T1 Mapping by Cardiac Magnetic Resonance Imaging - From Histological Validation to Clinical Implication

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Disclosures: none

Background

Diffuse myocardial fibrosis / extracellular matrix expansion is a landmark feature of various cardiac diseases and is associated with an unfavorable prognosis. Recently, cardiac magnetic resonance (CMR) T1-mapping has been proposed for the quantification of extracellular matrix.

Published series mainly used two T1 mapping sequences: 1. Modified Look-Locker Inversion recovery (MOLLI) T1 mapping, allowing the calculation of extracellular volume (ECV) [1], 2. Post-contrast multiple breath-hold T1 mapping [2]. In addition, native (pre-contrast) T1 mapping has gained increasing interest [3].

Although CMR T1 mapping is a very promising technique and has been advertised as the new “non-invasive myocardial biopsy”, validation data, particularly in heart failure patients, are sparse.

Methods

Patients. 531 consecutive patients without hypertrophic cardiomyopathy, including 20 with cardiac amyloidosis, referred to CMR were prospectively enrolled.

Of these, 39 patients underwent CMR T1 mapping and left ventricular biopsy within 4 weeks. This population consisted of 26 patients with heart failure, 9 with cardiac amyloidosis and 4 with valvular heart disease.

CMR protocols. All patients underwent a CMR study on a 1.5-T scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany). Studies consisted of functional and LGE imaging, according to standard protocols. Additionally, the following types of tissue characterization using T1-mapping techniques were performed:

1) Midventricular short-axis images were acquired previous to contrast agent application and 15-20 minutes post contrast using the modified look-locker inversion recovery (MOLLI) sequence. Regions of interest were defined manually, excluding areas with late gadolinium enhancement. The ECV (in %) was estimated by using the formula:

$$ECV = (1 - hematocrit)\frac{\left(\frac{1}{T1_{myo\ post}} - \frac{1}{T1_{myo\ pre}}\right)}{\left(\frac{1}{T1_{blood\ post}} - \frac{1}{T1_{blood\ pre}}\right)}$$

2) In addition, a multiple breath-hold ECG-triggered segmented inversion recovery spoiled gradient echo sequence with increasing inversion times was used to acquire a stack of 8 images in the middle short-axis over a range of inversion times from 115ms to 900ms 15 minutes after gadolinium injection.

Outcome analysis. A combined end-point of cardiovascular re-hospitalization and death was used to determine the association of ECV by CMR with cardiovascular mortality and morbidity.

Left ventricular biopsies taken during left heart catheterization were stained with modified Trichrome. Extracellular matrix was quantified with TissueFAXS and ImageJ using a color-threshold approach and is given in percent of total specimen area.

Results

In the whole cohort, MOLLI-ECV was 29±7%. When patients were divided into ECV quartiles (18.3-25.1%, 25.2-27.1%, 27.2-29.7% and ≥29.8%), patients with higher MOLLI-ECV were at significantly greater risk for cardiac events (log-rank test p<0.001), also when patients with cardiac amyloidosis were excluded (p=0.033). By multivariable Cox-regression model, including cardiovascular risk factors, comorbidities, age and NT-proBNP, MOLLI-ECV was still independently associated with outcome.

In the 39 patients who underwent myocardial biopsy, TissueFAXS-ECV was 33±16% of the myocardium, and MOLLI-ECV was 35±13%. The average post-contrast T1 time by the multiple breath-hold sequence was 411±79ms. Native MOLLI T1 times were 1009±73ms.

TissueFAXS-ECV was significantly correlated with MOLLI-ECV (r=0.915, p<0.001), with multiple breath-hold post-contrast T1 times (r=-0.683, p<0.001), and with native T1 times (r=0.657, p<0.001). When patients with cardiac amyloidosis were excluded, only MOLLI-ECV was significantly correlated with histology (r=0.491, p=0.015).

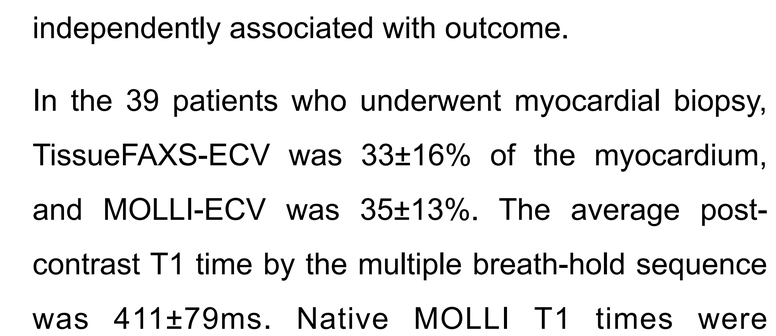

Figure 1: Correlation between MOLLI-ECV and TissueFAXS-ECV.
A: For all patients (r=0.915, p<0.001)
B: Excluding patients with cardiac amyloidosis (r=0.491, p=0.015)

