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Evaluation of the Relationship Between Iron Load, Age, and Cardiac Function in Children and Young Adults with Thalassemia Major

Talasemi Majorlü Çocuk ve Genç Yetişkinlerde Demir Yükü, Yaş ve Kardiyak Fonksiyonların İlişkisinin Değerlendirilmesi

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Abstract

Aim: To determine the structural and functional cardiac differences in children and young adults with thalassemia major (TM) compared to healthy subjects using pulsed-wave Doppler and tissue Doppler imaging methods and determine the relationship between iron overload and these differences.

Material and Method: We analyzed the data of pediatric and young adult TM patients (n = 44) aged 4–22 years and an age- and gender-matched control group (n = 40) in our hospital data system between Oct.01.2023 and Oct.01.2024. Height, weight, body mass index (BMI), systolic–diastolic blood pressure measurements, complete blood count, ferritin, cardiac T2* magnetic resonance imaging (MRI) values, and echocardiography results were recorded. Comparison of echocardiographic measurements between the two groups was performed. In addition, correlation analysis was performed between ferritin, cardiac T2*MRI, age and echocardiographic parameters of TM patients.

Results: Our study showed growth retardation (low height standard deviation score (SDS), low weight SDS and low BMI SDS), dilatation of the left cavities (high left ventricular internal diameter end diastole (LVIDd)), increased left ventricular muscle mass (high left ventricular mass index (LVMI)), cardiac distinctive diastolic (restrictive pattern: left ventricular (LV) peak early diastolic flow (E)/peak late diastolic flow (A) and E/early diastolic myocardial peak flow (E') high), and subclinical systolic (LV peak systolic flow low and LV Tei index high) dysfunction. In addition, iron load (ferritin and cardiac T2* MRI) was correlated with LVMI, and cardiac diastolic and systolic function indicators. As age increased, ferritin value did not change, but cardiac T2* MRI value decreased and diastolic–systolic parameters worsened.

Conclusion: Periodic cardiac T2* MRI and Doppler echocardiography examinations of patients with TM may detect subclinical myocardial dysfunction at an early stage, thus providing a window of opportunity for intervention.

Keywords: Thalassemia, cardiac functions, iron overload, cardiac T2 MRI, Doppler echocardiography

Öz

Amaç: Darbeli dalga Doppler ve doku Doppler görüntüleme yöntemleri kullanılarak talasemi majorlu (TM) çocuk ve genç yetişkinlerde sağlıklı kişilere göre kardiyak yapısal ve fonksiyonel farklılıklarının belirlenmesi; demir yükünün bu farklılıklar ile olan ilişkisinin ortaya konması amaçlanmıştır.

Gereç ve Yöntem: Çalışmamızı yaşları 4-22 arasında olan çocuk ve genç yetişkin TM lü hastaların (n=44) ve yaş-cinsiyet uyumlu kontrol grubunun (n=40) hastanemiz veri sistemindeki 01.10.2023 ile 01.10.2024 tarihleri arasındaki verilerinin incelenmesiyle oluşturduk. Hastaların boy, kilo, vücut kitle indexi (VKI), sistolik-diyastolik kan basıncı ölçümleri ile tam kan sayımı, ferritin, kardiyak T2*MRI değerleri ve ekokardiyografi kayıtları kaydedildi. İki grup arasında ekokardiyografik ölçümlerin karşılaştırılması yapıldı. Ek olarak TM hastaların ferritin, kardiyak T2*MRI,yaş ve ekokardiyografik parametreleri arasında korelasyon analizi yapıldı.

Bulgular: Çalışmamızda TM hastalarında büyüme gelişme geriliği (boy SDS, kilo SDS ve VKI SDS düşük), sol boşluklarda dilatasyon (LVIDd yüksek), sol ventrikül kas kitlesinde artış (LVMI yüksek), kardiyak aşikar diyastolik (restriktif özellikte olan: LV tepe erken diyastolik akımı (E)/tepe geç diyastolik akımı (A) ve E/erken diyastolik miyokardiyal tepe akımı (E') yüksek) ve subklinik sistolik (LV tepe sistolik akımı (Sm) düşük ve LV Tei indexi (TX) yüksek) fonksiyon bozukluğu olduğunu tespit ettik. Bununla birlikte demir yükü (ferritin ve kardiyak T2*MRI) ile LVMI, kardiyak diyastolik ve sistolik fonksiyon göstergeleri arasında ilişki mevcuttu. Yaş arttıkça ferritin değeri değişmezken kardiyak T2*MRI değerinin azaldığı; diyastolik ve sistolik parametrelerde kötüleşmelerin olduğu tespit edildi.

