Original Article

Evaluation of left Ventricular function correlation in patients with Thalassemia Major Beta with Iron deposition in Myocardial and Liver tissue using transverse relaxation T2 * calculated in Cardiovascular MRI

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ABSTRACT

background: Thalassemia is an autosomal genetic condition in which hemoglobin loses its natural structure and results in ineffective hemoglobin in the body. Blood transfusion to these patients is one of the most important causes of iron deposition in the body's organs (including the heart), which causes organ dysfunction. One of the best ways for patients to monitor their iron deposition is to use magnetic resonance imaging (MRI) and measure T2 * in their liver and heart. In this study, the relationship between left ventricular function of patients with thalassemia major Beta and iron deposition in myocardial and hepatic tissues using transverse relaxation T2 * time calculated by MRI was investigated. Methods: Twenty-two patients were randomly selected from Shaheed rajaei Cardiovascular and medical research center. Cardiovascular MRI was performed with the relevant protocols to measure the parameters. R2*, T2*, and cardiac function were extracted and then Student t-test was used and finally, the T2* To each of the desired cardiac performance indicators, the correlation and threshold of left ventricular changes in patients with iron deposition were determined. Results: In this study, it was found that there is a significant linear relationship between decrease in left ventricular ejection fraction with T2* values in patients and 55% of left ventricular ejection fraction decrease is due to iron deposition ($P < 0.05$). Conclusion: According to the results, proper follow up of patients with Beta thalassemia major, using MRI, at the right time we can be aware of the of iron deposition that could increase the risk of heart failure and arrhythmias and we can perform appropriate treatment to decrease complications.

Keywords: T2* relaxation time, Cardiac Magnetic Resonance imaging, Beta Thalassemia Major, left Ventricular ejection fraction.

Introduction

Thalassemia is an inherited single gene disorder caused by impaired synthesis of the globin chain of hemoglobin leading to various degrees of defective b- chain production, an imbalance in globin chain synthesis, ineffective erythropoiesis and anemia.

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Extremely different phenotypes exist within the thalassemia syndromes: at one end of the spectrum, there is thalassemia minor, a clinically silent, mildly hypochromic and microcytic anemia. At the other end, there is thalassemia major (TM) characterized by a severe anemia requiring lifelong transfusions to prolong survival and allow normal development. This leads to iron overload and toxicity, resulting in severe endocrine, liver and cardiac dysfunctions. [1] Cardiac failure due to iron overload remains the most common cause of death in patients with beta thalassemia major (TM) in developed countries, accounting for up to 71% of all deaths from this disease. A key feature of the clinical scenario is that iron- induced cardiomyopathy is reversible if intensive chelation treatment is instituted in time before the onset of overt left ventricular (LV) cardiac failure, which carries a poor prognosis. Thus, early detection of myocardial iron overload is important. [2]

Attempts to measure myocardial iron loading using T2 have been reported, but such methods have not received widespread use due to problems with motion artifacts, sensitivity, and reproducibility. T2-star (T2*) cardiac magnetic resonance imaging (MRI), which uses a single measurement in the mid-ventricular septum, has been validated for quantitative evaluation of myocardial iron overload. [3]

T2***** relaxation refers to decay of transverse magnetization caused by a combination of spin-spin relaxation and magnetic field inhomogeneity. T2***** relaxation is seen only with gradient-echo (GRE) imaging. T2***** relaxation is one of the main determinants of image contrast with GRE sequences and forms the basis for many magnetic resonance (MR) applications, such as susceptibility-weighted (SW) imaging, perfusion MR imaging, and functional MR imaging. GRE sequences can be made predominantly T2***** weighted by using a low flip angle, long echo time, and long repetition time. [4]

Review of similar articles:

In a study by Mark A. Westwood et al in 2005 on 67 patients it was demonstrated that Diastolic function was normal in a high proportion of the beta thalassemia major patients with normal myocardial iron (T2* > 20 millisecond), demonstrating good specificity. in patients with abnormal myocardial T2*, diastolic parameters showed correlations with falling myocardial T2*, indicating that diastolic function is abnormal in myocardial iron overload. However, the correlations were not strong, and most patients with abnormal myocardial iron had diastolic function that was within the normal range for a single measurement. Thus, the sensitivity for detecting myocardial iron overload by diastolic function was very limited. [2]

In another study by Selen Bayraktaroğlu et al in 2011 they found a normal left ventricular ejection fraction in patients with normal myocardial T2* values, but they detected a progressive decrease in the left ventricular ejection fraction with increasing myocardial siderosis. Left ventricular dysfunction was present in three patients. In all of these patients, the myocardial T2* values were indicative of myocardial siderosis. [5]

Also, in another study by Carlo Liguori et al in 2015 Significant differences were found between thalassemia major patients with iron overload and thalassemia major patients without iron overload: in thalassemia major patients with iron overload, decreased left ventricular and right ventricular ejection fraction and increased volumes were observed, compared to thalassemia major patients without iron overload. [1]

