Effects of Aging on Aortic Diameters and Distensibility in Marfan's Syndrome: Comparison With Healthy Subjects

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Abstract

The relationships between age, aortic diameter, and aortic distensibility were examined in patients with Marfan's syndrome. Aortic diameters were measured at the sinus of Valsalva, the ascending aorta, the aortic arch, and the abdominal aorta in 20 patients (aged 5–63 years) with Marfan's syndrome and 30 age-matched normal control subjects. The aortic distensibility was calculated as follows: aortic distensibility = 2 (change in aortic diameter) / (diastolic aortic diameter) (systolic pressure − diastolic pressure).

Aortic diameter increased with age in both groups. The diameters of the sinus of Valsalva and the ascending aorta were greater in the Marfan group than in the control group, and increased even after adolescence in patients with Marfan's syndrome. Aortic distensibility was the highest at the abdominal aorta and the lowest at the sinus of Valsalva in both groups. Aortic distensibility decreased with age in both groups, but aortas were less distensible in the Marfan group than in the control group at all ages.

The sinus of Valsalva and the ascending aorta dilate abnormally after adolescence in patients with Marfan's syndrome. However, aortic elastic properties in patients with Marfan's syndrome were abnormal even in childhood.

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Key Words
■ Aorta (distensibility) ■ Aortic diseases (Marfan's syndrome)
■ Echocardiography

INTRODUCTION

Marfan's syndrome is an inherited connective-tissue disorder with major manifestations in the ocular, skeletal, and cardiovascular systems. It is well known that the aortic dimensions in patients with Marfan's syndrome are greater than those in normal subjects[1–4]. Although most researchers emphasize that aortic dilation might progress gradually over many years[1], no study has addressed this matter specifically. Studies were recently conducted by echocardiography to detect the abnormal elastic properties of the aorta[5–9]. Some of these studies reported decreased aortic distensibility and an increased aortic stiffness in patients with Marfan's syndrome[8–10]. However, there have been few reports about the aortic elastic properties in children with Marfan's syndrome[9,10].

This study examines the relationships between age, aortic diameter, and aortic elastic properties in patients with Marfan's syndrome.

MATERIALS AND METHODS

Patients with a history of aortic surgery were excluded from the study. Twenty patients aged from 5 to 63 years who met the diagnostic criteria for Marfan's syndrome[11] were included in this study. Color Doppler echocardiography showed mild aortic regurgitation in 2 patients and mild mitral regurgitation in 4. Thirty age-matched normal control subjects were also studied. All subjects voluntarily underwent echocardiographic examina-

