Archivos de Cardiología de México

Volumen *Volume* 75 Número *Number* 2 Abril-Junio April-June 2005

Artículo:

Echocardiometric evaluation of cardiovascular abnormalities in Marfan syndrome

INVESTIGACIÓN CLÍNICA

Echocardiometric evaluation of cardiovascular abnormalities in Marfan syndrome

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Summary

Marfan syndrome is an inherited disorder of connective tissue with manifestations in various organ-systems including cardiovascular system. The aim of this study was to characterize and determine the frequency of cardiovascular alterations by echocardiography in 2 age cohorts of Mexican patients with Marfan syndrome and their comparisons with control groups. **Material and methods:** Sixty six with Marfan syndrome and 33 control patients were evaluated by echocardiography. Segments of the aorta and pulmonary artery were measured at different levels, cardiac valves were examined for prolapse and the interatrial septum was assessed for septal aneurysm. Numeric values were corrected for the body surface area and compared with the control group. **Results:** Mean significant values between group I (children) and Group II (adults) were as follows: aortic annulus 16.62 ± 4.57 mm/m^2 *vs* 12.81 ± 1.95 ($p < 0.001$), aortic root 23.30 ± 7.49 mm/m^2 *vs* 18.36 ± 2.97 ($p < 0.001$), sinuses of Valsalva 24.14 ± 7.29 mm/m^2 *vs* 19.84 ± 3.59 ($p < 0.001$), ascending aorta 18.43 ± 5.90 mm/m^2 *vs* 17.02 ± 4.79 ($p < 0.001$), aortic arch 16.12 ± 4.73 mm/m^2 *vs* 14.20 ± 2.68 ($p < 0.001$). Pulmonary valve prolapse was seen in 10/22 (45.5%) *vs* 7/44 (15.9%), $p \leq 0.03$. Interatrial septal aneurysm was found in 3/22 (13.6%) *vs* 20/44 (45.5%), $p \leq 0.03$. There was a significative diference in the presence of atrial septal aneurysm between the adult group and control group ($p < 0.001$). **Conclusions:** The incidence of cardio-

Resumen

VALORACIÓN ECOCARDIOMÉTRICA DE LAS ANOMALÍAS CARDIOVASCULARES EN EL SÍNDROME DE MARFÁN

El síndrome de Marfán es una enfermedad hereditaria del tejido conectivo con manifestaciones en varios órganos incluyendo el sistema cardiovascular. El objetivo del estudio fue caracterizar y determinar la frecuencia de las alteraciones cardiovasculares mediante ecocardiografía en 2 grupos de pacientes mexicanos con síndrome de Marfán en comparación con los grupos controles. **Material y métodos:** Se estudiaron mediante ecocardiografía a 66 pacientes con síndrome de Marfán y 33 pacientes del grupo control. Se midieron los segmentos de la aorta y de la arteria pulmonar a diferentes niveles, se valoró prolapso valvular y presencia de aneurisma del septum interatrial. Los valores numéricos fueron corregidos por área de superficie corporal y comparados con el grupo control. **Resultados:** Los variables con valor significativo entre el grupo I (niños) y el grupo II (adultos) fueron: Anillo aórtico: 16.62 ± 4.57 mm/m^2 *vs* 12.81 ± 1.95 ($p < 0.001$), raíz aórtica 23.30 ± 7.49 mm/m^2 *vs* 18.36 ± 2.97 ($p < 0.001$), senos de Valsalva 24.14 ± 7.29 mm/m^2 *vs* 19.84 ± 3.59 ($p < 0.001$), aorta ascendente 18.43 ± 5.90 mm/m^2 *vs* 17.02 ± 4.79 ($p < 0.001$), arco aórtico 16.12 ± 4.73 mm/m^2 *vs* 14.20 ± 2.68 ($p < 0.001$). Se encontró prolapso valvular pulmonar en 10/22 (45.5%) *vs* 7/44 (15.9%), $p \leq 0.03$. Aneurisma del septum interatrial en 3/22 (13.6%) *vs* 20/44 (45.5%), $p \leq 0.03$. Hubo diferencia significativa para la presen-