Materials and Methods:

This study was an analysis of myocardial T2* scans of TM patients who were referred to the Shaheed Rajaei Cardiovascular Medical and Research Center in Tehran, Iran. The study group included 22 patients (10 males and 12 females). The mean age of the study population was 22.0±4.6 years (range, 11−35 years). Patients with cardiac or vascular anomalies (congenital heart disease, valve disease, etc.) were not included in the study. This study was approved by the local Research Ethics Committee. All MRI examinations were performed with a 1.5 Tesla (T) scanner (Avanto, Siemens, Erlangen, Germany). The scans included measurement of the liver R2 value; the myocardial T2* value and left ventricular (LV) functions with following protocol: 3 Plane 2D True-Fisp Localizer.2 Chamber, 3 Chamber, 4 Chamber, Short Axis, RVOT Retrospective Cine 2D True-Fisp MR Imaging.4 Chamber,2 Chamber, Short-Axis 8-Echo-GRE & 12-Echo-GRE (T2* Mapping) MR Imaging. The lower limit of normality for $T2^*$ in the assessment of myocardial iron load has been considered 20 msec [6]. Patients with $T2^* > 20$ ms were considered to be free of cardiac iron overload, while patients with $T2^* < 20$ ms were considered to have cardiac overload. Ventricular volumes and ejection fractions were analyzed with CMRtools (CMRtools, Cardiovascular Imaging Solutions). The lower limit of normal for EF was considered to be 55%. Hepatic T2* >7.2ms and dry weight <5mg/g was considered as mild hepatic iron loading, T2* 3.3-7.2ms and dry weight 5-10mg/g as moderate hepatic iron loading and 2.2-3.3ms and dry weight 10-15mg/g as severe hepatic iron loading. Statistical analysis was performed using a computer software (Statistical Package for Social Sciences version 15.0, SPSS Inc., Chicago, Illinois, USA). Statistical significance was considered for $P < 0.05$.

Results:

In this study, it was found that there is a significant correlation between left ventricular ejection fraction in patients with cardiac T2 * values and 55% of left ventricular ejection fraction decrease was due to iron deposition (P <0.01). The linear relationship between EF and iron deposition in myocardial tissue is as follows: $Y = 0.22x + 45.94$.

There was no significant correlation between ejection fraction and liver T2* parameter in this study. ($p = 0.2$)

Also, no significant correlation was observed between liver T2* values and heart T2* values. ($p = 0.32$)

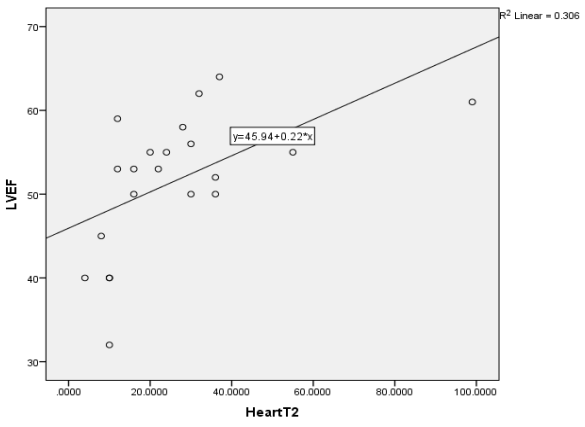

Figure 1:heart T2

Discussion:

Cardiac complications such as heart failure and arrhythmias are the significant causes of death in TM patients. Although heart dysfunction in TM patients is multifactorial in origin, heart failure is mainly attributed to iron toxicity [7]. In TM, the iron overload results from both excessive iron absorption from the gastrointestinal system and repeated blood transfusions. Transfusional iron is deposited in the reticuloendothelial system (RES); after the stores of the RES are saturated, iron deposition increases in parenchymal tissues such as endocrine glands, hepatocytes and the myocardium [8, 9]. In the literature, there are reported echocardiographic studies evaluating several functional and volumetric parameters in thalassemia patients [10, 11]. MRI techniques have recently been used to detect myocardial iron load and cardiac function [12, 13]. In this study, we evaluated Left Ventricular Function in Patients with Thalassemia Major Beta with Iron Deposition in Myocardial and Liver Tissue Using transverse relaxation T2 * Calculated in Cardiovascular MRI. We used myocardial and liver T2* and functional CMR imaging, which are considered to be the gold standard for assessment of cardiac and liver iron loading and cardiac function. We used a cut-off value for left ventricular impairment of 55%. We detected there is a significant correlation between decrease in left ventricular ejection fraction with cardiac T2 * values.

Conclusion:

Considering the significant relationship between reduction of left ventricular ejection fraction and T2 * values of the heart in this study, appropriate follow up of thalassemia major Beta patients using MRI as an accessible and noninvasive method at the right time it is possible to evaluate amount of iron deposition and with this method we could find the risk of heart failure and do appropriate treatment to reduce morbidity and mortality in thalassemia major Beta patients.

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