Different patterns of myocardial iron overload by T2* Cardiovascular MR as markers of risk for cardiac complication in thalassemia major.

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Introduction. Cardiac complications mainly related to myocardial iron overload (MIO) remain the main cause of morbidity and mortality in thalassemia major (TM) [1]. Thalassemia cardiomyopathy is treatable and partly reversible if appropriate chelation therapy is instituted in time. The validated multislice multiecho T2* Cardiovascular Magnetic Resonance (CMR) technique has permitted to quantify segmental and global myocardial iron burden detecting different patterns of iron overload [2]. Aim of our study was to verify the risk of cardiac complications related to different patterns of MIO in a large cohort of TM patients..

Materials and methods. We considered 812 TM patients for who CMR and cardiac data were collected in the Myocardial Iron Overload in Thalassemia (MIOT) central data base [3].
For the assessment of MIO, three short-axis views of the left ventricle (LV) were acquired and the myocardium was segmented into 16-segments standardized LV model. The T2* value on each segment was calculated as well as the global T2* value [2]. A conservative cut off of 20 ms was considered the limit of normal for the segmental and global T2* values.
Heart failure requiring medications was defined by a positive clinically and instrumentally documented or by CRM when left and/or right ejection fractions were ≤ 4SD from the mean value normalized to age and gender, defined using the data of 142 patients with no history of cardiac disease, normal electrocardiogram, no known risk factors, and no cardiac iron. A pulmonary hypertension was diagnosed if the trans-tricuspidal velocity jet was greater than 3.2 m/s. Arrhythmias were ECG documented and requiring medication.

Results. We identified 4 groups of patients: group I (17%) with homogeneous MIO (all segments with T2*<20 ms), group II (12%) with heterogeneous MIO (some segments with T2*<20 ms and others with T2*≥20 ms) and global heart T2*<20 ms; group III (29%) with heterogeneous MIO and global heart T2*≥20 ms; group IV (42%) with no MIO (all segments with T2*≥20 ms).
Table 1 shows the results of the comparison among the 4 groups. The groups were homogeneous for age and sex. The percentage of patients with cardiac complications was significantly different in the 4 groups. In particular, the percentage of patients with heart failure was significantly different in the 4 groups. No significant differences were found among groups in the percentage of arrhythmias and pulmonary hypertension. Odds Ratio for cardiac complications was 1.7 (1.0-2.7 OR 95% CI; P=.041) for patients with homogeneous MIO vs patients with no MIO. Odds Ratio for heart failure was 2.3 (1.3-4.2 OR 95% CI; P=0.004) for patients with homogeneous MIO versus patients with no MIO and 2.2 (1.1-4.2 OR 95% CI; P=.020) for patients with heterogeneous MIO and global heart T2*<20 ms versus patients with no MIO.

Table 1. *Comparison among the 4 identified groups.*

	Homogeneous MIO (N=138)	**Heterogeneous MIO and global Heart T2* < 20 ms (N=97)**	**Heterogeneous MIO and global Heart T2* ≥ 20 ms (N=238)**	**No MIO (N=339)**	**P**
Sex (M/F)	67/71	38/59	119/119	157/172	0.304
Age (years)	28.9 ± 7.4	30.8 ± 7.4	30.4 ± 8.9	31.1 ± 8.9	0.069
Hb pre-transfusion (g/dl)	9.7 ± 0.6	9.6 ± 0.5	9.7 ± 0.6	9.6 ± 0.8	0.309
Ferritin levels (ng/l)	2454 ± 1969	2043 ± 1796	1328 ± 1277	1114 ± 1004	<0.0001
Cardiac Disease, n (%)	34 (24.6%)	20 (20.6%)	20 (8.4%)	56 (16.5%)	<0.0001
Heart failure, n (%)	24 (17.4%)	16 (16.5%)	10 (4.2%)	28 (8.3%)	<0.0001
Arrhythmias, n (%)	13 (9.4%)	6 (6.2%)	8 (3.4%)	23 (6.8%)	0.112
Pulmonary Hypertension, n (%)	3 (2.2%)	1 (1.0%)	4 (1.7%)	14 (4.1%)	0.192

Conclusion. Homogeneous MIO predicts a significantly higher risk to develop cardiac complications, especially heart failure, suggesting an intensive chelation therapy in this group of patients.

References. [1] Borgna-Pignatti C et al. Haematologica 2004;89:1187-93. [2] Pepe A. et al. EJH 2006;76:183–192. [3] Meloni A et al. Int J Med Inform 2009;78(8):503-512.