Somatic Development in Children with Congenital Heart Defects

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Objectives Somatic development is impaired in children with congenital heart defects (CHDs), and head circumference seems to be a strong predictor of neurodevelopmental prognosis. The aim of this study was to generate up-to-date reference values for the somatic development (head circumference, body weight, and length/height) of children with CHDs.

Study design Our study population consisted of all patients included in the PAN study (Prävalenz angeborener Herzfehler bei Neugeborenen in Deutschland), which was conducted prospectively over a 3-year study period by the Competence Network for Congenital Heart Defects. All children with mild, moderate, and severe CHDs born in 2006-2009 in Germany were enrolled. For computing of *z*-scores, only children with the following characteristics were included: appropriate for gestational age, nonsyndromic disease, term or post-term delivery, and no cardiac surgery.

Results There were 2818 patients included. New *z*-scores for the described somatic measures of children with mild, moderate, and severe CHDs were computed. Comparisons with the KiGGS study (Gesundheit von Kindern und Jugendlichen in Deutschland) and the Berlin Longitudinal Study revealed significantly lower measurements for all measures—most notably in children with severe CHDs and/or cardiac surgery. In our cohort, no catch-up growth was seen after cardiac surgery.

Conclusion Children with severe CHDs demonstrated the most abnormal pattern in growth, including head circumference before and after cardiac surgery, which is indicative of accompanying brain pathology unrelated to operative injury. *(J Pediatr 2018;192:136-43).*

The improvement in diagnostics and both interventional and surgical approaches as well as pediatric cardiac intensive care has led to a increased long-term survival in children with congenital heart defects (CHDs). Thus, the influence of CHDs and their complex treatment during infancy and thereafter on somatic, psychomotor, and neurologic development is important.

Associated underlying malformations of the central nervous system and other prenatal pathologies (eg, intrauterine growth retardation) are possible contributors to impaired neurocognitive development.[1] Moreover, both intraoperative and postoperative factors (like circulatory arrest with or without hypothermia) may affect long-term neurologic prognosis.[2-9] Microcephaly in children with CHDs may be indicative of impaired central nervous system development, but may also be caused—at least in part—by impaired somatic development,[4,6,10,11] with problems in daily social life as well as in school performance.[12-15]

Most studies about the somatic development of children with CHDs have been limited to body weight and body length, with few studies assessing head circumference. The majority of studies demonstrated that body weight gain and growth (body length) is often impaired until the operative procedure is performed and that, in the postoperative period, catch-up growth occurs.[16-22] Conversely, head circumference typically remains abnormal after the operative procedure in comparison with healthy children.[4,23,24]

The aim of our study was to assess head circumference growth patterns in addition to body weight and length in children with the most common groups of CHDs and to develop *z*-scores for these children. To assess the role of cardiac surgery as a potential modifier of head growth, head circumference was measured before and after surgery in this cohort.

Methods

Our study population consisted of all patients included in the PAN-study[25] (Prävalenz angeborener Herzfehler bei Neugeborenen in Deutschland), which was

CHDs Congenital heart defect

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conducted from 2006 to 2011 by the Competence Network for Congenital Heart Defects, Berlin. In this study, the prevalence of CHDs in newborns in Germany was determined prospectively. Between 2006 and 2009, all children with CHDs who were born in Germany were enrolled and subsequently entered into the database. Information included demographic data as well as all medical and surgical data with regard to the underlying CHDs.

Data from the patient cohort from the PAN-study were entered into the German National Register for Congenital Heart Defects. In this database data about the clinical course of the disease, life expectancy, quality of life, medical/surgical treatment, and biologic samples were entered recorded. All data were stored pseudonymized and separated from personal identifying data.

After approval of the PANKU-study (Prävalenz angeborener Herzfehler bei Neugeborenen in Deutschland Kopfumfang) by the ethics committee at the Charité University Hospital, Berlin, Germany, in 2010, we set up an additional multicenter study that collected further data from every patient who took part in the PAN-study and the National Register for Congenital Heart Defects between July 2006 and June 2009 using a questionnaire. With this questionnaire, data from the German yellow screening booklet were collected. Parents or legal guardians were also provided with a detailed information leaflet containing information about data protection regulations, a declaration of consent, and a prepaid reply envelope.

