CLINICAL STUDY

Functional outcome of surgery for coarctation of the aorta

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Abstract

Aim of study: **Coarctation of the aorta (CoA) accounts for about 8 % of all congenital heart diseases. This represents about 30 new cases of coarctation every year in Slovakia, of which more than half will require surgical treatment. Over the past years, many children with this diagnosis have been successfully operated on at the Department of Cardiac Surgery of the Children's University Hospital, Bratislava. Thus, the need for a comprehensive follow-up and analysis of the postoperative well being of these young patients arises. Our study is therefore aimed at: 1) identifying factors affecting the incidence and persistence of postoperative systemic hypertension, as well as the need for heart failure and hypertension treatment, 2) assessing patients' psychomotor development following surgery for coarctation of the aorta.**

Methods and data: **Between January 1992 and December 2001, a total of 201 patients with aortic coarctation were operated on at our institution. The three classes of aortic coarctation namely: isolated coarctation, coarctation with ventricular septal defect and coarctation with complex cardiac anomalies were represented. Patients' medical records were retrospectively reviewed, with attention paid to such variables as the type of lesion, gradient across the site of coarctation, type of surgical technique employed and surgery-related complications. Subsequently, these patients were followed for a time period ranging between six months and ten years during which their psychomotor development and overall clinical state were evaluated.**

Results: **Of the 201 operated patients, 64 (33 %) had early postoperative hypertension, so-called paradoxical hypertension. There was a significant correlation between the incidence of early postoperative hypertension and patients' age at operation ($p<0.0001$). Age at operation was also a significant risk factor for late hypertension ($p=0.005$). In both cases we noticed a higher incidence of high blood pressure in patients operated on after the age of six years. The need for antihypertensive treatment of patients with early postoperative hypertension decreases with a younger age at operation. At five years of follow-up, the need for antihypertensive treatment was 15 %.**

Clinical psychological evaluation of 64 patients showed a normal distribution of patients' intelligence quotients. No surgery-related variable correlated with the incidence of delayed mental development. There was, however, a certain correlation between the presence of complex anomalies and low verbal IQ in examined patients ($p=0.04$)

Conclusions: **Early surgical treatment of aortic coarctation reduces the likelihood of early, as well as late postoperative hypertension. The preferred protocol in our institution is early surgical treatment of patients at about the age of two years. The need for antihypertensive treatment of patients at five years of follow-up is 15 %. Patients' psychomotor development following surgery for aortic coarctation is not affected by type of surgical procedure. On the whole, we can conclude that patients' psychomotor development does not differ from the rest of population. There is however, a certain correlation between complex cardiac anomalies and a delay in some components of patients' psychomotor development.** ***(Tab. 3, Fig. 4, Ref. 17.)***

Key words: coarctation of the aorta, hypertension in children.

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Patient population/data distribution

A total of 201 patients with coarctation of the aorta were operated on within the last ten years. 124 (62 %) of the operated patients were males and 77 (38 %) were females, M:F=1.5. 139 (69.2 %) of all operated patients had simple or isolated coarctation, 35 (17.4 %) had coarctation with ventricular septal defects (VSD), while 27 (13.4 %) had coarctation with complex intra cardiac anomalies including hypoplastic left heart syndrome, transposition of the great arteries, TGA, Shone syndrome and others.

The mean age at operation was 3.5 years (range 2 days to 18 years). About 60 % of all operated patients underwent surgery before the age of 2 years while 74 % of all patients were operated on before the age of six years (Tab. 1). This is in line with our preferred surgical protocol which favors correction of aortic coarctation as soon as it is diagnosed and the patient is deemed fit for surgery, usually before or at about age 2 years.

The mean weight at operation was 13.8 kg (range: 1.7 to 67 kg).

Associated anomalies:

135 (69 %) patients had at least one associated cardiac anomaly. The most common cardiac anomalies were various forms of valve lesions, occurring in about 44 % of cases. The most common valve anomaly was the bicuspid aortic valve, which occurred in 19 % of all cases of coarctation and in 43 % of all associated valve anomalies. We recorded 18 (9 %) cases of non-cardiac anomalies of which 4 (2 %) were cases of Turner's syndrome, 1 (0.5 %) case of Klippel Feil syndrome, 5 (2.6 %) cases of CNS lesions and 8 (4.4 %) cases of other anomalies ranging from gastrointestinal to metabolic disorders.