Sonuç: TM lü hastaların periyodik olarak kardiyak T2*MRI ile doppler ekokardiyografi incelemelerinin yapılmasıyla subklinik myokardiyal disfonksiyon erken dönemde tespit edilebilir; bu da bize gerekli müdahelelerin yapılması açısından fırsat penceresi sunabilir.

Anahtar Kelimeler: Talasemi, kardiyak fonksiyonlar, aşırı demir yükü, kardiyak T2 MRI, Doppler ekokardiyografi

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INTRODUCTION

Thalassemia major (TM) is an autosomal recessive disorder that causes chronic hemolytic hypochromic microcytic anemia due to a defect in the synthesis of one or more of the hemoglobin chains. TM patients need frequent and regular blood transfusions from an early age. Due to extramedullary hematopoiesis, bone marrow expansion and iron overload, various life-threatening complications occur. Endocrine system problems, including hypogonadism, growth retardation, hypoparathyroidism, hypothyroidism, glucose intolerance-diabetes susceptibility, adrenal insufficiency, decreased bone mineral density, and increased risk of bone fracture, are frequently encountered in patients with TM.[1] Complications that develop due to frequent blood transfusions include heart failure, pulmonary hypertension, impaired renal and hepatic functions, restrictive lung diseases, thrombosis, hepatosplenomegaly, leg ulcers, urinary system stones, depression-like psychiatric disorders, and viral infections.[2]

Frequent transfusions inevitably lead to iron accumulation in the body as ferritin binds iron up to a certain level; however, free plasma iron species such as labile iron, which increase in plasma, cause the production of reactive oxygen species and damage cells and organs. In addition, labile iron is directly cardiotoxic. The most common cause of life-threatening morbidity in TM patients is heart failure and arrhythmias due to iron accumulation in the heart (6.8% and 5.7% respectively);[3] this occurs mostly in adulthood. Therefore, close cardiac follow-up of the patients is very important for timely interventions. It is possible to detect subclinical cardiac dysfunction with methods such as pulsed-wave Doppler and tissue Doppler imaging in childhood before distinctive heart failure develops.[4] In our study, we aimed to determine structural and functional cardiac differences in children and young adults with TM compared to healthy subjects by using pulsed-wave and tissue Doppler echocardiography methods and to reveal the relationship between iron load and these differences.

MATERIAL AND METHOD

We conducted this retrospective study by examining the data of pediatric and young adult patients with TM aged 4–22 years between Oct.01.2023 and Oct.01.2024 in the data system of our tertiary university hospital where patients with TM are regularly followed up and treated. Patients had been receiving blood transfusions at regular intervals of two to four weeks for at least three years and were receiving oral iron chelation therapy. Height, weight, body mass index (BMI), systolic–diastolic blood pressure measurements, complete blood count, ferritin, cardiac T2* magnetic resonance imaging (MRI) values, and echocardiography records were included. The control group consisted of healthy individuals of similar age and gender to the patient group. We selected the control group from subjects who had a complete blood count. Ferritin and cardiac T2* MRI examinations were not performed in the control group. Patients with chronic systemic disease, congenital or acquired cardiac disorders, and those taking medications that may affect cardiac function were excluded.

Magnetic Resonance Imaging

Cardiac T2* MRI scans were performed using a single-breath-hold multiecho T2* protocol on a 1.5-T scanner (Magnetom Aera, Siemens Healthcare). The parameters were as follows: slice thickness, 8 mm; flip angle, 20°; matrix, 128x256; field of view, 400 mm; time to echo 2.6–16.7 ms with 2.0 ms increments; repetition time 20 ms; and sample bandwidth, 810 Hz/pixel. Mid-ventricular single-slice short-axis T2* maps were obtained. Images were analyzed using SyngoVia software. Measurements were taken from the septum, as measurements from the septum are a good indicator of global iron in the heart.[5] Since iron is preferentially deposited in the epicardium compared to the endocardium, a homogeneous region of interest is defined covering both epicardial and endocardial regions. The degree of cardiac iron overload was categorized as mild (15 ms<T2*<20 ms), moderate (10 ms<T2*<15 ms) and severe (T2*<10 ms).[6]

