



## Somatic growth in children with congenital heart disease at 10 years of age: Risk factors and longitudinal growth<sup>☆</sup>

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### ABSTRACT

**Background:** Children with congenital heart disease (CHD) are at risk of impaired growth.

**Aims:** To describe height, weight, head circumference (HC), and body mass index (BMI) at 10 years and identify risk factors for altered longitudinal growth in children with CHD.

**Study design:** Growth parameters were evaluated from birth until 10 years using z-scores. The impact of cardiac and noncardiac factors on longitudinal growth was investigated.

**Subjects:** A total of 135 children with different types of CHD who underwent cardiopulmonary bypass surgery, no genetic disorder.

**Outcome measures:** Head circumference, weight, height and BMI.

**Results:** At 10 years, z-scores for height and BMI did not differ from the Swiss population ( $P > 0.1$ ). Z-scores for weight and HC were significantly below the norm ( $-0.38$  and  $-0.71$ ,  $P < 0.01$ ). From 1 to 10 years, all growth parameters except BMI increased significantly ( $P \leq 0.001$ , BMI:  $P = 0.14$ ). Lower gestational age and longer length of hospitalization were associated with either impaired head circumference or length at 10 years, while lower socioeconomic status was associated with higher BMI and weight at 10 years (all  $P < 0.05$ ).

**Conclusion:** Despite partial catch-up, somatic growth remains impaired in children with CHD with weight and HC below the norm at 10 years. The only cardiac factor associated with impaired longitudinal growth was duration of hospital stay. Furthermore, lower socioeconomic background may pose a risk of overweight at older age. Close monitoring of growth parameters and parental counselling in all CHD children is advisable beyond early childhood to ensure optimal somatic growth.

### 1. Introduction

Thanks to the advanced medical treatment options, the vast majority of children with congenital heart disease (CHD) requiring open-heart surgery reach adulthood. [1] It is well known that children with CHD are at risk of impaired somatic growth [2–4] and neurodevelopment. [5] Multiple cardiac and patient factors are considered to impact growth,

including type and severity of the CHD, [2,3] weight at birth, [6,7] nutritional factors, [4,7,8] and hemodynamic instabilities. [8,9]

For early childhood, several studies have shown some catch-up for weight and height after corrective surgery [2,10] in children with CHD. Nonetheless, growth parameters may remain below the expected values for preschool aged children. [11,12] Similarly, lower head circumference at birth is frequently reported in infants with CHD. [10,13]

**Abbreviations:** CHD, Congenital heart disease; HC, Head circumference; BMI, Body mass index; CPB, Cardiopulmonary bypass; SES, Socioeconomic status; IQ, Intelligence quotient; SD, Standard deviation; IQR, Interquartile range; ECC, Extracorporeal circulation.

\* Clinical registration number: This is a prospective observational study that started 15 years ago and does not entail an intervention. Thus, this study does not have a clinical registration number.

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In contrast, information on growth parameters at school age is scarce and studies mainly include univentricular defects. [7,14] Further, there is little information on longitudinal growth. [3,15,16] In contrast to the impaired growth in younger children with CHD, studies in teenagers and young adults with CHD report a risk of overweight and obesity [15,17] comparable to the general population. Yet, little is known about BMI in prepubertal children. [3,15,16]

Thus, the aim of this study was to describe growth in a current population of 10-year-old children with CHD who underwent cardiopulmonary bypass (CPB) surgery. First, we compared growth parameters (height, weight, HC, and body mass index (BMI)) at the age of 10 years to the general population. Secondly, we investigated longitudinal growth trajectories until 10 years. Lastly, we aimed to identify cardiac and noncardiac risk factors for impaired long-term growth.

## 2. Patients & methods

### 2.1. Study population and measurements

The *Reachout* study is a prospective cohort study at the University Children's Hospital Zurich. Children received follow-up assessments at 1, 4, 6 and 10 years of age. The study was approved by the Ethics Committee of the Canton Zurich (May 16, 2014, KEK-ZH-Nr. 2014-0071) and written informed consent was obtained from each participant's parents or legal guardians.

Children born with CHD who underwent CPB surgery between 2004 and 2009 at the University Children's Hospital Zurich were prospectively enrolled. At the 10-year examination, children with a genetic disorder were excluded.

Neonatal growth data, cardiac diagnoses and medical risk factors were collected from hospital charts of the University Children's Hospital Zurich, growth at 1, 4, 6, and 10 years was assessed by a pediatrician or study nurse. HC was measured twice by means of a non-elastic tape, measuring the largest area of a child's head with the tape measure held above the eyebrows and ears. Length measurements were acquired using a roll-up measuring tape with wall attachment. Weight was measured using a digital scale. Heart defects were classified into univentricular or biventricular CHD. Furthermore, we recorded the total number of cardiopulmonary bypass surgeries and catheter interventions, and the use of cardiac medication at 10 years of age. Children requiring diuretics, angiotensin-converting-enzyme-inhibitors, beta-blockers or phosphodiesterase type 5 inhibitors were considered to have a cardiac insufficiency. A feeding disorder was considered if a child was tube fed, had swallowing difficulties or recurrent vomiting before the first CPB surgery. Socioeconomic status (SES) was calculated based on maternal education and paternal occupation at birth, ranging from 2 (lowest) to 12 (highest). [18] Additionally, intelligence quotient (IQ) was determined using the German version of the Wechsler Intelligence Scale for Children (WISC-IV). [19]

### 2.2. Statistics

Statistical analyses were conducted using SPSS version 24.0 (IBM Corp, Armond, New York) and R (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables are presented as frequencies and continuous variables as mean and standard deviation (SD) or median and interquartile range (IQR). All growth variables were converted into age- and gender-adjusted z-scores (standard deviation scores, SD) based on the Swiss growth charts. [20] Z-score of 0 represented the median of Swiss growth charts. For children born prematurely (<37 weeks of gestation), z-scores were corrected for gestational age [21] at birth and 1 year (except for BMI for which such adjustment is not available). Overweight was considered as BMI >90th (z-score > 1.282) and obesity as BMI >97th percentile (z-score > 1.881). [22]

For group differences, the Mann-Whitney-U test was applied. The association of growth measurements at 10 years with the corresponding

**Table 1**

Patient characteristics and cardiac factors for the total cohort (N = 135).

