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Original Article

Does malnutrition influence outcome in children undergoing congenital heart surgery in a developing country?

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Abstract

Background Most children undergoing cardiac surgery for congenital heart disease (CHD) in developing countries are malnourished. Malnutrition is known as a co-morbidity factor that might predict and influence outcomes after surgery.

Objectives To evaluate the effect of malnutrition and other associated risk factors on post-operative outcomes in children with CHDs underwent cardiac surgery.

Methods We conducted a retrospective cohort study in a single center tertiary pediatric cardiac intensive care unit (PCICU) in Indonesia. Our cohort included all children between 5 and 36 months of age undergoing congenital heart surgery with cardiopulmonary bypass from November 2011 until February 2014. Outcomes measured were the length of intubation and the length of ICU stay. Variables for potential influence investigated were the nutritional status, age, gender, type of cardiac anomaly (acyanotic vs. cyanotic), Aristotle score, cardiopulmonary bypass time, aortic cross-clamp time, and *Pediatric Risk of Mortality* (PRISM) III score.

Results Out of 249 patients included, 147 (59%) showed malnourishment on admission. Malnourished patients were significantly younger in age, presented with an acyanotic heart defects, and had higher PRISM III score. Additionally, they also had a longer mechanical ventilation time and ICU stay than those with a normal nutritional status. After adjusting for various variables using a multiple logistic regression model it could be demonstrated that a higher Z-score for weight to age was a significant protective factor for the intubation time of more than 29 hours with an odds ratio of 0.66 (95% CI 0.48 to 0.92, P = 0.012). Non-malnourished patients had a 49% significantly higher chance for extubation with a hazard ratio of 1.49 (95% CI 1.12 to 1.99, P= 0.007).

Conclusion Malnourishment is clearly associated in a linear fashion with longer mechanical ventilation and ICU stay. As one of significant and potentially treatable co-morbidity factors, prevention of malnourishment by early diagnosis and optimal timing for surgery is important. **[Paediatr Indones. 2015;55:109-16]**.

Keywords: *malnutrition; congenital heart disease; cardiopulmonary bypass; intubation time*

Congenital heart diseases (CHDs) are among the most frequent congenital anomalies presented at birth, with a reported incidence of 8 to 11/1,000 live

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births, and with a high impact on neonatal morbidity and mortality (up to 33%).[1] Additionally, several studies have consistently reported that malnutrition, ranging from mild undernutrition to complete failure to thrive,[2] is a common cause of morbidity in children with CHD.[3-5]

Multiple factors contribute to growth impairment and malnutrition in infants and children with CHD, such as prenatal and genetic factors, hypoxia and hemodynamic factors, such as congestive heart failure, inadequate nutritional intake, swallowing dysfunction, gastroesophageal reflux, immaturity of the gastrointestinal tract, a hypermetabolic state, and nutrient malabsorption,[6-8] as well as psychosocial and hormonal factors.[9,10] However, in medically partially underserved nations such as Indonesia, poor access to care leads to late presentation of patients with CHD and also contributes to malnutrition.

Children with CHD frequently require open heart surgery to repair the defect. However, to the authors' knowledge, only limited studies have been conducted in developing countries focusing on the link between malnutrition and other factors on the post-surgical outcomes in children who undergo congenital heart surgery with cardiopulmonary bypass. The present study was performed to verify whether malnutrition was an independent risk factor for the length of mechanical ventilation and the length of intensive care unit (ICU) stay in this specific group of patients.

Methods

This retrospective cohort study was performed from November 2011 until February 2014 and included all consecutive children aged 5 to 36 months admitted to the tertiary pediatric cardiac intensive care unit (PCICU) after congenital heart surgery with cardiopulmonary bypass. This age range was selected because this cohort showed homogenous characteristics and a tendency to require elective heart surgery over 5 months of age. We excluded patients with preexisting pulmonary disease, multiple congenital abnormalities, those who were subjected to tracheostomy, and those who died after the procedure.

The nutritional status was determined by using the Z-score of weight for age (W/A), based on *World Health Organization* (WHO) child growth standard curves.[11] Malnourishment was defined in those patients in which W/A was at least two Z-scores below the mean standard value, otherwise patients were included in the study and grouped as normal. The nutritional status could not be determined by body height because no height data could be retrieved from our database.