Surgical techniques

Four surgical techniques were employed in the treatment of our patients:

1) Resection and end-to-end anastomosis (RETE).
2) Extended resection and end-to-end anastomosis (RETE-ext.).
3) Patch aortoplasty (Vosschulte) (PA).
4) Subclavian flap aortoplasty (Waldhausen) (SFAP).

A fifth surgical technique entailed total aortic arch reconstruction (TAR) using a pericardial patch in some patients with associated aortic arch hypoplasia. On the whole, 101 patients (51 %) were treated by resection and end-to end anastomosis, 24 patients (12 %) by extended resection and end-to-end anastomosis, another 24 patients by the subclavian flap angioplasty and 44 patients (22 %) by the patch aortoplasty technique. Total arch reconstruction was performed in 6 patients (3 %). Over the last few years, the extended resection technique has become the procedure of choice especially in neonates and infants. On the contrary, there has been a considerable decline in the use of the subclavian flap technique and patch aortoplasty. Since the year 1997 we have not employed the subclavian technique, because the extended resection technique is more physiologic.

Tab. 1. Age distribution of operated patients.

Age	No of patients	Percentage
1–28 days	65	32
28–180 days	41	20
6 months–2 years	15	8
2–6 years	28	14
6–18 years	52	26
Total	201	100

Methods

Blood pressure monitoring: Patients' blood pressures were monitored by non-invasive methods. Pressure reference intervals for patients' age and body configuration were determined in line with the recommendations of the task force on blood pressure control in children (1).

Gradient across the site of coarctation repair

Gradients across the site of coarctation repair were detected first by non-invasive means using cuff manometer and echocardiography. On detecting gradients more than 20 mmHg, the patients involved were observed and echocardiography was repeated on several occasions. In cases of persistent high gradients and echo flow patterns suggestive of recoarctation, the patients were referred to catheterization for definitive diagnosis and balloon dilatation or surgery, where necessary.

Psychomotor development

Surgical repair of aortic coarctation is associated with some neurological complications either due to reduced perfusion during aortic cross clamping or as a result of left subclavian steal-syndrome following the subclavian flap technique (2). Other rare neurological complications such as cerebellar infarction, stroke and paraplegia due to spinal cord ischemia have been reported in some series (2). With these in mind we conducted an extensive psychomotor evaluation in collaboration with psychologists at the Children's Hospital in Bratislava. The psychomotor development study comprised two main parts:

1) Questionnaires covering the various stages in child development with emphasis on gross and fine motor development, attention deficit, speech impairment, cognitive functions and overall psychosocial interactions. The questionnaires were compiled in line with the Denver developmental screening test (3).

2) The second part entailed an assessment of the subjects by a clinical psychologist using the Standford-Binet intelligence scale (4).

The questionnaires were sent to a total of 160 patients and their parents, of whom 120 responded. For the purpose of evaluation, the questionnaires were divided into three areas representing early psychomotor development, cognitive development and emotional development. An answer was judged to be significant if it implied a delayed developmental process, in other words, if

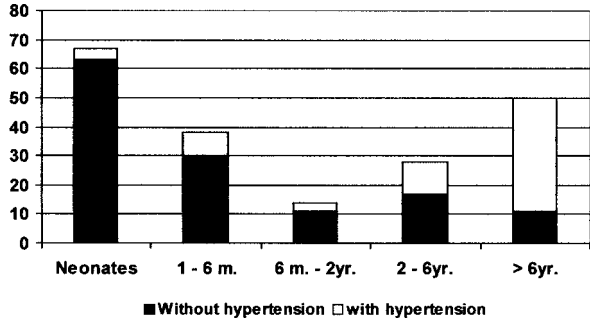

Fig. 1. Incidence of early (paradoxical) postoperative hypertension.

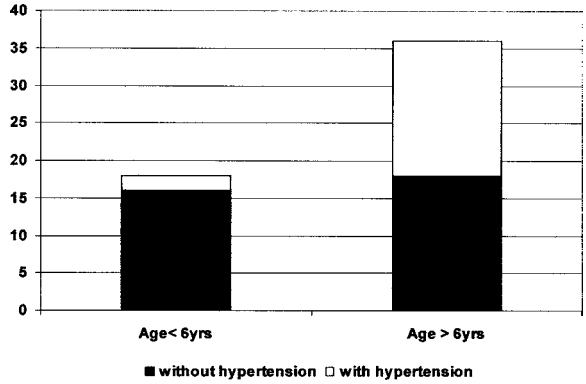

Fig. 2. Persistence of hypertension in patients after surgery.

it lay outside the upper 90th percentile as provided by the Denver developmental screening test (3). The more the number of significant answers, the higher the probability of psychomotor or cognitive/emotional impairment. A significant answer in any of the above-mentioned areas was scored "1" while a non-significant answer was scored "0". The scores were summed up for each section and the totals rated as follows:

0 to 1 – no suspected delay,

2 to 3 – suspected delay,

4 and above – highly suspected delay.