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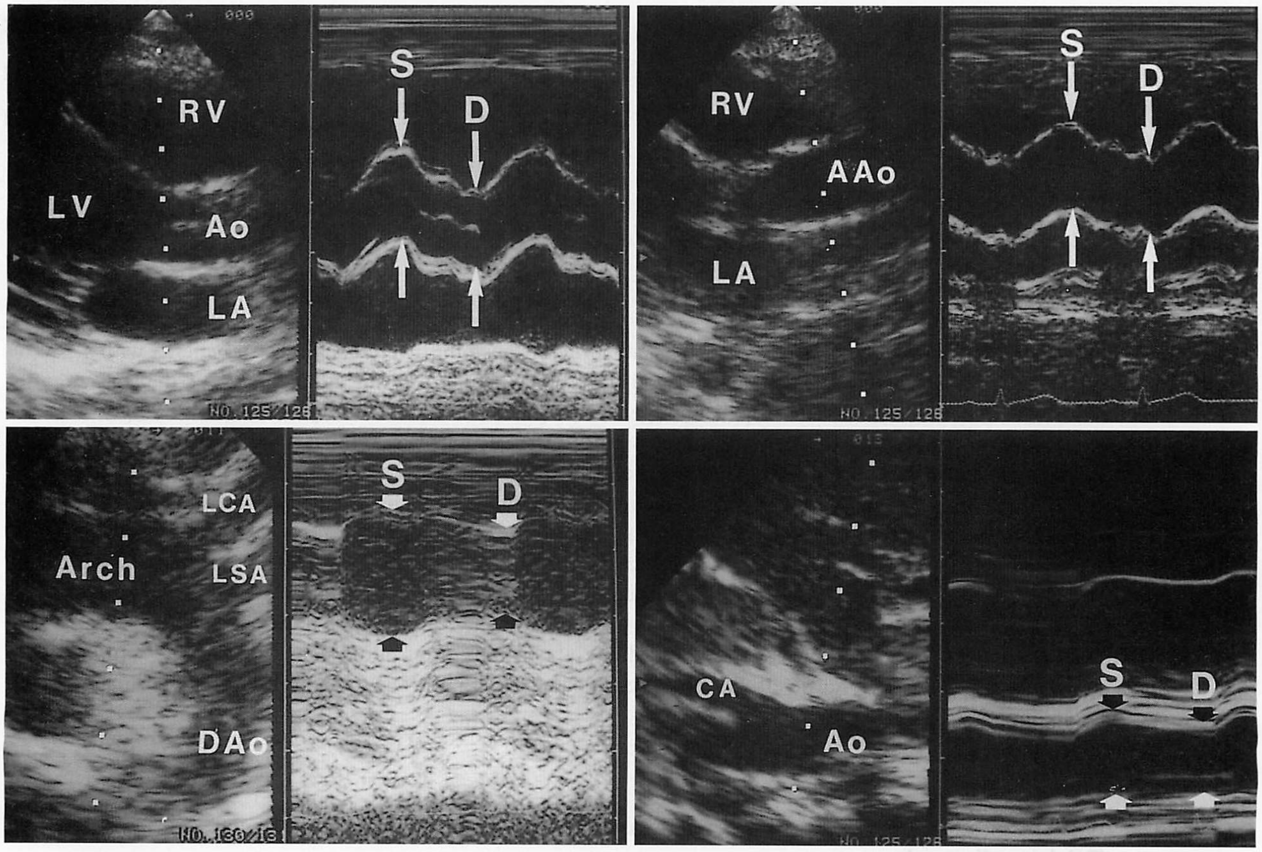

Fig. 1 Measurement of the aortic diameters at the sinus of Valsalva (*A*), ascending aorta (*B*), aortic arch (*C*), and abdominal aorta (*D*).
RV = right ventricle; LV = left ventricle; Ao = aorta; LA = left atrium; S = point of systolic measurement of aortic diameter; D = point of diastolic measurement of aortic diameter; AAo = ascending aorta; LCA = left common carotid artery; Arch = aortic arch; LSA = left subclavian artery; DAo = descending aorta; CA = celiac artery.

tion after informed consent was obtained. The subjects in the Marfan and control groups were divided into 2 groups by age: over 20 years and under 20 years. There was no subject aged 20 years.

After routine conventional echocardiographic examination, two-dimensional guided M-mode tracing was recorded at the center of the sinus of Valsalva, the ascending aorta (2 cm from the peripheral end of the sinus of Valsalva), the aortic arch (just before the branched left common carotid artery), and the abdominal aorta (just before the branched celiac artery) (**Fig. 1**). Systolic and diastolic diameters were measured at each part of the aorta. The diastolic diameter was measured at the peak of the QRS complex on the simultaneously recorded electrocardiogram, and the systolic diameter was measured at the point of maximal anterior motion of the aorta or at the end of the T wave on the electrocardiogram. The means of 5 measurements in sequential cardiac cycles were used for data analysis. Blood pressure was measured at the brachial artery by sphygmomanometry with the patient supine.

The ratio of aortic diameter to body height was calculated. Aortic distensibility was also calculated using the following formula:

Aortic distensibility = 2 (change in aortic diameter) / (diastolic aortic diameter) (systolic pressure − diastolic pressure).

