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Annals of Pediatrics & Child Health

Review Article

Association of Nutritional Deficiency with Postoperative Complications in Pediatric Cardiac Surgery

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Submitted: 20 April 2020

Accepted: 06 May 2020

Published: 08 May 2020

ISSN: 2373-9312

Keywords

- Nutritional status
- Heart diseases
- Surgery
- Complications

Abstract

Nutritional deficiency compromises the adequate immune and metabolic functions, and may cause repercussions during the postoperative period of pediatric patients submitted to cardiac surgery, thereby causing or aggravating clinical problems. Our aim was to investigate the association of operative complications with the nutritional deficiency of pediatric patients with congenital heart disease submitted to surgical correction. This was a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocol. Of the total number of studies, 16 were related to complications in pediatric cardiac surgery associated with malnutrition, and presented significantly statistical association measures. However, due to the heterogeneity of nutritional assessment methods, it was not possible to define a standard for clinical direction with variables to manage the preoperative period. PROSPERO Registration: CRD 42018111409.

ABBREVIATIONS

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

INTRODUCTION

Congenital heart diseases (CHDs), constitute a broad clinical spectrum, from asymptomatic defects, to those with high mortality rates [1]. They represent one of the most frequent malformations, the incidence of which varies from 8 to 10 per 1,000 live births, and are a significant cause of mortality during the first year of life [2]. Congenital heart disease patients often present with malnutrition and growth retardation, both due to structural damage and to an association with other factors, regardless of the nature of the cardiac defect and the presence or absence of cyanosis [3,4]. In Brazil, the prevalence of malnutrition in these children varies from 46.6% to 83.3%. It is estimated that the daily energy expenditure of children with CHD is 35% higher than that of healthy children of the same age and sex [5].

The inadequate biological use of available nutrients is the main factor responsible for malnutrition. The clinical conditions inherent to cardiac alterations lead to an increase in energy expenditure, thereby classifying children as part of a group of high nutritional risk, with a loss of body mass that has an overall effect on the body. Consequently, there is an increase in the risk of infection and for initiating the so-called nutritionally acquired immune deficiency syndrome, which may increase the chances of postoperative mortality [3,4,6]. In surgical procedures, malnutrition has a prominent role due to its influence on the prevalence of infections and postoperative metabolic complications [7].

Increased nutritional risk is generally not part of the clinical focus, and is therefore often underdiagnosed. Weight loss of between 5 and 10% during invasive treatment is a strong indicator of a poor prognosis, and this risk is particularly intensified with surgeries and hospitalization in intensive care units (ICU) [8]. Poor nutritional status may be associated with postoperative complications and is a key point in determining clinical results [9]. Nutritional imbalance, especially in younger children, is associated with factors of physiological instability, growth failure, longer hospital stays and increased hospitalization costs [10].

Despite the recommendations and positive gains of adequate nutritional therapy before surgical correction, there are currently

few studies on the subject, and results are inconsistent, mainly on the impact of nutritional care for rehabilitation after cardiac surgery [6,9]. However, independently, nutritional status has been identified as a risk factor for mortality amongst infants awaiting heart transplantation [11].

Nutritional deficiency in congenital heart patients compromises the adequate immune and metabolic functions in the postoperative period of cardiac surgery, and may cause and/or aggravate clinical problems. Therefore, investigating whether there is an association between malnutrition and intra- and postoperative complications may assist in the control of pediatric cardiac patients, with regard to pre- and postoperative nutritional conditions, since surgical correction depends on a number of factors, such as nutritional parameters. This study has aimed to determine the association of nutritional deficiency with operative complications in pediatric patients submitted to cardiac surgery.

METHOD

This was a systematic literature review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocol [12]. The question in this review was: What is the relationship between malnutrition and complications in pediatric cardiac surgery? Based on the strategy of the PICOS [13], framework, studies were considered eligible that included a population composed of pediatric patients submitted to cardiac surgery, assessed the influence of malnutrition on cardiac surgery, compared the outcomes between patients with nutritional changes and complications in the cardiac surgery, presented complications and/or death, and were clinical and/or observational studies.

