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Aortic Root Dilatation in Children and Adolescents at Al-Hawary General Hospital, and National Benghazi Cardiac Center -Libya

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Abstract: Isolated dilatation of the aortic root and/or ascending aorta is a rare but well-known cardiovascular manifestation, can be caused by a variety of congenital or acquired conditions; that lead to the weakening of the aortic wall. The study aimed to detect the cause and the rate of the aortic root dilatation in children and adolescents, and to assess the effect of the Beta-adrenergic blockers in preventing further dilatation in the aortic root. A case series study was perform with five years of follow-up at Al-Hawary General Hospital, National Benghazi Cardiac Center. A total of 91 patients were seen with ascending aortic dilatation and/or root dilatation during the period from 6/2016 - 6/2021 included in the study diagnosed by clinical examination, chest x-ray, and echocardiogram. The diagnosis in 34/91(37%) was Tetralogy of fallout (TOF) and truncus arteriosus, 57/91 (63%) was dilated aortic root, 25/57 (44%) bicuspid aortic valve (BAV), 22/57 (38.5%) Marfan syndrome, 4/57(7%) Noonan syndrome, 2/57(3.5%) Turner syndrome, 3/57(5%) Ehlers-Danlos syndrome, 1/57(2%) idiopathic**.** Follow-up results of three months – five years**:** 57/91 patients with aortic root dilatation were followed up, none of the Marfan syndrome and Ehlers-Danlos syndrome patients who received beta-blockers had shown progression in the dilatation of the aortic root, and all patients who had bicuspid aortic valve did not show any progression in the dilatation without using medication. Conclusions: Dilated aortic root is a common finding in Marfan syndrome, bicuspid aortic root, and Ehlers-Danlos syndrome, and its progress could be decreased by using beta-adrenergic blockers in rapidly progressing dilation.

Keywords: Aortic dilatation, Congenital heart disease, Marfan Syndrome, Bicuspid aortic valve.

INTRODUCTION

Isolated dilatation of the aortic root and/or ascending aorta is a rare, but well-known cardiovascular manifestation, which is usually encountered in patients with underlying connective tissue diseases (e.g. Marfan syndrome, Ehlers–Danlos and Turner syndrome) (Gott et al., 1999; Lin et al., 1998; Massih et al., 2002; Pfammatter et al., 2001). The dilatation of the aortic root may lead to secondary aortic valve regurgitation and expose the patients to the risk of acute aortic dissection or rupture. Pediatric patients rarely present with primary aortic valve regurgitation; in this case, the main mechanism of valve regurgitation is dilatation of the aortic root, of the aortic annulus, or spreading of the commissures at the sino-tubular level (Bonderman et al., 1999; Roman et al., 1987). Another small group of patients may suffer from dilatation of the supracoronary ascending aorta, with or without the presence of a bicuspid aortic valve. Bicuspid aortic valve (BAV) is associated with aortic root dilation and dissection in adults, but the age and conditions when dilation begins are unknown Patients with bicuspid aortic valve (BAV) have a higher risk of developing aortic valve dys-

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function and progressive proximal aorta dilatation, which can lead to aortic dissection. To this day, the identification of children at risk of developing severe aortic dilatation during their pediatric follow-up is still challenging because most studies were restricted to adult subjects (Blais et al., 2020).

If morphology of the aortic valve leaflets is normal, aortic root repair includes complete excision of the pathological aortic tissue with preservation of the normal aortic valve, either by reimplantation into a prosthetic graft or by remodeling the aortic root (Birks et al., 1999; David et al., 1995). Preservation of the native valve may have several advantages: excellent hemodynamic characteristics, avoidance of oral anticoagulation, and some growth potential in younger patients. However, controversy still exists regarding the durability of aortic valve-sparing procedures especially in the context of Marfan syndrome, in which the fibrillin defect involves not only the aortic wall but also the aortic valve leaflets as well (Cameron et al., 1996). Pediatric and adolescent patients presenting with aortic root dilatation with or without aortic valve regurgitation or isolated supracoronary dilatation of the ascending aorta usually demonstrate a progression of their disease (Bonderman et al., 1999; Roman et al., 1987). Beneficial effects of beta-adrenergic blockers have been demonstrated in some subsets of patients (Shores et al., 1994). Repair or replacement of the aortic root has been recognized as an established prophylactic procedure, which prevents aortic dissection and rupture, as well as the development of severe aortic valve regurgitation (Coady et al., 1997).

