The Impact of Delayed Cardiac Surgery on the Postnatal Growth of Children with Congenital Heart Disease in Bosnia and Herzegovina

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ABSTRACT

The aim of this study was to evaluate preoperative and postoperative growth in children with congenital heart disease (CHD) when cardio-surgical treatment is delayed. Growth data were analysed on 116 children with various types of CHD (cyanotic lesions (Group 1), left to right shunt (Group 2) and obstructive lesions (Group 3)), who underwent cardiac surgery after a certain period of waiting. Preoperatively, during the time (median 1.13 (0.55–2.39)) years of waiting for surgery, their mean weight z-score decreased from –1.38 (±1.19) to –1.41 (±1.28), and their mean height z-score from –0.65 (±1.41) to –0.81 (±1.36). Children in Group 1 developed a significant linear growth deficit, in Group 2 weight was more affected than height, while in Group 3 both growth parameters were gradually slowly, but not significantly reduced. Postoperatively weight and height z scores, although they showed a linear trend of improvement for all three groups, remained significantly reduced for two years after surgery. At the time of the last examination at the age 9.11 (5.66–13.10) years, the mean height z score –0.16 (±1.28), was significantly reduced p<0.0001, than predicted height 0.23 (±0.82). Growth catch-up was related to age at surgery and preoperative growth deficit. Delayed cardiac surgery in children with CHD aggravated growth deficit and caused slow and incomplete postoperative growth catch-up.

Key words: congenital heart disease, children, growth, cardiac surgery

Introduction

Somatic growth is the most important characteristic in childhood and at the same time a very sensitive index of good health in this period of life. Chronic diseases of all types account for a large proportion of growth disturbances. Children with congenital heart disease (CHD) have been reported as showing significant growth retardation1–8. Multiple extra cardiac factors such as extra cardiac anomalies, chromosomal malformations, other non-genetic disorders, low birth weight, and prematurity may contribute to poor growth in infants and children with CHD1,9,10. The most important effect of haemodynamic changes to their growth have been very well evidenced by most reviewers over time and worldwide7,8,11–14. The severity of the growth deficit depends on the type of cardiac lesion and its haemodynamic effects. The general evidence for this statement is the benefit of early surgical repair on long term growth in these children2,11–19. Surgical correction with restoration of a functionally normal circulation ensures survival for these children, appear of genetic growth potential and postoperative acceleration of growth and good quality of life. In developed countries the type and time of surgical treatment only depends on the type of CHD and its clinical presentation. It is preferred to perform surgical corrections for many cardiac malformations within the first year of life. In most undeveloped and transitional countries, cardiac surgery for congenital heart disease is not available. Surgical treatment of these children often depends on international humanitarian assistance. In this part of the world cardiac surgical treatment of children with congenital heart disease is often delayed due to administrative and transportation procedures. As a result of this delay we frequently encounter various cardiac complications and a high mortality rate20–23. The children who survive undergo surgery much later than this should be considered for individual lesions and for the severity of the disease.
The negative impact of delayed surgery on the quality of life in those children was shown in research by Tahirović et al. 200924. The hypotheses was that the long-term condition caused hemodynamic changes which led to significant somatic growth deficit in these children.

The aim of the present study was to evaluate the longitudinal growth of surviving children with various types of congenital heart disease when cardio surgical treatment is delayed. The steps of this study were evaluation: 1) preoperative growth assessment; 2) postoperative growth assessment and 3) actual growth in relation to their predicted height.

Patients and Methods

Geographical and population data

Bosnia-Herzegovina is a southern European state located between Croatia, Montenegro and Serbia (Figure 1), with an area of 51125 km and a population of 4.007.608 in 2004. The Tuzla Canton area is situated in the northern part of Bosnia-Herzegovina and has an area of 2,909.5 km, with a population of 502 418, including 85 526 children in the 0–14 age group (as of 31st December 2004). In 2004 the infant mortality rate was 6.8 per 1000 live births. Children suspected of having a heart disease are referred to the Paediatric Cardiology Unit, Department of Paediatrics in Tuzla. The state cardiac surgery service of congenital heart disease in period 1994–2004 was not available, during same interval in Tuzla Canton area 98 neonates and children with congenital heart disease died because no surgery could be performed. Despite post war condition, during this time children malnutrition was not registrated as a public health problem in this region.

