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DIAGNOSIS AND SURVEILLANCE OF AORTIC DILATION AT CHILDREN WITH CONGENITAL AORTHOPATIES

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REZUMAT

DIAGNOSTICUL ȘI SUPRAVEGHEREA DILATĂRII AORTICE LA COPIII CU AORTOPATII CONGENITALE

Cuvinte cheie: aortopatii congenitale, copii, tipuri de dilatări aortice.

Introducere. Aortopatiile congenitale (AoC) la copii implică remodelări vasculare la nivel de țesut vascular cu apariția unor dilatări de aortă, ce pot evolua în anevrisme, disecții sau rupturi de aortă.
Material si metode. A fost realizat un studiu analitic de urmărire pe un eșantion de 150 copii cu AoC. Diagnosticul AoC a fost stabilit conform criteriilor clinice și paraclinice ale unei malformații congenitale cardiace la copil. La acest grup de copii au fost evaluate datele ecocardiografice ale diametrelor aortice segmentate iar dilatarea aortei a fost apreciată conform scorurilor Z (Detroit Data).
Rezultate. S-au obținut următoarele tipuri de AoC: stenoza aortică (SAo) în 38,0% (n=57) respondenți, coarctație de aortă (CAo) au fost 32,0% (n=48), copii cu valvă aortică bicuspidă (VAB) au fost 26,0% (n=39), iar copii cu sindroame genetice au fost 4% (n=6). Un grup aparte l-au constituit patologiile combinate: SAo+VAB – 29,0% (n=43,5) din totalul subiecților iar, SAo+CAo — 17,0% (n=25). Tipurile de dilatări aortice au fost: dilatare de tip tubular, porțiunea ascendentă în 47,2% (n=42), porțiunea descendentă 33,6% (n=29), dilatare regiunea arcului aortic 11,2% (n=10), dilatare bulbară la nivelul sinusului Valsalva 8,0% (n=7) copii.
Concluzii. Dilatarea aortei este întâlnită frecvent la pacienții cu AoC. Cel mai frecvent tip de AoC la copii a fost SAo. Cel mai răspindit tip de dilatare aortică a fost dilatarea tubulară la nivelul aortei ascendente iar cel mai rar la nivelul arcului aortic.

РЕЗЮМЕ

ДИАГНОСТИКА И НАБЛЮДЕНИЕ ЗА РАСШИРЕНИЕМ АОРТЫ У ДЕТЕЙ С ВРОЖДЕННЫМИ АОРТОПАТИИ

Ключевые слова: врожденные аортопатии, дети, виды дилатации аорты.

Введение. Врожденные аортопатии (ВАо) у детей включают ремоделирование сосудов на уровне сосудистой ткани с появлением дилатаций аорты, которые могут развиваться в аневризмы, расслоения или разрывы аорты.
Материал и методы. Проведено последующее аналитическое исследование на выборке из 150 детей с ВАо. Диагноз ВАо устанавливали на основании клинических и параклинических критериев врожденного порока сердца у ребенка. В этой группе детей оценивали эхокардиографические данные диаметров сегментированной аорты и дилатацию аорты оценивали по шкале Z (Detroit Data).
Полученные результаты. Были получены следующие виды ВАо: аортальный стеноз (САо) у 38,0% (n=57) респондентов, коарктация аорты (КАо) у 32,0% (n=48), дети с двустворчатым аортальным клапаном (ДАК) у 26,0% (n=39), а детей с генетическими синдромами — 4% (n=6). Отдельную группу составила сочетанная патология: САо + ДАК – 29,0% (n=43,5) от общего числа обследованных и САо+КАо – 17,0% (n=25). Виды дилатации аорты: тубулярная дилатация, восходящая часть 47,2% (n=42), нисходящая часть 33,6% (n=29), дилатация области дуги аорты 11,2% (n=10), бульбарная дилатация на уровне синус Вальсальвы 8,0% (n=7) детей.
Выводы. Расширение аорты часто встречается у пациентов с ВАо. Наиболее частым типом у ВАо детей была САо. Наиболее распространенным типом дилатации аорты была тубулярная дилатация на уровне восходящей аорты и наиболее редкой на уровне дуги аорты.