Values were expressed as mean values ± standard deviation (SD). The Mann-Whitney *U*-test and regression analysis were used where appropriate for statistical evaluation. A p value less than 0.05 was considered statistically significant.

Table 1 Characteristics of the Marfan patients and control subjects under and over 20 years old

	Under 20 years old			Over 20 years old		
	Marfan's syndrome group ($n=12$)	Control group ($n=14$)	p value	Marfan's syndrome group ($n=8$)	Control group ($n=16$)	p value
Age (yr)	12±3	11±4	NS	43±13	39±14	NS
Body weight (kg)	48.5±16.6	44.5±20.0	NS	68.6±4.2	65.6±5.8	NS
Body height (cm)	169.4±25.9	149.2±24.2	<0.05	183.6±8.7	170.2±5.5	<0.005
Body surface area (m^2)	1.52±0.38	1.34±0.41	NS	1.88±0.12	1.78±0.10	NS

Values are mean±SD.

Table 2 Aortic diameters and distensibilities in Marfan patients and control subjects under and over 20 years old

	Under 20 years old			Over 20 years old		
	Marfan's syndrome group ($n=12$)	Control group ($n=14$)	p value	Marfan's syndrome group ($n=8$)	Control group ($n=16$)	p value
Diameter (cm)						
Sinus of Valsalva	2.58±0.44	2.12±0.37	<0.05	3.62±0.58	2.60±0.21	<0.0005
Ascending aorta	2.21±0.39	1.89±0.29	<0.05	3.33±0.46	2.33±0.21	<0.0005
Aortic arch	1.90±0.27	1.83±0.34	NS	2.73±0.30	2.32±0.18	<0.005
Abdominal aorta	1.32±0.24	1.18±0.27	NS	1.63±0.16	1.45±0.14	<0.05
Diameter/height $\times 10^{-2}$						
Sinus of Valsalva	1.54±0.22	1.42±0.14	NS	1.99±0.39	1.52±0.09	<0.0005
Ascending aorta	1.30±0.22	1.28±0.12	NS	1.82±0.31	1.37±0.11	<0.0005
Aortic arch	1.13±0.12	1.23±0.12	NS	1.44±0.20	1.36±0.09	NS
Abdominal aorta	0.77±0.05	0.79±0.09	NS	0.89±0.10	0.85±0.08	NS
Distensibility ($cm^2 \cdot dyn^{-1} \cdot 10^{-6}$)						
Sinus of Valsalva	1.34±0.71	2.69±0.99	<0.005	1.24±0.36	2.06±0.76	<0.01
Ascending aorta	2.34±0.78	4.09±0.84	<0.0005	1.61±0.55	3.13±0.77	<0.0005
Aortic arch	3.71±1.09	2.79±1.67	<0.05	1.49±0.72	3.47±1.81	<0.0005
Abdominal aorta	4.30±1.46	8.09±3.27	<0.005	2.11±1.05	4.68±1.73	<0.005

Values are mean±SD.

RESULTS

The demographic characteristics of the control and Marfan patient groups are compared in **Table 1**. There was no difference in age between the groups, but the patients in the Marfan group were taller than the controls.

The end-diastolic diameters of the sinus of Valsalva and the ascending aorta were greater in the Marfan group than in the control group (**Table 2, Fig. 2**). The significance of the difference was greater in the subjects more than 20 years old than in the subjects less than 20 years old. The diameters of the aortic arch and the abdominal aorta were greater in the Marfan patients than in the control subjects more than 20 years old.