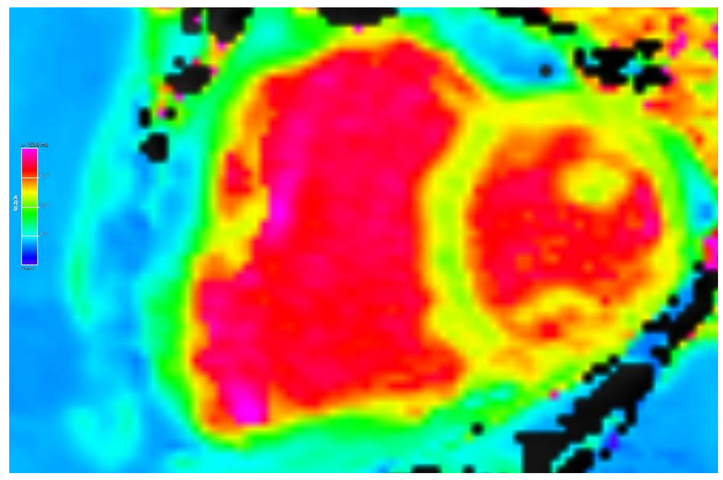

Figure 2: Color-encoded pre-contrast T1 map using MOLLI. In this heart failure patient, native MOLLI T1 time was 989ms and ECV was 30.8%. T1 time by post-contrast multiple breath-hold was 422ms.

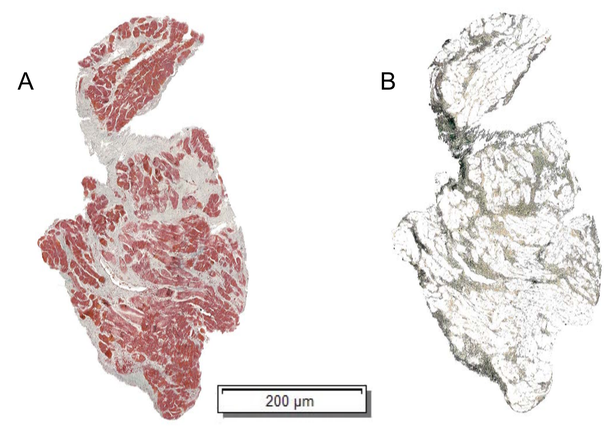

Figure 3: A. Myocardial specimen of the same patient as in Figure 2 with Trichrome staining. B. A color-threshold approach using ImageJ was used to quantify exctracellular matrix expansion which was 30.7% in this individual.

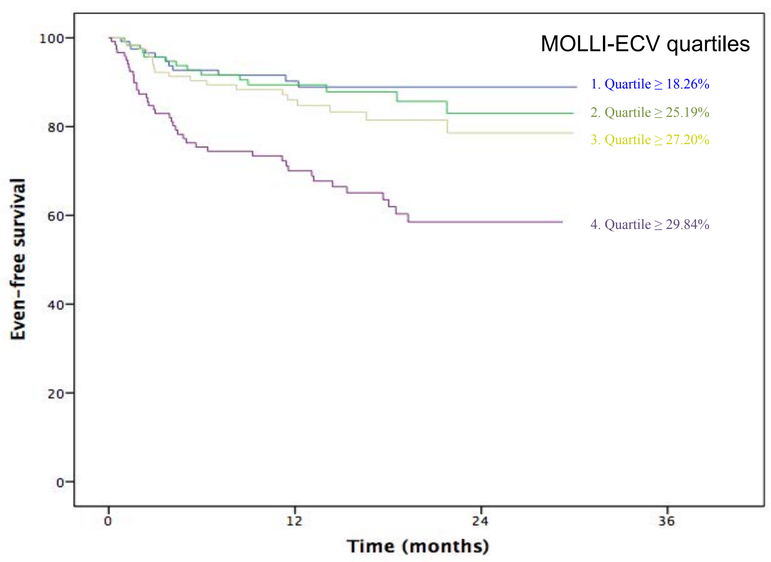

Figure 4: Kaplan-Meier plot for event-free survival (including 20 with cardiac amyloidosis). Log-rank-test p<0.001 (when excluding amyloidosis patients p=0.033)

Conclusion

In the present series, MOLLI-ECV appears to be the most accurate method for the quantification of extracellular matrix expansion when validated against myocardial biopsies. In a large cohort of patients with various cardiac diseases, higher MOLLI-ECV was associated with an increased cardiac event rate.

References.
1. White et al., JACC Cardiovasc Imaging. 2013 Sep;6(9):955-62.
2. Iles et al., J Am Coll Cardiol. 2008 Nov 4;52(19):1574-80.
3. Bull et al., Heart. 2013 Jul;99(13):932-7.