

Assessment of cardiac iron and right ventricular function by GRE-MRI in patients with thalassemia and sickle cell disease

J. Yamamura¹, R. Grosse², R. Engelhardt², J. Graessner³, G. Kurio⁴, R. Fischer⁴, G. Janka², and G. Adam¹

¹Diagnostic and Interventional Radiology, University Hospital Hamburg-Eppendorf, Hamburg, Hamburg, Germany, ²University Hospital Hamburg-Eppendorf, ³Siemens AG, ⁴Children's Hospital & Research Center, Oakland, USA

Introduction

In patients with thalassemia, left ventricular (LV) cardiomyopathy is related to cardiac iron burden in myocytes and mitochondria. Cardiac iron concentration and LV function can be measured by established quantitative MR methods. However, elevated or normal cardiac iron load with preserved LV function is often seen in patients with beta-thalassemia major (TM), intermedia (TI), and sickle cell disease (SCD), while right ventricular (RV) dysfunction caused by pulmonary hypertension may become the leading factor of heart failure.

Methods

In 10 splenectomized patients (4 TM, 4 TI, 1 SCD: age 26 – 43 y), in 5 SCD patients (age 19 – 24 y), and in 16 TM patients (age 11 – 32 y), the transversal relaxation rate R_2^* ($= 1/T_2^*$) was determined from mid-papillary short axis slices. Breathhold retrospective ECG gating was used on a 1.5 T imager (Symphony®, Siemens AG, Erlangen) acquiring data from 9 heartbeats with 8 echo times between 1.9 and 21.5 ms in end-diastole (TR = 223 ms, flip angle = 20°). LV function was assessed from 6 mm short and long axis slices of cine images (25 phases). RVEF was estimated from LV stroke volume and RV end-diastolic volume. Additionally, the left interventricular curvature ratio (LVCR) was derived from delineating the circular mid-systolic LV shapes between the RV junction points. RVEF was related to RV systolic pressure (RVSP) and N-Terminal pro-brain natriuretic peptide (NT-proBNP).

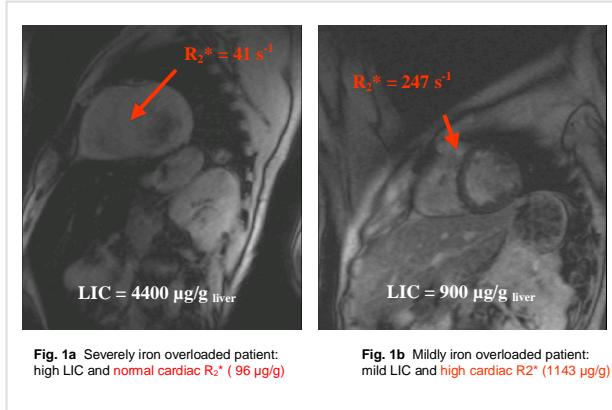


Fig. 1a Severely iron overloaded patient: high LIC and normal cardiac R_2^* (96 $\mu\text{g/g}$)

Fig. 1b Mildly iron overloaded patient: mild LIC and high cardiac R_2^* (1143 $\mu\text{g/g}$)

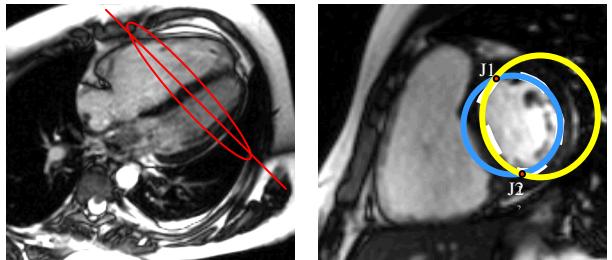


Fig. 2a Breathhold retrospective ECG triggered 4-chamber view of the heart in end-diastole from a splenectomized patient with β -thalassemia major (29 y, cardiac iron: 891 $\mu\text{g/g}$, RVEF: 39 %, NT-proBNP: 3598 ng/l)

Fig. 2b Short axis slice in early systole. Left interventricular septal radius R_{IVS} and free wall radius R_{FW} are determined from circular fits between the junction points J1 & J2 (yellow & blue circle). Low R_{FW}/R_{IVS} ($= 0.66$) may indicate PHT

Results

Cardiac relaxation rates of R_2^* above the widely accepted normal threshold of 50s^{-1} were determined in 5/10 splenectomized patients and in 6/16 TM patients. Patients with SCD did not differ from normals (range: 29 – 33 s^{-1}). The LVCR was determined between 0.6 and 0.9. Only in splenectomized patients, a decreased LVCR < 0.7 was found, which was correlated with a RVSP > 30 mm Hg indicating pulmonary hypertension. LVEF and RVEF were still normal. Only in two patients with extreme NT-proBNP levels (> 1000), a reduced RVEF $< 46\%$ at still normal LVEF was detected.

Discussion

Questionable signs of pulmonary hypertension in splenectomized patients are often caused by the chronic micro-thromboembolies. So far, the diagnosis for cardiomyopathy and arrhythmia assessed by ECG and LV function are not sufficient enough. In these patients however, the RV dysfunction caused by pulmonary hypertension may become a leading factor of heart failure. In this study, although normal LV function was found in nearly all of our thalassemia and sickle cell patients, we detected signs of pulmonary hypertension by the interventricular curvature ratio, especially in older splenectomized patients independent from their cardiac iron load.

Conclusion

Detection of early signs of pulmonary hypertension with MRI is possible by calculating the interventricular curvature ratio, which has proved to be a reliable indicator. On the one hand, measurement of cardiac iron by MRI- R_2^* is necessary for patients with Thalassemia. On the other hand, both LV-function and RV-function analysis are obligatory for sufficient diagnosis. The measurement of cardiac iron by MRI- R_2^* should be accompanied not only by the assessment of LV function, but also by analyzing the cine images for RV dysfunction and signs of pulmonary hypertension.