Echocardiographic Evaluation

Echocardiographic evaluation was performed by the same pediatric cardiologist using a Vivid S60N (GE Vingmed Ultrasound AS Strandpromenaden 45, 3191 Horten, NORWAY) and 3Sc-Rs sector probes. Three measurements were performed and averaged. Left ventricular (LV) M-mode measurements were obtained from the parasternal long axis window. LVMI was obtained by dividing LVM calculated by Devereoux formula by body surface area.[7]

To evaluate diastolic function, pulsed-wave Doppler measurements were obtained from the four-chamber window by placing mitral leaflets in the sample volume. Inflow peak early diastolic velocity (E) and inflow peak late diastolic velocity (A) measurements were performed. Tissue Doppler measurements were obtained by placing the sample volume on the left lateral wall through a four-chamber window. Annulus early diastolic myocardial peak velocity (E'), annulus late diastolic myocardial peak velocity (A') and peak systolic velocity (Sm) values were recorded. Myocardial performance index (Tei index (TX)) was obtained by dividing the sum of isovolumetric relaxation time and isovolumetric contraction time by ejection time.[8]

Statistical Analysis

The Statistical Package for the Social Sciences for Windows ver. 26.0 package program was used to conduct the study's statistical analysis. The term n (%) was utilized for categorical variables, whereas mean ± standard deviation was utilized for continuous variables when a normal distribution was followed, and median and inter-quantile range values were used when a normal distribution was not met. Analysis of the data's distribution and frequency was done using descriptive techniques, and the Kolmogorov–Smirnov test was done to check normal distribution. Two independent groups that fit the normal distribution were compared using the Student's t-test. When comparing two

independent groups that did not meet the normal distribution, the Mann–Whitney U test was employed. By using the Spearmann correlation coefficient (rho=r), the relationship between serum ferritin and cardiac T2* MRI values and echocardiographic parameters was determined. The Spearmann correlation coefficient was classified as follows: 0.00–0.19 = "extremely weak", 0.20–0.39 = "weak", 0.40–0.59 = "moderate", 0.60–0.79 = "strong", and 0.80–1.0 = "very strong". In all statistical studies, the significance level was determined to be less than 0.05.

Our study was approved by the ethics committee of our hospital with the date Oct.02.2024 and number 2024-16/8.

RESULTS

Our study consisted of 44 TM patients with a median age of 13.5 years (min 4, max 22) and 40 completely healthy controls with median age of 14 (4–22) years old. Patients had lower height standard deviation score (SDS), weight SDS and BMI SDS values than the control group (all three p<0.001). Systolic–diastolic blood pressure and heart rate did not differ between the two groups. The hematocrit value of the patients was 25.49±2.67%, while it was 38.1±2.53% in the control group (p<0.001). The median ferritin value of TM patients was 1,581 (220–6,214) ng/mL and cardiac T2* MRI value was 22.61±6.13 ms (**Table 1**).

Table 1. Comparison of basic demographic and clinical findings between groups.

	Thalassemia (n=44)	Control (n=40)	p
Age, years/Median (Min-Max)	13.5 (4-22)	14 (4-22)	0.795
Height, cm	141.43±22.04	151.65±23.64	0.044
Height, SDS	-1.2±0.58	0.23±0.53	<0.001
Weight, kg/Median (Min-Max)	45.5 (14-57)	54.5 (18-77)	0.004
Weight, SDS	-0.97±0.67	0.17±0.53	<0.001
BSA, m^2	1.23±0.33	1.4±0.37	0.031
BMI, kg/m^2	18.49±2.5	19.78±2.92	0.032
BMI, SDS	-0.43±0.63	0.06±0.47	<0.001
SBP, mm Hg	102.73±9.8	107±11.48	0.163
SBP, SDS	-0,02±0.36	0.1±0.25	0.521
DBP, mm Hg	60.77±4.57	62.53±4.04	0.067
DBP, SDS	-0,05±0.29	0,2±0,25	0.097
HR, beats per minute	72.7±7.1	70.4±6.6	0.127
Hb, g/dL	8.7±0.85	12.78±0.86	<0.001
Hct, (%)	25.49±2.67	38.1±2.53	<0.001
Ferritin, ng/mL/Median (Min-Max)	1581 (220-6214)		
Cardiac T2*MRI, ms	22.61±6.13		

BSA, body surface area; BMI, body mass index; SPB, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Hb, hemoglobin; Hct, haematocrit; T2*MRI, magnetic resonance imaging.