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Recibido: 3 de junio 2005
Aceptado: 10 de junio 2005

vascular abnormalities in our series is similar to that in the literature with the exception of the very high incidence of pulmonary valve prolapse *vs* control groups, then it suggests that the clinical manifestations of MFS are strikingly severe in the Mexican population. Also a high incidence of interatrial septal aneurysm (34.9%) in comparison to control groups (18.2%) was found.

cia de aneurisma del septum interatrial entre el grupo de adultos y el grupo control ($p < 0.001$). **Conclusiones:** La incidencia de anormalidades cardiovasculares en nuestra serie es similar a la reportada en la literatura excepto la alta incidencia de prolapso valvular pulmonar en relación al grupo control, lo que sugiere que las manifestaciones clínicas cardiovasculares del síndrome de Marfán son más severas en la población mexicana. Se encontró también una alta incidencia de aneurisma del septum interatrial (34.9%) en comparación al grupo control (18.2%).
(Arch Cardiol Mex 2005; 75: 133-140).

Key words: Marfan syndrome. Echocardiography. Interatrial septal aneurysm. Valve prolapse.
Palabras clave: Síndrome de Marfán. Ecocardiografía. Aneurisma del septum interatrial. Prolapso valvular.

Introduction

Marfan syndrome is one of the most common genetic disorders of connective tissue; it is characterized by skeletal, cardiovascular, and ocular abnormalities. The incidence of the disease is about 1 in 20,000, with life expectancy severely reduced because of cardiovascular problems.[1]

Mutations in the gene encoding the microfibrillar protein fibrillin-1 *(FBN1)* in the locus 15q15-21.1 of the long arm of chromosome 15 are now recognized as the cause of Marfan syndrome.[2-4] The syndrome lacks pathognomonic features; furthermore, it shows striking pleiotropism and clinical variability. Consequently, the physician is forced to reckon on the presence of a combination of clinical, echocardiographic and radiographic abnormalities for their diagnosis and follow-up.

Cardiovascular manifestations occur in 80% of the patients.[5] Significant structural cardiovascular abnormalities occur in the majority of Marfan syndrome patients. In children, mitral valve prolapse and mitral regurgitation are the most common cardiac manifestations, whereas, in the adult population, aortic root dilatation, aortic regurgitation, and aortic dissection predominate. Physical examination, although essential, is often insufficient to assess the severity and extent of cardiovascular abnormalities. Echocardiography is the most important imaging technique for diagnosis and follow-up of the cardiovascular manifestations.[6,7]

The aim of this study was to assess the incidence and nature of endocardic and great vessel abnormalities and to investigate the characteristics of the interatrial septum in 2 age cohorts of Mexican patients with Marfan syndrome compared with 2 control groups.

Material and methods

The study population consisted of 66 consecutive Mexican-mestizo patients with Marfan syndrome, who attended the outpatient Rheumatology clinic. Their Diagnosis was established according to the revised diagnostic criteria for the Marfan syndrome.[8]

Sixty six marfan patients were divided according to age (22 patients less than 16 years and 44 patients greater than 16 years) and compared to 33 age match controls (11 less than 16 years and 22 greater than 16 years). All 33 control patients were normal, paired by sex and age, and came to our institution with suspicions of cardiovascular disease.

Each patient had a complete medical history including cardiovascular clinical evaluation, chest X-ray, electrocardiogram, and echocardiographic examinations. The study protocol was approved by the ethics and medical research committees, and informed consent was obtained in all adult cases. In the group of patients less than 16 years old, parents gave consent.

Echocardiographic examination

All patients underwent transthoracic and/or transesophageal M-mode, two dimensional and Doppler echocardiograms with a Hewlett Packard Sonos 5500. An S3 electronic transthoracic probe and a multiplanar transesophageal probe were used. Mitral, tricuspid, aortic and pulmonary valves were evaluated in parasternal long and short axis and apical 4 chamber images. Left ventricular ejection fraction was calculated from apical 4 and 2 chamber images. Aortic annulus and ascending aorta were assessed in parasternal long axis. The aortic arch and the proximal portion of the descending aorta were assessed from

suprasternal images, and the abdominal aorta was examined in subcostal images. The interatrial septum was evaluated in apical 4 chamber and subcostal views.