The following databases were consulted until November 2019: *Cochrane Library, British Medical Journal (BMJ) Best Practice, National Library of Medicine National Institutes of Health* (PubMed / MEDLINE), *Science Direct* and Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS).

The search strategy was guided by the use of controlled vocabulary according to Health Sciences Descriptors (DeCs) as an expanded translation of Medical Subject Headings (MeSH). In the DeCs, research was conducted in Portuguese and the descriptors were obtained in English, and were combined using the Boolean operators “and” and “or”. The descriptors used for this study were: Child; Heart Disease; Child Malnutrition or Children’s Nutrition Disorders; Intraoperative Complications; Postoperative Complications or Post-Surgical Complications; Clinical Studies; Observational Studies.

The search for the studies was guided by the research question and by the combination of descriptors in the databases aiming to locate the term in the title, abstract and keywords. There was no restriction on the period or language, other than the use of gray literature as long as they were clinical and/or observational studies. The descriptors were combined two by two on each base and, when necessary, a triple combination was chosen.

Initially, the titles and abstracts of the studies were read, and each researcher registered agreement or not on the assessed study (1st stage). Discordant cases were discussed and submitted for assessment by a third researcher with greater experience in the subject (2nd stage). Subsequently, the selected articles were read in full in order to seek an answer to the review question (3rd stage). Figure 1 describes the flow of identification, selection, eligibility and inclusion of the studies.

Data extraction was performed by two researchers independently with the help of an electronic form prepared with Microsoft Excel®, and a data compatibility assessment was conducted by a third researcher, in order to assess data consistency and cleanliness. The critical assessment of the quality of the study data was undertaken using the *Oxford Center Evidence Based Medicine* method [14], as well as an assessment of the methodological quality of the studies according to the GRADE recommendations [15]. The data synthesis from this study was guided by PRISMA, followed by the IMRD structural logic - Introduction, Methods, Results and Discussion.

Aggregate data from the participating articles were used and a descriptive synthesis was developed. Assessments were conducted to determine whether there was an association between malnourished children who had undergone cardiac surgery, and the occurrence of complications. The methods section was published in the form of a Protocol based on PROSPERO - *International Prospective Register of Systematic Reviews* affiliated to the University of York, according to the CRD Identification Code 42018111409 and available for free access at: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018111409 and following this, the other steps of this study were conducted.

DISCUSSION & CONCLUSION

Nutritional Deficiency x Cardiac Surgery Complications

Sixteen studies [6,11,16-29], with a total of 6,123 participants, met the inclusion criteria for this review. Of the review articles [25,27], a total of 33 titles were included as the sample in the respective studies. The age of the participants included in the studies ranged from 1 (one) day of life <18 years of age, with ten studies (62.50%), that included children aged under 6 years. All studies sought to demonstrate the association of preoperative nutritional parameters with the occurrence of complications in pediatric cardiac surgery or used complications as a starting point in order to search for risk factors and/or causes (Table 1).

The articles were analysed in terms of quality and categorized by Grade of Recommendation and Level of Evidence. It was found that 93.75% (n = 15), of the articles were classified as grade B – moderate, and one article (6.25%), was classified as level of evidence 5, thereby constituting a grade D - very low. Of these, cohort studies were the most frequent types, 62.5% (n = 10), six were retrospective and four were prospective (Table 1).

Sixteen studies were included, of which, 62.5% (n = 10), were cohort studies, 12.5% (n = 2), clinical trials, 12.5% (n = 2), case-controls, 6.25% (n = 1), systematic reviews and, 6.25% (n = 1), a review. With regard to the relevance of the presented outcomes, there was agreement that 100% (n = 16), of the assessed studies presented results with scientific relevance, and 100% of the studies presented a clear methodology consistent with the main outcome (Table 1).