LVMI value was higher in patients with thalassemia major [95.57 (50.71–159.23)] compared to the control group [76.16 (34.67–93.91), p<0.001]. While the ejection fraction (EF), one of the indicators of systolic function, was similar in both groups (p = 0.583), LV Sm value was lower in TM patients (p<0.001). LV E/A and LV E/LV E' ratios, which are diastolic function indicators, were found to be higher in patients with thalassemia major (p<0.001 in both groups). However, LVTX value, which shows systolic and diastolic function together, was found to be high in TM patients (0.44±0.02 - 0.36±0.01, p<0.001) (**Table 2**).

Table 2. Comparison of M-mode, pulsed and tissue Doppler echocardiographic parameters between groups.

	Thalassemia (n=44)	Control (n=40)	p
EF, %	69.66±3.68	70.1±3.64	0.583
FS, %	39.02±3.05	39.33±3.12	0.654
IVSd, cm	0.85±0.19	0.8±0.16	0.264
IVSs, cm	0.97±0.18	0.92±0.16	0.337
LVIDd, cm	4.51±0.66	4.19±0.47	0.011
LVIDs, cm	3.08±0.62	3±0.49	0.529
LVPWd, cm	0.81±0.2	0.78±0.17	0.455
LVPWs, cm	0.94±0.19	0.940.17	0.873
LVM g	137.66 (32.36-245.68)	120.87 (27.42-168.45)	0.040
LVMI g/m^2	95.57 (50.71-159.23)	76.16 (34.67 (93.91)	<0.001
LV E, m/s	105.98±8.91	87.23±5.9	<0.001
LV A, m/s	61.93±2.77	62.82±2.61	0.133
LV E/A	1.71±0.19	1.39±0.11	<0.001
LV Sm, cm/s	7.21±0.73	8.15±0.80	<0.001
LV E', cm/s	13.68±0.83	13.28±1.06	0.053
LV E/E'	7.78±0.89	6.62±0.78	<0.001
LVTX	0.44±0.02	0.36±0.01	<0.001

EF, ejection fraction; FS, fractional shortening; IVSd, interventricular septal end-diastolic dimension, IVSs, interventricular septal end-systolic dimension, LVIDd, left ventricle end-diastolic dimension; LVIDs, left ventricle end-systolic dimension; LVPWd, left ventricle posterior wall end-diastolic dimension; LVPWs, left ventricle posterior wall end-systolic dimension; LVMI, left ventricle mass index, E, inflow peak early diastolic velocity; A, inflow peak late diastolic velocity; Sm, peak systolic velocity; E', annulus early diastolic myocardial peak velocity; TX, Tei index (myocardial performance index)

T2* MRI <10 ms was present only in one TM patient, who was aged 21 years. The mean age of patients with T2* MRI >20 ms was 11.29±5.36 years. The mean ferritin level was 3,200 ng/mL in patients with T2* MRI <10 ms and 1,154 (220–2,530) ng/mL in patients with T2* MRI >20 ms (**Table 3**).

Table 3: Age and ferritin levels of patients according to T2*MRI values

	T2*MRI <10 ms, (n=1)	T2*MRI 11-14 ms, (n=3)	T2*MRI 15-19 ms, (n=9)	T2*MRI >20 ms, (n=31)	Total (n=44)
Age, years	21	18.67±2.89	18±3.67	11.29±5.36	13.5 (4-22)
Age>18 years, n (%)	1 (10)	1 (10)	5 (50)	3 (30)	10 (100)
Age 4-17 years, n (%)	0 (0)	2 (5.9)	4 (11.8)	28 (82.3)	34 (100)
Ferritin, ng/mL	3200	2350 (2227-6214)	1860 (522-3600)	1154 (220-2530)	1581 (220-6214)

The T2* MRI value of TM patients age>18 years was 17.5 (8–25), while that of patients aged 4–17 years was 25 (11–29) ms (p<0.001). Ferritin value of TM patients aged>18 years was 1,855 (422–3,200) ng/mL, while that of patients aged 4–17 years was 1,489 (220–6,214) ng/mL (p<0.001) (**Table 4**).

