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Research Article

Assessment of Cardiac and Liver Iron Overload with MRI in Thalassemia Major Patients: Short Term Follow up in Pediatric and Young Adolescent Patients

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Abstract

Objectives: The aim of the study was assessment of cardiac and hepatic iron overload in young thalassemia patients

Materials and Methods: The authors reviewed medical records of thalassemia patients at pediatric hematology clinic who undergone cardiac and liver MRI scan between January 2017 and March 2018. Also demographic and clinic data of the patients were recorded.

Results: A total of 11 patients (5 males and 6 females) had cardiac and liver T2* MRI scan with the mean age at imaging 13,9 ± 4,48 years old. 3 patients had cardiac and all patients had hepatic iron overload according to MRI scan. 10 of the patients had a control MRI scan approximately one year later. Average serum ferritin level of the patients at initial MRI scan was 1820,87 ng/ml. There was strong negative correlation between ferritin level-cardiac T2* time (r = 0,729; P = 0,011) and blood hemoglobin level-hepatic T2* time (r = 0,601; P = 0,049). There was statistically significant decrease in average hemoglobin and ferritin level of 10 patients who had control imaging (P = 0,038 and P = 0,036) between initial and control imaging, but no significant increase in cardiac and hepatic T2*time.

Conclusion: Cardiac and liver T2* imaging is feasible method of assessment of cardiac and hepatic iron overload even before the iron overload complication and clinical signs appeared.

Keywords: *Thalassemia; Iron Overload; Magnetic Resonance Imaging*

Background

The patients having multiple blood transfusions because of anemia have a risk of secondary hemochromatosis. Thalassemia patients have more iron overload risk among other hereditary diseases [1]. Because of iron overload in thalassemia patients, cardiac disorders are the leading cause of mortality. Cardiac disorders include restrictive and dilative hearth failure, myocarditis, pericarditis and myocardial infarcts [2]. Other complications of iron overload in thalassemia patients are liver failure-cirrhosis and endocrine organ failure [3].

Serum ferritin level is a frequently used method of iron overload assessment but it doesn't manifest cardiac iron overload actually [4]. T2* weighted imaging gradient echo sequence is a Magnetic Resonance Imaging (MRI) parameter which decreases with iron-related magnetic inhomogeneity and quantitative value in milliseconds [5].

Objectives of the Study

In this study, assessment of cardiac and hepatic iron overload with MRI in transfusion-dependent thalassemia major patients was aimed.

Materials and Methods

Eskisehir Osmangazi University ethics committee approved this retrospective study. Patients diagnosed and treated for thalassemia major at pediatric hematology-oncology clinic and who undergone cardiac and liver MRI scan and also control MRI scan between January 2017 and March 2018 were retrospectively reviewed. Also, medical records of the eligible patients were reviewed. Demographic data, cardiac and liver T2* time, echocardiography findings, blood hemoglobin and ferritin levels and chelation therapy dose was obtained from hospital records. Blood hemoglobin and ferritin levels were defined as average of the last two years before the first MRI scan. And if the patient had a control MRI, chelation dose, mean blood hemoglobin and ferritin levels between two imaging was recorded.

All cardiac and hepatic T2* images obtained at 3 Tesla MR scanner (Figure 1 and 2). Cardiac T2* time was obtained from the ROI at mid septum on short axis view and liver T2* time was obtained from the ROI which was on right lobe of the liver and approximately 1 centimeter square on T2* map via computer software 'Cardiac VX™'. Cardiac T2* value was considered severe for < 10 ms and mild for ≥ 10 - 20 ms. Liver T2* value was considered mild for > 3,8 - 11,4 ms, moderate for > 1,8 - 3,8 ms and severe for ≤ 1,8 ms.