	Univentricular N = 28 (21%)	Biventricular N = 107 (79%)	P <sup>a</sup>
<b>Patient characteristics<sup>b</sup></b>			
Gestational age (weeks) <sup>c</sup>	39.02 (1.7)	39.02 (2.2)	0.568
Birth weight (kg)	3.34 (0.7)	3.15 (0.6)	0.359
Length at birth (cm)	49.2 (3.2)	48.8 (2.8)	0.455
Head circumference at birth (cm)	34.6 (1.6)	34.1 (1.7)	0.167
BMI at birth (kg/m <sup>2</sup> )	13.6 (1.7)	13.1 (1.7)	0.448
SES, median (IQR)	8 (7; 9)	8 (7; 10)	0.660
<b>Cardiac factors<sup>b</sup></b>			
Feeding disorder before 1st CPB, N (%)	6 (21.4%)	25 (23.4%)	0.867
Age at 1st CPB surgery (months), median (IQR)	2.9 (0.3; 5.3)	1.3 (0.3; 4.9)	0.792
Mean preoperative SpO <sub>2</sub> <sup>d</sup> at 1st CPB surgery	82.6 (8.8)	87.4 (10.4)	0.006
Lowest body temperature at 1st CPB (°C)	29.5 (5.9)	29.1 (3.6)	0.459
ECC time at 1st CPB surgery, min	157.2 (52.9)	166.5 (76.6)	0.534
Hospitalization at 1st CPB (days), median (IQR)	30.5 (17.5; 67.0)	23 (14; 33)	0.022

SD: standard deviation, IQR: interquartile range, BMI: body mass index, SES: socioeconomic status, CPB: cardiopulmonary bypass, ECC: extracorporeal circulation.

<sup>a</sup> Mann-Whitney-U test.

<sup>b</sup> Mean and standard deviation (SD) are presented if not otherwise stated (e.g. median and IQR).

<sup>c</sup> Of the total cohort, 16 (12%) children were born prematurely (<37 weeks of gestation).

<sup>d</sup> Arterial oxygen saturation (%).

growth parameter at birth was assessed using Spearman correlations. Risk factors from previous studies were considered; [4,7,8,23] those with too many missing data, low variance, or collinearity were not included into our risk factor analysis. Thus, cardiac risk factors included uni- vs. biventricular CHD, mean arterial blood saturation before the first CPB, feeding disorders, age at first CPB (log-transformed), lowest intraoperative temperature and extracorporeal circulation (ECC) time during first CPB, and length of hospitalization of first CPB (log-transformed). Patient characteristics included: SES, gestational age and growth parameters at birth.

The number of bypass surgeries was not analyzed as it strongly correlated with uni- vs biventricular CHD.

Multivariable regression analyses were performed with the different growth measurements at 10 years as outcome variables and the corresponding growth measurement at birth (e.g. height at birth for the outcome height at 10 years) as well as the above-mentioned risk factors as independent variables. Longitudinal analyses for each growth parameter (height, weight, HC, BMI) throughout childhood to 10 years of age were carried out using linear mixed models. A random child effect was included into the model to take into account dependencies due to repeated measurements of the same child along the years. Of note, only 1 to 10 year-measurements were included in the model, enabling us to summarize the catch-up growth of children with CHD over the years using just a linear slope, the observed drop in growth from birth to 1 year being already described in other studies. [9,24] In addition, risk factors that showed significant association with the growth outcome at 10 years were also introduced in the model, as main effect or interacting with age, enabling us to compare the growth trajectories for different levels of a risk factor. For the linear mixed models, z-scores higher in magnitude than +/-4 were set back to +/-4 in order to avoid our results to be driven by a few outlying values. Two-sided p-values <0.05 were considered statistically significant.

**Table 2**  
Distribution of univentricular and biventricular congenital heart disease in total cohort ( $N = 135$ ).

Univentricular heart defects	$N = 28$ (21%)
Double inlet left ventricle	8 (6%)
Hypoplastic left heart syndrome	7 (5%)
Pulmonary atresia (PA) with ventricular hypoplasia	4 (3%)
Double outlet right ventricle with ventricular hypoplasia	4 (3%)
Atrioventricular septal defect with ventricular hypoplasia	1 (1%)
Crisscross heart	1 (1%)
Functional single ventricle with dextro-transposition of great arteries (d-TGA)	1 (1%)
Ebstein anomaly	1 (1%)
Tricuspid atresia	1 (1%)
Biventricular heart defects	$N = 107$ (79%)
Dextro-transposition of great arteries (d-TGA)	36 (27%)
Ventricular septal defect	21 (16%)
Tetralogy of Fallot	12 (9%)
Atrioventricular septal defect	7 (5%)
Aortic coarctation	5 (4%)
Truncus arteriosus	5 (4%)
Pulmonary atresia (PA)	4 (3%)
Total anomalous pulmonary venous connection	4 (3%)
Aortic stenosis	3 (2%)
Atrial septal defect	3 (2%)
Pulmonary stenosis	2 (1%)
Double outlet right ventricle	2 (1%)
Anomalous left coronary artery from the pulmonary artery	1 (1%)
Taussig-Bing-anomaly	1 (1%)
Levo-transposition of great arteries (l-TGA)	1 (1%)

### 3. Results

#### 3.1. Study population

In total, 300 children with CHD were prospectively enrolled (Supplemental Fig. 4). At the 10-year examination, only children without genetic disorders were assessed (exclusion of 75 children). Overall, 63 children were lost to follow up and 27 died. Consequently, the population at 10 years accounted for 135 children.