INTRODUCTION

Congenital aortopathies (CAo) lead to increased global cardiovascular mortality, both in childhood and adulthood. These entities include: aortic stenosis (AoS), aortic coarctation (AoC), bicuspid aortic valve (BAV), Marfan syndrome (MS), Ehlers-Danlos syndrome, Turner syndrome, and others (1, 2). According to the estimated incidence in the specialty literature, aortic stenosis constitutes 2-11% of the total number of congenital heart diseases (CHD) in children, with a prevalence of 3-5 cases per 1000 live births. Aortic coarctation (AoC) accounts for 5-8% of cases, with a prevalence of 3 to 10.000 live births. Aortic dilatation occurs in 0.4% of patients with CAo, aortic valvulopathies (BAV) are the most common malformations (prevalence 1-2%) and have a risk of dissection up to 40% (2, 3). In children, as opposed to adults, aortopathies are sometimes completely asymptomatic, which camouflages the suspicion of developing a complication. Congenital aortopathies require early diagnosis and prompt therapy to improve the extremely unfavorable prognosis in some cases. These patients have the clinical symptoms of cardiac or vascular remodeling installed over time. In this context, the assessment of aortic dilation and the type of aortic dilation is essential for predicting possible complications in development at children with CAo.

Based on these assumptions and beliefs, we would like to emphasize the value of this research project in order to determine the prognostic elements capable of positively influencing the future of children with CAo.

MATERIAL AND METHODS

To achieve *the purpose and objectives of the research*, an analytical follow-up study was planned.

General design and study population. During 2016–2019, 150 children with CAo were examined, according to the developed study protocol. The study project was carried out within the IMPH IMC, at the Department of Pediatrics of the Pediatric Cardiology Clinic. At the initial stage, 150 selected children with CAo were complex examinated. Based on the obtained data (two-dimensional echocardiography) and the anthropometric parameters, the Z scores were calculated (Detroit Data) for each diameter of the aorta. Criterion that allowed us to appreciate the children with changes in diameter (dilation) at the level of the aorta was score Z>2 DS(4).

Inclusion criteria were: children aged 1 month to 17 years, 11 months and 29 days with CAo; diagnosis confirmed by AoS with PG>30 mmHg, CAo operated/unoperated; patients with BAV and genetic syndromes that involve the aorta: Marfan, Turner, etc.; presence of the agreement to participate in the study by the tutor and the assent from the children ≥14 years old. Exclusion criteria: children (parents or carers) who refuse to participate in the study; patients with severe concomitant pathologies (renal, hepatic impairment, terminal stage, with severe neurological pathologies); children with acquired (rheumatic) valvulopathies.

The evaluation of patients was performed in the following way:

Stage 1. Using the inclusion and exclusion criteria, 150 children with CAo were admitted to the research, who formed the general research sample, they were subjected to a thorough investigation, specifying the prenatal and postnatal history, disease history, current status, physical examination (anthropometric indices: weight, height, body surface area), laboratory examinations of an obstructive CHD, basic instrumental examinations (two-dimensional EcoCG and color Doppler.)

Stage 2. By means of the two-dimensional echocardiographic examination and the calculation of the Z score was obtained the batch of children with modifications of the aortic diameters (dilation). Initially the echocardiographic examination based on the morphology of the aorta was performed at 6 levels of the aortic segments: root of the aorta (diameter of the valvular ring, diameter of the sinus Valsalva, diameter of the sinotubular junction); ascending aorta; aortic arch (between the brachiocephalic trunk and left subclavian artery); descending aorta (immediately below the aortic isthmus). Morphometry of the aorta was performed according to Petterson's criteria with the Toshiba Aplio 300 MODUS TUS-A300 echocardiographic model, and the Z-score calculation — after Detroit Data (4). The diameter of the aortic ring was fixed at the distance between the points of articulation of the valves, during systole, in the long axis parasternal ultrasound dial. The diameter of the sinus Valsalva was assessed in the left parasternal section in the maximal size of the systole. Also in the same quadrant, the diameters of the sinotubular junction and the proximal ascending aorta were also appreciated. The diameter of the aortic arch was measured in the suprasternal echocardiographic quadrant, long axis, in the maximum systolic dimension between the brachiocephalic trunk and the left common carotid artery. And the diameter of the proximal descending aorta was measured in the suprasternal quadrant, long axis, in the maximal size of the systole in the immediate vicinity of the aortic isthmus, distal to the left subclavian artery.

