Somatic growth after corrective surgery for congenital heart disease

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SUMMARY Tokel K, Azak E, Ayabakan C, Varan B, Aşlamacı S, Mercan Ş. Somatic growth after corrective surgery for congenital heart disease. Turk J Pediatr 2010; 52: 58-67.

We report the somatic growth characteristics of 60 infants who underwent corrective surgery for congenital heart disease.

Patients were assigned to the following groups: Group 1, cyanosis with pulmonary hypertension (PH); Group 2, cyanosis without PH; Group 3, large left-to-right shunt and PH; and Group 4, left-to-right shunt or obstructive heart lesion and no PH. Weight, length, and head circumference measurements and z scores were obtained before the operation, at 45 days, and 3, 6, and 12 months after the operation. Details about dietary intake, socioeconomic status at presentation, length of stay in the intensive care unit, hospitalization period, and perioperative events were noted. The endpoint was reaching a z score >-1 for all anthropometric measurements.

At presentation, 51 patients (85%) had malnutrition. The family income, dietary intake, and presence of preoperative chronic malnutrition were interrelated and influenced the weight of the patient at all times during the postoperative follow-up (p<0.05 for all values). The severity of the heart defect had no significant influence on the postoperative anthropometric measurements (p>0.05). The lowest preoperative z scores for weight and height were observed in Group 3. Seven patients could not achieve the endpoint at the end of 12 months (4 in Group 3 and 3 in Group 2).

Catch-up growth is attained mostly in the first year after corrective surgery. Delays in reaching z scores >-1 are observed in the chronically malnourished children. If adequate calories are provided and early corrective surgery is performed, the normal growth potential may be fulfilled.

Key words: malnutrition, postoperative, catch-up growth, cardiac surgery.

Neonates with congenital heart disease may be normal weight for gestational age; however, significant malnutrition commonly occurs early in their lives^{1,2}. Several factors have been claimed to interfere with the normal growth potential in congenital heart disease, including inadequate caloric intake, increased energy expenditure, associated malabsorption, frequent respiratory infections, and associated genetic syndromes². Different types of cardiac lesions may lead to different patterns of growth retardation, which may have a notable effect on the outcome of the corrective surgery^{2,3}. There are several studies documenting the high prevalence of malnutrition in congenital heart disease and improvement in growth after corrective surgery³⁻⁹. However, most such studies are cross-sectional or retrospective in nature and include heterogeneous age groups. The fastest growth occurs during infancy and adolescence. Since most children with congenital heart disease are operated on during infancy, any growth impairment during this period may have a larger impact on the growth potential of the child. Therefore, in the present study, we aimed to report prospectively

the follow-up somatic growth characteristics of infants who underwent surgery for different types of congenital heart diseases. We also aimed to identify factors associated with suboptimal growth after surgery.

Material and Methods

Case Selection and Groups

The cohort consisted of 60 consecutive infants who underwent corrective cardiac surgery at Başkent University in a sixmonth period and whose one-year follow-up was completed at the pediatric cardiology department of Başkent University thereafter. Patients older than 18 months and those with known genetic malformations, dysmorphic features, hypothyroidism, or infection were not recruited.

All patients went through detailed physical and echocardiographic examinations, cardiac catheterization and angiography prior to the surgery in order to determine or confirm the cardiac diagnosis. Patients were assigned to four groups according to their diagnosis, similar to a previous study by Varan et al.³. Group 1 consisted of cyanotic patients with pulmonary hypertension (PH); Group 2 of cyanotic patients with normal pulmonary artery pressure; Group 3 of patients with large left-to-right shunt and PH; and Group 4 of patients with small leftto-right shunt or obstructive heart lesion and normal pulmonary artery pressure.

Assessment of Growth and Nutrition

Standardized measurements of weight, height, and head circumference were made by the same doctor (E.A.) at admission before the operation. The follow-up measurements were done by the same doctor in an outpatient clinic setting, at 45 days, and 3, 6, and 12 months after the operation (E.A.). The percentiles for weight, height and head circumference were determined with reference to the published standard values for age and sex in Turkish children¹⁰.

All patients' mothers were interviewed by the same doctor about dietary details. Mothers recalled and listed the dietary intake of their children in detail for three consecutive days, then the total energy and protein content of the diet was calculated by a dietitian. Dietary counseling was provided to mothers whose children had z scores for height and/or weight below -1 only at presentation.