Measurements

Detailed measurements of the aortic root were made in two-dimensional parasternal long axis views at three levels: annulus, sinuses of Valsalva and proximal ascending aorta during end-diastole. Aortic arch, descending aorta and abdominal aorta diameters were also measured. Measurements were made perpendicular to the long axis of the aorta using the leading edge technique in views showing the largest aortic diameters. Echocardiographic evaluations of great arteries were based on the internationally accepted maximum measurements.[9,11] Main pulmonary artery dimensions were assessed at two levels: 1) at pulmonary artery bifurcation, and 2) at pulmonary artery root as described by Nollen.[12] All measurements were corrected according to body surface area expressed in mm/m^2. BSA was derived from height (in cm) and weight (in kg) using the following equation.

$$BSA = weight^{0.5378} \times height^{0.3964} \times 0.024265$$

Mitral, tricuspid and aortic valve prolapse was diagnosed by previously established criteria.[13,15] Echocardiographic evidence of mitral valve prolapse corresponded to a posterior mitral displacement of at least 2 mm during late systole or a 3 mm displacement throughout systole on M-mode tracings, which was confirmed by billowing of one or both mitral leaflets superior to the plane of the mitral annulus in two-dimensional parasternal long axis views. Pulmonary valve prolapse was defined as the bowing of one or more leaflets into the right ventricular outlet.

The existence of an Interatrial septal aneurysm was sought. An interatrial septal aneuryms was defined as bulging of the interatrial septum equal to or greater than 0.8 cm into the left or right atrium with a base of 1.0 cm without pulmonary hypertension or other hemodynamic factors that could influence the movement of the interatrial septum.[16,17]

The characteristics of an aortic aneurysm (diameter > 40 mm) or aortic dissection (intimal flap) at any level were assessed using transesophageal technique.

Left atrium diameter and left ventricular end-diastolic and end-systolic diameters and wall thickness was assessed using a long parasternal view and left ventricular function was also evaluated in all patients by ejection fraction calculated by modified Simpson's rule.[18]

Statistical analysis

Qualitative variables are presented as proportions. Quantitative variables are presented as mean and standard deviation. For comparison of groups, when the distribution was normal or Gaussian, Student's t test was used. When the distribution was asymmetric the Mann Whitney non-parametric test or sum of ranges were used. Findings were considered statistically significant when p was ≤ 0.05. The χ^2 hypothesis was applied to the association of qualitative variables with a Yates correction when necessary. Linear correlation and Pearson's "r" regression test were used for the correlation of quantitative variables.

Results

Ninety-nine patients, entered the study, 50 females and 49 males. Ranging in age from 3 to 52 years (mean 23.8 ± 13.29 years). Demographic and anthropometric data are shown in *Table I*. The study population was divided into four groups: Group I) Patients with a mean age of

Table I. Demographic/anthropometric variables.

	Group I n = 22	Control I n = 11	p ≤ value	Group II n = 44	Control II n = 22	p ≤ value
Gender M/F	11/11	6/5	ns	21/23	11/11	ns
Age (years)	10.14 ± 3.44 (3-16)	10.27 ± 3.22 (5-15)	ns	30.48 ± 10.4 (17-52)	30.00 ± 9.81 (17-51)	ns
Height (cm)	151.0 ± 26.0 (88-189)	135.0 ± 18.0 (115-170)	0.05	185.0 ± 9.0 (153-210)	163.0 ± 10.0 (145-180)	0.001
Weight (kg)	37.53 ± 15.66 (15-68)	35.67 ± 15.32 (19-73)	ns	64.19 ± 13.82 (38-113)	67.57 ± 8.79 (49-86)	ns
Body Surface Area (m^2)	1.27 ± 0.37 (0.58-1.92)	1.14 ± 0.31 (0.77-1.84)	ns	1.78 ± 0.21 (1.42-2.50)	1.73 ± 0.15 (1.44-2.03)	ns

Table II. General characteristics.