64 patients were examined by a clinical psychologist using the fourth edition of the Stanford-Binet intelligence scale 44 of these patients had simple coarctation, 13 had coarctation with ventricular septal defect while 7 had coarctation with other complex intracardiac anomalies. Emphasis was laid mainly on those patients who underwent surgery within the first months of life. The median age at surgery of examined patients was 94 days. The psychological examination involved the assessment of verbal reasoning, abstract/visual reasoning, quantitative reasoning and short-term memory. On the whole 15 subtests were administered.

Raw scores were obtained for each subtest and subsequently converted to the standard age scores (SAS) to enable comparison between the various age groups. Overall scores or quotients obtained were compared to reference values for the normal population.

Statistical analysis of patients' data

Patients' data were analyzed using the JMP Statistical Discovery Software program version 4.04. The relationship (P) between two or more variables was determined by univariate or multivariate analyses. Unless otherwise stated, P values of less than or equal to 0.05 were assumed to be statistically significant.

Results

Early postoperative hypertension

Immediate postoperative systemic hypertension (so-called paradoxical hypertension) was recorded in 64 (33 %) of our patients. There was a significant correlation ($p<0.0001$) between the incidence of postoperative hypertension and the age at operation. About 80 % of these patients were those operated on after the age of two years (Fig. 1).

From Figure 1 it can also be concluded that the risk of paradoxical postoperative hypertension increases with age at operation. About 78 % of all the patients who underwent surgery after the age of six years had postoperative hypertension and required antihypertensive treatment for a varied period of time.

High blood pressure on follow-up

19 (35 %) of 54 of the patients with early postoperative hypertension presented with elevated blood pressure on follow-up. 10 (18.5 %) of these patients had severe hypertension while 9 (16.5 %) had blood pressure values slightly above the prescribed upper limit for their various ages. Contingency analyses identified age at operation as a major factor affecting the persistence of high blood pressure in patients after operation. From the graph in Figure 2, we can see that patients operated on after the age of 6 years were at a greater risk of having persistent high blood pressure than those operated on at an earlier age ($p=0.005$). Further analysis showed a decrease in the p value with an increase in age at operation. In other words, the higher the age at operation, the more likely patients are to have persistent hypertension. The corresponding value of p for age at operation of 10 years is 0.001

The high incidence of persistent hypertension in patients operated on after the pre-school age has been attributed to a change in sensitivity of their baroreceptors (5). Another factor affecting the incidence of late postoperative hypertension is the presence of residual or recurrent coarctation. In our series, there was no statistically significant relationship between the gradient across the site of repair and persistent high blood pressure in the 64 patients who had early postoperative hypertension ($p=0.8$). On the contrary, the relationship between high gradient across the site of repair and high blood pressure was quite significant in those patients who did not have early postoperative hypertension but later became hypertensive during the course of follow-up ($p=0.04$). Of the 16 patients with high echo gradient, 8 (50 %) had significant hypertension.

Response to antihypertensive medication

Most of the patients with early postoperative hypertension were discharged on antihypertensive medication. The duration of treatment was determined by individual patient's response to medication. On the whole, the majority of the patients no longer required any antihypertensive treatment six months after surgery. Figure 3 represents the "need for antihypertensive therapy". From the graph, it can be seen that only about 25 % of patients were on medication one year after operation. This number further declined to about 15 % at 4 years of follow-up.

A further look at all patients requiring antihypertensive medication postoperatively and who had been followed up for at least four years showed that older age at operation was a significant factor in persistent high blood pressure and thus, the need for prolonged treatment (p=0.01).

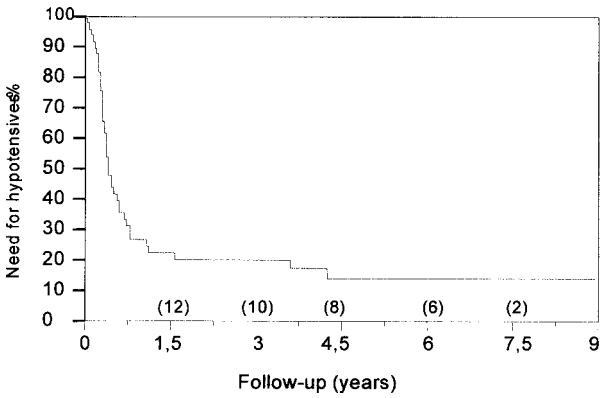

Fig. 3. The need for medication in patients with postoperative high BP. Patients at risk are in parenthesis.