Patients were considered as taking daily adequate energy when they ingested at least 120% of the estimated energy requirement under non-stressed conditions; namely, 120 Kcal/kg for patients 0-2 months old, 115 Kcal/kg for patients 3-4 months old and 100 Kcal/kg for patients >4 months old.

Information on socioeconomic level (monthly income, number of siblings, educational status of the parents), patient's birth weight, nutritional history (duration of breast-feeding, nutritional characteristics during weaning period), and medical history (infections and hospitalizations before operation, medications) were obtained through an interview with the parents. Low income was defined as both parents earning minimum monthly salaries as stated by the government, which is about 420 Euro. Families with incomes up to four times the minimum salary were considered as having average income.

Nutritional status of all patients was determined by comparing their weight for age values to standard references. Malnutrition was defined as the patient's weight being less than 89% of normal for age. Furthermore, by using height for age and weight for height standards, the duration of malnutrition was estimated. When the patient's height was less than 95% of standard height for that age, the condition was described as chronic malnutrition, in other words, the patient was stunted. When the patient's weight for height was less than 90%, it was considered as acute malnutrition; the patient was wasted. If the patient was both wasted and stunted, then acute malnutrition was recently added to chronic malnutrition¹¹. The endpoint of the catch-up growth was reaching a z score more than -1 for all anthropometric measurements.

Disease Severity

Measurements of pulmonary and systemic flows (for patients with left-to-right shunt), pulmonary artery and aortic systolic pressures and aortic oxygen saturation were available for all patients. Mean pulmonary artery pressure above 25 mmHg was considered as PH. Severity of disease was determined by the following criteria (Table I):

		Severity of CHD			
Type of CHD		Variable	Mild	Moderate	Severe
PH (+)	(cyanotic or acyanotic)	PA/Ao systolic pressure	< 0.5	0.51-0.75	> 0.75
		Qp/Qs	< 2.1	2.1-3	> 3.1
PH (-)	cyanotic	O ₂ saturation	≥90%	75-89%	< 75%
	acyanotic	Pressure gradient	<50 mmHg	50-75 mmHg	>75 mmHg

Table I. Classification of the Severity of Congenital Heart Disease (CHD)

PH: Pulmonary hypertension. PA: Pulmonary artery. O_2 : Oxygen. Qp: Pulmonary flow (L/min/m²). Qs: Systemic flow (L/min/m²).

Aortic oxygen saturation while breathing room air was used for disease classification in cyanotic patients with normal pulmonary artery pressure (Group 2). For patients with PH (Groups 1 and 3), the ratio of the pressures in the main pulmonary artery and the aorta was used. For patients with left-to-right shunt (in Group 3 and some in Group 4), the ratio of pulmonary and systemic flows was also considered. In patients with obstructive lesions (Group 4), the gradient across the lesion was considered in determining the severity of the disease. Table II summarizes the distribution of the disease severity in the different groups.

Other Data

Perioperative events, including length of stay in the intensive care unit, hospitalization period, infections, and administration of total parenteral nutrition and diuretics were also noted.

Complete blood count, serum iron, total iron binding capacity, transferrin, and ferritin values were used to determine iron deficiency anemia among patients, and the tests were repeated at each outpatient visit. Routine biochemical tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatinine, total protein, albumin, prealbumin, and serum zinc levels were determined preoperatively and repeated at 6 and 12 months of follow-up.

The study was approved by the Başkent University Committee on Ethics and Clinical Investigation. The parents were informed about the details of the study and signed an informed consent in order to participate.

Statistics

Categorical data were analyzed using chi-square

or Fisher's exact test. Comparisons were made between the groups using Mann-Whitney U for independent variables, and Kruskal-Wallis or Student t test for dependent variables. Correlations were done with Spearman or Pearson tests. Data were analyzed with a software program, SPSS 11.5 for Windows. Values of p < 0.05 were considered statistically significant.

Results

Demographic Characteristics

The mean age of the patients at presentation for operation was 8.7 ± 4.8 months (range: 1-17 months); of these, 32 patients were male and 28 were female.

Thirty-five patients (58.3%) were from a low income family and 25 (41.7%) were from an average income family. Only 10 patients (16.7%) resided in a rural area whereas 50 patients (83.3%) lived in an urban area (town or city center). Six patients (10%) were born prematurely. Among all, the birth weights of 15 patients (25%) were < 2500 g and 6 patients (10%) were > 4000 g.