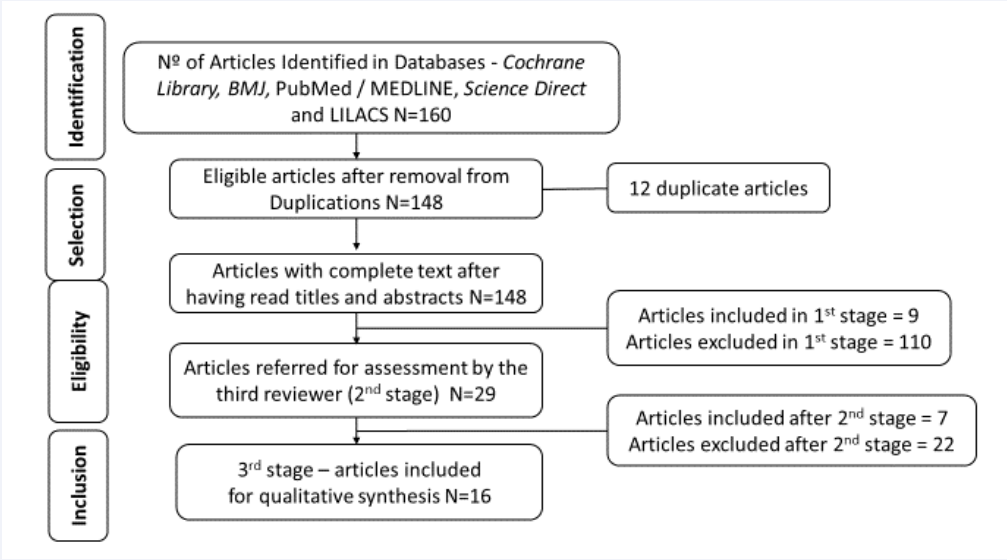

Figure 1 Results Flow Diagram of the Research Strategy and Study Selection.

Table 1: Studies on malnutrition and its association with postoperative complications in pediatric patients submitted to cardiac surgery.

Study and Year of Publication	LE	Type of Study	Sample Size and Age	Nutritional Parameters	Postoperative Complications	RR or OR CI 95% and/or p-value	Conclusions
Leite et al., 1995 [16]	3B	Case-control	50/3 to 11.6 years	Brachial Circumference Brachial Muscular Circumference Pre-albumin	Brachial Circumference / Brachial Muscle Circumference x Cardiac arrhythmia, Cardiogenic Shock, CHF, Cardiac Tamponade, Lobar Atelectasis, Pneumothorax, Hemothorax, Pneumonia, Mediastinitis, Sepsis, Incision Infection, Acute Otitis Media, Bleeding Disorders, Metabolic Acidosis and MODS & AKI Pre-albumin x Infections	*p* 0.0019 / *p* 0.0419 *p* <0.01	The classification for nutritional risk proved to be a good method to identify the subgroups of children with an additional risk of postoperative morbidity.
Leite et al., 2005 [17]	3B	Case-control	30/3 months to 11 years	Albumin	Infection Mortality	*p* 0.0026 *p* 0.0138	The data suggest that the 3.0 g/dL concentration of preoperative serum albumin may be associated with increased risks of mortality and post-surgical infection.
Sano et al., 2009 [18]	2B	Retrospective Cohort	62/1 to 57 days	Body Weight	Mortality	9.75 [2.6-36.3] *p* 0.007	Body weight less than 2.5 kg was associated with mortality.
Vaidyanathan et al., 2009 [19]	2B	Prospective Cohort	476 / < 5 years	Malnutrition [weight/age, height/age and weight/height < - 2 Z-score]	Persistent Postoperative Malnutrition	All variables presented *p* < 0.05	Persistent malnutrition after corrective intervention is predicted by nutritional status at presentation, birth weight and parental anthropometry.

