

**2009 Annual Meeting of the
American Society of Hematology**

Highlights Report

**Prevalence of Cardiac Dysfunction in Patients with
Thalassemia Major with Respect to Cardiac Magnetic
Resonance**

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Abstract 2013

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**Prevalence of Cardiac Dysfunction in Patients with Thalassemia Major with
Respect to Cardiac Magnetic Resonance (Abstract # 2013)**

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Despite advances in clinical management, heart failure secondary to cardiac iron overload is responsible for most deaths in transfused patients with β -thalassemia, and may contribute to mortality in other transfusion-dependent patients including those with MDS.^{1,2} Cardiac magnetic resonance (CMR) can be used to assess the level of iron accumulation in the heart, and may be useful to predict the likelihood of future cardiac events and plan commencement of protective iron chelation therapy in most at-risk individuals.

This analysis estimated the predictive power of myocardial iron load, as assessed by the relaxation parameter T2* by CMR, for cardiac disease (CD). A total of 318 transfusion-dependent thalassemia patients were analyzed and were characterized as having CD if they experienced left ventricular shortening fraction <30%, arrhythmia or requiring therapy with cardiac medications for clinically-evident heart dysfunction. The predictive power of T2* was estimated by reviewing the cardiac events that occurred in individuals without CD, during a period of follow-up.

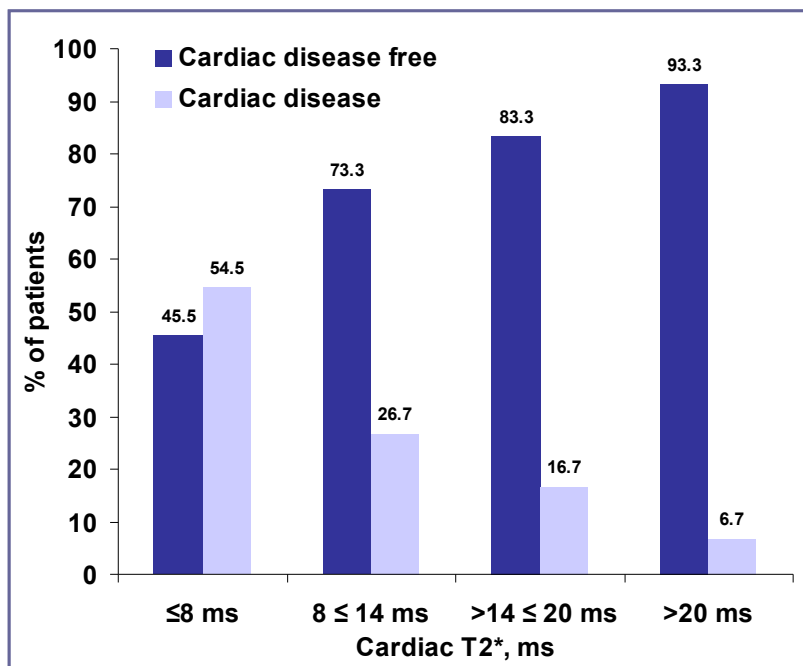
The proportion of CD-free patients increased in line with the cardiac T2* (Table 1, Figure 1).

Table 1. Cardiac T2* in CD and CD-free patients

n (%)	≤8 ms	8 ≤ 14 ms	>14 ≤ 20 ms	>20 ms	Total
CD-free	30 (45.5)	44 (73.3)	35 (83.3)	140 (93.3)	249 (78.3)
CD	36 (54.5)	16 (26.7)	7 (16.7)	10 (6.7)	69 (21.7)
Total	66 (100)	60 (100)	42 (100)	150 (100)	318 (100)

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Figure 1. Cardiac T2* in CD and CD-free patients



The relative risks of experiencing CD with a T2* <8 vs 8–14, 14–20 and >20 ms were 3.3, 6 and 16.8, respectively (Table 2).

Table 2. Relative risks of CD between different cardiac T2* groups

T2*	Odds	P value
<8 vs >20	16.8	<0.001
<8 vs 8-14	3.3	0.002
<8 vs 14-20	6	<0.001
<8-14 vs 14-20	1.8	0.23
<8-14 vs >20	5.1	<0.001
14-20 vs >20	2.8	0.05

T2* data were interrogated to assess ability to discriminate between CD and CD-free patients, and a receiver operating characteristic (ROC) analysis estimated an area under the curve of 0.79. At T2* cut-off values of 20, 17, 14 and 10 ms, sensitivity/specificity are 85.3/56%, 77.9/62.8%, 75/70% and 63.2/79.6%,

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respectively. The value of initial CMR T2* values for predicting future cardiac events in cardiac disease-free patients was 2.9/100 patient years for T2* < 8 ms, 0.9 for T2* between 8-20 ms, decreasing to 0.4/100 patient years for T2* > 20 ms.

Cardiac MRI is a sensitive tool in determining the risk for potential cardiac dysfunction in chronically-transfused patients with thalassemia major and for monitoring the need for, and efficacy of, iron chelation therapy. The introduction of novel iron chelating agents and consequent alteration in the cardiac morbidity and mortality of transfused patients may be a reason for its poor predictive power in this study.

Expert commentary: Dr John Porter, University College London, UK

One of the problems with this analysis is the grouping of cardiac arrhythmia and LV dysfunction under a single diagnosis of CD. Whereas the risk of developing left ventricular failure has been clearly linked to myocardial iron (mT2) in large prospective cohorts, the risk of cardiac arrhythmias persists, even after (mT2*) has been normalized. The second flaw in the design of this study is its cross-sectional nature, rather than a prospective design. At present there is no evidence to support the speculation by these authors that the relatively low predictive value of mT2* in this study relates to changes in chelation therapy.*

References

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2. Takatoku M, Uchiyama T, Okamoto S *et al.* Retrospective nationwide survey of Japanese patients with transfusion-dependent MDS and aplastic anemia highlights the negative impact of iron overload on morbidity/mortality. *Eur J Haematol* 2007;78:487-494.