There were no significant differences between groups with respect to age, socioeconomic status, number of siblings, history of prematurity, or birth weight (p>0.05 for all variables).

Disease-Related Characteristics

In the study group, 28 patients (46.7%) had severe disease, whereas 25 patients (41.6%) had moderate and 7 patients (11.7%) had mild disease. Table II shows the characteristics of the groups and distribution of the severity of the congenital heart disease in the different groups. The majority of the patients (45 patients, 75%) did not have adequate energy intake for age. Only 25% (15 patients) had adequate intake. Although Group 4 had more patients with sufficient energy intake for age, the difference among groups was not statistically significant (p>0.05). Dietary energy intake was similar among patients grouped according to the severity of the congenital heart defect (p>0.05).

At presentation, 51 patients (85%) had malnutrition. Among these, 35 patients (58.3%) had acute, 8 (13.3%) had chronic, and 8 (13.3%) had acutely exacerbated chronic malnutrition. Only 9 patients (15%) were normally nourished. Table III depicts the distribution of the type of malnutrition among groups at presentation and throughout the study. Chronic malnutrition was most frequently seen in Group 3; in fact, none of the patients in Group 1 and Group 4 had chronic malnutrition. However, the rates of chronic malnutrition observed in Groups 2 and 3 were similar (15% of patients in Group 2, 20% of patients in Group 3). On the contrary, acute malnutrition was most frequent in Group 3 (68% of Group 3 patients) (Table III). The number of patients having z scores less than -1 for weight was significantly more in Groups 2 and 3 (p<0.001).

Preoperative anthropometric measurements (weight, height and head circumference) and the severity of malnutrition were mostly influenced by factors like family income and energy intake. Preoperative energy content of the diet was also correlated with family income (r=0.61; p<0.001). Conversely, preoperative variables like gestational age, birth weight, severity of the cardiac lesion, and previous hospital admissions were not correlated with the preoperative anthropometric measurements (p>0.05).

Preoperative z scores for weight were correlated with postoperative number of complications and infections (p<0.05). However, they were not correlated with the length of the intensive care therapy or the total hospitalization time. On the other hand, preoperative energy content of the diet had correlations with length of intensive care therapy (r=-0.43; p=0.003), total hospitalization time (r=-0.65; p<0.001) and the postoperative z scores for weight (r=-0.70; p<0.001).

Iron deficiency anemia was seen in 57.3% of the patients preoperatively, but only 7.8% of the patients were receiving iron replacement therapy. The distribution of iron deficiency anemia before the operation was parallel to the distribution of malnourished children and was more frequent among patients in Groups 2 and 3; however, the mean ferritin levels were similar among all groups. On the other hand, 45 days after the operation, Groups 2 and 3 had significantly higher ferritin levels (127.45±52.29 ng/dl and 126.52±77.19 ng/dl, respectively) compared to Groups 1 and 4 (97.83±62.38 ng/dl and 73.11±28.72 ng/dl, respectively; p=0.019). We believe this difference was due to postoperative blood transfusions. Serum zinc levels and prealbumin levels were also similar among groups throughout the study (p>0.05).

Postoperative Follow-Up

Figures 1 and 2 show the change in z scores of height and weight, respectively, after corrective surgery. At the 3rd month after the operation, all the height and head circumference measurements were above 3rd percentile for age. All patients in Groups 1 and 4 reached the endpoint (z scores > -1) by the end of the 6th month; however, this was still not observed in 7 patients at the end of the study. The most remarkable change in z scores for weight after the operation was observed in Group 3. The z score increased 3.08 ± 1.63 in Group 3, compared to 1.67 \pm 1.21 in Group 1, 1.20 \pm 1.15 in Group 2, and 2 ± 1.22 in Group 4 at the end of the study (p=0.001). On the other hand, the change in z scores for height was similar among all groups (p>0.05).

We observed that only patients in Group 2 continued to lose weight shortly after the operation and had lower z scores for weight than the initial measurements. Although patients in Group 3 had the lowest z scores at 45 days after the operation, these values were higher than the initial measurements and therefore were a reflection of improvement (Fig. 2).