Patient characteristics and cardiac factors stratified for uni- and biventricular CHD are presented in Table 1. The 63 children lost to follow up by the 10-year examination did not differ from the final study population regarding patient characteristics except for SES, which was significantly lower in the children lost to follow up ( $P < 0.047$ ). Regarding cardiac factors, age at first CPB surgery was older in the children lost to follow up ( $P < 0.005$ ), mean preoperative blood saturation and lowest body temperature were significantly higher ( $P < 0.005$  and  $P = 0.007$ ), ECC time and hospital stay were significantly shorter in the children lost to follow up ( $P = 0.013$  and  $P < 0.005$ ). Detailed cardiac diagnoses of our final study population are listed in Table 2. Most children (67%) underwent one CPB until the age of 10 years (range 1–4) and were operated within their first year of life (95%). The majority (76%) had one interventional heart catheterization until 10 years (range 0–11). Mean age at 10-year follow-up was 10.2 years (SD: 0.3 years) with 81 (60%) male participants. At 10 years, 11 children were considered to have a cardiac insufficiency based on the need for cardiac medication (univentricular:  $N = 6$ ). Mean IQ at 10 years was within the normal range, but significantly lower than in the normal Swiss population (mean IQ 96, SD = 13,  $P = 0.023$ ).

#### 3.2. Longitudinal growth from 1 to 10 years of age

As illustrated in Fig. 1, median z-scores for height, weight, and HC significantly increased from 1 until 10 years of age (height:  $P < 0.001$ , weight:  $P = 0.001$ , HC:  $P < 0.001$ ), except BMI ( $P = 0.136$ ). Of note,

between birth and 1 year, all growth parameters but BMI significantly decreased (height:  $P < 0.001$ , weight:  $P < 0.001$ , HC:  $p < 0.001$ , BMI:  $P = 0.134$ ).

#### 3.3. Risk factors for longitudinal growth from 1 to 10 years of age

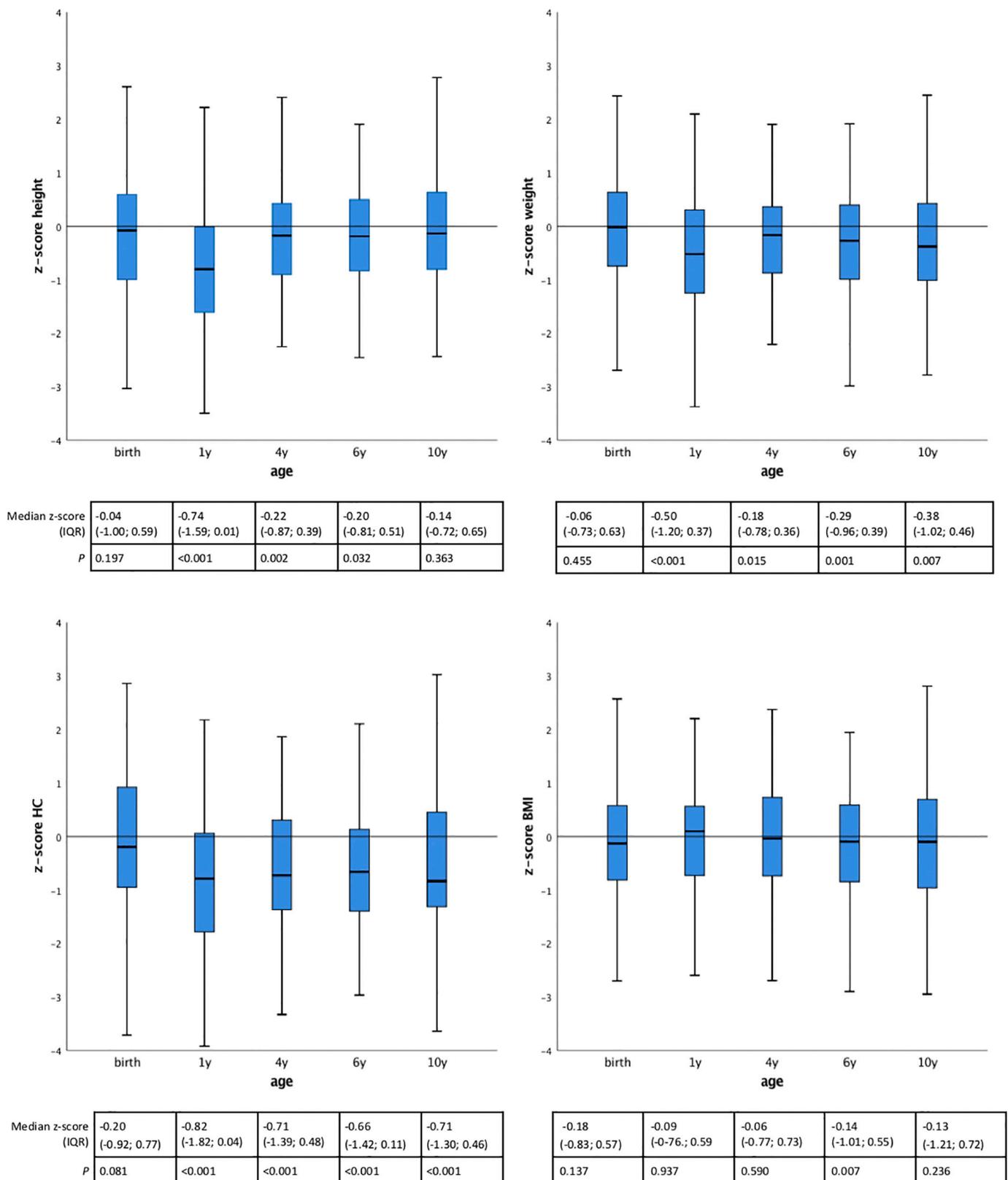
Table 3 summarizes the results of the linear mixed models describing growth trajectories from 1 to 10 years of age. When introducing the corresponding growth parameter at birth as a main effect in the linear mixed model, we found a significant result for height ( $P < 0.001$ ), weight ( $P < 0.001$ ) and HC ( $P < 0.001$ ), but not for BMI ( $P = 0.121$ ), while an interaction with age was never significant (all  $P > 0.1$ ). This meant that the catch-up growth between 1 and 10 years of age described in the previous paragraph was on average similar for those children with a high value and for those children with a low value of height, weight or HC at birth, the former remaining at higher levels than the latter over the years, the growth trajectories being thus roughly parallel. Length of hospitalization at first CPB was significant as a main effect for height ( $P = 0.007$ ) and for weight ( $P = 0.021$ ), but not for HC ( $P = 0.137$ ) and for BMI ( $P = 0.357$ ), while not interacting significantly with age (all  $P > 0.3$ ), children with a shorter hospitalization remaining on average taller and heavier over the years than those children with a longer hospitalization (see Fig. 2 for an illustration). The risk factor SES was never significant as a main effect (all  $P > 0.05$ ), but significantly interacted with age for weight ( $P = 0.045$ ) and BMI ( $P < 0.001$ ), resulting in a more pronounced increase in weight and BMI along the years for children with lower SES compared to those with higher SES (see Fig. 3 for an illustration). Gestational age as a main effect was significant only for height ( $P = 0.004$ ), children being on average taller over the years when the gestational age was higher, while an interaction of gestational age with the age of the child was significant only for weight ( $P = 0.004$ ), the catch-up in weight along the years being more pronounced when the gestational age was low than when it was high (see Supplemental Fig. 5 for an illustration). Finally, we similarly introduced IQ at 10 years in the linear mixed model and found no significant interaction with age (all  $P > 0.1$ ), meaning that the growth trajectories were not significantly associated with IQ at 10 years.

