.006) (Table 2).

The anthropometric indicators, low BMI/A (OR= 4.84; CI95%=1.57-14.94; *p*=0.006), low W/H (OR=4.15; CI95%=1.29-13.35; *p*=0.017) and low W/A (OR=5.4; CI95%=1.57-18.52; *p*=0.007) as well shown association with mortality. Compared to patients with adequate nutritional status, malnourished patients had shown 4 times more chances of death (OR=4.57; CI95%=1.07-16.84; *p*=0.039) (Table 2).

After adjusting analysis for the confounding factors (Table 3), there were no associations of PNI, CRP, albumin, TLC and H/A with mortality. Patients classified as malnourished were 4 times more likely to die. (OR=4.11; CI95%=1.26-13.40; *p*=0.019).

The anthropometric indicator low BMI/A had shown association with mortality even after adjusting for confounding factors (OR=4.14; CI95%=1.26-13.61; *p*=0.019), as well as low W/H (OR= 4.15; CI95%=1.29-13.35; *p*=0.017) and low W/A (OR=5.20; CI95%=1.39-19.43; *p*=0.014) (Table 3).

Discussion

Cardiovascular diseases are the most common congenital malformations worldwide and are an important cause of early morbidity and mortality.[14] The present study evidenced that older children were less likely to die after cardiovascular surgery. One of the possible hypothesis would be that patients who underwent surgery at older age usually have less complex cardiovascular diseases,[15] and therefore, show higher chances of survival after surgery.

The use of stratification of cardiovascular surgeries by relatively similar levels of complexity, such as performed in our study, is necessary to the mortality analysis due to the high number of different surgical procedures in patients with congenital cardiovascular diseases.[16] Agreeing with the present results, a comparative study between two tools of mortality stratification, STS-EACTS tool among

Table 1

Clinical and demographic characteristics of patients, São Luís - MA, 2021.

Variables	N/ Mean or Median	%/ SD or P_{25}-P_{75}
Sex		
Male	56	57.1
Female	42	42.9
Age (years)		
<2	49	50.0
≥2	49	50.0
CRP		
<0.5 mg/ L	21	21.4
≥0.5 mg/L	77	78.6
Albumin	3.4	0.57
TLC	3690.3	796 - 12600
Cardiovascular disease*		
IAC	33	33.7
IVC	33	33.7
PAVSD	3	3.1
PAD	19	19.4
CoA	10	10.2
Pulmonary stenosis	15	15.3
Aortic stenosis	1	1.0
IAA	1	1.0
TGA	3	3.1
Tetralogyof Fallot	14	14.3
TAPVD	9	9.2
Tricuspid Atresia	6	6.1
Ebstein Anomaly	1	1.0
Pulmonary Atresia	7	7.1
Endocarditis	2	2.0
Tricuspid insufficiency	6	6.1
Hypoplastic left heart syndrome	3	3.1
Single ventricle	2	2.0
STS-EACTS mortality score		
Category 1	38	39.2
Category 2	34	35.1
Category 3	4	4.1
Category 4	21	21.6
Type of cardiovascular disease		
Acyanotic	62	63.3
Cyanotic	36	36.7
PH		
No	80	81.6
Yes	18	18.4
PNI classification		
Low	68	69.4
High	30	30.6
Malnutrition		
No	71	72.5
Yes	27	27.5
Low H/A		
No	64	65.3
Yes	34	34.7
Low BMI/A		
No	67	68.4
Yes	31	31.6
Low W/H		
No	49	69.0
Yes	22	31.0
Low W/A		
No	49	57.0
Yes	37	43.0
Death		
No	82	83.7
Yes	16	16.3
Total	98	100.0

SD = Standard Deviation; CRP=C Reactive Protein; TLC = Total Lymphocyte Count; IAC – Interatrial Communication; IVC = Interventricular Communication; PAVSD = Partial atrioventricular septal defect; PAD = Patent ductus arteriosus; CoA = Coarctation of the aorta; IAA = interrupted aortic arch; TGA = Transposition of Great Arteries; TAPVD = Total Anomalous Pulmonary Venous Drainage; STS-EACTS= Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; PH = Pulmonary Hypertension, PNI = Nutritional Prognostic Index; H/A = Height for Age; BMI/A = Body Mass Index for Age; W/H = Weight for Height; W/A = Weight for Age.

Table 2

Association of mortality with demographic and clinical characteristics of patients, non-adjusted analysis, São Luís - MA, 2021.

Variable	Non-adjusted analysis		
	OR	CI95%	*p*
Sex			
Male	1.00		
Female	1.04	0.35; 3.07	0.937
Age (years)			
<2	1.00		
≥2	0.27	0.08; 0.92	0.036
STS-EACTS mortality score			
Category 1	1.00		
Category 2	0.82	0.17; 3.97	0.808
Category 3	8.50	0.92; 78.92	0.058
Category 4	4.25	1.07; 16.84	0.039
Pulmonary Hypertension			
No	1.00		
Yes	1.61	0.45; 5.76	0.457
Type of cardiovascular disease			
Acyanotic	1.00		
Cyanotic	5.01	1.57; 15.95	0.006
CRP			
<0.5 mg/L	1.00		
≥0.5 mg/L	0.53	0.16; 1.75	0.300
Albumin	1.16	0.45; 2.95	0.760
TLC	1.00	0.99; 1.00	0.760
PNI Classification			
High	1.00		
Low	0.68	0.22; 2.11	0.515
Malnutrition			
No	1.00		
Yes	4.57	1.50; 13.98	0.008
Low H/A			
No	1.00		
Yes	2.03	0.68; 6.01	0.198
Low BMI/A			
No	1.00		
Yes	4.84	1.57; 14.94	0.006
Low W/H			
No	1.00		
Yes	4.15	1.29; 13.35	0.017
Low W/A			
No	1.00		
Yes	5.4	1.57; 18.52	0.007