Family income, dietary intake, preoperative weight, and presence of preoperative chronic

Table II. Characteristics of the Groups and Sevenity of Disease						
Groups	n	Severity of CHD				
		Mild (%)	Moderate (%)	Severe (%)		
1: Cyanotic PH (+)	6	0	3 (50%)	3 (50%)		
2: Cyanotic PH (-)	20	0	13 (65%)	7 (35%)		
3: Acyanotic PH (+)	25	0	7 (28%)	18 (72%)		
4: Acyanotic PH (-)	9	7 (78%)	2 (22%)	0		
TOTAL	60	7 (11.7%)	25 (41.6%)	28 (46.7%)		

Table II Changestanistics of the Change and Sevenity of Disease

CHD: Congenital heart disease. PH: Pulmonary hypertension.

	Tab	le III. Type of Ma	alnutrition in t	the Four Group	ps	
		Preoperative	45 th day	3 rd month	6 th month	1 st year
- ·	acute	4 (67%)	5 (83%)	2 (33%)	2 (33%)	0
Group 1	chronic	0	0	0	0	0
n=6	acute+ chronic	0	0	0	0	0
	acute	10 (50%)	10 (50%)	8 (40%)	4 (20%)	2 (10%)
Group 2	chronic	3 (15%)	3 (15%)	2 (10%)	1 (5%)	1 (5%)
n=20	acute+ chronic	3 (15%)	2 (10%)	1 (5%)	0	0
	acute	17 (68%)	14 (56%)	7 (28%)	5(20%)	1 (4%)
Group 3	chronic	5 (20%)	4 (16%)	3 (12%)	2 (8%)	3 (12%)
n=25	acute+ chronic	3 (12%)	2 (8%)	2 (8%)	1 (4%)	0
	acute	4 (44%)	3 (33%)	1 (11%)	1 (11%)	0
Group 4	chronic	0	0	0	0	0
n=9	acute+ chronic	2 (22%)	0	0	0	0
	acute	35 (58%)	32 (53%)	18 (30%)	12 (20%)	3(5%)
Total	chronic	8 (13%)	7 (12%)	5 (8%)	3 (5%)	4 (7%)
n=60	acute+ chronic	8 (13%)	4 (7%)	3 (5%)	1 (%)	0

malnutrition were interrelated and influenced the weight of the patient at all times during the postoperative follow-up. The presence of acute or chronic malnutrition and the z scores for weight at the end of the study were correlated with the severity of the residual cardiac defect as well (p < 0.05 for all values). The length of the intensive care therapy, number of complications and infections and total hospitalization time determined the severity of malnutrition in the early (45 days) as well as the late (1 year) postoperative period by affecting the z scores for weight (Table IV). Interestingly, the severity of the congenital heart defect itself and the length of diuretic therapy had no significant influence on the postoperative anthropometric measurements (p>0.05).

At the end of the study, only 7 patients could not achieve the desired catch-up endpoint for growth. Among these, 3 patients all had z scores below -1, whereas the remaining 4 had only z scores for weight below -1. When these 7 patients were studied separately, the following were determined to influence their low weight: low socioeconomic status (6/7 patients), preoperative chronic malnutrition

	Severity	of malnutrition	on
	Preoperatively	45 th day	1 st year
Family income	r= -0.47	r= -0.56	r= -0.51
Dietary intake	p≤0.001 r= -0.40	p < 0.001 r = -0.56	p< 0.001 r= -0.70
Preoperative weight SD score	p=0.002 r= -0.86	p<0.001 r= -0.68	p<0.001 r= -0.34
Preoperative chronic malnutrition	p< 0.001 r= 0.42	p<0.001 r= 0.42	p= 0.007
Time in intensive care unit	p= 0.001	p= 0.001 r= 0.51	p > 0.05 r = 0.34
Postoperative complications/infections	p > 0.05 r = 0.38	p < 0.001 r = 0.55	p=0.021 r=0.86
Total hospitalization time	p= 0.003	p < 0.001 r = 0.54	p<0.001 r= 0.52
Severity of heart defect	p>0.05	p<0.001	p< 0.01
Length of diuretic therapy	p>0.05	p>0.05	p>0.05
postoperatively Residual defect	NA	p > 0.05 r = 0.39	p > 0.05 r = 0.66
CD . Standart deviation	p>0.05	p= 0.002	p<0.001

Table IV. Variables Correlating with the Seven	ity of Malnutrition Pre- and Postoperatively
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SD : Standart deviation. NA : Not available.