#### 3.4. Growth at 10 years of age

Growth parameters from birth until 10 years of age of our cohort are depicted in Fig. 1. At 10 years, median height z-scores did not differ from the normal Swiss population ( $P = 0.363$ ), while median weight and HC z-scores were significantly below the norm ( $P = 0.007$  and  $P < 0.001$ , respectively). Median BMI z-scores were similar to the normal Swiss population ( $P = 0.236$ ) and the number of overweight ( $N = 11$ , 8.2%) and obese children ( $N = 9$ , 6.7%) was only slightly elevated ( $P = 0.043$ ). The 11 children with cardiac insufficiency had a larger HC compared to children without (median z-scores: 0.74 vs  $-0.79$ ,  $P = 0.015$ ). Other growth parameters did not differ in children with cardiac insufficiency ( $P > 0.05$ ). IQ was not significantly correlated with HC ( $\rho = 0.160$ ,  $P = 0.072$ ), weight ( $\rho = -0.079$ ,  $P = 0.365$ ), height ( $\rho = 0.043$ ,  $P = 0.625$ ), or BMI ( $\rho = -0.154$ ,  $P = 0.076$ ) at 10 years of age. There was no significant sex difference in height, weight, HC or BMI ( $P > 0.05$ ).

#### 3.5. Risk factors for growth at 10 years of age

Height, weight, and HC, but not BMI at 10 years were significantly correlated with the corresponding growth parameter at birth (height:  $\rho = 0.284$ ,  $P = 0.001$ , weight:  $\rho = 0.172$ ,  $P = 0.048$ , HC:  $\rho = 0.432$ ,  $P < 0.001$ , BMI:  $\rho = 0.015$ ,  $P = 0.862$ ). Table 4 illustrates the results of the multivariable linear regression analysis examining risk factors for growth at 10-years of age. When adjusting for the corresponding growth parameter at birth, length of hospitalization at first CPB was associated to height and head circumference at 10 years. Gestational age was associated with height and BMI and SES was



**Fig. 1.** Growth parameters (z-scores) at different ages from birth until 10 years of age. The blue box shows the median (black horizontal bar) and is defined by the interquartile range (IQR). The black lines above and under the blue box indicate the minimum and maximum values. For better readability outliers are not marked. The tables below the boxplots show the corresponding median z-scores and p-values of median z-scores when testing for difference between median z-scores and 0 as median of normal population. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

**Table 3**  
Risk factor analysis for growth trajectories from 1 to 10 years of age.

	Height at 10 years			Weight at 10 years			Head circumference at 10 years			BMI at 10 years		
	Beta	CI 95%	P	beta	CI 95%	P	beta	CI 95%	P	Beta	CI 95%	P
Height at birth (z-score)	0.32	0.21	0.45	0.33	0.19	0.46	0.42	0.29	0.54	0.1	-0.03	0.23
Weight at birth (z-score)												
HC at birth (z-score)												
BMI at birth (z-score)												
GA	0.11	0.03	0.18	0.04	-0.04	0.11	0.05	-0.05	0.14	0.322	0.991	0.04
LOH (log)	-0.21	-0.36	-0.06	-0.19	-0.34	-0.03	-0.15	-0.34	0.05	0.137	0.351	0.09
SES	-0.03	-0.11	0.04	-0.07	-0.15	0.01	0.07	-0.02	0.16	0.143	0.971	0

Beta: unstandardized beta, CI 95%: 95% confidence interval, GA: gestational age, HC: head circumference, BMI: body mass index, SES: socioeconomic status, length hosp: length of hospitalization at first cardiopulmonary bypass surgery, LOH: Length of hospitalization.

associated to weight and BMI. Of note, severity of CHD (uni-versus biventricular) was not associated to any growth parameter at 10 years.

#### 4. Discussion

In this study, we analyzed a large data set of prospectively collected longitudinal growth parameters for 135 children with CHD from birth until 10 years of age. We were able to show catch-up growth in height and to a lesser extent in weight and head circumference by 10 years. However, somatic growth remained impaired with weight and head z-scores below the norm at 10 years. BMI was comparable to the Swiss population from birth until 10 years of age for the total cohort. Our paper expands the literature on growth in children with CHD [3,15,16] by focusing on longitudinal growth and BMI.