Psychomotor development

Questionnaire results

On univariate analysis two factors were shown to be associated with delay in early stages of psychomotor development. The factors in question are complex cardiac anomalies and severe pre- and post-operative course (Tab. 2).

Patients with complex cardiac anomalies in association with aortic coarctation were at a higher risk of early psychomotor developmental delay than were patients without complex cardiac anomalies (p=0.02). Patients with severe pre- or postoperative complications and a long period of hospital stay also had a high risk of delay in early psychomotor development. 13 (21 %) of 62 patients under the age of 1 year were hospitalized for a period longer than 30 days, 5 of these patients had signs of early psychomotor impairment. These 5 patients constituted 72 % of all patients with signs of early psychomotor developmental delay (p=0.003 on Fisher's exact test).

On multivariate analysis, a complicated postoperative course proved to be a more significant risk factor for early psychomotor retardation than the presence of complex cardiac anomalies (p=0.01).

Hence, there was no statistically significant difference in early psychomotor development between patients with complex anomalies, who had a good pre- or postoperative course and those with simple lesions (p=0.7).

Further analyses showed that despite a delay in early psychomotor development, many of the subjects with prolonged childhood illness compared quite well with their peers in late psychomotor development. In other words, there was no significant difference in emotional and cognitive development between the two groups as mirrored by their performance at school, p=0.7 and 1.0, respectively.

Tab. 2. Factors associated with early psychomotor developmental delay in children undergoing surgery for coarctation of the aorta.

Factors	Univariate analysis p	Multivariate analysis p
Complex cardiac anomalies	0.02	0.1
Length of hospital stay >30 days	0.003	0.01

Results of clinical psychological examinations

There was a normal IQ distribution amongst the patients. (Fig. 4) 10 (16 %) of the 64 examined patients had IQ below average while 8 (13 %) had above average IQ.

Analysis of the various IQ components showed that patients obtained the highest scores in the abstract/visual aptitude tests (mean 103.2±15.2) and the lowest scores in short term memory tests (mean 94.7±14.7)

Further statistical analyses did not show any significant correlation between low patient IQ and surgery-related variables. As shown on Table 3, the only statistically significant relationship was between complex cardiac anomalies and low verbal components of the patients' intelligence quotient.

Discussion

The need for early surgical treatment of aortic coarctation in order to minimize the risk of postoperative hypertension has been emphasized by several authors. Our study of 201 patients of whom 64 had early postoperative hypertension over a period of one to ten years, identified age at operation as a very significant risk factor for both early and late (persistent) high blood pressure in operated patients. The occurrence of early or "paradoxical" hypertension has been attributed to increased catecholamine secretion following surgical stimulation of sympathetic nerve fibers (6) but the fact remains that just like late hypertension, it is age-related and can be minimized by early timing of surgery. Our findings agree with those of Seirafi et al (7) of the New England Medical Center in Boston, Massachusetts who, in their study of 176 patients undergoing repair of coarctation of the aorta, identified older age at operation as a risk factor for persistent hypertension. While the work of Seirafi et al favored surgical treatment before the age of one year, our study showed that the risk of persistent hypertension was highest in those undergoing sur-

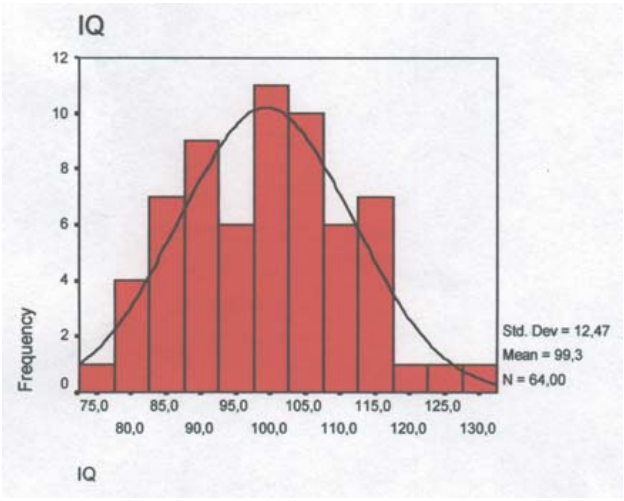

Fig. 4. Patients' IQ distribution.