Other potential predictors for clinical outcomes, such as age, gender, the diagnosis of heart defect (acyanotic vs. cyanotic), Aristotle score (the score to indicate the complexity of surgery), cardiopulmonary bypass (CPB) time (the time when patient was on CPB machine), aortic cross-clamp time (the time when the aorta was clamped until the clamp was released), P*ediatric Risk of Mortality* (PRISM) III score (the score to predict mortality, consist of physical examination and laboratory results) on ICU admission were also assessed for their compromising effects with the nutritional status. The Glasgow coma scale was excluded from PRISM III score computation, as our patients were all sedated during ICU admission. The outcome variables were the length of mechanical ventilation and the length of ICU stay. As our patients varied in surgical complexities, the length of mechanical ventilation was categorized as prolonged if it was greater than 75th percentile of our cohort's intubation time that was 29 hours post surgery.

Power Analysis and Sample Size (PASS) for *Windows* software (*version 11.0*) was used to calculate the sample size needed to verify the association between malnutrition and length of intubation time using the Cox regression method; with 5% alpha error, 10% beta error, it yielded that a total of 193 patients were required, based on an expected 90% prevalence of malnutrition and expected relative morbidity risk of 1.70 in CHD children with a weight/age Z-score $\leq$-2.[11] All data collected were assessed for their normal distribution before being statistically analyzed. Subsequently, because the data distribution was not normal, we analyzed group differences using the Mann-Whitney test. We used x^2 test and simple logistic regression to study the associations between the predictor variables (categorical and continuous variables, consecutively) and the binary outcome variables (length of intubation longer or shorter than 75th percentile). All significant predictor variables were then analyzed in a multiple logistic regression model (forward stepwise). A Kaplan-Meier survival curve was generated to verify the influence of the nutritional status on the length of mechanical ventilation using the log rank test to compare the groups. Those which yielded P-value < 0.05 was considered as statistically significant. Data were expressed as mean and standard error of mean (SEM). All statistical analyses were performed using the *SPSS for Mac* software (*version 21.0*).

Results

Out of a total of 1206 PCICU admissions (aged 0 to 18 years) from November 2011 until February 2014, only 547 patients were within the age range of 5-36 months. Of that number, 298 patients had incomplete or missing data. Hence, only 249 patients were eligible for the analysis presented. Our hospital had an overall 6.2% mortality rate for children aged 0 to 18 years undergoing congenital heart surgery. In our study,

Table 1. Main characteristics of patients studied

Characteristics	Normal (Z score > -2) (n = 102)	Malnourished (Z score ≤ -2) (n = 147)	P value
Mean age (SEM), months	17.91 (0.89)	14.90 (0.71)	0.01
Male gender, n(%)	52 (51.0)	87 (59.2)	0.24
Mean body weight (SEM), kg	9.2 (0.24)	6.4 (0.14)	<0.001
Mean Z score for A/W (SEM)	-1.04 (0.11)	-3.02 (0.06)	<0.001
Cyanotic heart defect, n (%)	54 (52.9)	56 (38.1)	0.03
Heart defect diagnosis, n (%)			
Acyanotic			
ASD, VSD, iAVSD, SVD	40 (39.2)	72 (49.0)	
cAVSD	6 (5.9)	9 (6.1)	
Coarctation of the aorta, IAA	2 (2.0)	5 (3.4)	
Cyanotic			
TOF	30 (29.4)	27 (18.4)	
PA-IVS, PA-VSD	7 (6.9)	0	
DORV	4 (3.9)	7 (4.8)	
TGA, MGA	6 (5.9)	9 (6.1)	
Truncus arteriosus	1 (1.0)	2 (1.4)	
APVD, TAPVD	2 (2.0)	7 (4.8)	
Others, n (%)	4 (3.9)	9 (6.1)	
Surgical procedures, n (%)			
ASD, VSD, iAVSD closure	42 (41.2)	72 (49)	
cAVSD repair	5 (4.9)	4 (2.7)	
Total correction TOF	29 (28.4)	27 (18.4)	
Rastelli procedure	3 (2.9)	0	
Arterial switch operation	2 (2.0)	6 (4.1)	
BCPS, atrial septectomy	15 (14.7)	15 (10.2)	
Coarctation/IAA repair	2 (2.0)	4 (2.7)	
Truncus repair	0	2 (1.4)	
APVD, TAPVD repair	2 (2.0)	7 (4.8)	
Others	2 (2.0)	10 (6.8)	
Mean Aristotle score (SEM)	7.15 (0.15)	7.00 ± 0.14	0.33
Mean CPB time (SEM), minutes	97.68 (5.25)	93.73 (4.96)	0.31
Mean cross-clamp time (SEM), minutes	54.93 (3.47)	53.64 (3.09)	0.62
Mean PRISM III score (SEM)	3.77 (0.47)	5.12 (0.47)	0.02