Patients

The growth data on 116 survived children who had undergone surgery for CHD were analysed. They underwent the surgery during 1994–2004 through the assistance of an international humanitarian organization, in different cardio surgical world centres, after a certain period of waiting for surgery. Poor financial condition, establishment of a contact with a foreign humanitarian and cardiac surgery institution, administrative and transport organisational problems were some major reasons for the delay cardio surgical treatment of these children. Preoperative and postoperative follow-up for all patients was performed at the Paediatric Cardiology Unit, Department of Paediatrics, Tuzla, Bosnia-Herzegovina. The study only included children in which the clinical and hemodynamic data at the time of diagnosis indicated cardiac surgery. Children with extra-cardiac anomalies, chromosomal malformations, other non-genetic disorders, prematurity, these who were born as small for their gestational age and these who had significant postoperative residual lesions were not included in the present study.

Diagnosis of CHD was made using the medical history, physical examination, chest X-ray, electrocardiogram and echocardiogram based on a sequential segmental approach. By utilising the established information about similar patterns of growth in children with CHD, all the children were divided into three different hemodynamic groups: Group 1 children with complex cyanotic CHD, Group 2 children with CHD with left to right shunt (on the atrial, ventricular or arterial level) and Group 3 children with CHD with simple obstructive lesions (obstruction of the systemic circulation and the pulmonary obstruction without cyanois) (Table 1).

Methods

All the case material was obtained from the clinical records from 1992 to 2006 year of the Department of Paediatrics in Tuzla, Bosnia-Herzegovina. The data for birth weight and gestation age was provided from available documentation for 102 children, for others 14 children from parental anamnesis. Longitudinal growth was estimated from the data of age, weight and height: (a) at the time of diagnosis; (b) preoperative – at the time of admission for surgical correction; (c) postoperative – 6 months, 1 year and 2 years (with variations of±15 days) after surgical correction; and (d) at the time the latest clinical examination. The children were measured using standard anthropometric techniques25, with same measuring device and by two nurses. Weight and height were compared with standard reference data for British children based on studies published by Tanner and Whitehouse26,27; and expressed as standard deviation scores (z-scores). Anthropometric data from all three groups were analysed separately and compared with mean standard data for age and with each other. Catch-up growth was defined as the difference between the best postoperative z-score and the preoperative z-score for each individual patient, expressed as a standard deviation (SD) gain. Parental height was measured at the time of assessment. The predicted height of patients was calculated by the standard formula for mid-parental height and then corrected for sex25.

![Fig. 1. Geographical location of the Tuzla Canton area (Bosnia-Herzegovina).](image-url)
TABLE 1
DIAGNOSTIC GROUPS, INDIVIDUAL CARDIAC LESIONS AND SEX STRUCTURE OF CHILDREN WITH SURGICAL TREATMENT FOR CHD

<table>
<thead>
<tr>
<th>Diagnostic groups</th>
<th>Diagnosis</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (complex cyanotic lesions)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased pulmonary flow</td>
<td>TGA</td>
<td>31</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Decreased pulmonary flow</td>
<td>TOF</td>
<td>16</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Group 2 (left to right shunt)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shunt on the atrial level</td>
<td>ASD</td>
<td>20</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Shunt on the ventricular level</td>
<td>AVSD</td>
<td>6</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Shunt in the arterial level</td>
<td>VSD</td>
<td>27</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Group 3 (obstructive lesions)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstruction of the pulmonary circulation</td>
<td>PS</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Obstruction of the systemic circulation</td>
<td>AS</td>
<td>7</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>(ASD) atrial septal defect; (VSD) ventricular septal defect; (AVSD) atroventricular septal defect; (PDA) patent ductus arteriosus; (APW) aortopulmonary window; (PS) pulmonary stenosis; (AS) aortic stenosis; (COA) coarctation of the aorta; (TGA) transposition of the great artery; (TAPVR) totally anomalous venous connection; (TOF) tetralogy of Fallot; (PA) pulmonary atresia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical analysis

Abnormally distributed data sets were described by the median (interquartile range) and normally distributed data sets by X ± SD. Normality was tested using the Shapiro-Wilk test. A single-sample t-test was used to compare the mean z-score with the reference general population with a mean of 0, the two-sample t-test to compare the mean z-score between the groups and at different times. In the case of abnormally distributed data, one or both variables of the Mann-Whitney test were used. A two-sided p value < 0.05 was considered statistically significant. Correlations were tested between growth parameters and age at surgery by Spearman rank coefficients. In the analysis, we used the statistical package Arcus QuickStat, Biomedical version.