gery at about the age of six years or more. Our protocol, however, is surgery before the age of two years. Similarly, in a study of 571 patients, Cohen et al (8) showed that late hypertension occurred in 7 % of those operated on in infancy (i.e. before the age of one year) as opposed to 33 % who had undergone repair after the age of 14 years. A most probable explanation for persistent high blood pressure in our patients could be a change in the sensitivity of their baroreceptors and thus, an overall change in arterial reactivity as noted by Beekman et al (5). High postoperative pressure gradient across the site of repair (i.e. recurrent coarctation) was not a significant risk factor for late high blood pressure in this group of patients. Studies have shown an increased endocrine activity during exercise in patients treated for coarctation of the aorta. Elevated arginine vasopressin and lowered atrial natriuretic factor have been associated with hypertension in coarctation patients and this state tends to persist even after surgical treatment.

In a recent study by de Divitiis et al (9) titled "vascular dysfunction after repair of coarctation of the aorta", the authors demonstrated an impaired conduit artery function, with abnormal responses to flow-mediated dilatation (FMD) and dilatation by sublingual nitroglycerin in patients after repair of aortic coarctation. They also demonstrated that early surgical treatment was associated with preserved elastic properties of conduit arteries, but concluded that reduced reactivity remained. Other studies by Gardiner et al (10), Kimball et al (11), Weber et al (12) and Balderston et al (13) have pointed out endocrine factors, impaired vascular reactivity as well as discrepancies in aortic growth as likely causes of exercise-induced hypertension in patients after coarctation repair. While early surgical treatment has been shown to minimize the risk of late hypertension in coarctation patients, Gardiner and colleagues (10) in their study demonstrated abnormal small and large vessel function in the "pre-coarctation" arm vessels even in subjects who had undergone repair in the neonatal period. It becomes expedient to state at this juncture that early surgery does not solve all problems of late hypertension in patients, hence it has been suggested that coarctation of the aorta may be a manifestation of a generalized vascular abnormality (14). Further studies are required to determine the state of these patients undergoing early surgery for CoA in the long run (for example 20 to 30 years after surgery) vis-à-vis the normal population.

Tab. 3. Some variables and their relationship to patients' IQ scores.

Variables	Univariate analysis p
Complex cardiac anomalies	0.04
Total aortic arch reconstruction (circulatory arrest)	0.3
Subclavian flap angioplasty	0.8
Age at operation <30 days	0.1

Psychomotor development

The overall picture of patients' psychomotor development following surgery for aortic coarctation was quite encouraging. Early psychomotor development as evaluated by the questionnaire showed that those patients with complex anomalies were at the highest risk of being impaired. The early psychomotor impairment in most of these patients was, however, shown to be transient by later psychomotor evaluations. Clinical psychological evaluations identified a correlation between associated cardiac anomalies in coarctation patients and low verbal IQ component. No surgery-related variables were found to be in correlation with delayed mental development. Our decision to evaluate the psychomotor development of patients undergoing surgery for coarctation of the aorta was informed by the need to have a complete picture of the postoperative well being of all children treated in our institution for various forms of congenital heart diseases. The recent use of intra-operative circulatory arrest (also in coarctation patients undergoing total arch reconstruction) has also called for the evaluation of the influence of this procedure on the mental development of patients. In addition, the use of the subclavian flap technique has been associated with the so-called "steal syndrome", which implies a reduced perfusion of the brain especially during exercise.

The link between complex cardiac anomalies and impaired psychomotor development as noted in our series has also been pointed out by the few studies in this field. In their work titled "Neurodevelopmental outcomes after complex infant heart surgery", Mahle and Wernovsky (15) of the Children's Hospital of Philadelphia outlined the preoperative, intra-operative as well as postoperative risk factors for neurological impairment in patients undergoing complex heart surgery. Among the intra-operative risk factors were cooling time, acid-base strategy, inflammatory response, embolic risk and deep hypothermic circulatory arrest. In a randomized trial performed in Boston (16) involving patients operated on for transposition of the great arteries (TGA), the mean IQ at 4 years of age was 92.6±14.9, which was significantly lower than the normal population. The mean IQ of patients in our series is 100 and does not differ from the rest of population, however, further studies are required in this area.

The psychomotor development of patients with complex cardiac anomalies such as TGA is presently being investigated in our institution.

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