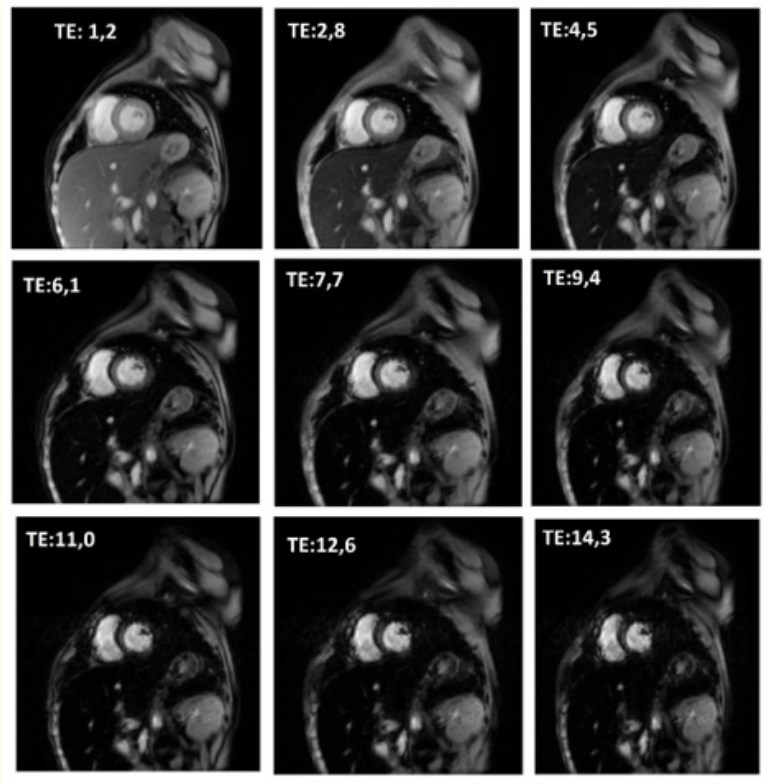

Figure 1: *16 years old female patient. There is severe cardiac iron overload causing signal decrease with higher TE value.*

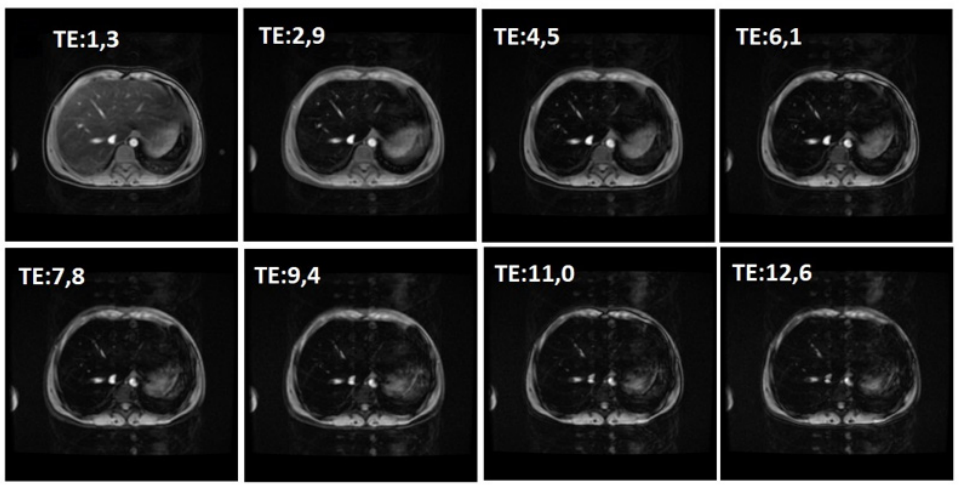

Figure 2: *11 years old male patient. There is severe hepatic iron overload causing signal decrease with higher TE value.*

The IBM SPSS (version 20.0, New York, USA) was used for statistical analysis. Since values were non-parametric, Spearman Rank correlation coefficient was used to asses correlation, Mann Whitney U and Wilcoxon test to asses mean values between independent and dependent groups. P values less than 0,05 was considered statistically significant.

Results

A total of 11 patients (5 males, 6 females), who undergone cardiac and liver MRI scan with 3 Tesla MRI scanner, diagnosed with thalassemia major and having regular blood transfusions were identified. And also, 10 patients of total 11 patients had undergone a second control MRI scan approximately one year after the initial imaging (mean time between scans was 476 (± 57,5) days).

The mean age of the patients at the time of first MRI scan was 13,9 years (9 - 21). All of the patients had no cardiac dysfunction in echocardiography results. 6 patients had monthly and 5 patients had every three weeks blood transfusion. Except one patient, all of the patients had oral deferasirox chelation therapy and mean dose was 1025 (± 362,28) mg per day.

There were 3 patients with cardiac siderosis; one of them had severe and two of them had mild siderosis. The age of these patients were 9, 14 and 15 years. All of the patients had iron overload in liver; 4 patients mild, 5 patients moderate and 2 patients severe (Table 1).

Mild		Hepatic iron overload		
		Moderate	Severe	
Cardiac Siderosis	Positive	1 (9,1%)	1 (9,1%)	1 (9,1%)
	Negative	3 (27,3%)	4 (36,4%)	1 (9,1%)

Table 1*: Distribution of cardiac and hepatic iron overload.*

The mean blood ferritin level of total 11 patients was 1820,87 ng/ml. Patients having cardiac siderosis had 3373,88 ng/ml and having no cardiac siderosis had 1238,49 ng/ml blood ferritin level, so there was statistically significant difference between them (P = 0,041).

There was a statistically significant negative strong correlation between cardiac T2* time and blood serum level (r = 0,729; P = 0,011). There was no statistically significant correlation between hepatic T2* time and blood ferritin level (r = -0,255; P = 0,45).