In so doing, we collected data about the diagnosis and all relevant somatic variables (head circumference, body weight and length at birth and over the course of time until the second year of life). Furthermore, we assessed both maternal measures (age of the mother at birth, multiple pregnancy, fetal echocardiography) and existing comorbidities (gestational age, associated syndromes and other organ malformations, familiar CHDs).

At defined examination points, we used the medical examinations from U1 to U7 that were recorded in the yellow screening booklet (U1, at birth; U2, 3rd-10th days of life; U3, 4th-6th weeks of life; U4, 3rd-4th months of life; U5, 6th-7th months of life; U6, 10th-12th months of life; and U7, 21st-24th months of life).

All data were entered into a remote data entry system using electronic case report forms. These were saved in the database of the National Register for Congenital Heart Defects using Oracle 10g (Oracle, Redwood City, CA).

Small for gestational age was defined as a body weight below the 10th percentile and large for gestational age as a bodyweight of greater than the 90th percentile. Microcephaly was defined as a head circumference below the 3rd percentile. Congenital heart defects were grouped in 3 categories: mild CHDs, including ventricular septal defect (small or muscular), atrial septal defect, patent ductus arteriosus, pulmonary stenosis, and others; moderate CHDs, including ventricular septal defect others than small or muscular, atrioventricular septal defect, aortic stenosis, coarctation of the aorta, partial anomalous pulmonary venous drainage, and others; and severe CHDs, including univentricular heart defect, tetralogy of Fallot, pulmonary atresia, double outlet right ventricle, dextro-transposition of great arteries, congenital corrected transposition of the great arteries, truncus arteriosus communis, interrupted aortic arch, total anomalous pulmonary venous drainage, Ebstein's anomaly, and others.

We compared our medians of head circumference for moderate and severe CHDs with and without cardiac surgery with the head circumference percentiles of the Berlin Longitudinal Study[26] and our medians of body weight und length/height for moderate and severe CHDs with and without cardiac surgery were compared with the percentiles of the KiGGS Study.[27] For purposes of clarity, results from children with mild CHDs were not displayed because of only very minor differences when compared with the group of moderate CHDs.

To evaluate catch-up growth of the group of children who underwent cardiac surgery, patients with cardiac surgery before completion of the first year of life were examined separately.

The statistical analysis was done in cooperation with the Institute for Medical Biometry, Epidemiology and Medical Informatics at the Medical faculty of the University of Saarland, Homburg/Saar, Germany. The datasets were exported from the database of the National Register for Congenital Heart Defects into an Excel document (Microsoft Corp, Redmond, WA). After encoding them, they were imported into SPSS using IBM SPSS Statistics Version 19 (IBM Corp, Released 2010; IBM SPSS Statistics for Macintosh, Version 19, Armonk, NY). Results are depicted as absolute numbers, mean, median, and SD. Linear regression was used to determine statistically significant correlates of somatic development.

Results

There were 2818 patients who took part in his study (1348 male; in 1 case no sex was provided). Demographic characteristics of our study population are detailed in **Table I** and frequencies of CHDs in our cohort are depicted in **Table II**.

Table I. Patient characteristics

	Study population (including ventricular septal defect)	
Patient's characteristics	**Male**	**Female**
Total	1348	1469
Small for gestational age	131 (9.7)	217 (14.8)
Appropriate for gestational age	1043 (77.4)	1147 (78.1)
Large for gestational age	131 (9.7)	71 (4.8)
Age of mother at birth, years	31.4 ± 5.1	31.8 ± 5.0
Multiple pregnancy	90 (6.7)	109 (7.4)
Gestational age	38.2 ± 2.9	38.2 ± 2.9
Preterm	231 (17.1)	261 (17.8)
Term	1075 (79.7)	1172 (79.8)
Postterm	4 (0.3)	9 (0.6)
Surgery	363 (26.9)	298 (20.3)
First surgery with CPB	286 (21.2)	230 (15.7)
No. of operative procedures with CPB	1.0 [0.8]	1.0 [0.7]

CPB, Cardiopulmonary bypass.
Values are n, n (%), mean ± SD, or median [SD].
Percentage refers to the total count of male and female patients are given in brackets.