Myocardial Fibrosis in Heart Failure

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DECLARATION OF CONFLICT OF INTEREST

• Nothing to declare
Myocardial fibrosis

- Present in all aetiologies of heart failure
- Focal/regional (replacement fibrosis)
- Diffuse (reactive interstitial fibrosis)

Mewton et al. JACC 2011;57:891–903
Fibrosis and MRI
Myocardial Gadolinium Kinetics

Contrast Injection

Delayed Enhancement

Normal Myocardium

Scarred Myocardium

>10 min
LGE identifies regional but not diffuse myocardial fibrosis.
Diffuse myocardial fibrosis evaluated with cardiac magnetic resonance imaging predicts heart failure symptoms in non-ischaemic cardiomyopathy

Aim

To establish the relationship between non-invasive assessment of diffuse myocardial fibrosis and symptoms of heart failure
Quantifying Diffuse Fibrosis

• As the inversion time increases there are alterations in tissue signal intensity

• Ten images taken (mid-ventricular short axis) with varying inversion times (50-1000ms) and the entire myocardium was identified for each image

• Images were then processed to generate $T_1$ maps
Calculating $T_1$ Relaxation Time
9 patients post-transplantation

Histologic collagen content quantified from endomyocardial biopsy sample

Correlated with post-contrast T₁ time on CMR

*Iles et al JACC 2008;52:1574–80*
T₁ times shorten in heart failure

- T₁ mapping
- 25 CCF
- 20 controls

- T₁ times shorter in CCF cf controls
  383±17ms vs. 564±23ms, p<0.0001

- T₁ times shorter in CCF even when LGE+ areas were excluded
  429±22ms vs 564±23ms, p<0.0001

Iles et al JACC 2008;52:1574–80
Diastology, collagen and heart failure symptoms

- LV stiffness correlates with myocardial collagen fraction in hypertensive pts
  - *Diez et al Circ 2002;105:2512-7*

- Diastology correlates with NYHA class in hypertrophic cardiomyopathy
  - *Matsumura et al Heart 2002 Mar;87(3):247-51*
Diastology and collagen in HFNEF

- 26 pts with HFNEF
- 15 controls

Kasner et al JACC 2011;57:977–85
Methods

• 75 patients with non-ischaemic cardiomyopathy
  – Mean age = 55±13 yrs
  – 67% male
  – Mean LVEF=33±14%

• Patients were excluded if clinically unstable, acute myocarditis, contraindications to MRI (including device therapy)

• Clinical data including NYHA class collected
Methods

- Cardiac MRI successfully completed in all 75 patients
- In addition to standard imaging, post-contrast $T_1$ mapping sequence acquired
- Experienced cardiologist blinded to clinical parameters calculated myocardial $T_1$ times
### Univariate Predictors of NYHA Class

<table>
<thead>
<tr>
<th></th>
<th>NYHA I/II (n=52)</th>
<th>NYHA III/IV (n=23)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>56±14</td>
<td>52±12</td>
<td>0.79</td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td>36±14</td>
<td>25±11</td>
<td>&lt;0.01</td>
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<tr>
<td><strong>LVEDVI</strong></td>
<td>133±50</td>
<td>172±50</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>34/52 (65%)</td>
<td>16/23 (70%)</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>LGE</strong></td>
<td>26/52 (50%)</td>
<td>13/23 (57%)</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>T₁ time</strong></td>
<td>459±125</td>
<td>378±85</td>
<td>0.01</td>
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# Univariate Analysis of T₁ Times

<table>
<thead>
<tr>
<th></th>
<th>Pearson’s $r$</th>
<th>$p$</th>
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<tbody>
<tr>
<td>Age</td>
<td>-0.005</td>
<td>0.97</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.191</td>
<td>0.10</td>
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<tr>
<td>LVEDVI</td>
<td>-0.195</td>
<td>0.09</td>
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<tr>
<td>NYHA</td>
<td>-0.275</td>
<td>0.02</td>
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<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td></td>
<td>= 410±107ms</td>
<td>= 482±131ms</td>
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<table>
<thead>
<tr>
<th>LGE</th>
<th>LGE+ = 437±124ms</th>
<th>LGE- = 432±117ms</th>
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<tr>
<td></td>
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<tr>
<td></td>
<td></td>
<td>0.86</td>
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NYHA Class correlates with post-contrast T₁ time in heart failure

- T₁ times shortened as NYHA class increased

- NYHA I/II = 459 ± 125 ms vs NYHA III/IV = 378 ± 85 ms (p=0.02)
## Multivariate Predictors of NYHA Class

<table>
<thead>
<tr>
<th>Predictor</th>
<th>partial r</th>
<th>p</th>
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<tbody>
<tr>
<td>LVEDVI</td>
<td>0.106</td>
<td>0.38</td>
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<tr>
<td>LVEF</td>
<td>-0.209</td>
<td>0.08</td>
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<tr>
<td>Male</td>
<td>-0.099</td>
<td>0.41</td>
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<tr>
<td>$T_1$ time</td>
<td>-0.239</td>
<td>0.04</td>
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Diastology and $T_1$ Times

- How does this relate to diastolic function?
- 13/75 with echocardiogram within 7 days of CMR (mean 2±2 days)
- Diastology assessed by a cardiologist blinded to CMR findings
Diastology and $T_1$ Times
(within 7 days)

$r=0.67$, $p=0.01$

$n=13$
Conclusion

Contrast-enhanced cardiac MRI using $T_1$ mapping quantifies diffuse myocardial fibrosis, which is a significant contributor to symptoms of heart failure in non-ischaemic cardiomyopathy
Acknowledgements

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Thank you for your attention