Soares et al., 2010 [20]	2B	Retrospective Cohort	101 / < 3 years	Body weight	SIRS-CPB	$p < 0.05$	Risk group for SIRS-CPB. This group has predisposing factors: lower weight [5.3 ± 1.9] kg and longer CPB time. Patients with SIRS-CPB stay longer on mechanical ventilation, in the intensive care unit and in hospital. Higher weight [OR = 0.68, p 0.01] was identified as a protective factor.
Vivanco-Muñoz et al., 2010 [21]	2B	Retrospective Cohort	289 / < 3 years	Malnutrition [<90% of the weight/age at birth and Z-score <-2 for the BMI]	Mortality Long Hospital Stay	3.447 [1.006–11.812] p 0.049 2.772 [1.282–5.995] p 0.010	Malnutrition at birth and before surgery increases both the length of hospital stay and mortality after cardiac surgery. Early nutritional support reduces length of hospital stay and mortality.
Anderson et al., 2011[22]	2B	Retrospective Cohort	55 / 1.6 to 6 years	Z-score of weight/age	Infections	p 0.006	A Z-score of weight/age less than 2.0 is associated with a higher rate of severe postoperative infections, which are associated with longer hospital stays.
Rodriguez et al., 2013 [23]	2C	Non-randomized Clinical Trial	28 / > 28 days and < 1 year	Malnutrition [weight/age under the 3rd percentile] and Albumin	Infections	73.3% With Malnutrition 53.7% Hypoalbuminemia $p < 0.05$.	The group of malnourished children presented a higher number of infectious complications, related to hypoalbuminemia.
Costello et al., 2014 [24]	2B	Prospective Cohort	78 / <3 years	weight/age height/age weight/ height Growth Failure	Longer Hospital Stay	p 0.003 p 0.025 p 0.042 p 0.009	Growth failure during the pre-admission period and lower growth parameters were associated with a longer hospital stay.
Godown et al., 2014 [11]	2B	Retrospective Cohort	2712 / 2 to 18 years	BMI	Lower Survival After Heart Transplant	2.17 [1.28-3.68] p 0.004	Severe malnutrition and obesity are independent risk factors for mortality in pediatric patients with cardiomyopathies.
Mangukia et al., 2014 [25]	5	Review	21 Articles / < 18 years	Protein-calorie malnutrition	Mediastinitis	NA	Malnutrition and others were definitive risk factors for mediastinitis.
Radman et al., 2014 [26]	2B	Prospective Cohort	71 / < 5 years	Tricipital Skinfold Total Fat Mass Pre-albumin Albumin	Longer Hospital Stay in ICU, Longer time on MV, Longer period on Inotropic Support and Higher Levels of B-Type Natriuretic Peptide	All variables presented $p < 0.05$	Lower total body fat mass and acute and chronic malnutrition are associated with poorer results in children submitted to surgery.
Hill et al., 2016 [27]	2A	Systematic Review	12 Articles / < 18 years	Nutritional Variables	Infection	NA	Malnutrition can be predictive of postoperative complications of infection in children.
Grippa et al., 2016 [28]	2B	Prospective Cohort	72 / > 30 days and ≤ 15 years	weight/age height/age arm muscle area/age	Increased time on MV	RR 2.73 [1.44-5.18] RR 2.49 [1.44-4.28] RR 5.22 [1.19-22.76]	Malnutrition was associated with a longer period of time on mechanical ventilation.

Ross et al., 2017 [29]	2B	Retrospective Cohort	2088 / < 5 years	Z-scores of height/age, weight/age and weight/height	Cardiac Arrest Infections Longer MV Time Longer stay in ICU Longer Hospital Stay Mortality <30 Days	All variables presented $p < 0.05$	Significant association between malnutrition and mortality in 30 days and adverse outcomes after pediatric cardiac surgery.
Santos et al., 2017 [6]	2C	Non-randomized Clinical Trial	11 / > 30 days and ≤ 5 years	BMI	Longer Stay in ICU	NA	An appropriate nutritional status of children with heart disease prior to surgical correction is essential for a good postoperative evolution.
Abbreviations/Legend: NA: Not Assessed; **L**E: Level of Evidence.							