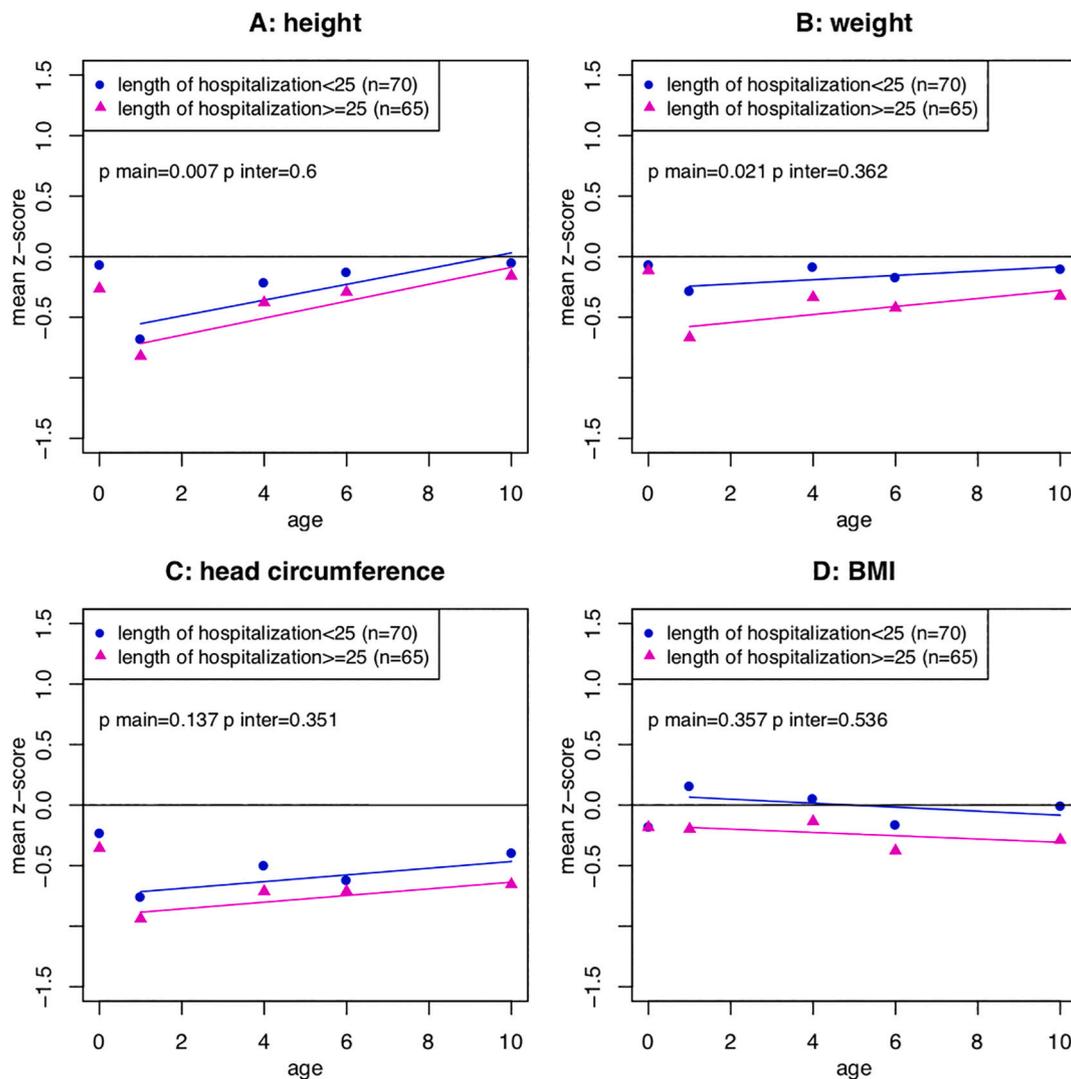
At 10 years of age, growth in children with CHD remains impaired. Similar findings have been described in other studies in CHD; most of these focused on growth in younger children. [2,4,8,10,11] Although studies in different types of CHD have reported impaired growth in prepubertal children [7,25] and teenagers, [3] one study on children with tetralogy of Fallot found a normalization of height and weight at 14 years. [6] Studies in single-ventricle defects report conflicting results on the extent of growth impairment: in some studies, weight is more impaired than height, whereas in others the findings are vice versa with height being more affected than weight. [7,12,25,26] Thus, the pattern of growth impairment in CHD remains heterogeneous with HC, weight, and height being inconsistently affected. These dissimilarities may be attributed to differences in patient populations, demographics, medical services, and countries of residence.

Impaired head growth has been frequently described and linked to neurodevelopment in young children with CHD. [8,11,13] However, the literature on HC and neurodevelopment at 10 years of age and older is scarce. [27] Although HC was the most impaired of the growth parameters in our cohort, a link to cognitive functioning could not be established. Although HC is associated with neurodevelopment in younger children, this association may diminish over time with no detectable association at adolescent. [27] Further, HC may not reflect brain growth; for example, it has been shown that ventricular spaces were enlarged and brain volumes were smaller in children with Fontan completion. [28] Instead, measurements of brain volumes acquired by cerebral MRI are better correlates of brain function, as has been shown by von Rhein et al. [27]

Longitudinal growth between 1 and 10 years of age showed a significant increase over time in all growth parameters except BMI, which remained within the norms over the years. Thus, we were able to show a potential for catch-up growth in the CHD population, which is consistent with other studies. [3,6,16] This is most likely attributable to cardiac surgical intervention restoring cardiac circulation and oxygen saturation. Interestingly, this effect was similar for children with uni- and biventricular CHD. Once again, studies in children with univentricular CHD report both impaired growth and catch-up growth after cardiac surgical intervention. [7,12,25,26] These differences may be attributed to differences between patient populations and the heterogeneity of number of cardiac interventions. Children with univentricular CHD seem to have the potential for catch-up growth, and thus ensuring optimal medical care and nutrition in these children is crucial.