Stage 3. Subsequently, the values of the Z score were calculated, online, by introducing the values of the aortic diameter (cm) relative to the area of the child's body surface (height — cm, weight — kg), based on which the study sample appreciated children with diameter changes in the aorta (Z score>2 DS) and children without diameter changes in the aorta (Z score≤2 DS). The first batch consisted of 89 children — 62 boys and 27 girls, with an average age of 102.8 ± 7.13 months, and the second of 91 children (30 ineligible children with Z =2 DS score), respectively 61 children — 48 boys and 13 girls, with an average age of 121.4 ± 7.2 months.

Stage 4. All forms of CAo found in the research were investigated, the types of aortic dilatations being evalu-

ated as the risk factors in the development of a complication of the CAo such as aneurysm, dissection, aortic rupture.

Ethical considerations. The consent of the parents or the legitimate guardian and the consent of the children aged ≥14 years were obtained; they were not paid, they did not bear financial expenses related to the study participation. The study was approved by the Research Ethics Committee of the State University of Medicine and Pharmacy Nicolae Testemitanu (report No. 76 of 12.05.2017).

The given scientific research is an analytical tracking study, in which several statistical methods were used: historical, comparative, biostatistic, observational, mathematical.

Statistical analysis. The statistical analysis of the obtained results was performed by several methods of assessing the truthfulness: the $\chi 2$ matching criterion, U-Fisher criterion, t-Student criterion of comparing the mean values, correlation analysis, Odds Ratio (OR), discriminant analysis and the analysis logistic regression.

RESULTS

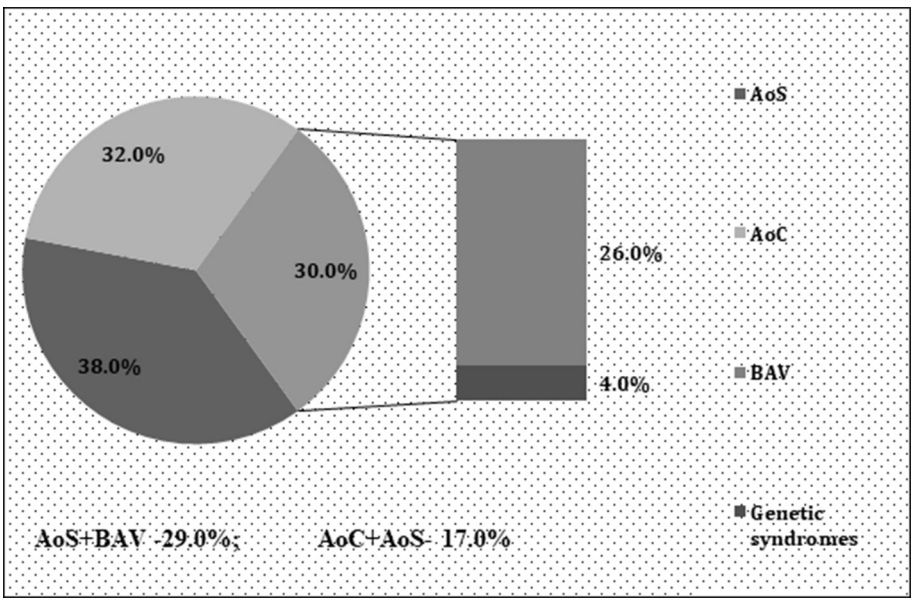
Despite the multiple researches that had as objective the evaluation and definition of the evolutionary particularities of the CAo, there are still many obscure and contradictory moments regarding to the interpretation of the character and structural changes in dynamics in the context of the clinical manifestations in children with these pathologies. The essence of the correct and timely approach of a child with CAo is to evaluate the risk of developing a complication (dilatation, aneurysm, dissection) with the potential for premature death, and one of the main components of this approach is the long-term follow-up, with the appreciation of the elements displayed by expansion to certain levels of the aorta.

Analysis of the distribution of the study participants according to age groups. The study included children aged 1 month to 17 years 11 months and 29 days (mean age =10 ± 5.19 months or 9.2 years). These children were divided into two groups according to the aortic diameter changes presented. One batch of children were those with expanded diameters and another with unchanged diameters. Group I consisted of 89 children (59.3%), of whom 18 (20.2%) aged≤1 year (≤12 months), 11 (12.4%) aged 1– 5 years (12–60 months), 29 (32.6%) aged 5-12 years (60–144 months) and 31 (34.8%) aged >12 years. Group II consisted of 61 (40.6%) children, of which one (1.6%) under the age of ≤ 1 year (≤12 months), 10 (16.4%) aged between 1 and 5 years (12–60 months), 26 (42.6%) 5–12 years (60–144 months) and 24 (39.6%) over 12 years.