A study by Leite et al. (1995) [16], reported an association between brachial circumference below the 5th percentile (p 0.0019) and brachial muscle circumference below the 5th percentile (p 0.0419), with the following postoperative complications: cardiac arrhythmia, cardiogenic shock, congestive heart failure (CHF), cardiac tamponade, lobar atelectasis, pneumothorax, haemothorax, pneumonia, mediastinitis, sepsis, infected incision, acute otitis media, bleeding disorders, metabolic acidosis, multiple organ dysfunction syndrome (MODS), and acute kidney injury (AKI). When assessing the levels of pre-albumin vs. infections, the authors identified that the mean value was significantly lower in patients who developed postoperative infection when compared to those who did not develop infectious complications (p <0.01).

In 2005, Leite et al. [17], assessed preoperative albumin as a predictor of outcomes in children submitted to cardiac surgery, and reported that concentrations below 3.0 g/dL were associated with infections (p 0.0026) and with an increase in postoperative mortality (p 0.0138).

Sano et al. (2009) [18], demonstrated that body weight <2.5 kg was associated with mortality (OR 9.75 - 2.6-36.3 - p 0.007). Taking into account the variable body weight, Soares et al. (2010) [20], observed that children with lower weight were considered a risk group for the development of the systemic inflammatory response syndrome after cardiopulmonary bypass (SIRS-CPB) (p <0.05), and in the multivariate analysis, higher weight (OR 0.68 and p 0.01), was identified as a protective factor.

Vaidyanathan et al. (2009) [19], confirmed that weight/age, height/age and weight/height less than -2 in the Z-score were associated with persistent postoperative malnutrition (p <0.05). Vivanco-Muñoz et al. (2010) [21], reported that <90% of weight/age at birth and a Z-score of less than -2 for BMI before surgery were associated with increased mortality (OR 3.447 - 1,006 -11.812 - p 0.049), and prolonged hospitalization (OR 2.772 - 1.282-5.995 - p 0.010).

When assessing the Z-Score of weight/age, Anderson et al. (2011) [22], observed that values less than 2.0 in the Fontan procedure were associated with a higher rate of severe postoperative infections (p 0.006), and that, in turn, children who developed serious infections presented a longer hospital stay.

Rodriguez et al. (2013) [23], reported that 73.3% of children were malnourished and that in this group there was a greater number of infectious complications, and that hypoalbuminemia was present in 53.7%, and was associated with a greater number of infectious complications (p <0.05).

An increase in the length of hospital stay was reported as an outcome by Costello et al. (2014) [24]. The authors associated this outcome with values less than -2 in the Z-score for weight/age (p 0.003), height/age (p 0.025), weight/height (p 0.042), and growth failure (p 0.009).

Godown et al. (2014) [11], when examining the influence of nutrition on children on a waiting list and results after heart transplants, observed that BMI levels were associated with lower survival after heart transplant (OR 2. 17 - 1.28-3.68 - p 0.004).

With a greater number of anthropometric variables, Radmann et al. (2014) [26], demonstrated that lower values of tricipital skin fold, total fat mass, pre-albumin and albumin presented a significant association (p <0.05 for all variables), with an increase in the length of stay in ICU, a longer time on mechanical ventilation (MV), a longer period of time on inotropic support and an increase in the levels of B-type natriuretic peptide.

Grippa et al. (2016) [28], demonstrated that malnutrition based on anthropometric variables was associated with an increase in the MV time (weight/age RR 2.73 - 1.44-5.18; height/age RR2.49 - 1.44-4.28; arm muscle area/age RR 5.22 - 1.19-22.76).

When assessing the impact of preoperative malnutrition on outcomes after pediatric cardiac surgery, using the Z-score for height/age, weight/age and weight/height, Ross et al. (2017) [29], confirmed a significant association of all the variables (p <0.05), with cardiac arrest, occurrence of infections, longer time on MV and in ICU and in hospital, and increased mortality in the first 30 days after surgery.

Santos et al. (2017) [6], reported that lower BMI values in the preoperative period were associated with a longer ICU stay, however they did not describe the value of the association measure that was performed.

The two reviews included in this study demonstrated an association between malnutrition and infectious complications. Mangukia et al. (2014) [25], observed that malnutrition and other variables were a definite risk factor for post-surgical mediastinitis, and Hill et al. (2016) [27], in their systematic review, demonstrated that malnutrition may be predictive.