Results

All 116 children (63 male and 53 female) were full term newborn (median gestation age 39 (38–40) gestation week) with appropriate birth weight for gestational age (mean birth weight z-score –0.27 (±1.12)). Median age at diagnosis for all 116 was 0.80 (0.30–3.52) years. Surgical correction was performed at median age 2.89 (1.39–6.28) years, in only 13 underwent surgery in the first year of age (11%), in the second 17 (15%), and the others 86 (74%) at an older age. Median time of waiting for surgical correction was 1.13 (0.55–2.39) years. The age of latest examination was 9.11 (5.66–13.10) years. Time of growth follow up was 6.83 (4.90–8.83) years (Table 2).

Preoperative growth assessment

The initial preoperative measurement performed at the time of diagnosis, the mean weight z-score for all 116 children was –1.38 (±1.19), mean height z-score –0.65 (±1.41) and mean weight-for-height z-score –1.37 (±1.73), which showed a statistically significant deficit for all parameters (p < 0.05) compared to the reference general population (Table 3). There was no gender difference found for mean weight z (p = 0.207) and mean height z-scores (p = 0.112) at the time of diagnosis. At the time of diagnosis, the mean weight and height z-scores in children Groups 1 and 2 were statistically significantly reduced, with weight more significantly than height in both groups. Growth retardation was mostly pronounced in children with CHD with left to right shunt. At the same time, the values of weight and height z-scores in children in Group 3 were gradually reduced. At the initial measurement 35% of all children had weight less than the 2 SD, and 21% had height less than 2 SD. During the time of waiting for surgery the trend of reduced mean weight z-score and mean height z-score in children in Group 1 aggressively increased, with a statistically significant difference from the value at the time of diagnosis, and with the height z-score more affected. Weight in children in Group 2 slowly improved (Table 3). During the time of waiting for the operation, the percentage of children with weight (from 39 to 48%) and height (from

TABLE 2
REVIEW OF AGE AT DIAGNOSIS, AGE AT SURGICAL CORRECTION, AGE AT THE LATEST EXAMINATION WITH TIME OF WAITING FOR SURGERY AND DURATION OF FOLLOW UP

<table>
<thead>
<tr>
<th>Diagnostic groups (N)</th>
<th>Age at diagnosis Median (years)</th>
<th>Age at surgical correction Median (years)</th>
<th>Time of waiting for surgery Median (years)</th>
<th>Age at latest examination Median (years)</th>
<th>Duration of follow-up Median (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (31)</td>
<td>0.30 (0.12–0.71)</td>
<td>1.50 (1.20–2.87)</td>
<td>1.10 (0.45–1.84)</td>
<td>8.84 (4.74–12.12)</td>
<td>8.15 (2.37–11.73)</td>
</tr>
<tr>
<td>Group 2 (62)</td>
<td>1.29 (0.48–4.76)</td>
<td>3.08 (1.51–6.53)</td>
<td>1.08 (0.52–2.03)</td>
<td>8.63 (5.40–12.73)</td>
<td>6.39 (4.17–7.73)</td>
</tr>
<tr>
<td>Group 3 (23)</td>
<td>1.88 (0.48–6.08)</td>
<td>6.31 (2.90–9.22)</td>
<td>2.22 (0.87–4.29)</td>
<td>7.68 (6.31–8.54)</td>
<td>7.68 (6.31–8.54)</td>
</tr>
<tr>
<td>Total (116)</td>
<td>0.80 (0.30–3.52)</td>
<td>2.89 (1.39–6.28)</td>
<td>1.13 (0.55–2.39)</td>
<td>9.11 (5.66–13.10)</td>
<td>6.83 (4.90–8.83)</td>
</tr>
</tbody>
</table>
Postoperative growth assessment