In the control group under 20 years old, a correlation was found between age and the diameters of the sinus of Valsalva ($r=0.86$), the ascending aorta ($r=0.88$), the aortic arch ($r=0.83$), and the abdominal aorta ($r=0.84$). No correlation was found between age and the aortic diameters in control subjects over 20 years old. In the Marfan patients under 20 years old, a correlation was found between age and the diameters of the aortic arch ($r=0.59$), the abdominal aorta ($r=0.83$), but not the sinus of Valsalva and the ascending aorta. In contrast, in patients over 20 years old, a correlation was found between age and the diameters of the sinus of Valsalva ($r=0.71$) and the ascending aorta

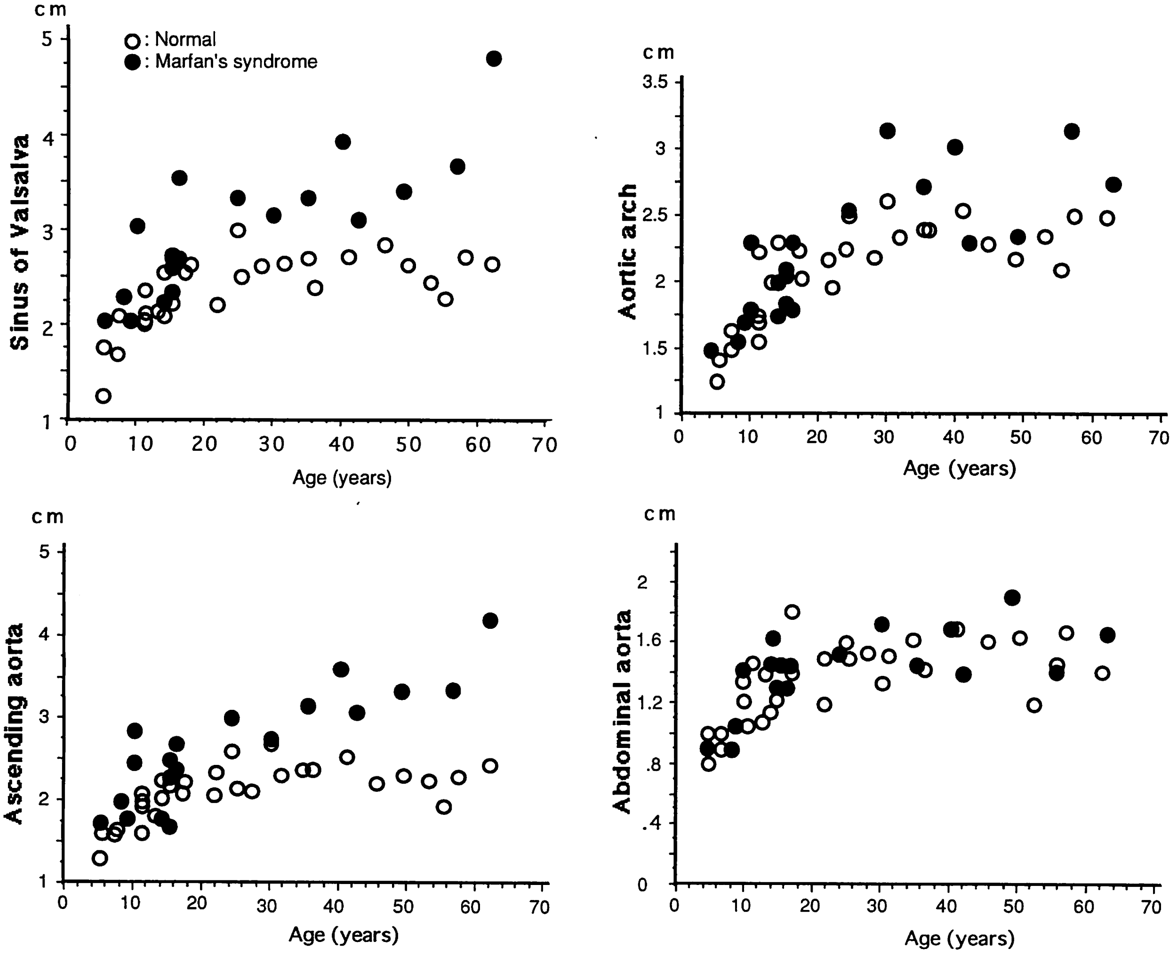

Fig. 2 Relationships between age and aortic diameters in normal control subjects and patients with Marfan's syndrome

$(r = 0.79)$.