ASD: atrial septal defect, VSD: ventricular septal defect, iAVSD: incomplete atrioventricular septal defect, SVD: sinus venosus septal defect, cAVSD: complete atrio-ventricular septal defect, TOF: tetralogy of Fallot, PA: pulmonary atresia, IVS: intact ventricular septum, VSD: ventricular septal defect, DORV: double outlet right ventricle, TGA: transposition of the great arteries, MGA: malposition of the great arteries, IAA: interrupted aortic arch, (T)APVD: (total) anomalous pulmonary venous return drainage, BCPS: bidirectional cavo-pulmonary shunt, CPB: cardiopulmonary bypass, PRISM: *Pediatric Risk of Mortality.*

Table 2. Outcomes observed based on the nutritional status

Outcomes	Normal	Malnourished	P value
Length of intubation (n= 249)	n= 102	n= 147	
Mean (SEM), hours	27.51 (4.91)	39.89 (6.12)	0.005
Min – max, hours	3.0 - 295.0	3.5 – 545.0	
Length of ICU stay (n= 238)	n= 99	n= 139	
Mean (SEM), days	2.75 (0.38)	4.30 (0.67)	0.018
Min – max, days	1.0 – 25.0	1.0 – 61.0	

Table 3. Characteristics of the patients, influence of other variables on the length of intubation

Characteristics	Length of intubation ≤ 29 hours (n=188)	Length of intubation > 29 hours (n=61)	P value
Mean Z score for W/A (SEM)	-2.08 (0.10)	-2.61 (0.15)	0.01
Range	-4.66 – 7.57	-6.82 – 0.43	
Mean age (SEM), months	16.93 ± 0.65	13.68 ± 1.05	0.01
Gender (male), n (%)	105 (55.9)	34 (55.7)	1.00
Cyanotic heart defect, n (%)	76 (40.4)	34 (55.7)	0.04
Mean aristotle score (SEM)	6.86 (1.11)	7.70 (0.24)	0.001
Mean CPB time (SEM), minutes	84.76 (2.92)	127.98 (10.79)	<0.001
Mean cross-clamp time (SEM), minutes	44.90 (2.23)	72.08 (5.79)	<0.001
Mean PRISM III score (SEM)	3.71 (0.30)	7.35(0.97)	0.002

The intubation time of 29 hrs is the 75th percentile of the ventilation time of the cohort. 75% of the patients were extubated within 29 hours after admission to the PCICU, 25% were ventilated more than 29 hours.

however, as only those aged 5 to 36 months were included, mortality was only 3.4%.

Table 1 illustrates the baseline characteristics of children with normal nutrition status as compared to its counterpart group. Approximately 59% of the patients studied had a Z-score for W/A under minus 2. Overall, the two groups were comparable, except for age and presence of cyanotic heart lesions. Those with normal nutrition were of older age and presented predominantly with a cyanotic heart defect.

Additionally, atrial/ventricular septal defect (A/VSD) remained the leading cardiovascular malformations among all cases of acyanotic CHD; followed by tetralogy of Fallot (ToF) that accounted for the most frequent cyanotic lesion of CHD. There was no difference of perioperative variables (Aristotle score, CPB time, cross-clamp time); however PRISM-III scores showed a statistically significant difference between both nutrition groups; patients with malnourishment had a significantly higher PRISM-III score than those with normal nutrition status.

Despite comparable preoperative variables, our cohort showed a significant association between the nutritional status and the morbidity outcomes as judged by the length of intubation and the length of ICU stay, as depicted in **Table 2**. Malnourished patients clearly showed a tendency (P=0.005) to have a longer length of intubation, i.e., mean 39.89 (SEM 6.12) hours when compared with those with a normal nutritional status who have mean intubation time of 27.51 (SEM 4.91) hours. The other morbidity factor measured was the length of ICU stay, which also showed a significant result. The mean difference between these two groups was about 2 days, the malnourished children stayed 4. 3 days in the PCICU, the non malnourished only 2. 75 days. The longest ICU stay in the cohort group with Z-score for W/A above 2 was 25 days; while those in the group of malnourished patients may have a prolonged ICU stay until 61 days.

