

Echocardiographic findings and clinical spectrum of pediatric Marfan syndrome

¹Esma ŞEN RIŞVAN

²Nurdan EROL

¹Department of Pediatrics, University of Health Sciences, Turkey. Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center, Istanbul, Turkey

²Department of Pediatric Cardiology, University of Health Sciences, Turkey. Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center, Istanbul, Turkey

ORCID ID

EŞR : 0009-0008-3496-4154

NE : 0000-0002-9650-2077



ABSTRACT

Objective: Marfan syndrome is more than a genetic diagnosis; it poses a significant cardiovascular risk, with critical structures such as the aortic root potentially affected before clinical symptoms appear. This study evaluated the echocardiographic profiles and characteristic clinical features of genetically confirmed pediatric Marfan syndrome patients in a tertiary center.

Material and Methods: Pediatric patients with confirmed Marfan syndrome who underwent transthoracic echocardiography between October 2018 and May 2025 were retrospectively reviewed. Aortic dimensions and valvular pathologies were assessed according to American Society of Echocardiography criteria. Clinical data, family history, and anthropometric features were also documented.

Results: Ten patients (8 females, 2 males; mean age 12.4±5.6 years) were included. Aortic root dilatation was observed in two patients, mitral valve prolapse in nine patients, and mitral regurgitation in six patients based on their most recent outpatient follow-up evaluations. Four patients received medical therapy; however, treatment adherence was inconsistent and outcomes varied. Most patients exhibited tall stature and had a positive family history. No cardiovascular surgeries were performed during the follow-up period.

Conclusion: In pediatric Marfan syndrome, severe cardiovascular complications may remain clinically silent until advanced stages. Our findings indicate that even in genetically confirmed cases, early echocardiographic evaluation frequently detects valvular abnormalities and aortic involvement before clinical deterioration. These results underscore the critical importance of early diagnosis and regular echocardiographic surveillance to optimize follow-up and prevent delayed recognition of potentially fatal complications.

Keywords: Aortic root dilatation, Marfan syndrome, pediatric cardiology.

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Correspondence: Esma ŞEN RIŞVAN, MD. Sağlık Bilimleri Üniversitesi, İstanbul Zeynep Kamil Kadın ve Çocuk Hastalıkları Sağlık Uygulama ve Araştırma Merkezi, Çocuk Sağlığı ve Hastalıkları Kliniği, İstanbul, Türkiye.

Tel: +90 534 634 98 50 **e-mail:** esmasen95@gmail.com

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INTRODUCTION

Marfan syndrome (MFS, MIM #154700) is an autosomal dominant connective tissue disorder affecting multiple organ systems. It is genetically caused by pathogenic variants in the FBN1 gene, which encodes the extracellular matrix protein fibrillin-1.^[1–3] While the mutation exhibits high penetrance, its expression varies among individuals. As a result, clinical manifestations are heterogeneous and age-dependent. The most commonly affected systems are skeletal, ocular, and cardiovascular.^[4]

Cardiovascular manifestations include mitral valve prolapse (MVP), mitral regurgitation (MR), left ventricular dilatation, aortic root dilatation, aortic regurgitation, and pulmonary artery dilatation. Among these, aortic root dilatation is the most critical complication, as it may lead to aortic dissection and sudden cardiac death.^[1–3] These features may appear during childhood, and some cases may present with symptoms during the neonatal period, especially in severe phenotypes.^[5,6]

This study aimed to evaluate the cardiovascular findings and follow-up of genetically confirmed pediatric MFS cases monitored at our Pediatric Cardiology outpatient clinic.

MATERIAL AND METHODS

Study Population and Echocardiographic Evaluation

This study included patients with genetically confirmed Marfan syndrome who underwent at least one transthoracic echocardiographic examination between October 2018 and May 2025 at our Pediatric Cardiology outpatient clinic. Data on age, sex, height, weight, percentiles, body mass index (BMI), family history of MFS, systemic manifestations, medical treatments, and surgical interventions were collected retrospectively from hospital records.

Echocardiographic assessments were performed using the Vivid 3 S26 (GE Medical Systems) device. Standard M-mode, 2D, and color Doppler techniques were used. Measurements and evaluations were based on criteria established by the American Society of Echocardiography (ASE). Aortic annulus and sinus of Valsalva dimensions were assessed, and Z-scores were calculated using a database-based tool according to age, sex, and body surface area. Z-scores $\geq +2$ were considered diagnostic for annular or aortic root dilatation. Valve insufficiencies were classified as trace, mild, moderate, or severe.

Statistical Analysis

The data were recorded in Microsoft Excel. Descriptive statistics were applied. Continuous variables are presented as mean \pm standard deviation, and categorical variables as frequencies and percentages. No inferential statistical tests were performed due to the limited sample size.