Table 4: T2*MR and Ferritin levels of patients under and over 18 years of age

	Age >18 years, (n=10)	Age 4-17 years, (n=34)	Total, (n=449	p
T2*MRI, ms	17.5 (8-25)	25 (11-39)	22.61±6.13	<0.001
Ferritin, ng/mL	1855 (422-3200)	1489 (220-6214)	1581 (220-6214)	<0.001

Hematocrit and EF were not associated with any echocardiographic parameters. Ferritin was weakly associated with LVMI; and moderately associated with E/A, E/E', LVTX and LV Sm. Cardiac T2* MRI associated strongly with LVMI, E/E', LVTX, LV Sm; and very strongly with E/A (**Table 5**, **Figure 1**). Ferritin was not associated with age, whereas cardiac T2* MRI was strongly associated with age (**Table 5**, **Figure 2**).

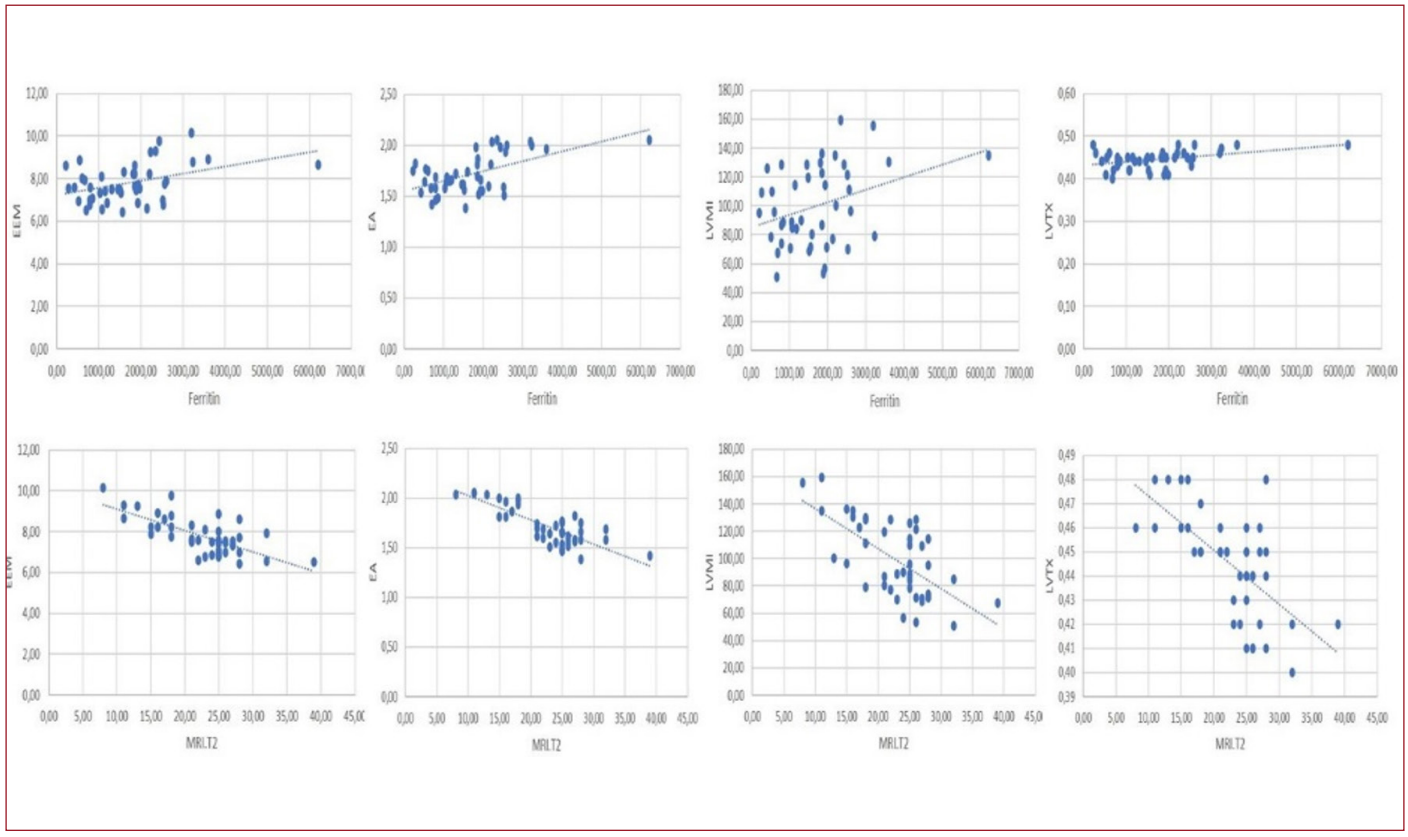

Figure 1. Spearmann correlation of ferritin, cardiac T2*MRI and echocardiographic parameters.
LVMI, left ventricle mass index, E, inflow peak early diastolic velocity; A, inflow peak late diastolic velocity; E', annulus early diastolic myocardial peak velocity; TX, Tei index (myocardial performance index).

