Myocardial fibrosis by CMR LGE in a large cohort of pediatric thalassemia major patients

Antonella Meloni[1], Maddalena Casale[2], Aldo Filosa[2], Rosellina Rosso[3], Antonino Vallone[4], Gianluca Valeri[5], Daniele De Marchi[1], Vincenzo Positano[1], Massimo Lombardi[1], and Alessia Pepe[1]

[1]CMR Unit, Fondazione G.Monasterio CNR-Regione Toscana and Institute of Clinical Physiology, Pisa, Italy, [2]UOSD Centro per le Microcitemie, AORN Cardarelli, Napoli, Italy, [3]U.O. Talassemie ed Emoglobinopatie, Ospedale Ferrarotto CT Az. Osp. Universitaria Policlinico Vittorio Emanuele, Catania, Italy, [4]Istituto di Radiologia, Az. Osp. "Garibaldi" Presidio Ospedaliero Nesima, Catania, Italy, [5]Dipartimento di Radiologia, Azienda Ospedaliero-Universitaria Ospedali Riuniti "Umberto I-Lancisi-Salesi", Ancona, Italy

Introduction. CMR by late gadolinium enhancement (LGE) allows to detect myocardial fibrosis [1]. Myocardial fibrosis was shown to be a relative common finding in large cohort of Italian thalassemia major (TM) patients mainly related to HCV infection [2], but specific studies involving only pediatric patients are not available. This study investigated the prevalence and clinical-instrumental correlates of myocardial fibrosis in pediatric TM patients.

Materials and methods. We studied retrospectively 76 pediatric patients with TM (44 boys, 4.2 -17.9 years old, mean age 13.6±3.4 years) enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) Network [3]. All patients were well transfused and chelated since the early childhood. LGE images were acquired to detect myocardial fibrosis. Myocardial iron overload (MIO) was measured by T2* multislice multiecho technique [4]. Biventricular function parameters were quantitatively evaluated by cine images.

Results. Myocardial fibrosis was detected in 12 (15.8%) patients. In all patients the location of the fibrosis was epi-mesocardial, with no ischemic pattern. The youngest patient showing myocardial fibrosis had 13 years of age.
The Table shows the comparison between patients with and without myocardial fibrosis. A significant higher MIO was detected in patients with myocardial fibrosis. The left atrial area, all the left ventricular (LV) indexed volumes, the LV mass index and the bi-ventricular stroke volume indexes were significantly higher in the fibrosis group than in the no-fibrosis group.

	Fibrosis group (N=12)	No-fibrosis group (N=64)	P-value
Sex (M/F)	10/2	34/30	0.062
Age (years)	15.4 ± 1.8	13.3 ± 3.5	0.073
Transfusions starting age (years)	1.2 ± 0.9	1.3 ± 0.8	0.691
Chelation starting age (years)	3.1 ± 1.8	3.1 ± 2.3	0.705
HCV antibodies	0	3 (4.8%)	0.437
Hb pre-transfusion (g/dl)	9.7 ± 0.3	9.5 ± 0.7	0.757
Ferritin levels (ng/l)	3012 ± 2167	2225 ± 1396	0.226
Global Heart T2 (ms)*	20.9 ± 13.9	30.6 ± 9.7	0.022
Pts with global heart T2<20 ms, N (%)*	7 (58.3)	12 (18.8)	0.008
*N. of seg. with abnormal T2**	9.0 ± 7.0	3.8 ± 5.2	0.030
Left atrial area (cm^2)	18.3 ± 3.1	15.9 ± 3.9	0.050
Right atrial area (cm^2)	16.9 ± 4.3	14.9 ± 3.5	0.169
LV EDVI (ml/m^2)	102.9 ± 23.5	87.0 ± 16.3	0.005
LV ESVI (ml/m^2)	42.0 ± 12.1	35.1 ± 8.9	0.022
LV SVI (ml/m^2)	60.7 ± 12.4	51.8 ± 10.7	0.012
LV mass index (g/m^2)	65.3 ± 11.4	53.8 ± 11.4	0.003
LV EF (%)	59.2 ± 4.4	59.7 ± 5.9	0.368
RV EDVI (ml/m^2)	96.9 ± 25.6	81.6 ± 17.1	0.089
RV ESVI (ml/m^2)	36.9 ± 13.7	32.3 ± 8.3	0.458
RV SVI (ml/m^2)	61.5 ± 11.6	48.9 ± 14.1	0.005
RV EF (%)	62.6 ± 4.4	60.2 ± 7.1	0.175

Conclusions. In pediatric TM patients myocardial fibrosis is not a rare finding to keep in mind in the cardiological management. When appropriate treatment has been administered since early childhood, CMR LGE can be postponed until 13 years of age. By the natural history of this large cohort of pediatric patients where HCV infection has been appropriately prevented, myocardial fibrosis seems to be associated with MIO and high cardiac output.

References. [1] Mahrholdt H. et al. Eur Heart J 2005;26:1461-74. [2] Pepe A et al. Heart 2009;95:1688-93. [3] Meloni A et al. Int J Med Inform 2009;78:503-12. [4] Pepe A et al. JMRI 2006;23:662-8.