We observed a significant decrease of all growth parameters but BMI from birth until 1 year of age, as frequently described in the literature. [9,24,28] This impaired growth is likely attributable to multiple factors, such as poor preoperative blood oxygenation and perfusion, duration of hospitalization, age at surgery, and neurological abnormalities. [9,24,28]

With regard to BMI measurements, our cohort was mainly within the norm, similarly to other studies. [12,14] We were able to show that BMI did not change over time in the total cohort. The percentage of overweight and obese children in our study was lower than in other studies. [15,17] However, those studies assessed children with CHD with a wider



**Fig. 2.** Growth trajectories in function of length of hospitalization for A: height, B: weight, C: head circumference, D: BMI. Length of hospitalization has been here divided into two groups (below 25 days and above/equal 25 days) for illustration purpose, but was kept as a continuous variable in the model to test for its significance as a main effect (p main), or for its interaction with age (p inter). Circles/triangles represent the empirical means of the growth parameters over the years (calculated from the raw data for the different groups) and lines show the linear fit achieved by the model.

age range, different demographics, and different percentile curves. Despite our cohort being from high SES, we found low SES to be associated with increasing BMI over time. Similarly, Andonian et al. [17] reported significant differences in risk of obesity in children and adults with CHD depending on the level of health education. Thus in our cohort, children with low SES in particular may face a similar risk of abnormally elevated BMI as the general population.

We were able to demonstrate a long-term influence of growth parameters at birth on growth beyond early school age. Other factors associated with an altered growth pattern in our cohort were gestational age and length of hospitalization at first CPB. Similarly to healthy preterm-born children, our preterm-born CHD children showed a more pronounced increase of weight than term-born children. [29] In contrast to other studies, [7,11,25,26] and as mentioned above, we did not find any influence of CHD type on somatic growth. The only cardiac factor associated with growth in our cohort was length of hospital stay: children with longer hospitalization at first CPB showed similar growth over time but on a lower growth trajectory than those with shorter hospitalization. Similar findings have been reported for younger children with CHD. [4,30] Length of hospital stay may be considered a proxy for the overall health of a child, reflecting a complex interplay of several medical and environmental factors before and after corrective surgery

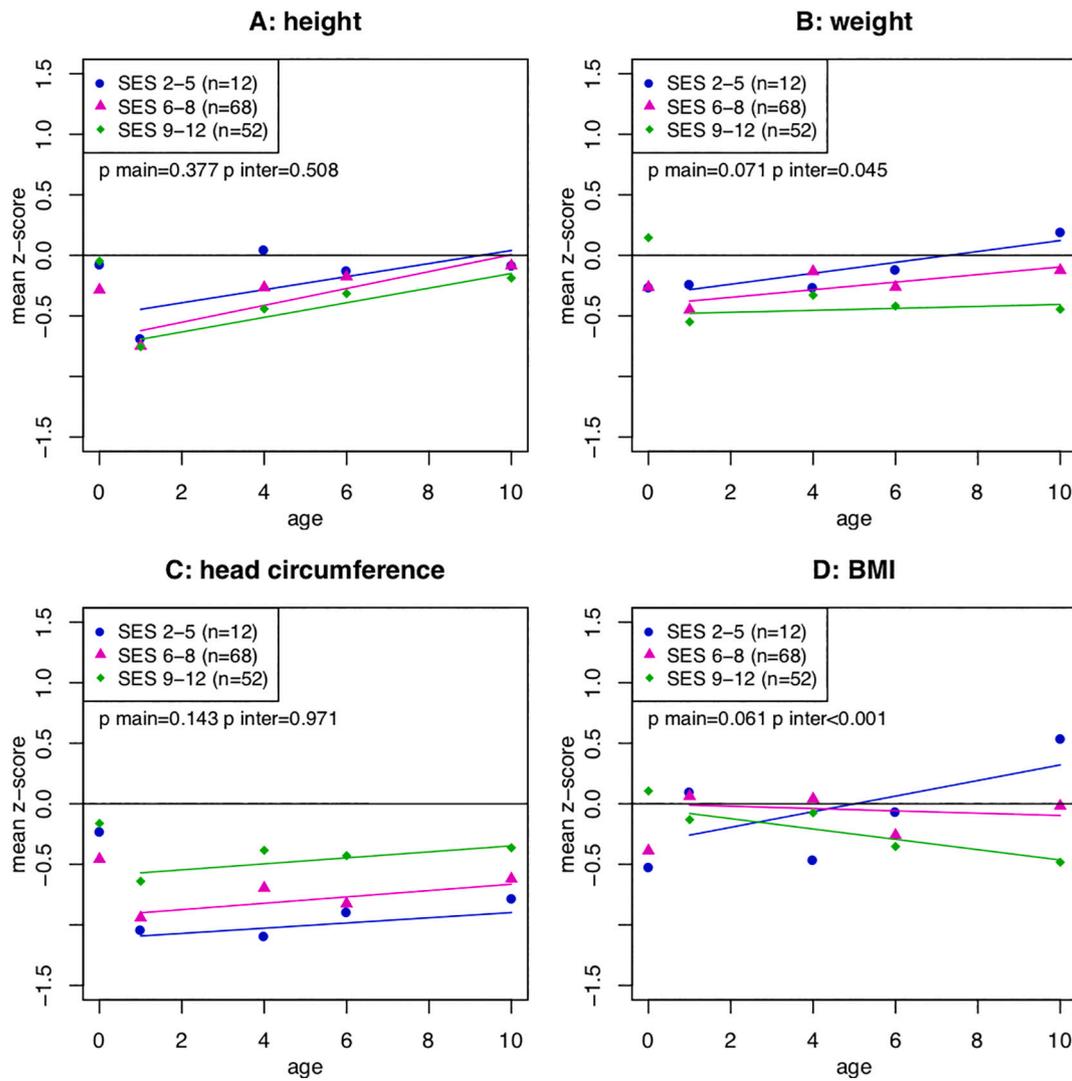
for CHD.