Fig. 1. Changes in mean \boldsymbol{z} scores of height after corrective surgery.



Fig. 2. Change in mean z scores of weight after corrective surgery.

(4/7 patients), inadequate diet (5/7 patients), residual heart defect (5/7 patients), diuretic use more than 3 months (5/7 patients), and 2 or more serious infections during follow-up (4/7 patients). Four of these patients were in Group 3 and 3 were in Group 2. Two of them were reoperated because of residual cardiac defects. We followed these patients beyond 12 months and observed that all patients achieved catch-up growth within 27 months.

Discussion

We found that malnutrition was very frequent in children with congenital heart disease, and recovery of somatic growth was achieved in most of the patients after corrective surgery. However, there was a small group with suboptimal growth even one year after surgery. These patients had low family income, inadequate diet, and preoperative chronic malnutrition in common, as well as residual cardiac defects requiring lengthy diuretic use postoperatively.

Children with congenital heart disease may become malnourished due to multiple factors, such as the type of cardiac lesion, low energy intake, hypermetabolism, age at the time of operation, and prenatal factors². When chromosomal disorders, dysmorphic syndromes and intrauterine infections are associated with congenital heart disease, prenatal factors become more considerable in the growth pattern. Since patients with these characteristics were excluded from our study, the influence of prenatal factors was insignificant in our group. Among all causes, socioeconomic variables like family income, adequate dietary intake, and the type of congenital heart disease (especially being in Group 3) were more influential on preoperative malnutrition.

Several studies have emphasized that different patterns of growth retardation may be observed in different types of congenital heart defects. In a previous study from our department, children with congenital heart disease were studied in similar groups in terms of the type of congenital heart disease³. Cyanotic patients with PH had the most severe growth retardation, emphasizing the additive effects of hypoxia and PH on nutrition and growth. In the present study, however, acyanotic patients with PH were the leading group in terms of growth retardation. Several factors may have influenced the divergence between the two observations. Fewer patients in Group 1 (cyanotic and pulmonary hypertensive group) made the comparisons and interpretations difficult. Although the age was not significantly different among groups, the patients in Group 1 were younger at presentation; therefore, they were only acutely malnourished when the symptoms had commenced. Most of the patients in Group 3 had large ventricular septal defects and were medically treated at younger ages with an anticipation of spontaneous closure of the defect; the latter group, therefore, was more chronically malnourished. The discrepancy in the pattern of growth retardation in Group 1 from previous studies may be due to the acute nature of their malnutrition, predominantly affecting weight but not height.

Height was the predominantly affected variable in obstructive heart lesions according to Mehrizi and Drash⁴. In our study, however, neither height nor weight was affected considerably in Group 4. This can be attributed to the small number of patients in this group and because their obstructive lesions were mostly mild; only two out of seven patients had moderate disease. In fact, severe congenital heart defects were most frequent in Group 3, corresponding to the most severe growth retardation.

Studies from developed countries have documented significant catch-up growth with normalization of somatic growth when corrective surgery for congenital heart defect is performed early in life^{6,7,12-15}. However, in developing countries, where malnutrition is an independent issue and prevalence of malnutrition is high among patients with heart defects, studies concerning somatic growth after corrective surgery are inadequate^{1,8}. The prevalence of preoperative malnutrition may change from 45% to 65% in developing countries, depending on the study population^{1,3,9}. The frequency of malnutrition was 85% in our study group. The higher prevalence observed in the present study is impressive, but may be in part due to a selected patient population referred to a tertiary cardiac center for operation. Similarly, Cameron et al.16 reported 80% acute malnutrition in hospitalized infants with congenital heart disease.

Factors such as low family income and inadequate dietary intake are certainly interrelated, and together with the severity of the congenital heart disease, have an impact on the severity of the preoperative malnutrition. These in turn affect the catch-up growth rate in the follow-up. Although we could not demonstrate a correlation between the severity of the congenital heart defect and the preoperative anthropometric measurements, we did observe that patients in Group 3 had more severe heart disease, and were affected more in terms of growth delay.