The ratios of aortic diameter to body height were not different in the Marfan patients and control subjects under 20 years old (**Table 2**). The ratios at the sinus of Valsalva and at the ascending aorta were greater in the Marfan patients than in the controls over 20 years old.

The ratios in the control subjects were constant at all ages (**Fig. 3**). There was a correlation between age and the ratios at the sinus of Valsalva $(r = 0.75)$ and at the ascending aorta $(r = 0.82)$ in Marfan patients over 20 years old.

In both groups, aortic distensibility decreased with age (**Fig. 4**), and was the lowest at the sinus of Valsalva and increased distally. Aortic distensibility in the Marfan patients was less than that in the control subjects at all ages (**Table 2, Figs. 4, 5**).

DISCUSSION

The age range of the subjects in this study was very wide. Therefore, we divided the subjects into 2 groups, under 20 years old (during growth) and over 20 years old (after growth).

In this study, the aortic diameters were greater in the Marfan group than in the controls. However, the Marfan patients were taller than the control subjects. The aortic dimension should therefore be expressed in both the Marfan and normal patients as a function of height.

Body height is a useful, alternative means of standardization. Aortic dimension correlates closely with age, height, weight, and body surface area, but height is the best independent predictor and has a linear relationship to aortic root dimension[12]. Another large study of normal aortic annular, left