Our study has limitations worth mentioning. Although a broad range of different types of CHD was included in the study, we were not able to perform subanalysis for specific types of CHD or prolonged cyanosis due to the small sample sizes. Further, the data on nutritional parameters was evaluated retrospectively and was only available at preoperative assessment.

In conclusion, partial catch-up growth can be found in children with CHD up to 10 years of age, but somatic growth remains impaired with weight and HC below the norm. The only cardiac factor significantly associated with impaired growth was duration of hospital stay. Despite normal prepubertal BMI, children from lower socioeconomic backgrounds may be at risk for overweight at older age. Close monitoring of growth parameters in all CHD children is advisable beyond early childhood to ensure optimal growth.

#### CRediT authorship contribution statement

I declare that I participated in the design, execution, and analysis of the paper by Hapuoja and colleagues entitled “Somatic growth in children with congenital heart disease at 10 years of age: Risk factors and longitudinal growth” that I have seen and approved the final version and that I have



**Fig. 3.** Growth trajectories in function of SES for A: height, B: weight, C: head circumference, D: BMI. SES has been here divided into three groups (2-5, 6-8 and 9-12) for illustration purpose, but was kept as a continuous variable in the model to test for its significance as a main effect (p main), or for its interaction with age (p inter). Circles/triangles/diamonds represent the empirical means of the growth parameters over the years (calculated from the raw data for the different groups) and lines show the linear fit achieved by the model.

**Table 4**  
Multivariabel risk factor analysis for growth parameters at 10 years of age.

	Height at 10 years			Weight at 10 years			Head circumference at 10 years			BMI at 10 years		
	$\beta$	CI 95%	P	$\beta$	CI 95%	P	$\beta$	CI 95%	P	$\beta$	CI 95%	P
Height at birth (z-score)	0.35	0.18	0.52	0.35	0.17	0.52	0.43	0.25	0.61	0.23	0.01	0.46
Weight at birth (z-score)			<0.001			<0.001						0.016
HC at birth (z-score)												0.047
BMI at birth (z-score)												0.016
Gestational age	0.22	0.05	0.39	-0.04	-0.21	0.13	0.02	-0.17	0.22	0.23	0.01	0.46
Uni- vs. biventricular CHD	-0.07	-0.25	0.10	-0.05	-0.23	0.12	0.07	-0.12	0.26	-0.27	-0.50	0.016
Feeding disorder pre 1st CPB	-0.05	-0.22	0.12	-0.10	-0.27	0.08	0.01	-0.19	0.21	0.01	-0.18	0.948
Mean saturation pre 1st CPB	-0.04	-0.22	0.14	-0.02	-0.21	0.16	-0.18	-0.38	0.01	0.922	-0.27	0.297
ECC time 1st CPB	-0.06	-0.26	0.14	-0.08	-0.21	0.16	-0.04	-0.25	0.17	-0.04	-0.23	0.15
Age 1st CPB	-0.10	-0.29	0.10	-0.08	-0.27	0.12	0.02	-0.19	0.23	-0.10	-0.31	0.360
Lowest T° 1st CPB	0.00	-0.20	0.20	-0.03	-0.23	0.17	-0.20	-0.41	0.00	-0.10	-0.30	0.17
LOH (log)	-0.26	-0.48	0.016	-0.18	-0.39	0.04	-0.32	-0.54	-0.10	-0.10	-0.32	0.364
SES	-0.01	-0.18	0.15	-0.25	-0.42	0.09	0.09	-0.08	0.27	-0.32	-0.49	0.362
	Adjusted R <sup>2</sup> = 0.188, p < 0.001			Adjusted R <sup>2</sup> = 0.171, p < 0.001			Adjusted R <sup>2</sup> = 0.243, p < 0.001			Adjusted R <sup>2</sup> = 0.112, p < 0.010		

no conflict of interest.

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**Compliance with ethical standards**

The ethics committee of the Canton of Zurich in Switzerland approved this study and written informed consent was obtained from the parents or legal guardian of the children.

**Data availability**

The deidentified data are available from the corresponding author upon reasonable request.

**Declaration of competing interest**

The authors report no competing interests.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.earlhumdev.2021.105349>.

**References**

- [1] P. Moons, L. Bovijn, W. Budts, A. Belmans, M. Gewillig, Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium, *Circulation*. 122 (22) (2010) 2264–2272.
- [2] C. Daymont, A. Neal, A. Prosnitz, M.S. Cohen, Growth in children with congenital heart disease, *Pediatrics*. 131 (1) (2013) e236–e242.
- [3] D.C. Aguilar, G.W. Raff, D.J. Tancredi, L.J. Griffin, Childhood growth patterns following congenital heart disease, *Cardiol. Young* 25 (6) (2015) 1044–1053.
- [4] C.L. Costello, M. Gellatly, J. Daniel, R.N. Justo, K. Weir, Growth restriction in infants and young children with congenital heart disease, *Congenit. Heart Dis.* 10 (5) (2015) 447–456.
- [5] B. Latal, Neurodevelopmental outcomes of the child with congenital heart disease, *Clin. Perinatol.* 43 (1) (2016) 173–185.
- [6] M.M. Cheung, A.M. Davis, J.L. Wilkinson, R.G. Weintraub, Long term somatic growth after repair of tetralogy of Fallot: evidence for restoration of genetic growth potential, *Heart*. 89 (11) (2003) 1340–1343.
- [7] K.N. Vogt, C. Manlhiot, G. Van Arsdell, J.L. Russell, S. Mital, B.W. McCrindle, Somatic growth in children with single ventricle physiology impact of physiologic state, *J. Am. Coll. Cardiol.* 50 (19) (2007) 1876–1883.
- [8] B. Medoff-Cooper, C. Ravishankar, Nutrition and growth in congenital heart disease: a challenge in children, *Curr. Opin. Cardiol.* 28 (2) (2013) 122–129.
- [9] Williams RV, Zak V, Ravishankar C, Altmann K, Anderson J, Atz AM, et al. Factors affecting growth in infants with single ventricle physiology: a report from the Pediatric Heart Network Infant Single Ventricle Trial. *J. Pediatr.* 2011;159(6): 1017–22.e2.
- [10] Poryo M, Paes LA, Pickardt T, Bauer UMM, Meyer S, Wagenpfeil S, et al. Somatic development in children with congenital heart defects. *J. Pediatr.* 2018;192: 136–43.e4.
- [11] Heye KN, Rousson V, Knirsch W, Beck I, Liallahi R, Bernet V, et al. Growth and intellectual abilities of six-year-old children with congenital heart disease. *J. Pediatr.* 2019;204:24–30.e10.
- [12] Burch PT, Ravishankar C, Newburger JW, Lambert LM, Pemberton VL, Granger S, et al. Assessment of growth 6 years after the norwood procedure. *J. Pediatr.* 2017; 180:270–4.e6.
- [13] Miller TA, Zak V, Shrader P, Ravishankar C, Pemberton VL, Newburger JW, et al. Growth asymmetry, head circumference, and neurodevelopmental outcomes in infants with single ventricles. *J. Pediatr.* 2016;168:220–5.e1.
- [14] Cohen MS, Zak V, Atz AM, Printz BF, Pinto N, Lambert L, et al. Anthropometric measures after Fontan procedure: implications for suboptimal functional outcome. *Am Heart J.* 2010;160(6):1092–8, 8.e1.
- [15] J.M. Steele, T.J. Preminger, F.G. Erenberg, L. Wang, K. Dell, T. Alsaied, et al., Obesity trends in children, adolescents, and young adults with congenital heart disease, *Congenit. Heart Dis.* 14 (4) (2019) 517–524.