According to the data presented in Table 1, there is a presence of CAo with changes in diameter at the level of the aorta (score Z>2 DS) in subjects aged ≤1 year (≤12 months) in 20.2% cases, confirming the possibility of installation of the expansive type complications (dilation, dissection, aortic rupture) from an early age.

Analysis of the study participants distribution according to the environment of origin. The prevalence of children from rural versus urban areas was recorded in the study, the same legality being maintained in the research groups, respectively 74 (83.1%) of children from group I and 51 (83.6%) from group II were from the rural area vs 15 (16.9%) and 10 (16.4%) children of urban origin ($\chi 2 = 0.006$; $p>0.05$).

The structure of the subjects included in the research according to the model of congenital / genetic aortopathy. The general group of children included the



Note: AoC-Aortic coarctation, AoS-Aortic stenosis, BAV-bicuspid aortic valve

Figure 1. ***Structure of the subjects included in the research according to the type of congenital and genetic aortopathy and their combinations.***

following subgroups of aorta pathologies: first group was represented by children with AoS – 38.0%, second with AoC – 32.0%, third with BAV – 26.0%, and the fourth group included children with the genetic syndromes – 4.0%, a separate group constituted the combined pathologies: AoS + BAV – 29.0% of the total subjects and, AoS + AoC – 17.03%, **(Figure 1)**.

Existing studies demonstrate an increased rate of complications in subjects with CAo, especially in combination cases (AoC + BAV). Aortic dilatation can occur in different aortic segments, appearing in a bulbar form that is installed at the root of the aorta, and the tubular form — at the level of the ascending aorta. Knowing the design of dilation and the level of impairment in a given CAo facilitates the prediction of aneurysm, dissection or aortic rupture. Two pathologies are known to have an increased risk of aortic dissection: aortic bicuspid valve(risk of dissection estimated at 0.4%) and Marfan syndrome (≈ 40% of the subjects develop acute acute aortic dissection).

Analysis of the forms of dilatations at the level of the aorta as risk factors in the specific complications of congenital aortopathies in children. Having confirmed the types of CAo in children and performing at the initial stage the distribution of the general group according to the presence or absence of aortic dilation in relation to anthropometric indices (Z score), we considered it essential to assess the form of this dilation as a risk factor in the occurrence of a complication of giant aneurysm and/or aortic dissection. The results obtained are shown in **Figure 2**.

In this research, evaluating the dilated aortic diameters, we found that on the first place is the dilation of the ascending aorta, which usually has a tubular dilation — 42 (47.2%) of children. On the second place is the dilation of the descending aorta — the isthmus, recorded in 29 (33.6%) participants in the study. Subsequently, 10 (11.2%) cases showed dilatation in the diameters of the aortic valve ring and transverse aortic arch, and in the Valsalva sinus — bulbar dilation in only 7 (8.0%) children.