Ethical Considerations

The study protocol was approved by the Ethics Committee of Zeynep Kamil Women and Children's Training and Research Hospital (approval number: 99, date: 25/12/2024). The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

Eighteen pediatric patients with genetically confirmed MFS were identified. Eight patients without echocardiographic data were excluded. The remaining ten cases were analyzed.

The mean age was 12.4 ± 5.6 years; eight patients were female and two were male. Height percentiles were above the 95th percentile in eight cases, and weight percentiles were below the 50th percentile in two cases. BMI ranged from 12.6 to 30.8 kg/m², with a mean of 19.8 ± 6.1 kg/m².

Among the ten patients, two were siblings and one was a cousin. A positive family history of MFS was identified in nine of ten patients. Parental consanguinity was reported in three of ten families.

Four of ten patients (40%) were prescribed enalapril therapy. In the first case, aortic root dilatation was present, and early initiation of medical therapy resulted in normalization of the aortic root Z-score during follow-up, with no subsequent increase observed. In the fifth case, enalapril therapy was initiated at the age of 9 years, continued for one year, and subsequently discontinued by the patient herself. In the seventh case, there was no consanguinity and no family history of Marfan syndrome, and the case was identified as a de novo mutation. In the eighth case, the patient's mother was diagnosed only after the patient was evaluated and had recently undergone both valvular and aortic surgery. The final findings of the cases are summarized in Table 1.

The most recent echocardiographic findings revealed Z-scores ranging from -1.2 to +3.28. During follow-up, two patients had an aortic root Z-score $>+2$, indicating aortic root dilatation. MVP was identified in nine cases, and MR was noted in six of these, four of which were graded as trace regurgitation. The 1-year-old infant had only a patent foramen ovale (PFO) without other abnormalities. The distribution of cardiac findings is presented in Table 2.

Three patients had undergone lens surgery, and one patient had undergone rhinoplasty. No cardiovascular surgeries were reported.

DISCUSSION

Marfan syndrome affects 1 in 3,000 to 5,000 individuals, regardless of race or gender.^[1–3] Clinical diagnosis is based on the Ghent criteria established by an international expert panel, but definitive diagnosis is genetic.^[7]

In one striking case within our study, Patient 7 was identified as having a de novo mutation, consistent with the approximately 25% rate reported in the literature.^[1–4] The mothers of Patients 5 and 6 had also been diagnosed with MFS. These observations highlight variable intrafamilial expression and emphasize the importance of early identification and screening of at-risk relatives.

Clinically, the cohort displayed classic Marfan features such as tall stature, long limbs, arachnodactyly, scoliosis, pectus deformities, and increased arm span.^[1–3] Three patients had undergone lens surgery due to lens subluxation, aligning with the reported 40–56% prevalence in pediatric patients.^[1]

Except for the infant, all cases demonstrated mitral valve prolapse, and most had associated mitral regurgitation. Aortic root dilatation was observed in 20% of cases, which may be underestimated due to

Table 1: Summary of the demographic, medical history, echocardiographic findings and medication records

Case number	G	Age	Weight	Height	BMI	Parental con.	Family Marfan history	EKO	Aortic annulus	Aortic sinus	LVDD	Medication
Case 1	F	10	72.6	183.7	21.5		Yes	MVP, MR (trace)	20.07	23.7	44.67	Enalapril
Case 2	F	18	62	180	19.1			MVP (mild)	20.3	24.7	41.75	
Case 3	F	8	24	138	12.6		Yes	MVP, MR (mild), aortic root dilatation	17	28	46.5	Enalapril
Case 4	F	18	100	180	30.8	Yes	Yes	MVP, Aortic root dilatation (mild)	22	33	48.5	
Case 5	F	13	55	172	18.5	Yes	Yes	MVP, MR (trace)	21	30	45.9	Enalapril for 1 year at age 9, discontinued
Case 6	F	15	58	170	20	Yes	Yes	MVP, MR (mild)	20.5	30.5	51	Enalapril
Case 7	F	7	23.4	130	13.6			MVP(mild)	15.5	17.5	38.8	
Case 8	F	1	11.6	84	16.4		Yes	PFO	12	15	25	
Case 9	M	17	112	195	29.4		Yes	MVP, MR (trace)	24	39	55	
Case 10	M	13	43.3	185	15.7		Yes	MVP, MR (trace)	24	29.7	48.6	

G: Gender; F: Female; M: Male; Con: Consanguinity; MVP: Mitral valve prolapse; MR: Mitral regurgitation; PFO: Patent foramen ovale; LVDD: Left ventricular end-diastolic diameter.

the younger age distribution. Across all patients, aortic root Z-scores ranged from -1.2 to +3.28 during follow-up. As age increases, the incidence of dilatation and related complications is known to rise.

Angiotensin-converting enzyme inhibitors, such as enalapril, have demonstrated efficacy in reducing the progression of aortic complications.^[8–10] However, in our cohort, only four patients were receiving medical therapy, and adherence was suboptimal. One patient discontinued therapy prematurely on their own initiative, while others did not consistently adhere to the prescribed regimen.

