Comparison of Cardiac Iron Overload Assessment by MRI Susceptometry and R2* in Thalassemia Patients

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Introduction

In recent years, it became obvious that the previously accepted assumption of a positive correlation between liver iron concentration and cardiac iron concentration (CIC) did not hold in well-chelated patients. Methods for quantitative iron assessment, especially MRI-R2*, have been used to assess the cardiac iron level [1]. The septal R2* in the short axis view of a mid-papillary heart slice is used for artifact-free cardiac iron measurements [2]. Based on normal control studies, a risk threshold of T2* < 20 ms or R2* > 50 s^{-1} for developing cardiomyopathy [1] has been suggested. However, It has been controversial whether the R2* method reliably reflects the tissue iron level because R2* is sensitive to shimming and susceptibility artifacts. Therefore, MRI Cardio-Susceptometry (MRI-CS) has been developed as an alternative and more direct method for cardiac iron quantification. In this study, we compare cardiac iron levels assessed with both techniques in a group of thalassemia patients.

Materials and Methods

The studies were conducted on Philips Intera 1.5T scanners. MRI-CS measurement was completed with a previously described method [3]. The magnetic susceptibilty differences $\Delta\chi$ (in SI units) of the apical cardiac wall relative to the left ventricular oxygenated blood (endo-myocardium susceptibility) and relative to the intercostal muscle (epi-myocardium susceptibility) were measured. The cardiac R2* was measured from a short axis slice [2] and a transverse slice going through the area of the susceptibility measurement using multiple gradient echoes (7 to 17 echoes with TEs up to 18 ms). All data analyses were conducted using internally developed software written in IDL.

Eleven control subjects (6 male, 5 female, age range 21 to 41 years, median 24.5) have been studied. In 9 control subjects, T2* at the septum and at apex near the chest wall, and MRI cardiac susceptometry data were acquired. Reproducibility of MRI-CS and R2* was tested in two controls. Nine thalassemia patients (5 female, 4 male, age range 5.6 to 39.5 years, median 16.0) were studied. R2* was derived from measurements of septal short axis images and apical images near the chest wall. MRI-CS study was completed in all 9 patients.

Results

From control subjects, expected T2* values were obtained for the septum (mean ± sd = 35.2 ± 5.4 ms) and for the apex of the anterior cardiac wall (32.1 ± 6.2 ms). The R2* values from the two regions were correlated (r = 0.72, p <0.02). For control subjects, $\Delta\chi_{endo} = (-0.06 \pm 0.09)\cdot 10^{-6}$ and $\Delta\chi_{epi} = (0.21 \pm 0.18)\cdot 10^{-6}$ (mean ± s.d.) were obtained. Reproducibility (mean ± s.e.m.) in control subjects from repeated scans was found for T2* (n=5) as 36.8 ± 3.0 ms for septum, 31.2 ± 2.2 ms for apex, and for relative cardiac magnetic susceptibilities (n=4) as $\Delta\chi_{endo} = (0.13 \pm 0.01)\cdot 10^{-6}$ and $\Delta\chi_{epi} = (0.45 \pm 0.03)\cdot 10^{-6}$.

Based on a previous gerbil model study [4], a specific magnetic susceptibility for wet tissue iron of $\Delta\chi = 1.54\cdot 10^{-6}$ per [mg Fe/g] is used. In control subjects, the gradient of cardiac iron distribution is negligible, and the average of iron concentration in the control hearts has been reported as 0.05 mg Fe/g wet tissue [5], corresponding to $\Delta\chi_{endo} = -0.06\cdot 10^{-6}$ and $\Delta\chi_{epi} = 0.21\cdot 10^{-6}$ found in this study. Based on these data, the endo- and epi-myocardial iron concentrations are given by CIC_{endo}(mg Fe/g wet tissue) = $0.086 + 0.65\cdot 10^{6}\,\Delta\chi_{endo}$, and CIC_{epi} (mg Fe/g wet tissue) = $-0.090 + 0.65\cdot 10^{6}\,\Delta\chi_{epi}$. The quantity $CIC_{ave} = (CIC_{endo} + CIC_{epi})/2$ is calculated as an average cardiac tissue iron concentration.

In patients, R2* of the septum and apex regions are well correlated (r = 0.97, p < 0.0001). The regression analysis yields $R2^*_{apex} = 1.05\cdot R2^*_{septum} + 6.9$ (s^{-1}). In addition, R2* and CIC_{ave} are strongly correlated (r = 0.93, p < 0.001). The linear regression yields CIC_{ave} (mg Fe/g wet tissue) = $0.01665 + 0.005048 \cdot R2^*_{septum}$ (s^{-1}) (solid thick line in the figure).

Discussion and Conclusions

We have shown that R2* at septum and near apex are in good agreement. Based on this, we studied the correlation between apical CIC measured by MRI-CS and septal R2* and found a good agreement between both measurements. The relationship between CIC and R2* was found to be very similar to that of Ghugre et al from an autopsy study of one newly deceased patient [6] (thin blue line in the Figure). Ghugre et al [6] did not have data points with R2* < 180 s^{-1}, but the slope of their regression line is in close agreement with ours.

One issue is whether the MRI-CS method provides better iron quantification than the R2* method at the risk threshold of T2* = 20 ms. According to our linear relationship, a R2* of 50 s^{-1} (T2* = 20 ms) corresponds to a CIC of 0.27 mg Fe/g wet tissue. This translates into $\Delta\chi_{endo} = 0.28\cdot 10^{-6}$ and $\Delta\chi_{epi} = 0.55\cdot 10^{-6}$. The value of $\Delta\chi_{endo}$ is beyond 2 s.d. of normal values ($\Delta\chi = (-0.24 - 0.12)\cdot 10^{-6}$), but the value of $\Delta\chi_{epi}$ is within 2 s.d. of the normal values {$\Delta\chi = (-0.15 - 0.57)\cdot 10^{-6}$}. Therefore, endo-myocardial magnetic susceptibility may be more sensitive to mild elevation of cardiac iron than R2*. One patient with a septal R2* of 50 s^{-1} is at the risk threshold for normal controls [1]. However, the susceptibility measurement clearly showed elevated iron. This case demonstrates the value of the MRI-CS method for patients with borderline R2* values.

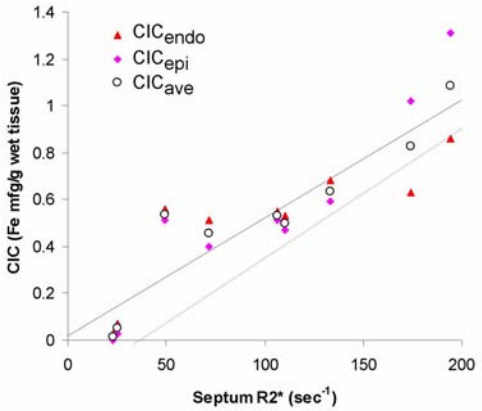

Figure. Correlation of R2* and the cardiac iron concentration measured by MRI susceptometry.

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