It was demonstrated in previous studies that children with weight for age z scores between -1 and -2 are twice as likely to die from infectious diseases compared to the children with better nutritional status¹⁷. Therefore, preoperative malnutrition and growth retardation may increase the mortality and morbidity of the cardiac surgery and may complicate the postoperative care. None of our patients died during our study, but we observed that preoperative energy intake was correlated with the total hospitalization time, length of the intensive care therapy, and number of postoperative complications and infections. This suggests that preoperative severity of malnutrition is indeed related to the perioperative events. This study was designed as an outpatient surveillance program, and the variables in the intensive care unit were not assessed in detail. Further studies are needed to define the effects of malnutrition exclusively in the intensive care setting.

Similar to the findings of Vaidyanathan et al.¹, preoperative chronic malnutrition affected weight on follow-up; height recovery was faster than weight recovery in all our groups. Especially in Group 3, chronic malnutrition was observed more than in the others; hence, the catch-up growth was later in the postoperative period. It is noteworthy that none of the patients in our study had height measurements below the 3rd percentile at presentation, except for three patients in Group 3. This implicates that if the patient presents late or the corrective surgery is delayed, the nutritional status and the growth potential may be affected unfavorably. Other studies report that improvement in growth was largely completed by 12 months after operation for infants¹². In our study, suboptimal recovery of somatic growth following corrective surgery was seen in seven patients (11.6%) by 12 months. Catch-up growth was further delayed by 27 months in these patients.

Freedom from residual cardiac defects is an important factor in gaining normal growth potential. Residual defects were observed in

18.3% (11 patients) of our patients. Among these, five patients could not achieve the desired growth pattern by the end of the first year. Patients with residual defects are more likely to receive lengthy diuretic therapy after the operation. Diuretics are usually a marker of more severe cardiac disease. Furthermore, they can lead to renal losses of several important micronutrients that are important for normal growth¹⁷. However, we could not demonstrate any correlation between the length of diuretic therapy and postoperative malnutrition. We believe earlier and more aggressive dietary intervention in patients with residual defects may eliminate suboptimal growth in these patients12,13,15.

In our study, inadequate dietary intake seems to be the central factor causing impairment of growth both preoperatively and postoperatively. Inadequate calories occur when children with congenital heart disease lose their appetite because of medications (i.e. diuretics, digoxin). Compressive hepatomegaly secondary to congestive heart failure may reduce gastric volume and increase the likelihood of gastroesophageal reflux and aspiration. Moreover, congestive heart failure may be responsible for decreased splanchnic flow, edema and hypoxia of the gut with subsequent dysmotility and malabsorption^{2,17}. Feeding difficulties may be due to decreased cardiac output and increased respiratory effort. Among all these factors related to the severity of the hemodynamic disturbance, inadequate intake due to disadvantageous socioeconomic status seems to be the most important in our study, given that the severity of the disease itself was not correlated with the preoperative anthropometric measurements.

Most of our patients were living in urban areas with easier access to healthcare facilities; however, 58.3% were members of a low income family. Almost all patients with suboptimal growth at the end of the first year were from a low income family and had inadequate dietary intake, mainly consisting of breast-milk. Although breast-milk has immunologic and nutritional advantages over formulas, adequate calories are not achieved in most patients with congenital heart disease who are mainly breastfed. Therefore, additional calories often need to be supplemented.

Limitations

We can not speculate on the true achievement of normal genetic growth potential postoperatively. because variables like mid-parental height were not assessed in this study. Our study was observational and designed to determine the possible factors that contribute to postoperative catch-up growth. Larger prospective studies are necessary to examine whether tight control of dietary intake improves outcome. Our study population consisted of a small and heterogeneous group of patients, with fewer patients especially in Groups 1 and 4. This may have caused some bias while interpreting certain statistical data; however, presence of some limitations does not undervalue the findings of this study.

In conclusion, children with congenital heart defects are frequently undernourished. Our data suggest that catch-up growth is inversely correlated with the severity of the initial growth disturbance. Catch-up growth is largely completed by the end of the first year after corrective surgery. Delays are observed in the chronically malnourished children. Energy malnutrition due to low caloric intake is easily preventable and should be addressed more energetically. Optimal growth may be possible even for the chronically ill child if adequate calories are provided and early corrective surgery is performed before severe malnutrition develops. Preventive actions can be taken by providing free dietary counseling and dietary supplements especially for patients with a higher risk of malnutrition and for those living in impoverished and deprived conditions.

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