History	Group I n = 22	Control I n = 11	p ≤ value	Group II N = 44	Control II N = 22	p ≤ value
Family/Genetic History	19 (86.4%)	0 (0%)	0.001	26 (59.1%)	0 (0%)	0.001
Smokers	0 (0%)	0 (0%)	ns	8 (18.2%)	1 (4.6%)	ns
Cerebral Vascular Event	0 (0%)	0 (0%)	ns	5 (11.4%)	0 (0%)	ns
Systemic Hypertension	0 (0%)	0 (0%)	ns	3 (6.8%)	0 (0%)	ns

Table III. Echocardiographic variables corrected for BSA.

(mm/m^2) ± SD	Group I n = 22	Control I n = 11	Values of p <	Group II N = 44	Control II n = 22	Values of p <
Aortic annulus	16.62 ± 4.57	14.25 ± 1.88	0.04	12.81 ± 1.95	10.80 ± 1.17	0.001
Aortic root	23.30 ± 7.49	17.95 ± 3.34	0.008	18.36 ± 2.97	14.84 ± 1.85	0.001
Sinus of Valsalva	24.14 ± 7.29	18.23 ± 2.84	0.002	19.84 ± 3.59	14.96 ± 1.78	0.001
Ascending aorta	18.43 ± 5.91	14.82 ± 2.08	0.016	17.02 ± 4.79	12.41 ± 1.43	0.001
Aortic arch	16.12 ± 4.73	13.77 ± 1.88	ns	14.20 ± 2.69	11.12 ± 1.19	0.001
Descending aorta	13.78 ± 3.90	11.89 ± 1.54	ns	13.26 ± 4.53	9.80 ± 1.33	0.001
Abdominal aorta	10.88 ± 2.57	9.46 ± 1.30	0.043	11.27 ± 4.57	8.19 ± 1.36	0.001
Pulmonary annulus	18.96 ± 5.62	13.70 ± 2.86	0.001	14.25 ± 2.60	10.45 ± 1.32	0.001
Main pulmonary artery	19.83 ± 6.54	15.37 ± 2.61	0.01	14.42 ± 2.19	11.80 ± 1.78	0.001
Left atrium	22.97 ± 5.55	24.83 ± 3.58	ns	19.36 ± 5.88	18.78 ± 3.30	ns
Interventricular septum	6.26 ± 1.88	5.70 ± 1.27	ns	5.33 ± 0.99	4.90 ± 0.69	0.045
LV posterior wall	5.92 ± 1.72	5.27 ± 0.91	ns	5.06 ± 0.78	4.64 ± 0.46	0.008
LV diastolic diameter	34.46 ± 8.22	35.72 ± 6.02	ns	26.92 ± 4.71	25.38 ± 2.81	ns
LV systolic diameter	23.81 ± 7.75	21.55 ± 3.30	ns	17.00 ± 3.47	15.22 ± 1.86	0.01

LV: Left ventricular, SD: Standard deviation, mm/m^2: Millimeters/meter square, BSA: Body surface area.