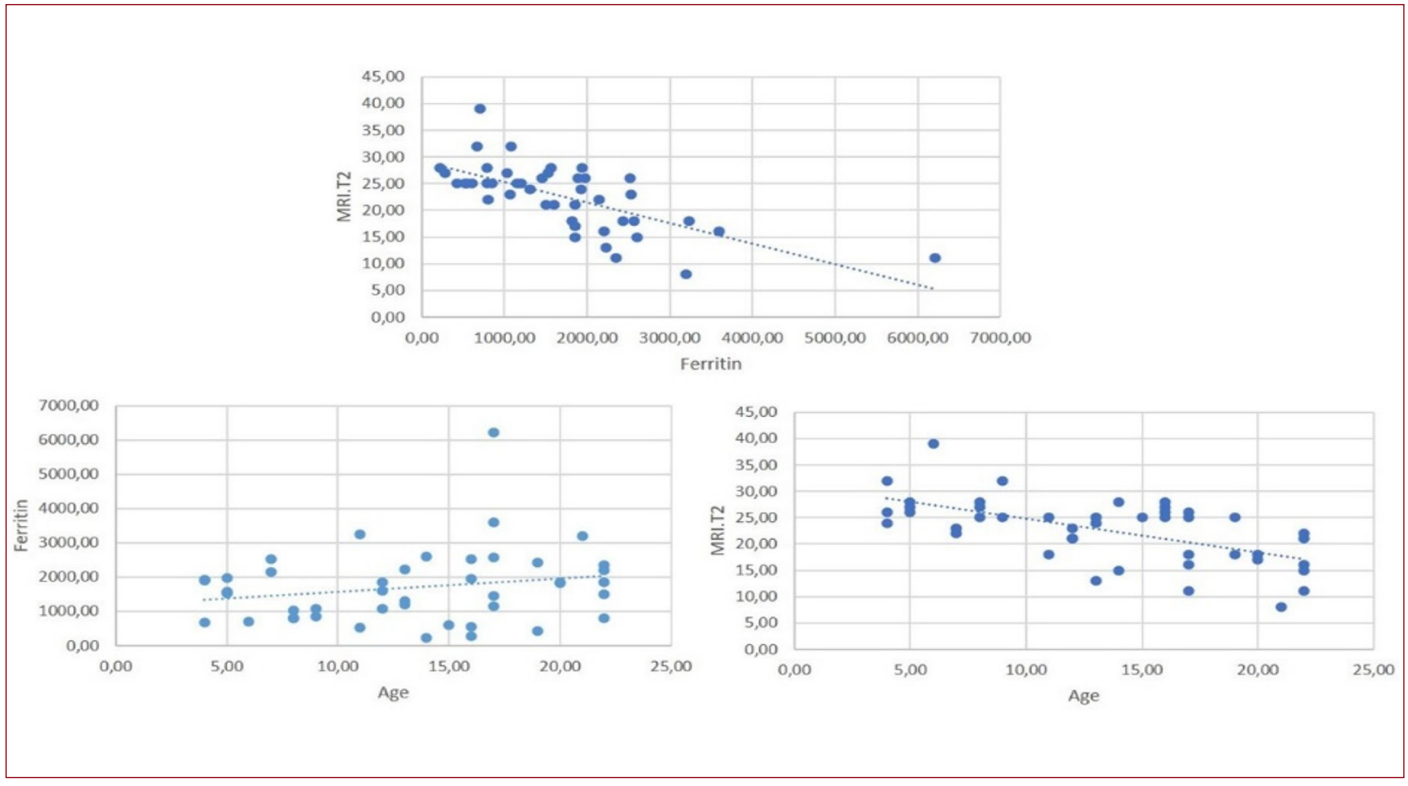

Figure 2. Spearmann correlation of ferritin and T2*MRI each other; and ferritin and T2*MRI with age.
T2*MRI, magnetic resonance imaging

Table 5: Spearmann correlation coefficient matrix of serum Hct, Ferritin levels, T2*MRI and echocardiographic parameters (rho=r).