The timing of surgery is crucial in these patients. While difficult to determine in some patients, it is related to the aortic diameter, the rate of progression of the dilatation, and the function of the aortic valve.

Aortic root diameter in excess of 50 mm, should be considered for elective composite graft repair of the aorta (Cameron et al., 1996; Coady et al., 1997; Yacoub et al., 1998).

Aim of the study: To detect the cause of aortic root dilatation in children and adolescence. To determine the rate of progression of aortic dilatation in these patients. To assess the effect of the Beta-adrenergic blockers in preventing further dilatation in the aortic root.

MATERIALS AND METHODS

This is a case series study of children with dilated aortic root, with five years follow-up.
A total of 91 patients seen with aortic dilatation ascending and/or root dilatation followed at the National Benghazi Cardiac center and General Al Hawary Hospital during the period from 6/2016 to 6/2021 were included in the study. All patients' names, ages, gender were registered and all patients were examined and diagnosed by clinical examination, to find any dysmorphic features, in addition to chest x-ray, ECG, and Echocardiography: we performed a transthoracic echocardiogram during routine medical follow-ups. Proximal aorta diameters were measured in the parasternal long-axis. We used echo machines: Philips IE 33, Vivid 3, Vivid 5, Vivid 7, and Vivid 9, and GE 59.

We measured the diameters of the aortic root, annulus, and sinotubular junction. The aortic root was considered dilated when the diameter was > the Z score diameter according to the weight and height of the patients. These *Z* score equations were developed in a population of children with normal hearts and have been validated against a separate population of healthy children.

Follow-up methods: Six months to five years follow-up. All patients were evaluated in the cardiac clinic with aortic root dilatation. Aortic dimensions were measured by echocardiography and patients were followed up with annual physical and echocardiog-

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raphy examinations to detect any change in aortic diameter over the subsequent five years.

RESULTS

A total of 91 patients had dilated aorta. 34/91(37%) patients with dilated ascending aorta 31/34 patients had Tetralogy of fallout (TOF), and 3/34 patients had Truncus arteriosus.

57/91(63%) patients had a dilated aortic root. Their Gender was 30 Males, 27 Females. The ratio was almost the same. 25/57(44%) had bicuspid aortic valve (BAV), their age ranged from 9 months to 15 years. 22/57(38.5%) had Marfan syndrome, and their age ranged from 2 to 24 years. 4/57 (7%) had Noonan syndrome, their age ranged from 3 to 10 years. 2/57(3.5%) had Turner syndrome, their age was five years and seven years. 3/57(5%) had Ehlers-Danlos syndrome, their age was 3, 5, and 7 years. 1/57(2%) had idiopathic aortic root dilatation, and the age of the patient was 4 years, discovered by accidental finding by chest x-ray due to chest infection. Figure 1).

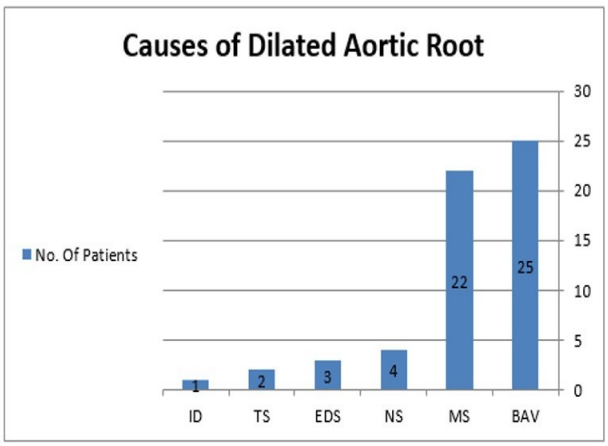

Figure (1): Distribution of the studied Aotric dilatation according to etiology.

BAV: bicuspid aortic valve, MS: Marfan syndrome, NS: Noonan Syndrome, EDS: Ehlers-Danlos syndrome, TS: Turner Syndrome, ID:Idiopathic

Medical treatment:
Most of the patients of Marfan syndrome received Beta- bloker drugs, only 2 patients not received the drug and they had rapidly progression in dilatation, and all patients with Ehlers-Danlos Syndrome received medical treatment as show in table (1)

Table (1) below illustrates the number of patients who received beta-blockers and their diagnosis.