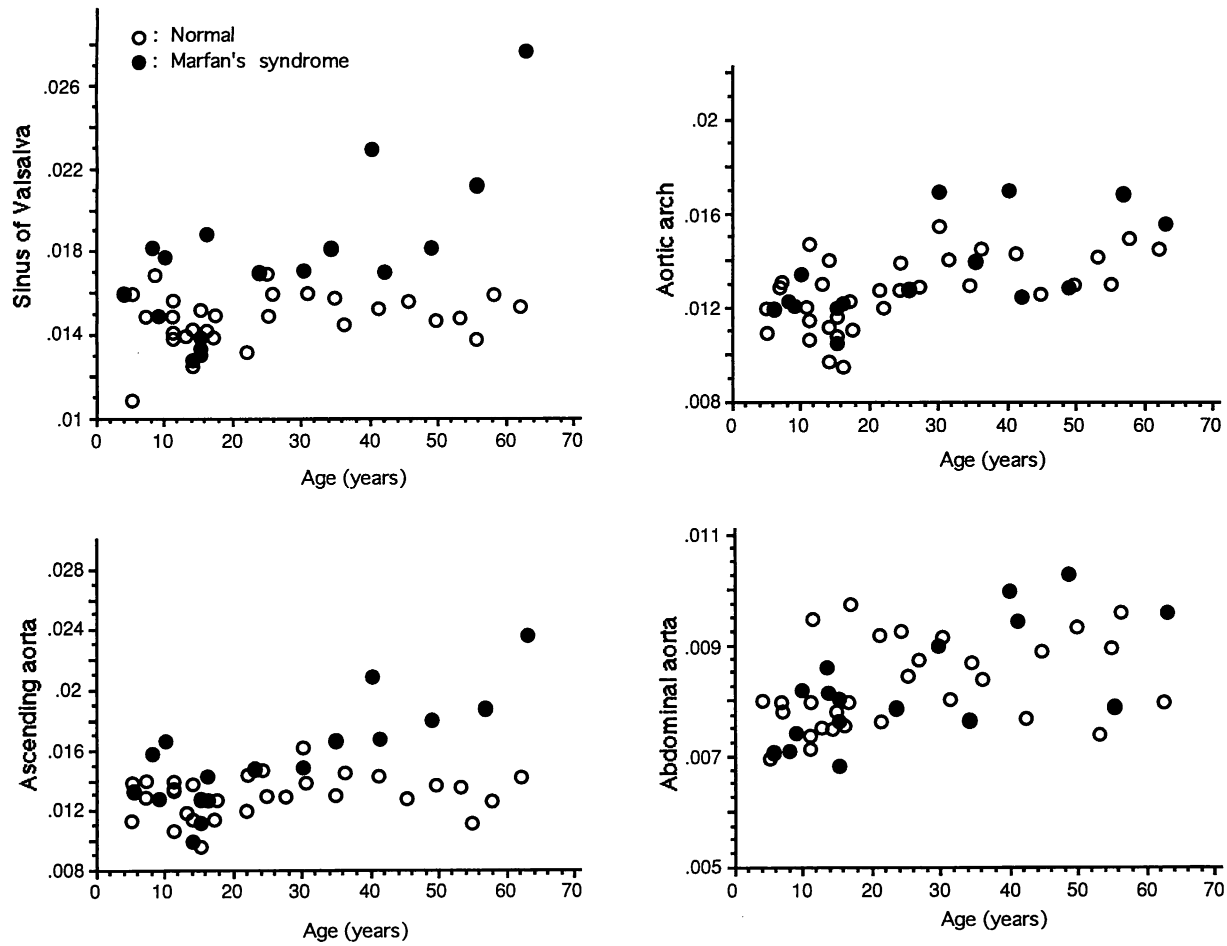

Fig. 3 Relationships between age and the ratio of aortic diameters to body height in normal control subjects and patients with Marfan's syndrome

atrial, and left ventricular end-diastolic dimensions found a striking linear relationship of all 3 dimensions to height, suggesting that cardiac dimensions increase primarily in response to skeletal growth[13]. Height is probably a better indicator than body surface area because the latter is a changeable condition and as such will be counteracted by the very lean body tendencies of the Marfan individual.

The greater initial aortic root dimension and the more rapid rate of aortic dilation cause risks of aortic complication such as death or surgery on the ascending aorta[14]. This study demonstrates that diameters of the sinus of Valsalva and the ascending aorta in patients with Marfan's syndrome increased even after adolescence, when the aortic diameters in normal subjects are constant. This means that the risk of an aortic complication increases with age after adolescence.

A substantial proportion of Marfan patients die of aortic dissection with an aortic root dimension in the 50- to 60-mm range[15]. However, the diameters of aortic roots in all of the patients in this study were under 50 mm and none had undergone surgery for ascending aortic dissection or aneurysm. The patients in this study were thought to be in a low risk subgroup of patients with Marfan's syndrome, and consequently the results of this study do not reflect the natural course of Marfan's syndrome, as the rate of aortic root dilation should be generally more rapid.

The aorta becomes stiffer with age[16,17]. The elastin laminae in the tunica media are considered to be the basal structural elements bearing the pulsatile load of ventricular ejection[18,19]. With aging, fragmentation of the elastin laminae occurs[20], and a greater load is then placed on the stiffer collagen fibers. This study also showed that aortic elasticity decreased with age in both normal subjects and