	Hct	Ferritin	T2*MRI	EF	LVMI	E/A	E/E'	LVTX	Age	Sm
Hct (r)	-	-0.258	0.222	-0.081	-0.290	-0.180	-0.216	-0.126	-0.180	0.212
(p)	-	0.091	0.148	0.602	0.056	0.243	0.159	0.415	0.243	0.166
Ferritin (r)	-0.258	-	-0.681	0.222	0.341	0.560	0.408	0.417	0.203	-0.501
(p)	0.091	-	<0.001	0.148	0.023	<0.001	0.006	0.005	0.187	0.001
T2*MRI (r)	0.222	-0.681	-	-0.078	-0.648	-0.801	-0.716	-0.648	-0.605	-0.617
(p)	0.148	<0.001	-	0.614	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
EF (r)	-0.081	0.222	-0.078	-	0.010	0.084	-0.101	-0.056	-0.128	-0.60
(p)	0.602	0.148	0.614	-	0.950	0.586	0.516	0.717	0.407	0.700
LVMI (r)	-0.290	0.341	-0.648	0.010	-	0.630	0.609	0.602	0.941	-0.200
(p)	0.056	0.023	<0.001	0.950	-	<0.001	<0.001	<0.001	<0.001	0.192
E/A (r)	-0.180	0.560	-0.801	0.084	0.630	-	0.821	0.747	0.628	-0.709
(p)	0.243	<0.001	<0.001	0.586	<0.001	-	<0.001	<0.001	<0.001	<0.001
E/E' (r)	-0.216	0.408	-0.716	-0.101	0.609	0.821	-	0.602	0.583	-0.617
(p)	0.159	0.006	<0.001	0.516	<0.001	<0.001	-	<0.001	<0.001	<0.001
LVTX (r)	-0.126	0.417	-0.648	-0.056	0.602	0.747	0.602	-	0.630	-0.648
(p)	0.415	0.005	<0.001	0.717	<0.001	<0.001	<0.001	-	<0.001	<0.001
Age (r)	-0.180	0.203	-0.605	-0.128	0.941	0.628	0.583	0.630	-	-0.187
(p)	0.243	0.187	<0.001	0.407	<0.001	<0.001	<0.001	<0.001	-	0.224
Sm (r)	0.212	-0.501	-0.617	-0.60	-0.200	-0.709	-0.617	-0.648	-0.187	-
(p)	0.166	0.001	<0.001	0.700	0.192	<0.001	<0.001	<0.001	0.224	-

Hct, haematocrit; T2*MRI, magnetic resonance imaging; LVMI, left ventricle mass index, E, inflow peak early diastolic velocity; A, inflow peak late diastolic velocity; E', annulus early diastolic myocardial peak velocity; TX, Tei index (myocardial performance index); Sm, peak systolic velocity

DISCUSSION

The incidence of hemoglobinopathies has been reported to be one in 0.1–0.4 million per year worldwide and thalassemias are the most common. It is frequently observed in Mediterranean, Middle Eastern, and Southeast Asian countries.[9] For beta thalassemia major to occur, both parents must be carriers. As in developed countries, screening of men and women for thalassemia before marriage is a legal obligation in Turkey. Although the incidence of TM patients has decreased in recent years, it is still seen as a public health problem due to immigrants relocating to Turkey from other Middle Eastern countries. In our study, 14 of 44 patients (31.8%) were immigrants to Turkey in recent years.

Various endocrinologic problems occur due to iron accumulation in the organs; chronic hypoxia caused by chronic anemia, and growth retardation also occur in TM patients.[1,10,11] In our study, we found low height, weight, and BMI SDS values in TM patients.

Patients with TM have hypertrophy of the heart because of iron accumulation in the heart and enlargement of the cavities due to chronic anemia.[12] Studies have shown LV end-systolic and end-diastolic dilatation and increased LVMI levels in patients with TM.[13-15] Similarly, in our study, we found that high left ventricular internal diameter end diastole (LVIDd) and left ventricular mass index (LVMI) measurements were higher in patients with TM compared to the control group. In addition, LVMI increased with increasing age.