Although inferential statistical analysis was limited by the small sample size, descriptive analyses were performed to illustrate trends among treated patients. In Patient 1, therapy was initiated when the aortic root Z-score was 1.14; during treatment, values fluctuated between -1.0 and +0.57, and at the last follow-up the Z-score was 1.71, without significant progression. In Patient 3, therapy began at a Z-score of 2.3; after 7 months, the Z-score increased to 3.28. This patient had previously received enalapril at an external center but discontinued the medication independently during the COVID-19 pandemic. Therapy was subsequently restarted at our center, and follow-up continued under treatment. In Patient 5, medical therapy was initiated at a Z-score of 2.31 but discontinued by the patient after one year; subsequent Z-scores ranged from -0.29 to +1.95, and

Table 2: Distribution of cardiac findings

Cardiac finding	n	%
Aortic root dilatation	2	20
Mitral valve prolapse	9	90
Mitral regurgitation	6 (4 trace, 2 mild)	60

clinical follow-up continued without medication. In Patient 6, therapy was initiated at a Z-score of 1.86, but the patient demonstrated poor adherence, with the most recent follow-up revealing a Z-score of 1.71. With the exception of Patient 5, all treated patients remain under ongoing medical therapy and surveillance.

Among the treated cases, follow-up Z-scores showed fluctuations rather than a consistent trend, reflecting both individual biological variability and inconsistent treatment adherence. These findings highlight the challenges of maintaining long-term therapy and follow-up in pediatric populations. Regular echocardiographic monitoring and multidisciplinary follow-up, including general pediatrics, ophthalmology, and orthopedics, remain essential for the optimal management of children with Marfan syndrome.

The 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease provided updated recommendations on surveillance intervals, medical therapy, and surgical thresholds, emphasizing individualized management and care at experienced centers.^[11] It also highlighted the need for lifelong follow-up, earlier consideration of surgery in high-risk patients, and the use of β -blockers or angiotensin receptor blockers (ARBs) as first-line medical therapy.^[10,11]

Building on these principles, the 2024 AHA Scientific Statement on Cardiovascular Management of Aortopathy in Children specifically addressed pediatric populations. It emphasized growth- and Z-score-based definitions of aortic dilatation, risk stratification by progression rate, and the role of genetic diagnosis in tailoring management.^[12] In children, surgical decisions are not solely guided by absolute dimensions but also by rapid aortic enlargement, severity of regurgitation, and family history of dissection.^[11,12] Furthermore, the statement introduced more individualized recommendations for lifestyle and exercise, advocating shared decision-making between clinicians and families.^[12] These considerations are directly relevant to our cohort, given early aortic root dilatation, variable adherence to therapy, and heterogeneity of follow-up.

Kemna et al.^[13] proposed a root-to-descending aorta ratio ≥ 2 as highly sensitive and ≥ 2.3 as highly specific. Gautier et al.^[14] provided nomograms for Valsalva diameters. A French multicenter study reported a 7.6% cardiovascular event rate in pediatric Marfan patients, with 82.9% undergoing aortic surgery. Cumulative incidence increased from 5.3% at 18 years to 19.4% at 25 years.^[6] Identified risk factors included an annual Z-score increase ≥ 0.1 , annual diameter growth ≥ 5 mm, aortic regurgitation ≥ 2 , and a Z-score ≥ 3 before the age of 16.^[6] Recent studies have also suggested that the aortic sinus cross-sectional area-to-height ratio (5–7cm²/m) may aid surgical decision-making in children.^[15]

No patients in our cohort underwent cardiovascular surgery, likely due to the outpatient and referral-based nature of our clinic. While moderate physical activity may be permitted, contact sports and intense physical exertion remain contraindicated in children with Marfan syndrome.^[12]

CONCLUSION

In this case series, the clinical and cardiovascular characteristics of pediatric Marfan syndrome were consistent with previously reported findings in the literature. Notably, the presence of aortic root dilatation at diagnosis in some children highlights the need for early and systematic surveillance. Although β -blockers or angiotensin receptor blockers (ARBs) are recommended as first-line therapy, our experience illustrates the challenges of long-term treatment adherence in pediatric patients. In our series, treatment outcomes varied, reflecting the impact of adherence and continuity of follow-up on aortic root progression.

In line with current guidelines,^[12] children with Marfan syndrome should not only be followed by pediatric cardiology but also require a multidisciplinary approach, including general pediatrics, ophthalmology, and orthopedics. When necessary, collaboration with genetics and surgical specialties should also be considered to optimize individualized management.

Early recognition, sustained treatment adherence, and structured multidisciplinary follow-up remain the cornerstones for preventing major adverse outcomes in children with Marfan syndrome.

Statement

Ethics Committee Approval: The Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Clinical Research Ethics Committee granted approval for this study (date: 25.12.2024, number: 99).

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