- [16] C. Tamayo, C. Manlhot, K. Patterson, S. Lalani, B.W. McCrindle, Longitudinal evaluation of the prevalence of overweight/obesity in children with congenital heart disease, *Can J Cardiol.* 31 (2) (2015) 117–123.
- [17] C. Andonian, F. Langer, J. Beckmann, G. Bischoff, P. Ewert, S. Freilinger, et al., Overweight and obesity: an emerging problem in patients with congenital heart disease, *Cardiovasc Diagn Ther.* 9 (Suppl. 2) (2019) S360–S368.
- [18] R.H. Largo, D. Pfister, L. Molinari, S. Kundu, A. Lipp, G. Duc, Significance of prenatal, perinatal and postnatal factors in the development of AGA preterm infants at five to seven years, *Dev. Med. Child Neurol.* 31 (4) (1989) 440–456.
- [19] R.G. Schmid, U. Petermann, F. Petermann, C. Weiß, M. Daseking, Leistungen des HAWIK-IV in der Intelligenzdiagnostik im Schulalter, *Monatsschrift Kinderheilkunde.* 157 (6) (2009) 587–594.
- [20] Braegger C, Jenni OG, Konrad D, Molinari L. Neue wachstumskurven für die Schweiz. *Paediatrica: Bulletin der Schweizerischen Gesellschaft für Pädiatrie = Bulletin de la Société Suisse de Pédiatrie.* 2011;22(1):9–11.
- [21] M. Voigt, C. Fusch, D. Olbertz, K. Hartmann, N. Rochow, C. Renken, et al., Analyse des neugeborenenkollektivs der bundesrepublik deutschland, *Geburtshilfe Frauenheilkd.* 66 (10) (2006) 956–970.
- [22] Malatesta D. Gültigkeit und Relevanz des Body-Mass-Index (BMI) als Massgrösse für Übergewicht und Gesundheitszustand auf individueller und epidemiologischer Ebene. *Gesundheitsförderung Schweiz [Health Promotion Switzerland] working paper, Bern.* 2013.
- [23] B.S. Marino, P.H. Lipkin, J.W. Newburger, G. Peacock, M. Gerdes, J.W. Gaynor, et al., Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association, *Circulation.* 126 (9) (2012) 1143–1172.
- [24] W. Knirsch, W. Zingg, V. Bernet, C. Balmer, A. Dimitropoulos, R. Prêtre, et al., Determinants of body weight gain and association with neurodevelopmental outcome in infants operated for congenital heart disease, *Interact. Cardiovasc. Thorac. Surg.* 10 (3) (2010) 377–382.
- [25] K. François, T. Bové, J. Panzer, K. De Groote, K. Vandekerckhove, H. De Wilde, et al., Univentricular heart and Fontan staging: analysis of factors impacting on body growth, *Eur. J. Cardiothorac. Surg.* 41 (6) (2012) e139–e145.
- [26] M.I. Cohen, D.M. Bush, R.J. Ferry, T.L. Spray, T. Moshang, G. Wernovsky, et al., Somatic growth failure after the Fontan operation, *Cardiol. Young* 10 (5) (2000) 447–457.
- [27] M. von Rhein, A. Buchmann, C. Hagmann, R. Huber, P. Klaver, W. Knirsch, et al., Brain volumes predict neurodevelopment in adolescents after surgery for congenital heart disease, *Brain.* 137 (Pt 1) (2014) 268–276.
- [28] K.N. Heye, W. Knirsch, B. Latal, I. Scheer, K. Wetterling, A. Hahn, et al., Reduction of brain volumes after neonatal cardiopulmonary bypass surgery in single-ventricle congenital heart disease before Fontan completion, *Pediatr. Res.* 83 (1–1) (2018) 63–70.
- [29] A.M. Euser, C.C. de Wit, M.J. Finken, M. Rijken, J.M. Wit, Growth of preterm born children, *Horm. Res.* 70 (6) (2008) 319–328.
- [30] D.K. Kelleher, P. Laussen, A. Teixeira-Pinto, C. Duggan, Growth and correlates of nutritional status among infants with hypoplastic left heart syndrome (HLHS) after stage 1 Norwood procedure, *Nutrition.* 22 (3) (2006) 237–244.