Name of the disease with dilated aortic root	Number of patients received Beta-blocker	Percentage
Marfan syndrome	20/22	91%
Ehlers-Danlos	3/3	100%
Bicuspid Aortic valve	1/25	4%
Noonan syndrome	1/4	25%
Turner syndrome	0/2	0%
Idiopathic	0/1	0%

Follow-up results: We excluded 34 patients who had TOF and truncus arteriosus from follow-up.
We performed five years follow-up of 57 patients with dilated aortic root.

25/57 patients had bicuspid aortic valve and aortic root dilatation:
3/25 patients without aortic stenosis.
8/25 patients with mild aortic stenosis.
6/25 patients with moderate aortic stenosis.
6/25 patients with severe aortic stenosis.
Five patients operated on: Two patients with valve replacement, one with Ross operation, and two patients with transcatheter aortic ballooning valvuloplasty. Only 2 patients with bicuspid aortic valves had mild aortic regurgitation.

Associated lesions with bicuspid aortic valve: Four patients with coarctation of aorta (COA)

One patient with subaortic membrane One patient with post-COVID Kawasaki disease and had dilated coronary artery (Table 2).

Only one patient with BAV received a beta-blocker due to associated supraventricular

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tachycardia.None of the patients with BAV had any progression in aortic root dilatation during these five years of follow-up, and no surgical graft replacement of the aortic root had been performed in these patients.

Table: (2) Associated lesions with bicuspid aortic valve (BAV)

Number of patients with BAV	Associated lesions
3	No AS
8	Mild AS
6	Moderate AS
6	Sever As
2	Mild AR
4	COA
1	SAM
1	Post-COVID 19 Kawasaki with dilated coronary

AS: aortic valve stenosis, AR: aortic valve regurgitation, COA: coarctation of aorta, SAM: subaortic membrane

Marfan syndrome patients were 22/57: The majority of patients were asymptomatic. All patients had associated mitral valve prolapse. 20/22 of Marfan syndrome patients received beta-blockers, and two of them had an Ace inhibitor added. 2/22 who did not receive a beta-adrenergic blocker had shown rapid progression one of them the aortic root dilatation progressed to 4.3 cm in diameter. The age of this patient was 17 years, and the second patient was 24 years old with an aortic root dilatation that progressed to 4.0 cm.

In Marfan syndrome: the patients who received beta-blockers had no progression in the dilatation of the aortic root according to Z score while the patients who did not receive a beta-blocker showed progression in the dilatation of the aortic root. No patients with Marfan syndrome had surgical graft replacement of the aortic root during these five years of follow-up.

Also, no patients with Noonan, Turner, Ehlers-Danlos syndromes, and the idiopathic root dilatation had surgical graft replacement of the aortic root during these five years of follow-up. All patients with Ehlers-Danlos syndrome had received beta-adrenergic blockers and had not shown any progression in the dilatation of the aortic root

DISCUSSION

Dilatation of the aorta is a common complication of Marfan syndrome and may manifest at an early age. Furthermore, aortic dilatation can progress rapidly (Gott et al., 1999; Harringer et al., 1999; Lin et al., 1998; Massih et al., 2002; Pfammatter et al., 2001; Roman et al., 1987; Yacoub et al., 1998).

Although pediatric and adolescent patients presenting with aortic root dilatation with or without aortic valve regurgitation or isolated supracoronary dilatation of the ascending aorta usually demonstrate a progression of their disease [5,6]. In the current study, the patients who received beta-adrenergic blockers did not show any progression in the dilatation of the aortic root. Beneficial effects of beta-adrenergic blockers have been demonstrated in some subsets of patients. In the current study, there is evidence that beta-blockade therapy can slow down the rate of dilatation of the aorta and has clinical benefits on children and adolescents with Marfan syndrome (Shores et al., 1994; Tierney et al., 2007).

In this study, the results showed an overall very slow and clinically insignificant proximal aorta *Z* score progression over time during childhood in bicuspid aortic valve (BAV) with or without correction of the presence of Aortic valve dysfunction (Blais et al., 2020).