The mean blood hemoglobin level of total 11 patients was 8,33 g/dl. There was no statistically significant difference between cardiac siderosis groups (P = 0,759). But there was a strong negative correlation between hepatic T2* time and hemoglobin level (r = 0,601; P = 0,049).

There was no statistically significant difference in cardiac T2* and hepatic T2* time between genders both first and control imaging.

The mean hemoglobin and ferritin levels of 10 control patients were 8,31 g/dl and 1686,05 ng/ml before the first imaging. Between the first and control imaging the mean hemoglobin and ferritin levels were 8,12 g/dl and 1260.23 ng/ml. Both ferritin and hemoglobin levels reduced statistically significant between first and control imaging (P = 0,038 and P = 0,036). The mean cardiac T2* and hepatic T2* time was 21,07 ms and 3,62 ms at first imaging; 23,01 ms and 3,72 ms at control imaging. But there were no statistically significant increase in cardiac and hepatic T2* time.

Discussion

Because of ineffective hematopoiesis; anemia appears in thalassemia and intestinal absorption of iron is also increased. Treatment of thalassemia with blood transfusions is another cause of iron overload. İron overload leads to oxidative stress and impairment to cell membrane. At the end, cardiac, hepatic and endocrine glands are having functional impairment as well as skeletal changes due to bone marrow excessive activation [1].

Between complications of thalassemia, cardiac iron overload and cardiac complications (heart failure and aritmia) are the leading mortality factor [6]. Hepatic complications due to iron overload include inflammation, fibrosis and finally cirrhosis [7].

Serum ferritin level is the most common option in monitoring iron overload which is very sensitive but not specific. Because serum ferritin level can increase with inflammation as acute phase reactant, in metabolic disorders and hepatitis [8]. Echocardiography is a modality that can diagnose cardiac iron overload related complications only after heart failure begins [9].

According to literature, there is lower cardiac and hepatic T2* time in thalassemia major patients and also strong negative correlation between serum ferritin level and T2* times [10]. In our study there was strong negative correlation between serum ferritin level and initial cardiac T2* time as expected. But there was no significant correlation between serum ferritin level and initial hepatic T2* time and also between cardiac and hepatic T2* times. Result of the iron chelation therapy effect on liver can be increased because of the iron storage duty of liver and this may explain why there is no significant correlation between cardiac and hepatic T2* time; also ferritin levels and hepatic T2* time.

There was a negative correlation between blood hemoglobin level and initial hepatic T2* time in our study which reveals the importance of lower targeted hemoglobin levels of blood and less blood transfusion in order to avoid iron overload. A moderate transfusion regimen which targets hemoglobin level between 9-10 g/dL is already recommended in literature [11]. But the mean hemoglobin levels of the patients in our study was 8,33 g/dL and this may suggest lower hemoglobin levels can be targeted as long as patients are asymptomatic.

In our study, there was a statically significant decrease in mean ferritin and hemoglobin levels between first and control imaging of 10 patients. The decrease of mean hemoglobin level can be result of lower blood transfusion rate and the decrease of mean ferritin level can be result of both lower transfusion rate and also better chelation compliance which suggests that assessment of iron overload may have an influence on patients having iron overload and clinicians about chelation compliance and transfusion regimen. But there was no statically significant influence of lower ferritin levels on cardiac and liver T2* times which suggest that effect on iron overload at myocardia and liver parenchyma can require more than one year.

Yang., *et al.* reported that there could be cardiac siderosis in pediatric thalassemia patients as young as 6 years in case of bad chelation therapy [12]. In our study, the youngest patient having cardiac siderosis was 9 years even tough having chelation therapy. Because of the patients have no clinical symptom, assessment and following up of iron overload with MRI scan have a crucial role even in younger patients.

According to our experience, both cardiac and hepatic T2* MR scanning is possible in a session with a single breath hold time due to acquiring time of gradient echo T2* sequence is very short. This result with imaging is possible without anesthesia even with younger patients.

This study had some limitations. It was retrospective design, having small number of patients and single hospital study. So results cannot be generalised overall thalassemia patients. Also, there was no cardiac functional imaging to correlate cardiac functions with other parameters. The other limitation of the study was no histopathological assessment of iron amount at liver and myocardia.

Conclusion

To conclude; cardiac and liver T2* imaging is feasible method of assessment of cardiac and hepatic iron overload even before the iron overload complication and clinical signs appeared.

Authors Contribution

All authors contributed to design, data gathering-analysis and preparation of manuscript of the study.

Conflict of Interests

None declared.

Ethical Considerations

The institutional ethical committee approved this retrospective study (25403353-050.99-E.54477).

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