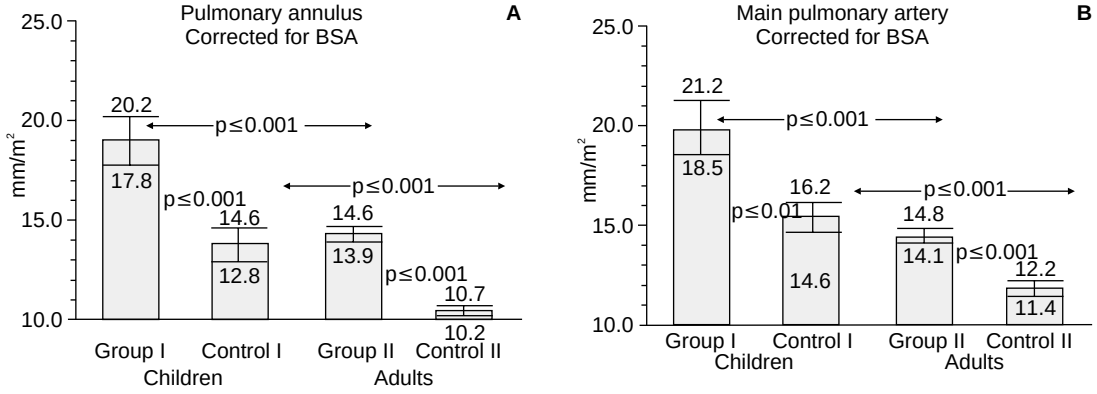

Fig. 1a, b. These graphics show significative differences between studied and control groups related with values corrected to BSA of pulmonary annulus and main pulmonary artery.

10.14 ± 3.44 years, Control I) with a mean age of 10.27 ± 3.22 years, Group II) Patients with a mean age of 30.48 ± 10.4 years and Control II) with a mean age of 30.00 ± 9.81 years.

Nineteen (86.4%) patients in Group I and twenty-six (59.1%) in Group II had positive family and/or genetic history (parent, child, or sibling who meet the MFS diagnostic criteria independently), with a statistically significant difference between both studied groups ($p < 0.02$). In Group II, 8 (18.2%) patients were smokers, 5 (11.4%) had cerebral ischemic events and three (6.8%) systemic hypertension. In the control groups only one case had systemic hypertension *(Table II)*.

Table III shows the echocardiometric variables. Mean significant values corrected by body surface area between Group I and Group II were as follows: aortic annulus 16.62 ± 4.57 mm/m^2 *vs* 12.81 ± 1.95 ($p < 0.001$), aortic root 23.30 ± 7.49 mm/m^2 *vs* 18.36 ± 2.97 ($p < 0.001$), sinuses of Valsalva 24.14 ± 7.29 mm/m^2 *vs* 19.84 ± 3.59 ($p < 0.001$), ascending aorta 18.43 ± 5.90 mm/m^2 *vs* 17.02 ± 4.79 ($p < 0.001$), aortic arch 16.12 ± 4.73 mm/m^2 *vs* 14.20 ± 2.68 ($p < 0.001$).

Aortic dilatation was found in 8 patients from Group I and 15 patients from Group II (36.4%

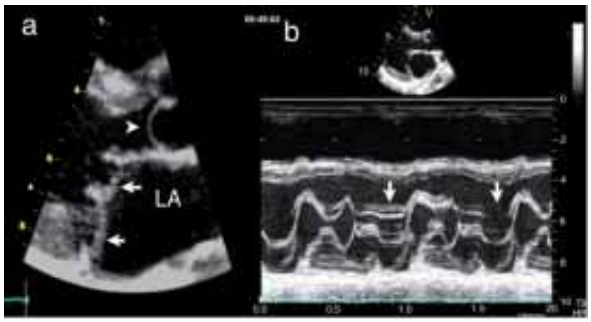

Fig. 2. (a) Two-dimensional parasternal long axis image shows prolapse of both mitral leaflets (arrows) and prolapse of the noncoronary aortic leaflet (head arrow). (b) M-mode echogram at the level of the mitral leaflet during systole shows the image of a hammock (arrows). LA= Left atrium.

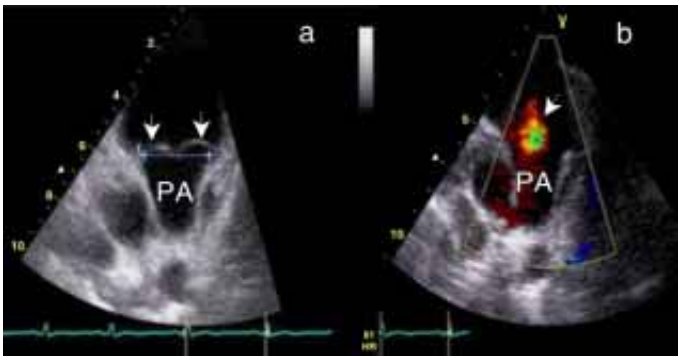

Fig. 5. (a) Two-dimensional parasternal short axis image shows bulging of the pulmonary leaflets toward the right ventricular outlet (head arrows). (b) With color Doppler pulmonary regurgitation is evident (arrow). PA= Pulmonary artery.