We further investigated not only the nutritional status, but also other possible independent variables, which may be associated with the length of intubation. As shown in **Table 3.,** besides malnutrition (measured as lower Z-score), younger age, cyanotic heart defect, a higher Aristotle score, longer CPB time, cross-clamp time, and PRISM-III score were found significantly different in the group of patients with an intubation

Table 4. Univariate and multivariate analyses of predictive factors for an intubation time longer than 29 hours (analyzed with multiple logistic regression)

Variables	Unadjusted Odds Ratio (95% CI)	P value	Adjusted Odds Ratio (95% CI)	P value
Z score W/A	0.64 (0.51 to0.81)	<0.001	0.66 (0.48 – 0.92)	0.01
Age, months	0.93 (0.90 to0.96)	<0.001		0.10
Gender (male)	1.01 (0.56 to1.80)	1.00		0.80
Cyanotic heart defect	1.15 (0.70 to1.89)	0.61		0.08
Aristotle score	1.86 (1.04 to 3.33)	0.04		0.23
CPB time	1.01 (1.01 to 1.02)	<0.001		0.09
Cross-clamp time	1.02 (1.01 to 1.03)	<0.001	1.02 (1.01 – 1.03)	0.001
PRISM III score	1.09 (1.02 to 1.15)	0.01	1.14 (1.06 – 1.22)	<0.001

CPB : cardiopulmonary bypass

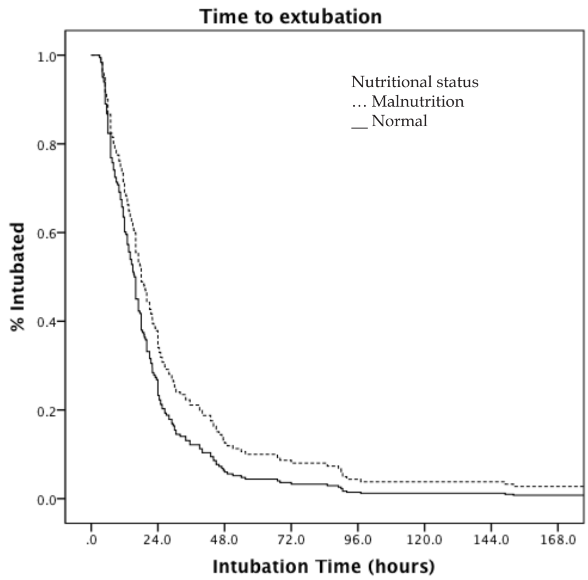

Figure 1. Kaplan–Meier curve of time to extubation for normal and malnourished subjects with 7 days censor time (adjusted for cross clamp time and PRISM III score). Statistics by Cox proportional hazards: hazard ratio for those normal nutrition patients was 1.49 (95% CI 1.12 to 1.99, P= 0.007) compared to malnourished group.

time of more than 29 hours (i.e. the 75% percentile of the cohort). To assess the predictive magnitude of those significant variables, we entered these variables into a simple and multiple logistic regression analysis, and the results as presented in **Table 4**. A lower Z-score for body weight to age as continuous variable, a longer cross-clamp time, and a higher PRISM-III score statistically significant increased the length of intubation significantly with an adjusted OR of 0.66 (95% CI 0.48 to 0.92, P = 0.012), 1.02 (95% CI 1.01 to 1.03, P = 0.001), and 1.14 (95% CI 1.06 to 1.22, P = <0.001), respectively.

A Kaplan-Meier survival analysis of intubation time was then conducted and is illustrated in **Figure 1.** In consistency with our results this curve depicts that well-nourished patients tend to have a shorter length of intubation compared to the other group, even after being adjusted for cross-clamp time and PRISM-III score.

Discussion

It is well known that CHD may cause malnutrition and that malnutrition accompanies and contributes to morbidity in CHD. We investigated in this retrospective study the potential influence of malnutrition in this patient group on the immediate postoperative course. Our results clearly showed that malnourished patients had a statistically significant higher length of mechanical ventilation and ICU stay after a corrective cardiac surgery procedure despite comparable baseline characteristics. On average, our malnourished patients tended to be extubated 12 hours after those counterpart patients with normal nutritional status; this is consistently reported in many different sets of patients.[5,12-14] In comparison to our study, a study[14] investigated the influence of the nutritional status based on skinfold thickness, instead of weight for age.[14] According to the study, a lower total body fat mass, as well as acute and chronic malnourishment were associated with worse clinical outcome, assessed by the length of ICU stay, duration of mechanical ventilations, and duration of dopamine and milrinone infusion.[14]

The other characteristics of our cohort were that malnourished patients were of younger age, presented more often with acyanotic heart defects at the time of congenital heart surgery, and had higher PRISM III score. A previous study reported that heart failure, older age at corrective surgery and lower growth potential (lower birth weight, small for gestation, lower parental anthropometry and associated genetic syndrome) emerged as significant predictors of malnutrition at the presentation of the patients.[15] The fact that our cohort of malnourished patients presented at younger age and more often with acyanotic types of CHD indicates that they suffered from earlier and more pronounced congestive heart failure due to unrestrictive pulmonary blood flow, that might be complicated postoperatively by more severe pulmonary hypertension.[4] In general, this group of patients requires earlier corrective surgery. The severity of illness as depicted by PRISM III score has also been reported to be associated with prolonged mechanical ventilation with a similar odds ratio as our study.[16,17]

