No Evidence for Iron Overload in the Heart of Multitransfused Elderly Patients with Sideroblastic Anemia (RARS): A Quantitative T2* weighted MRI study

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Introduction: Iron overload is a well known complication in multitransfused patients with myelodysplastic syndromes (MDS), contributing to morbidity and mortality. The presence of non transferrin bound iron (NTBI), a catalyst in generation of reactive oxygen species, has also been documented (1) resulting in impaired function of the mitochondria in the heart. T2* MRI allows accurate noninvasive evaluation of iron in different body organs. Studies in thalassemia demonstrated that there was no direct correlation between the amount of iron deposited in liver and heart.

Purpose: The purpose of the present study was to evaluate using T2* the degree of iron overload in the heart and liver of transfused patients with the sideroblastic form of MDS.

Methods: MRI measurements were performed using 1.5T, GE MRI system. Scans included left ventricular volumetric and function measurements, and a breath-hold multi echo gradient echo T2* sequence: TR 35 ms, FA 30^o, 128X256 matrix, FOV 36 cm, SW 8-10 mm, 16 echos starting with TE 1.9 ms. Only the even TEs were used for T2* calculations following Anderson et. al.(2). T2* values across regions of interest located at the cardiac septum and at the subphrenic part of liver were evaluated.

Results: Reported myocardial and liver T2* values for healthy volunteers are 52 ± 16 ms and 33±7 ms, respectively, where cardiac iron overload is below 20 ms (2). The present results in the controls are in line with those values and are displayed in the table:

Diagnosis	MDS	MDS	MDS	MDS	MDS	**HEMPAS**	**Controls**(4)
Age/ Gender	75/M	87/M	84/F	80/M	69/M	52/F	34-68/3F,1M
No. of PC units	67	50	58	30	43	0	0
Ferritin (ng/ml)	3920	1853	1790	NA	1930	1280	
LVEF (%)	70	63	59	15	70	46	82-196
T2* liver (ms)	3-5	<2	<2	18-21	25-35	<2	27-37
T2* Heart (ms)	42-46	15-20	33-40	47-50	35-5	3-5	41-47

In 4 out of 5 MDS patients who received up to 67 transfusions throughout a period of 1 to 5 years, there was no evidence of iron accumulation in the heart, while in one untransfused patient with Congenital dyserythropoietic anemia type II (HEMPAS) despite chelation with Desferrioxamine and Deferiprone there was a lot of iron in the heart. Moreover, in spite of their advanced age, 4 out of 5 patients had normal left ventricular ejection fraction. The one exception (LVEF-15%) has severe atherosclerotic heart disease. On the other hand, 4 of 5 patients had a lot of iron in their liver. There was no correlation between serum ferritin levels and the T2* measurements.

Conclusions: These preliminary results suggest that iron accumulation in elderly patients with refractory anemia with ringed sideroblasts (RARS) who received more than 30 blood units is primarily in the liver and not in the heart. In order for the heart to be involved higher number of transfusions and/or a longer duration of the disease may be required. Moreover, the mechanism of iron deposition in the heart seems to be different in congenital anemias, where intravascular premature hemolysis results in release of iron, and accumulation in the heart even without transfusions. The present findings indicate that there is a rationale for iron chelation in MDS patients at least from the liver and possibly also from the heart. The mode of chelation will have to be designed accordingly, since the efficacy of the available chelators is not the same. T2* MRI may be used to follow quantitatively and noninvasively the effect of these drugs.

References:

1. Winder et al, Blood 2003;102:916a
2. Anderson et al, Eur Heart J 22:2171,2001