MAGNETIC RESONANCE IMAGING ASSESSMENT OF EXCESS CARDIAC IRON IN THALASSEMIA MAJOR: WHEN TO INITIATE?

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Introduction

Thalassemia major(TM) is common in southern China. Patients with TM should get appropriate transfusion and chelation therapy before cardiac symptoms are presented. Cardiac complications such as arrhythmia, dysfunction or heart failure are the most common causes of death in TM and primarily result from iron accumulation[1], demonstrating its early diagnosis importance. Serum ferritin and liver iron have no or weak correlation with cardiac iron, which are not ideal surrogates for cardiac iron measurement [1] or, according to Kolnagou, A et al [2], may even mislead for estimating cardiac iron load. Cardiac MRI T2* has been proved to be a validated and valuable non-invasive tool to detect excess cardiac iron as well as hepatic, splenic or pancreatic iron. It also can detect pre-clinical cardiac iron overload and is regarded as the central to early identification of cardiac iron overload in TM. As early systolic and diastolic dysfunction can occur in TM patients younger than 10 years old even in asymptomatic patients, a proper early initial age for cardiac MRI T2* assessment is absolutely necessary and crucial. Although Wood's and Fernandes et al [3,4] suggested 7 or 8 years old as the initial age of cardiac MRI screening, it's still disputable at what age T2* screening should be initiated. In the recent study from Berdoukas, V et al [5], detectable cardiac iron can occur even at patients as young as 6.5 years old. We therefore initiated a project to explore the optimal initial age of cardiac MRI T2* assessment in patients with TM.

Methods

The study was approved by the Committee of Clinical Investigation at Sun Yat-Sen Memorial Hospital. Consents were not obtained for MRI examinations since these were performed for clinical indications. 102 patients (age,11.4±5.1years, male,62.7%) between June of 2012 and September of 2013 were included. Children under 7 years of age will be studied freely breathing under sedation if they cannot hold breath cooperatively with the scanning. The study was examined with a 1.5-T Philips MRI scanner. A mid-ventricular short axis slice was obtained with a black blood T2*sequence at 8 echo times (TE) from 1.7 to 20.3 ms at approximately 2.7 ms increments. Other parameters were as follow: flip angle=20°, matrix size=248×90 , sample bandwidth=790.6 Hz/pixel, slice thickness 10 mm and field of view(FOV)=400 mm. To calculate the T2* value of myocardium, region of interests (ROI) were drawn in the ventricular septum, avoiding blood pool and cardiac vessels. A series of short axis images were acquired with Balance-SSFP sequence to measure the left ventricular ejection fraction (LVEF). It was performed with 8 breath-holdings and each one took 8 seconds.The hepatic T2* scanning was performed with parameters as follow: TR/TE1/delta TE: 200/0.85/0.9 ms, FOV of 400×200 mm, flip angle of 20°, matrix of 160×65, slice thickness of 10 mm. liver T2* was measured from a single midhepatic slice or slice between the first and second hepatic porta. ROI was drawn around the right liver boundary, excluding obvious hilar vessels or breathing artifacts. Image analysis was performed using Thalassaemia tools (a plug in of CMRtools). Mean, standard deviation were calculated from all pixels within the ROI. Measurements and analyses for all images were performed by two experienced investigators. All statistics were performed by using software (SPSS, version 16.0). Linear regression was calculated to correlate the cardiac, hepatic T2* values and ferritin. Scatterplots and Spearman regression were calculated to analyze the associations between cardiac T2* and patient age. A p value of < 0.05 was considered significant.

Results

Using the T2*cut-off of 20ms, no patient under 5 years of age showed detectable cardiac iron. 3/19(15.8%) patients under 7 years of age had a cardiac T2*≤20ms (5.5 to 7 years) but none≤10ms; while 35/83(42.2%) patients above 7 years old had a cardiac T2*≤20ms (5.5 to 32 years) and 18 of them≤10ms (8 to 21 years). Cardiac T2* correlated weakly with ferritin and liver T2* (r=-0.39, 0.41 respectively, both p<0.001), but not with patient age(P>0.05) (Figure1).Serial data from 6 patients showed that cardiac T2* value was improved over time, one of them even from abnormal to normal (Figure2,3). The average increment is 2.7±2.6ms.

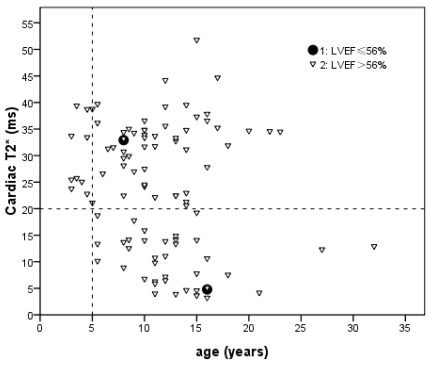

Figure 1. Associations between cardiac T2* and age.

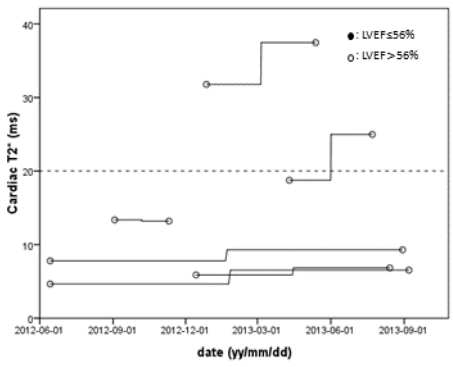

Figure2. Serial data in 6 TM patients.

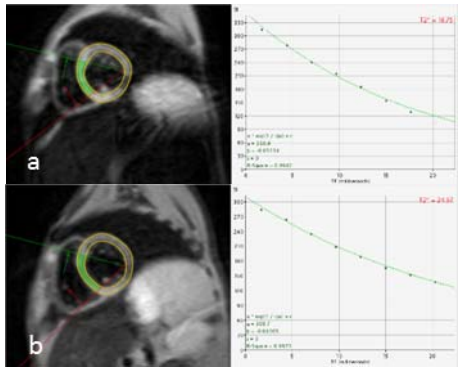

Figure3. a TM patient of 5.5 years old with detectable cardiac iron at the first MRI screening(a) showed normal cardiac iron level in serial scanning(3.5 months latter) after improved chelator dose with better compliance (b).

Discussion and Conclusions

Cardiac iron overload can occur in young patients with TM as young as 5.5 years old. Assessment of cardiac iron with MRI T2* should be initiated as early as 5 years of age even in asymptomatic patients.

Cardiac complications, resulted from iron deposition, is the most severe consequence of organic iron overload and is the most common causes of death in patients with TM. It is much slower and more difficult to remove cardiac iron than liver iron, especially in the severe degree. So it seems sensible to diagnose it at the early age and modify chelation therapy positively to reverse it at the early stage rather than make a change passively until severe cardiac iron overload developed. Thus, from our study, it seems prudent to start monitoring cardiac iron load with MRI T2* as early as 5 years of age if suboptimal chelation is performed, even in asymptomatic patients.

References

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