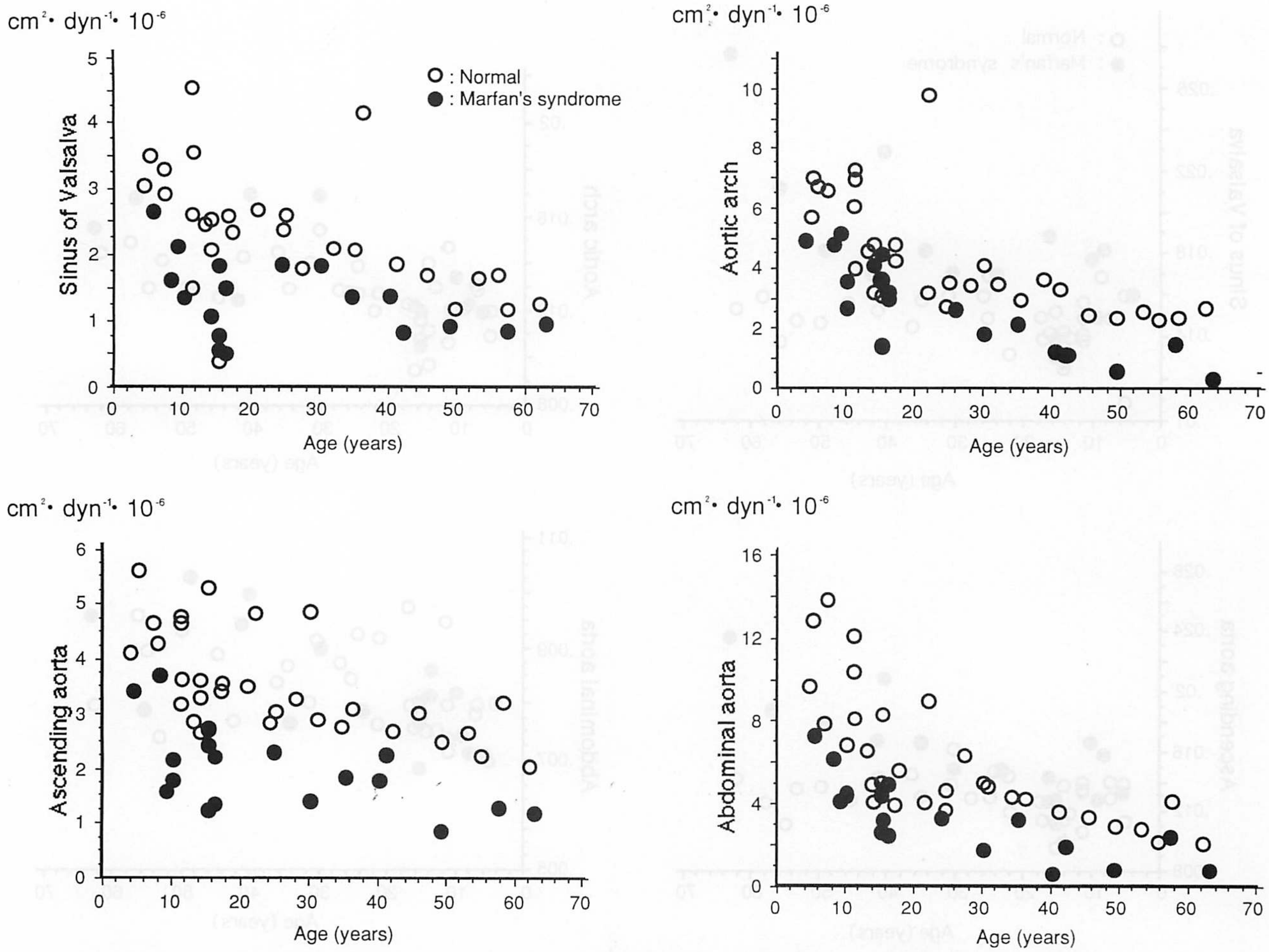

Fig. 4 Relationships between age and aortic distensibility in normal control subjects and patients with Marfan's syndrome