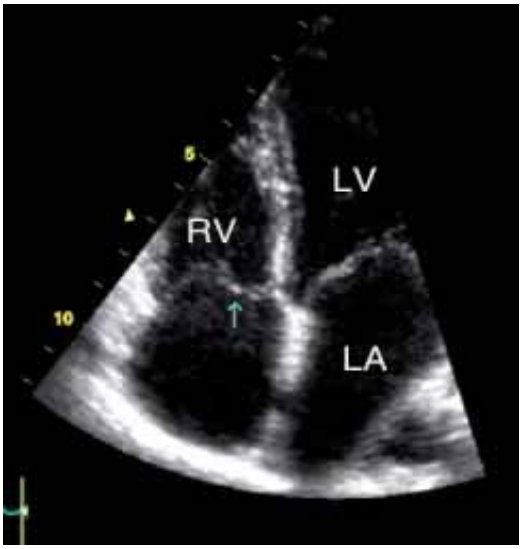

Fig. 3. Arrow points to prolapse of the septal leaflet of the tricuspid on four chamber apical image. LA= Left atrium, LV= Left ventricle, RA= Right atrium, RV= Right ventricle.

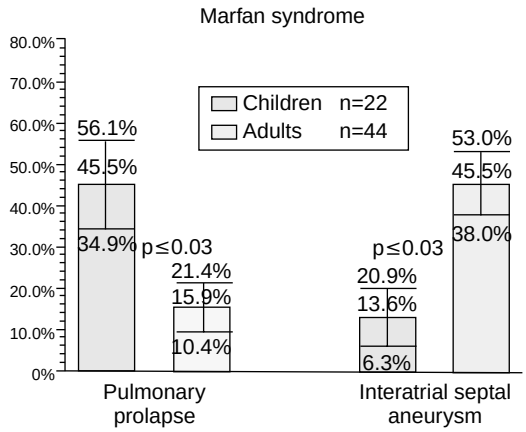

Fig. 6. These graphics show significative differences of pulmonary prolapse and interatrial septal aneurysm between studied groups.

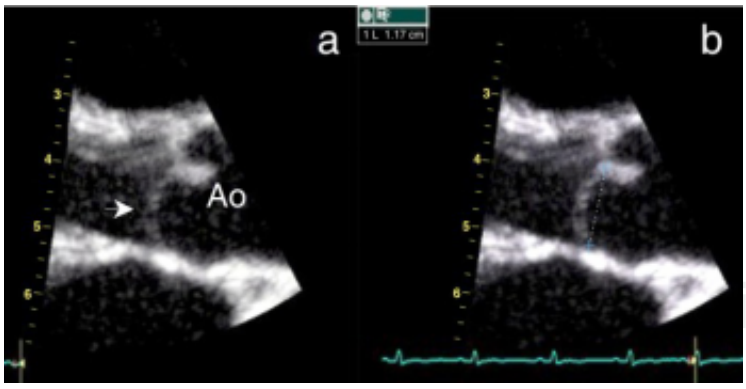

Fig. 4. (a) Parasternal long axis image shows prolapse of the noncoronary leaflet of the aorta (arrow). (b) Displacement of the leaflet toward the left ventricular outlet is seen. Ao= aorta.

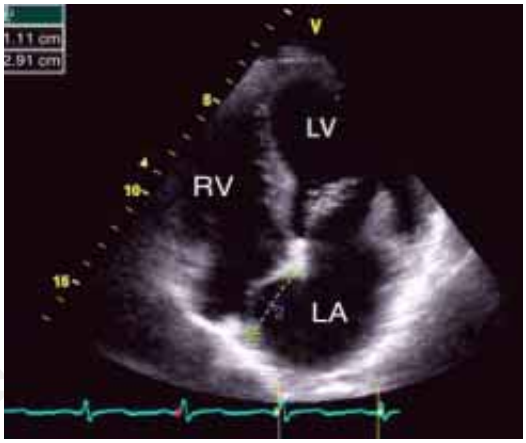

Fig. 7. Apical four chamber image shows IASA bulging to the right. The base is 2.91 cm and the displacement is 1.1 cm. LA= Left atrium, LV= Left ventricle, RV= Right ventricle.

vs 34.1%, p = ns). Five adult patients (11.4%) had aortic dissection.