At postoperative follow-up weight and height z scores showed a linear trend of improvement over time for all three groups but still remained significant reduced up to two years after surgery. At one year after surgery weight and height z scores in children in Groups 1 and 2 were statistically reduced, as well as at two years after surgery, excluding the mean height z score of children in Group 2. At the time of the latest examination all growth parameters in children in these two Groups were still slightly abnormal, only the weight z score in children in Group 1 remained significantly reduced compared to the reference normal population (Table 3). The proportion of children with weight and height below 2 SD, also decreased significantly (<0.0001). Table 4 shows the worst preoperative, the best postoperative and the difference of weight and height mean z scores. Growth catch-up was defined as the change of these parameters, was statistically significant for all growth parameters in all children. Figure 2 shows the course of preoperative growth by age and postoperative catch up for weight and height in all three diagnostic groups. Growth catch-up was correlated negatively with the age at surgery. No statistically significant correlation was found between catch-up weight and age at surgery (Spearman r= –0.161; p=0.079) or statistically significant correlation between catch-up height and age at surgery (Spearman r= –0.251; p=0.006). Correlations between preoperative weight deficit and catch-up of weight (Spearman r=...
Actual growth in relation to their predicted height

The mean height z scores in all children, at the time of the latest examination, were significantly lower than those predicted by mid-parental height (actual height z score –0.16 (±1.28); predicted height z-score 0.23 (±0.82); p<0.0001). The separate analysis of the groups shows that deviation in height z scores at the time of the latest examination from predicted height was more pronounced in children in Group 1 (actual height z-score –0.47 (±1.04); predicted height z-score 0.19 (±0.52); p<0.0001), followed by children in Group 2 (actual height z-score –0.10 (±1.05); predicted height z-score 0.21 (±0.95); p=0.034). Mean height z scores in children in Group 3 did not differ from predicted height (actual height z score 0.42 (±1.04); predicted height z-score 0.37 (±0.74); p=0.958).

Discussion

This study was conducted at a time when the negative impact of CHD on growth in childhood and the catch-up effects of early cardiac surgery were very well established by numerous pieces of research. At the same time this study was performed in one of many parts of the world where paediatric cardiovascular service is poorly developed. The mortality rate of children with CHD born during the latest decade of the twentieth century in this region was 25.9%, with 86% of deaths occurring in the first month of life. From this time surviving children underwent surgery much later than should be considered for individual CHD and for the severity of lesions. A primary goal of this study was to evaluate preoperative growth disturbances and postoperative growth catch-up, mainly during that time, in surviving children where surgery is not performed in good time.

Preoperative growth assessment

The available data in this study show lower birth weight. Although children were excluded from the sample who had statistically low birth weight and those with incomplete data, they deserved attention as an indicator that their postnatal growth started with a moderate prenatal growth deficit. This deficit of birth weight, explained by alterations of the fetal circulation, has already been described, but for other, still unknown reasons in the foetus. Important discrepancies between this study and other studies, are the much later age of diagnosis. Such differences in comparison with previous epidemiological research in this region, can explain that many children, born with hemodynamically significant CHD, died at an early age in this period. Another possible explanation for this delayed referral to a paediatric cardiologist is the deficiency of the health service in general in the conditions of post war economic devastation and major migrations of the population.

Initially, the most severe growth retardation was found in children with CHD with left-right shunt and cyanotic lesions. Children with obstructive lesions had slightly reduced, but non-significant growth retardation. In children with left to right shunt, weight was more affected than height, which is sign of acute under nourishment. Congestive heart failure and pulmonary overload in children with CHD with large left to right shunt are well known causes of this type of growth deficit. Although the degree of growth retardation is in good correlation with the severity of hemodynamic changes, significant malnutrition was found in children with small asymptomatic left to right shunts. Lower weight

Fig. 2. The age course of preoperative growth and catch up for weight and height in all three diagnostic groups. The arrow shows age of surgical correction.
than height in the present study was found in children with cyanotic lesions initially (median age 0.30 (0.12–0.71) years). During the time of waiting for surgical repair, both growth parameters decreased rapidly, height more so, leading to linear growth retardation, as a sign of chronic under nourishment. This is a well-known pattern of growth retardation caused by the negative effects of general tissue hypoxia and in some cases combined with congestive heart failure in cyanotic lesions2,7,9,11. This rapid worsening of growth parameters, in the present study, showed the definitely unfavourable effects of altered hemodynamics during the critical age of rapid growth20. During the time of waiting for surgery, the weight of children with left to right shunt was slightly improved. This minimal weight improvement, as a positive effect of medical treatment of congestive heart failure and nutritional support, confirms observations reported by other authors3,5,6. Although growth in children with non-critical obstructive lesions has been reported as normal2, in this study we found at initial measurement, slightly reduced weight, with progressive normalisation in the preoperative period. This may partially be the result of increased parental care for the nutrition of these children, but also, this may be explained by individual genetic growth potential. An exact conclusion regarding the growth of children in this diagnostic group is not possible since this is relatively small sample. In literature there are limited comparable reports for long term growth in children with non critical obstructive lesions, although impairment in linear growth relative to weight has been observed in children with pulmonary stenosis and coarctation of the aorta2. Gender growth differences reported in some studies3,5,8 were not found in our children.