In patients with TM, non-transferrin-bound iron accumulates in the heart as in many organs. It leads to the formation of toxic oxygen metabolites via the Fenton reaction, which damage cell and membrane lipids, proteins, and nucleic acids in mitochondria. In addition, iron accumulation in the heart causes iron overload cardiomyopathy.[16,17] The causes of death of 2,797 TM patients in the United States between 1999 and 2020 were analyzed, and it was reported that the leading cause, with 26%, was cardiovascular diseases.[18] In patients with TM, distinctive heart failure secondary to systolic dysfunction is observed in the late stages of the disease; until then, EF measured by conventional methods remains within normal limits. However, early changes in tissue Doppler Sm and TX values indicating subclinical systolic dysfunction have been shown in studies.[16,19-21] In our study, there was no difference between TM patients and the control group in terms of EF, which is an indicator of systolic function. However, a tissue Doppler imaging study showed that patients with TM had low LV Sm and high LVTX, indicating subclinical systolic dysfunction. In addition, LV Sm decreased and LVTX increased with increasing age.

Studies have shown that patients with TM have diastolic myocardial dysfunction in the early stages. In restrictive myocardial diastolic dysfunction, the E value and E/A ratio is high. Restrictive diastolic myocardial dysfunction also occurs in patients with TM due to iron accumulation in the heart.[16,23-25] In our study, E/A and E/E' ratios indicating restrictive diastolic myocardial dysfunction were high. It was also found that E/A and E/E' ratios increased with increasing age.

The volume of iron load caused by periodic blood transfusions can be detected by MRI in the liver, pancreas, and heart.[26] Silvilariat et al. reported a correlation between ferritin level, cardiac T2* MRI value, and diastolic function parameters in their study of 77 TM patients with a median age of 14 years.[27] El-Shanshory et al. reported that there was a correlation between cardiac T2* MRI value and LVTX; and T2* MRI value decreased with increasing age in their study of 100 children with TM with a mean age of 10.9±3.7 years.[28] Khezri et al. compared ferritin and cardiac T2* MRI results in 1,959 adults

with TM and reported that the ferritin cut-off value for predicting high cardiac iron load (cardiac T2* MRI above 20 ms) was 2,027 ng/mL.[29] Güzelbey et al. reported that cardiac T2* MRI follow-up would be very useful in the evaluation of cardiac iron accumulation in TM patients.[30] In our study, the median ferritin level of TM patients was 1,581 (220–6,214) ng/mL. Severe cardiac iron accumulation (T2* MRI level below 10 ms) was detected in a 21-year-old patient; moderate iron accumulation (11–14 ms) was detected in three patients aged 13, 17 and 22 years. All patients with significant cardiac iron accumulation (T2* MRI below 20 ms) were older than 11 years. There was a strong correlation between ferritin and cardiac T2* MRI levels (rho = -0.681, p<0.001). T2* MRI decreased with increasing age (rho = -0.605, p<0.001), whereas ferritin levels did not change with age (rho = 0.203, p = 0.187).

CONCLUSION

In our study, we found that TM patients had growth retardation (low height SDS, low weight SDS and low BMI SDS), LV dilatation (high LVIDd), increased LV cardiac muscle mass (high LVMI), distinctive cardiac diastolic dysfunction (restrictive pattern: high LV E/A and E/E') and subclinical systolic (low LV Sm and high LVTX) dysfunction. However, there was a correlation between iron load (ferritin and cardiac T2* MRI) and LV muscle mass, and cardiac diastolic and systolic function indicators. While ferritin value did not change with increasing age, cardiac T2* MRI value decreased, and diastolic and systolic parameters worsened. Ferritin levels were higher and T2* MRI values were lower in patients with TM older than 18 years compared to younger patients. It may be possible to prevent advanced stages of cardiac dysfunction in patients with TM by not interrupting blood collection periods and making iron chelation therapy more disciplined. In addition, periodic cardiac T2* MRI and Doppler echocardiography examinations may detect subclinical myocardial dysfunction at an early stage, which may provide an opportunity for necessary interventions. However, the main principle in the fight against TM is to identify potential parents who are thalassemia carriers and prevent the emergence of individuals with TM from the very beginning.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval for our study was obtained from the Bursa City Hospital Clinical Research Ethics Committee (Date: 02.10.2024, Decision no: 2024-16/8).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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