Dilatation of the pulmonary annulus was found in 47 patients (70%) with associated dilatation of the main pulmonary artery in nine (13.5%) *(Figs. 1a, b)*.

Mitral valve prolapse was found in 21 patients (95.5%) of Group I and in 32 (72.7%) of Group II (p = ns, *Figs. 2a, b*). Tricuspid valve prolapse was detected in 18 (81.8%) patients of Group I and in 26 (59.1%) of those in Group II (p = ns, *Fig. 3*). Aortic valve prolapse was found in 5 patients (22.7%) of Group I and in 5 (11.4%) of Group II (p = ns, *Figs. 4a, b)*. Furthermore, pulmonary valve prolapse was found in 10 patients (45.5%) of Group I and in 7 (15.9%) of Group II (p < 0.03, *Table IV*, *Figs. 5a, b*). In contrast, mitral, tricuspid, aortic and pulmonary valve prolapse was not observed in both control groups (p < 0.001) *(Fig. 6)*.

Forty-two patients (63%) had lesions in two or more heart valves, 15 (22.7%) in a single valve, and in 9 (13.6%) no valve lesion was found.

Interatrial septal aneurysm was found in 23 patients (34.9%). In 12 of these, bulging of the septum was to the right, in 7 towards the left, and in both directions in 4 instances. Three of the patients with interatrial septal aneurysm pertained to Group I (13.6%) *vs* 3 of control I (27.2%) and 20 patients to Group II (45.5%) *vs* 3 of control II (13.6%), *(Fig. 7)*, with a significative difference between these last both (p < 0.001). Interatrial septal aneurysm coexisted with mitral valve prolapse in 21 cases (21/23, 91%). In one case, from Group II interatrial septal aneurysm was associated with a ischemic cerebral vascular event, *(Table IV)*.

Myocardial involvement in Marfan syndrome has been previously studied.[19] Myocardial hypertrophy and fibrosis as well as hypertrophic cardiomyopathy had been described. The absolute and corrected measurements of heart chambers appear in *Table III*. Nine patients (13.4%) had left atrial dilatation, 6 of whom also had concentric left ventricular hypertrophy and 3 left ventricular dilatation secondary to regurgitant valves.

Discussion

Cardiovascular complications are responsible for the vast majority of premature deaths in this syndrome. Such abnormalities can be detected and followed by echocardiography in the great majority of patients with Marfan syndrome. As expected, it appears that as body surface area increases in the first 3 decades of life, the aortic root also grows. Thereafter, between 30 to 50 years of age, there is minimal increase in the size of the aortic root. After 50 years of age, aortic size seems to gradually increase again.[9,10] This latter observation has been attributed to age-related changes in the collagen and elastin content of the aorta.[15] We have studied all of the aortic segments and have found that when measurements are corrected for the body surface area, the curves show that segments of the aorta are smallest in Group I (patients less than 16 years of age) and that the values increase with patient age (Group II). However, comparison of the two groups showed no significant difference in the sizes of the descending and abdominal aorta.

In two series of MFS patients, mitral valve prolapse has been found in up to 80% of cases. This percentage is in agreement with our findings of

Table IV. Valve and interatrial abnormalities.