On multivariate analysis, the other commonly known factors (i.e. Aristotle and PRISM III score, bypass time and cross clamp time) play a role in predicting the duration of intubation but nevertheless malnutrition is another independent and equally important factor. A lower Z score for body weight to age indicated a more severe malnourishment and remained a significant factor for predicting a longer intubation time ($>75^{th}$ percentile of our cohort intubation time that was more than 29 hours), along with the cross-clamp time and PRISM III score. The PRISM III score has repetitively been reported by other studies to be associated with and may predict length of intubation, ICU stay, and mortality rate.[17,18] Cox regression and Kaplan-Meier survival curve were then conducted to show differences in the length of intubation in those patients with a normal nutrition when compared to the malnourished counterpart group. Again a longer intubation time in the malnourished group even after adjustment for cross-clamp time and PRISM-III score could be demonstrated. Malnutrition alters many systemic functions, especially in those who are critically ill. Many studies have consistently reported that malnutrition is associated with a lowered immune response, atrophy, and an increased permeability of the intestinal epithelial barrier, which facilitates infection and bacterial translocation.[12] Additionally, impaired healing of wounds, a higher incidence of pneumonia and sepsis, low T3 syndrome, low cardiac output syndrome, muscle weakness and other conditions which can lead to increased mortality, prolonged length of intubation and hospital stay, and finally increased health care costs are confounding factors influenced by malnutrition.[12,19]

Considering these detrimental effects of malnutrition, it seems evident to improve the nutritional status of the patients before and after surgery. It may be postulated and hypothesized that restoration of the nutritional status of the patients whilst waiting for surgery may improve the postsurgical clinical outcomes. In addition the post-operative nutritional intake is frequently inadequate and may be affected by a combination of genetic factors, increased metabolic demands, inefficient nutrient absorption, postsurgical fluid restriction, oro-pharyngeal dysfunction, and frequent interruptions of enteral feeding. Therefore even after surgery nutritional support plays an important role for improving outcome.[13] Most patients presenting late suffered from malnourishment due to relatively poor access to medical care in Indonesia, where waiting times for surgeries are often extended to months, well beyond Western standards. The only way to improve this is to improve access to care. This problem may be attenuated by creating a more efficient health care system and increasing resources for congenital heart disease patients in Indonesia.

The present study has several limitations. First, it was a retrospective cohort study; hence, it has the limitations inherent in this type of study. Secondly, it was conducted in a single center and therefore the results may not be able to be extrapolated to other ICUs with different characteristics. Nevertheless the setting of the ICU is highly comparable to settings in comparable countries. Additionally, we have a very homogenous sample (aged 5 to 36 months). This approach however was chosen to have comparable groups and to obtain reliable data. And lastly as our study determined the nutritional status based on weight and age only, so we were able to observe more acyanotic patients with W/A malnutrition (underweight). Wasted (W/H) and stunted (H/A) condition could not be evaluated because no body height data were recorded.

Considering the results of the study presented and the limitations cited above, we recommend further studies to assess the influence of the nutritional status (age, weight, height) on other outcomes, such as the low cardiac output syndrome, the use or necessity of inotropic support, possible biomarkers available (e. g., brain natriuretic peptide) and sepsis. In addition a nutritional guideline for malnourished children who suffer from a congenital heart defect and who will be scheduled for corrective surgery should be established and evaluated. Due to its positive influence on energy metabolism and the potential effect on the postoperative low cardiac output syndrome (LCOS) it may be helpful to conduct a further therapeutic study along with thyroid hormone supplementation peri-operatively, which may improve the physiologic response and impede the morbidities and mortalities associated with malnutrition. Finally additional recommendations for clinicians and medical communities need to be elaborated to improve the early detection and screening for congenital heart defects, enable early access to corrective surgery and to improve the nutritional status beforehand whilst waiting. This should be possible within national health care system coverage.

In conclusion, our results show that malnutrition is common among children with congenital heart defect in a developing country who have to undergo corrective surgery. It is associated with higher morbidity especially with longer mechanical ventilation and ICU stay. Pediatricians, cardiologists, intensivists, surgeons, and nutritionist support teams should recognize and address this important risk factor. The health care system should be enabled to screen and identify these patients early to avoid possible detrimental outcomes.

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Conflict of interest

None declared

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