Postoperative growth assessment with actual growth in relation to their predicted height

From the first investigations of growth characteristics in children with CHD, the answer has been sought to the question of how surgical treatment affected their growth2,3,8,9,10. All these studies came to the general conclusion that surgical correction has a positive effect on the growth of children with CHD. They showed the surprising acceleration of growth during the first postoperative months. The results of growth catch-up was different according to the type and severity of CHD, degree and pattern of preoperative growth deficit, age at surgery, residual hemodynamic changes and the time of follow-up. The children in this study had accelerated growth after surgery, with the best velocity of growth during the first six months and first postoperative year. Catch-up of growth was also extended in children with cyanotic heart disease and uncompleted. This uncompleted growth catch up was explained by the time lost waiting for the operation. Our data indicate that postoperative height catch-up is in correlation with age at surgery, as well as with the severity of initial growth deficit as in similar research7. Height in children in this study was significantly reduced in relation to predicted height from parental height, in contrast to the results of Cheng et al.2, who reported fulfillment of genetic growth potential in 45 children after surgery tetralogy of Fallot. Some older studies described slight growth improvement after surgical repair of CHD3, postoperative weight gain, but no improvement of height5, or much slower growth improvement2. Several recent studies reported complete growth catch-up within two years9, or in the first postoperative years11, even when several forms of heart disease are involved7,11,13. The main reason for these different results is age at the time of cardio-surgical correction. Children in the present investigation, preoperatively, had a similar pattern of growth deficit and nearly the same degree of growth deficit as in some recent comparable studies, but extended and uncompleted growth catch-up is more similar to the studies dated from the time when surgical correction occurred much later than nowadays.

Conclusions

The pattern and degree of preoperative growth deficit in children with CHD in our study were expected according type and severity of hemodynamic changes. Delayed cardiac surgery in children with cyanotic lesions and those with left to right shunt caused slow and incomplete postoperative growth catch-up, and failure to reach predicted height. This segment of negative outcome deserves attention in terms of improvement care for timely cardiac surgery and long-term follow-up of general health and quality of life for this demanding patient population.

REFERENCES

UTJECAJ ODGOĐENE OPERACIJE SRCA NA POSTNATALNI RAST U DJECE SA PRIROĐENOM BOLEŠĆU SRCA U BOSNI I HERCEGOVINI

SAŽETAK

Cilj istraživanja je bio procjena preoperativnog i postoperativnog rasta djece sa prirođenim bolestima srca u uslovima odgođenog kardiokirurškog liječenja. Analizirani su podaci o rastu 116 djece sa različitim tipovima prirođene srčane bolesti (cijanogene lezije (Grupa 1); lezije sa lijevo-desnim šantom (Grupa 2) i opstruktivne lezije (Grupa 3)) koji su podvrgnuti operaciji srca nakon određenog perioda čekanja. Tokom preoperativnog vremena (median 1,13 (0,55–2,39) godina čekanja na operaciju, njihov srednji z skor tjelesne težine je smanjen od 1,38 (±1,19) na –1,41 (±1,28), a njihov srednji z skor tjelesne visine od –0,65 (±1,41) na –0,81 (±1,36). Djece iz Grupe 1 su razvila značajan linearni deficit rasta, u Grupi 2 tjelesna težina je bila više pogodena od tjelesne visine, dok su u Grupi 3 oba parametra rasta bila blago, ali ne značajno snižena. Postoperativni skor tjelesne težine i visine su pokazali linearni trend poboljšanja u sve tri grupe, ali su ostali značajno niži u periodu od 2 godine nakon operacije. U vrijeme posljednjeg pregleda u dobi od 9,1 (5,66–13,10) godina, srednji skor tjelesne visine –1,16 (±2,28) bio je značajno manji (p<0,0001) u odnosu na očekivano procijenjeni 0,23 (±0,28). Nakon pada rasta je bila u skladu s dobi operacije i preoperativnim definitom rasta. Odgođena operacija srca u djece sa prirođenom srčanom bolesću uzrok je deficit rasta i spore i nepotpune postoperativne nadoknade rasta.