	Group I n = 22	Group II n = 44	All n = 66	Values of Chi	Values of p ≤
Pulmonary prolapse + regurgitation	9 (40.9%)	5 (11.4%)	14 (21.2%)	7.66	0.006
Pulmonary regurgitation	11 (50.0%)	8 (18.2%)	19 (27.3%)	5.77	0.02
Pulmonary prolapse	10 (45.5%)	7 (15.9%)	17 (25.8%)	5.24	0.03
Tricuspid regurgitation	16 (72.7%)	19 (43.2%)	35 (53.0%)	5.14	0.03
Tricuspid prolapse + regurgitation	13 (59.1%)	16 (36.4%)	29 (43.9%)	3.08	ns
Tricuspid prolapse	18 (81.8%)	26 (59.1%)	44 (66.7%)	2.46	ns
Mitral prolapse	21 (95.5%)	32 (72.7%)	53 (80.3%)	3.46	ns
Mitral regurgitation	9 (40.9%)	21 (47.7%)	30 (45.5%)	0.28	ns
Mitral prolapse + regurgitation	9 (40.9%)	18 (40.9%)	27 (40.9%)	0.0	ns
Aortic prolapse	5 (22.7%)	5 (11.4%)	10 (15.2%)	1.47	ns
Aortic regurgitation	1 (4.5%)	6 (13.6%)	7 (10.6%)	0.50	ns
Aortic prolapse + regurgitation	0 (0.0%)	1 (2.3%)	1 (1.5%)	—	—
IASA	3 (13.6)	20 (45.5%)	23 (34.8%)	5.21	0.03
IASA + Mitral prolapse	3 (13.6%)	18 (40.9%)	21 (31.8%)	3.85	0.05

mitral valve prolapse in 80.3%.[13,14] The mitral was the most commonly affected heart valve, followed by the tricuspid and pulmonary valves. In this cohorts there was a sizable percent of cases (21.2%) with pulmonary valve prolapse in association with pulmonary regurgitation, which was significantly more frequent in Group I ($p = 0.006$) when it was compared with control groups. Recent surgical and pathologic studies have demonstrated myxomatous degeneration of aortic, tricuspid and mitral valves. At present, prognostic implications of isolated pulmonary valve prolapse or in association with pulmonary valve regurgitation have not been explored in Marfan syndrome. Since the pulmonary valve is made up of essentially the same tissue as the aortic valve, it would be reasonable to assume that both valves could be equally affected in patients with Marfan syndrome. Moreover, it has been suggested that the abnormalities are not confined to a single valve but may involve all of the endocardial tissue, leading to multivalvular compromise. Indeed, in our series 63% of patients had involvement of two or more heart valves

Interatrial septal aneurysm has been seldom reported in Marfan syndrome. Generally it is found in association with congenital heart disease, such as patent foramen ovale, atrial and ventricular septal defects, mitral valve prolapse and Ebstein's anomaly, or in acquired conditions like valve disease, cardiomyopathy, systemic and pulmonary hypertension. The reported prevalence of interatrial septal aneurysm in autopsy series is 1-4%. Recently, it has been associated with cerebrovascular disease (ischemia or infarction in up to 20% of cases).[17]

This is the first report of a large number of interatrial septal aneurysm in patients with Marfan syndrome, with a frequency of 34.8% in our series, and 7.6% of these had cerebral ischemic events. In the majority (31.8%), interatrial septal aneurysm coexisted with mitral valve prolapse but never with patent foramen ovale. Isolated interatrial septal aneurysm or interatrial septal aneurysm associated with mitral valve prolapse was significantly more common in adults than in children, $p < 0.03$ and $p < 0.05$, respectively. This suggests that in Marfan syndrome the connective tissue abnormality also involves the interatrial septum. The prognostic significance of interatrial septal aneurysm in Marfan syndrome is yet to be determined. Furthermore interatrial septal aneurysm has been shown to be a major source of thrombi, and when it occurs concomitantly with mitral valve prolapse it could potentiate the cardioembolic risk as was previously described.[20]

To our knowledge this is the first report of echocardiometry in a Mexican-mestizo Marfan cohort and we consider it will provide the basis for comparisons among other populations with different genetic background.

Conclusions

The incidence of cardiovascular abnormalities in our series is similar to that in the literature with the exception of the very high incidence of pulmonary valve prolapse in relation to control groups (0%), it suggests that the clinical manifestations of Marfan syndrome are strikingly severe in the Mexican population.

Our patients also had a high incidence of interatrial septal aneurysm (34.9%) *vs* control groups (18.2%). Only isolated cases associated with Marfan syndrome have been reported heretofore. The measurements of segments of the aorta should be corrected to body surface area, as they are different in children and adults.

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