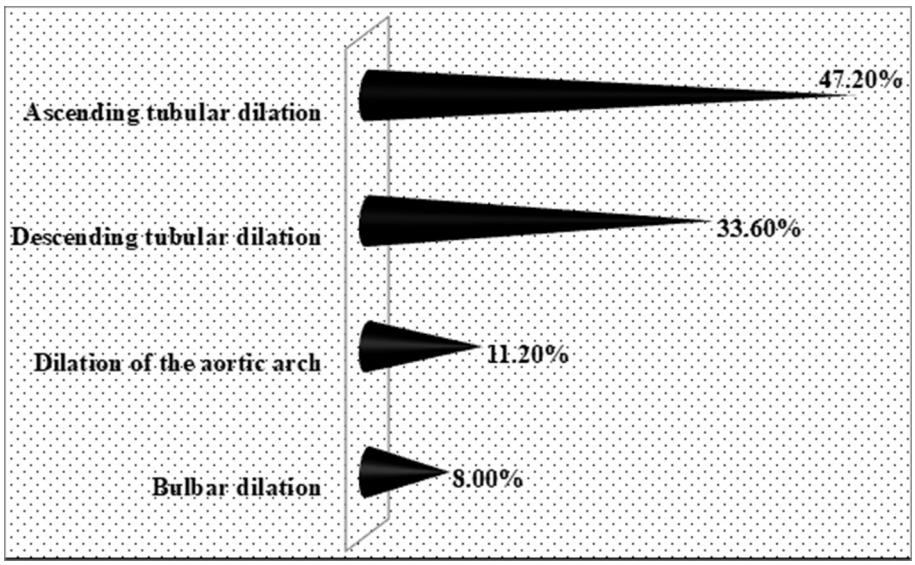


Figure 2. ***Forms of dilatations in children with congenital aortopathies***

Association of dilated segments of the aorta is commonly found in CAo. In about 7.9% (n=7) of cases, children showed dilatation of diameters at the level of two different aortic portions: the segment of ascending aorta and descending aorta and the level of the aortic valvular ring with the portion of the sinus Valsalva. In 4.5% (n=4) cases they developed aortic diameter dilatation concomitantly at the level of the aortic valve ring and in the isthmus portion of the descending aorta; the rest of the combinations were recorded in unique cases. The specificity of the development of the complications within the congenital aortopathies is depending on the model of aortic dilatation which in turn depends on the profile of congenital aortopathy confirmed. Thus, studies have shown that ascending tubular dilation has tropism over the bicuspid aortic valve and aortic stenosis, and both are most commonly complicated with aortic dissection (5). Bulbar dilation is a greater risk of developing an aortic rupture dissection and we may have it at a higher rate in the genetic syndromes with aortic defect (Marfan syndrome) (6). Within aortic coarctations and genetic syndromes, such as Turner syndrome, the descending tubular dilatation is associated with the risk of aortic aneurysms (7).

DISCUSSIONS

The researches reported in recent years pay close attention to the factors that may favor the development of major complications in CHD (8). In this context, a particular role is played by an obstructive category of valvulo-vascular CHD, with major risk of developing lethal complications, because they arise with an expansive mechanism post-obstruction (1, 5). This group of cardiac malformations are congenital aortopathies (CAo) — relatively new concept in pediatric cardiology of the Republic of Moldova. We initiated this research,

because the incidence of CAo (about 10-15% from the total CHD) in children is increasing (1, 6).

Congenital aortopathies lead to rised global cardiovascular mortality, both in childhood and in adulthood. In children, as opposed to adults, aortopathies are sometimes completely asymptomatic, which camouflages the suspicion of developing a CAo complication (9). Congenital aortopathies require early diagnosis and prompt therapy to improve the extremely unfavorable prognosis in some cases. Recently, the Global Burden Disease Project 2010 demonstrated that the overall mortality rate from CAo complications (aneurysms, dissections, aortic rupture) increased from 2.49 to 2.78 at 100.000 inhabitants in period of 1990-2010, with higher rates for males (2, 10). The information presented demonstrates the importance of its research and that the topic is actual. The treated subject is fundamental and extremely interesting regarding the consequences that we can monitor by studying the evolution of a certain type of congenital aortopathy. Researching the factors involved in the occurrence of a complication, as aortic dilation, can prevent a complication from CAo which sometimes can be fatal. These factors have a predictive role in the prophylaxis of valvulo-vascular remodeling, developed progressively in children with CAo (11).

The discriminant selective analysis of the study group allowed to highlight groups of risk factors for probability of occurrence of a specific CAo complication: factors related to the form of CAo and factors related to the model of aortic dilation.

CONCLUSIONS

1. The type of CAo, according to the obtained results plays an important role in the appearance of dilation, aneurysm, dissection, aortic rupture. In the study being recorded not only CAo as isolated entities (AoS, AoC, BAV, genetic syndromes), but also valvulo- vascular combinations (BAV + AoS, BAV + AoC, BAV + genetic syndromes etc.)
2. The analysis of the variety of aortic dilations as risk factors in the complications of CAo in children found that the dilatation of the ascending aorta is on the first place, which usually has a tubular dilation (47.2%); on the second place is the dilation of the descending aorta (33.6%), in 10 (11.2%) cases, there were dilations in the diameters of the aortic valve ring (11.2%), the transverse aortic arch (11.2%) and the Valsalva sinus (8.0%).

CONFLICT OF INTERESTS

The authors do not declare any conflict of interest.

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