The progression of the dilatation of aortic root in Marfan syndrome patients who didn't receive Beta-adrenergic blockers, and the absence of progression in dilatation in aortic root in other causes without receiving beta-blocker medication could question the benefit and the rule of this drug in preventing the progressive dilatation of the aortic root**.** (Tierney et al., 2007)could be explained by

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the rapid progression of the aortic root dilatation that only happens in Marfan syndrome and Ehlers-Danlos syndrome and not in bicuspid aortic valve in children (Bonderman et al., 1999; Gao et al., 2011; Gidding, 2011; Gott et al., 1999; Kouchoukos & Dougenis, 1997; Massih et al., 2002; Miller, 2003; Pfammatter et al., 2001; Roman et al., 1987; Wenstrup et al., 2000; Wenstrup et al., 2002).

2-dimensional echocardiography is a useful for the diagnosis and follow-up of aortic root dilatation and aneurysms in children. There is a strong association between mitral valve prolapse and dilated aortic root in Marfan syndrome. In this study, similar associations were found (Boudoulas et al., 2020; Knadler et al., 2019; Rybczynski et al., 2011).

CONCLUSION

Aortic root dilatation is a common finding in Marfan syndrome, and Ehlers-Danlos syndrome and is also frequently seen in bicuspid aortic valve. The progression of the dilatation of the aortic root was rapid in Marfan syndrome patients without medical treatment.
The beneficial effects of beta-adrenergic blockers were demonstrated in this study, and this is show the role of this medication in preventing the rapid progression of aortic root dilatation. However, further clinical trial studies are required to prove this role.

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اتساع جذر الشريان الابهر لدى الاطفال والمراهقين في مستشفى الهواري العام ومركز بنغازي الوطني للقلب – ليبيا

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المستخلص: توسع جذر الشريان الابهر هو أحد مشاكل القلب والأوعية الدموية النادرة ولكن المعروفة، ويمكن أن ينتج عن مجموعة متنوعة من الحالات الخلقية أو المكتسبة التي تؤدي إلى إضعاف جدار الأبهر. أجريت هذه الدراسة لمعرفة أسباب ومعدل اتساع جذر الشريان الأبهر عند الأطفال والمراهقين وتأثير الدواء في منع تفاقم هذا الاتساع. اجريت الدراسة على 91 طفل ومراهق لديهم توسع في الأبهر الصاعد أو اتساع جذر الشريان الأبهر الذين يتابعون عيادات التشوهات الخلقية في المركز الوطني للقلب ومستشفى الهواري العام وقد تم تشخيصهم باستخدام صورة الأشعة للصدر وتخطيط صدى القلب في الفترة ما بين - 6/2016 6/2021 وكانت الأسباب هي: 91/34 (37%) منهم بسبب رباعي الفالوت والجذع الشرياني المستديم وكان عدد 91/57 (63%) لديهم اتساع في جذر الشريان الاورطي وكان 57/25 (44%) لديهم الصمام الأبهري ثنائي الشُرف، 57/22 (38.5%) لديهم متلازم المارفن ، 57/4 (7%) متلازم النونان، 57/2 (3.5%) متلازم الترنر، 57/3 (5%) متلازم اهلر دانلوس، 57/1 (2%) كان التوسع مجهول السبب. تم متابعة 57 حالة توسع الجذر في مدة ما بين 3 أشهر إلى 5 سنوات وقد وجد أن لا أحد من مرضى المتلازم المارفن ولا الاهلر دانلوس زاد التوسع بعد استخدام العلاج وكذلك لم يزد التوسع في مرضى لديهم الصمام الأبهري ثنائي الشُرف بدون استعمال الدواء. تم التوصل إلى أن توسع الشريان الأبهر هو حالة شائعة في متلازمة المارفان والصمام الأبهري ثنائي الشرف ومتلازمة الاهلر دانلوس، ومن الممكن منع تفاقم الحالة باستخدام الدواء في الحالات التي يتسع فيها الشريان الأبهر بسرعة.

الكلمات المفتاحية: اتساع الشريان الأبهر، التشوهات الخلقية للقلب، متلازم المارفن، صمام الأبهر الثنائي الشُرف.

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