This systematic review made it possible to demonstrate that there is evidence that the nutritional variables that indicate states of malnutrition in pediatric patients are associated with surgical complications, especially during the postoperative period.

Most of the studies were classified as being of moderate quality and with a grade B of recommendation. This may be justified due to the scarcity of randomized controlled clinical trials. However, all those that used measures of association reported statistical significance and, according to their samples and specific characteristics, were able to demonstrate that variables related to malnutrition were associated with the presence of complications in the postoperative period, the repercussions of which were an increase in morbidity and mortality of the pediatric population with congenital cardiovascular malformations submitted to surgical correction.

To assess malnutrition, several anthropometric variables were used and/or measured when dealing with serum markers, such as pre-albumin or albumin. However, it should be noted that due to the heterogeneity of these variables, it was not possible to group the data and compare one study with another.

Assessments based on Z-Scores for height/age, weight/age and weight/height and BMI were the most common variables; this fact is frequent and justified by the routine use of these indicators in routine nutritional assessment, since they follow international WHO recommendations, mainly from the 2000s. When using these variables, the authors used data previously collected by professionals in their daily lives, which is why the retrospective nature is more frequent, thereby bringing scientific data closer to reality, given that in the absence of resources in the health services, more sophisticated parameters for research would be difficult to implement in the services. .

Metha et al. (2013) [30], in a study that aimed to determine the best definition of malnutrition, emphasized that it would continue to evolve with a better understanding of the processes that lead to and complicate the treatment of this condition. A uniform definition should allow for future research that focuses on the impact of child malnutrition on functional outcomes and helps to solidify the scientific basis founded on practical evidence of nutrition. Possibly due to this dynamism in the concept of malnutrition, the articles included herein presented different parameters of assessment.

A number of complications were associated with malnutrition. However, the occurrence of infection, extended hospital stay, an increase in the time required for mechanical ventilation and increased mortality were the most frequent events. It is important to reflect that such factors are common to major surgeries [10], especially in children, however, it should be highlighted that several parameters indicating nutritional deficiency were associated with such complications, thereby raising the need to rethink the assessment and nutritional conducts for this population in order to reduce the occurrence of events that increase morbidity and mortality.

The use of the results from this review should take into account the characteristics of each study base, since, as previously mentioned, there was no pattern of variables investigated to seek an association with complications. Another important point is that although most studies included children aged under six years, others chose to include patients aged up to 18 years. The heterogeneity of the findings is justified due to the complexity of the research question. The authors sought to frame as many studies as possible, respecting the methodological criteria, but aiming to achieve a reflection of the various variables that are used in clinical practice. A specific standard for preoperative nutritional assessment is difficult to implement, since the local characteristics of the population must be taken into account, together with the infrastructure and availability of human and diagnostic services in hospital environments.

In conclusion, the studies demonstrated the association of variables that characterize malnutrition with several types of complications after cardiac surgery. No studies, however, assessed complications during surgery. There was evidence that associated malnutrition as a predictive factor for postoperative complications in children submitted to cardiac surgery, thus contributing to the morbidity and mortality of this group. The variety of nutritional assessment methods used in research does not enable a standard to be defined for clinical direction, for variables to manage the preoperative period. However, it would appear that these are often used in isolation or together, therefore studies of greater magnitude are needed in order to investigate all the possible prognostic relationships.

CONFLICT OF INTEREST

The authors, being responsible for the content of the work and declare that there are no possible ethical and interest conflicts.

ACKNOWLEDGEMENTS

We would like to express our thanks to the support received from the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) - Financing Code 001 - CAPES Ordinance No. 206, on September 4, 2018.

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Cite this article

Batista Cabral JV, da Silveira MMBM, Reis EM, Cordeiro HL, Sobral Filho DC, et al. (2020) Association of Nutritional Deficiency with Postoperative Complications in Pediatric Cardiac Surgery. Ann Pediatr Child Health 8(3): 1179.