OR = Odds Ratio; CI = Confidence Interval; STS-EACTS = Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; CRP = C Reactive Protein; TLC = Total Lymphocyte Count; PNI = Prognostic Nutritional Index; H/A = Height for Age; BMI/A = Body Mass Index for Age; W/H = Weight for Height; W/A = Weight for Age.

them, identified that children with higher scores, that is, with need for more complex surgeries, had shown higher mortality risk.[17]

The results of this study corroborates the hypothesis that the postoperative nutritional status can be decisive to increase the chance of mortality after cardiovascular surgery.[18,19] The presence of malnutrition in studied patients increased the chance of mortality 4 times, reinforcing negative effects of malnutrition that are widely documented in the literature as factors of morbimortality in cardiovascular surgery.[18-21]

Table 3

Association of mortality with demographic and clinical characteristics of patients, adjusted analysis, São Luís - MA, 2021.

Variable	Adjusted analysis		
	OR	CI95%	*p*
CRP*			
<0.5 mg/L	1.00		
≥0.5 mg/L	0.45	0.12; 1.61	0.223
Albumin*	1.34	0.50; 3.55	0.558
TLC*	1.00	0.99; 1.00	0.634
PNI classification*			
High	1.00		
Low	0.41	0.11; 1.45	0.168
Malnutrition			
No	1.00		
Yes	4.11	1.26; 13.40	0.019
Low W/A†			
No	1.00		
Yes	2.59	0.80; 8.40	0.114
Low BMI/A†			
No	1.00		
Yes	4.14	1.26; 13.61	0.019
Low W/H†			
No	1.00		
Yes	4.15	1.29; 13.35	0.017
Low W/A†			
No	1.00		
Yes	5.20	1.39; 19.43	0.014

OR = Odds Ratio; CI = Confidence Interval; CRP = C Reactive Protein; TLC = Total Lymphocyte Count; PNI = Prognostic Nutritional Index; H/A = Height for Age; BMI/A = Body Mass Index for Age; W/H = Weight for Height; W/A = Weight for Age; Variables adjusted for modulation of multivariate ordinal logistic: * Malnutrition; † Cyanosisand Pulmonary Hypertension.

The described association may be explained by the postoperative metabolic response, characterized by altered energetic demands, complex inflammatory status and higher protein catabolism, [3,22] added to malnutrition, which can by itself impair the results of the corrective surgery.[19]

Thus, postoperative nutritional diagnosis in cardiovascular surgeries allows for early therapeutic intervention, decreasing risks of postoperative complications.[23] Although these results are not recent, they reinforce the relevance of routine nutritional assessment in patients with congenital cardiovascular diseases, specially before surgery.

One of the combinations of albumin with the TLC found in the literature is the PNI, by Onodera *et al.*,[8] which is easy to calculate[24-26] using preoperative laboratory data,[25] which in turn are objective markers of low cost.[24] Initially associated with surgical risk for patients with gastrointestinal malignancy,[8] PNI is currently used as a nutritional marker predictive of mortality in patients with several diseases, such as cancer,[25,26] Non-tuberculous mycobacterial infection,[27] chronic kidney disease,[28] burn wounds[29] and cardiovascular diseases.[9,24,30]

The exact mechanisms for which PNI is related to postoperative prognosis are not well comprehended, however, some of these potential mechanisms were reported. Firstly, the serum albumin level is widely used to assess nutritional and inflammatory systemic aspects of patients[26,28,29] and secondly, the lymphocytes represent a major role in immune response, and their functions and values are deeply altered after sepsis and other acute lesions such as complex surgeries.[29]

Regarding cardiovascular surgeries, it was observed that patients with coronary artery disease, with a mean follow-up of 7 years, had higher incidence not only of mortality by all causes, but also of cardiac mortality when presented lower preoperative PNI.[24]

A study carried out with 131 patients over 18 years old, accompanied for one year, in order to investigate the impact of the PNI in mortality by infectious endocarditis, demonstrated an association of this index with the mortality rate, being the PNI identified as independent predictor of mortality during hospitalization.[30] It was also observed an association with mortality in the postoperative period of cardiovascular surgery in adult patients, moreover, a higher PNI was related to a better survival rate.[9]

In the current study, this association was not observed. Factors such as sample size, small number of outcomes and assessed age group might explain this finding. This demonstrates that despite of having a well-proven prognostic value in abdominal and gastrointestinal surgeries,[29] there is little evidence about this tool in pediatrics.

We can mention the missing data as another limitation of our study, which was partially solved by multiple imputation. This method has been recommended once the exclusion of observations with missing data and analysis restriction to complete observations diminish the sample size and generates biased estimates.[13]

The strengths include the analysis of association of the PNI with mortality in children and adolescents who underwent cardiovascular surgery, with evidence that it is one of the first studies to approach such association, besides the multiple logistic regression analysis adjusted to the variables represented by the DAG, allowing for the adjustments to be executed by confounding variables, averting spurious associations.

We conclude that age, STS-EACTS mortality score, cyanotic cardiac disease, malnutrition, low BMI/A, W/H and W/A had shown significant association with mortality. In spite of being an indicator of nutritional status of easy application, there was no observed association of the PNI with mortality in children with cardiovascular disease after cardiovascular surgery.

Author's contribution

Silva BM: conception and writing of the article; collection, analysis and interpretation of data. Batista CLC, Pires BRF, Oliveira EC and Lima Jr. JRM: critical review.

Barros TA: data collection. Cruvel JMS: analysis and interpretation of data. Statistical analysis and writing. All authors approved the final version of the article and declare no conflict of interest.

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