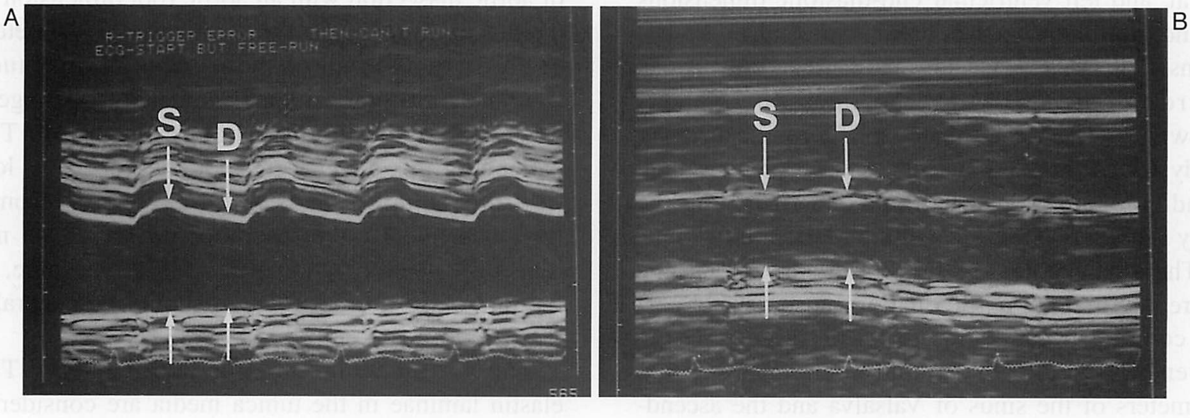

Fig. 5 M-mode echograms of the abdominal aorta in a 13-year-old normal girl (*A*) and a 15-year-old girl with Marfan's syndrome (*B*)

The change of the aortic diameter between systole and diastole was very small in the patient with Marfan's syndrome, indicating decreased elasticity of the aortic wall.
Abbreviations as in Fig. 1.

patients with Marfan's syndrome.

There is currently very little information about the elasticity of different parts of the aorta. This study demonstrated that aortic elasticity increased in proportion to distance from the heart. This characteristic was recognized in both the controls and patients with Marfan's syndrome at all ages.

Vascular pathology in Marfan's syndrome is caused by defective synthesis, secretion, and extracellular matrix formation of the fibrillin protein, which is widely distributed in elastic tissues[21]. This study demonstrated that aortic distensibility in patients with Marfan's syndrome was less than that of normal subjects at all ages, as reported by Jeremy *et al.*[10]

In Marfan's syndrome, the sinus of Valsalva and the ascending aorta dilate abnormally after adolescence. Aortic distensibility decreases in all parts of the aorta, even in childhood. In Marfan's syndrome, the aortic root cannot bear the pulsatile load of ventricular ejection and dilates after adolescence, because its elasticity is low.

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要　約

Marfan症候群における大動脈径および伸展性の加齢変化

市橋　光

Marfan症候群では加齢とともに大動脈基部が拡大してくるといわれているが，具体的なデータはわずかである．近年，本症候群の動脈壁の弾性の低下を超音波検査で測定する試みがなされているが，小児期におけるMarfan症候群の動脈壁の弾性についての報告もまた少ない．本研究では，Marfan症候群の大動脈径および動脈の伸展性の加齢変化を超音波検査により検討した．

対象は，5−63歳のMarfan症候群20例である．年齢が同等な健常者30例を対照群とした．超音波検査はBモード断層像を指標として，Mモード法にてValsalva洞中央，上行大動脈，大動脈弓，腹部大動脈の径を計測した．さらに安静時血圧を測定し，以下の式により大動脈伸展性を求めた．

大動脈伸展性＝2(大動脈収縮期径−拡張期径)/(大動脈拡張期径)(拡張期血圧−収縮期血圧)

大動脈径はMarfan症候群患者，健常者ともに加齢とともに増加した．Valsalva洞と上行大動脈の径はMarfan症候群で拡大していたが，思春期以降も増大する特徴があった．大動脈伸展性はMarfan症候群，健常者ともに加齢に従い低下し，Marfan症候群患者でより低値であった．

以上よりMarfan症候群患者では，大動脈基部は思春期以後に拡大するが，動脈壁の弾性の低下はすでに小児期に始まっていることが認められた．

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