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Plasma Tenascin-C: a novel prognostic biomarker in heart failure with preserved ejection fraction

Authors:
P Kanagala¹, JR Arnold², JN Khan², A Singh², GS Gulsin², DCS Chan², ASH Cheng³, J Yang⁴, Z Li⁴, P Gupta², IB Squire², GP Mccann², LL Ng², ¹Aintree University Hospital - Liverpool - United Kingdom of Great Britain & Northern Ireland, ²NIHR Biomedical Research Unit in Cardiovascular Disease - Leicester - United Kingdom of Great Britain & Northern Ireland, ³Kettering General Hospital - Kettering - United Kingdom of Great Britain & Northern Ireland, ⁴Bristol-Myers-Squibb - Princeton - United States of America,

Topic(s):
Heart Failure with Preserved Ejection Fraction

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National Institute for Health Research Leicester Cardiovascular Biomedical Research Centre overall project Grant (IRS_BRU_0211_20033)

Background
Tenascin-C is reportedly associated with adverse outcomes in heart failure with reduced ejection fraction but its role in heart failure with preserved ejection fraction (HFpEF) is unknown.

Purpose
To assess whether plasma Tenascin-C is related to prognosis in HFpEF.

Methods
Prospective, observational study of age and sex-matched HFpEF n=130 and controls n=42 (age 73±9, males 50%) who underwent comprehensive phenotyping with plasma biomarkers, cardiovascular magnetic resonance imaging, echocardiography and 6-minute-walk-testing (6MWT).

Results
Tenascin-C was higher in HFpEF (13.7 vs 11.1 ng/ml [controls], p<0.0001). During follow-up (median 1428 days), there were 61 composite end-points (21 deaths, 40 HF hospitalizations). 28 univariable predictors were noted (p<0.1). In multivariable Cox regression, Tenascin-C (adjusted hazard ratio [HR] 1.755, 95% confidence interval [CI] 1.305–2.360; p<0.0001) and indexed extracellular volume (HR 1.465, CI 1.019-2.106; p=0.039) were the only parameters that remained significant when added to a base prognostic model comprising age, prior HF hospitalization, diastolic blood pressure, lung disease, NYHA, 6MWT distance, haemoglobin, creatinine, BNP and E/E’.

Conclusions
Tenascin-C is a strong prognostic marker in HFpEF

<table>
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<tr>
<th>Clinical/imaging parameters</th>
<th>Hazard Ratio (p value)</th>
<th>Plasma biomarkers</th>
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<tr>
<td>*Age (years)</td>
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<td>Tenascin-C</td>
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<td>Growth differentiation factor-15 (GDF-15)</td>
<td>1.495</td>
</tr>
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<td><em>NYHA class III/IV</em></td>
<td>1.703</td>
<td>(0.033)</td>
<td>Tissue inhibitor of metalloproteinase-1 (TIMP-1)</td>
<td>1.610</td>
</tr>
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<td><em>6 minute walk distance</em></td>
<td>0.659</td>
<td>(0.019)</td>
<td>Matrix metalloproteinase-2 (MMP-2)</td>
<td>1.527</td>
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<td><em>Haemoglobin</em></td>
<td>0.727</td>
<td>(0.010)</td>
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<td>1.279</td>
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<td><em>Creatinine</em></td>
<td>1.312</td>
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<td>Matrix metalloproteinase-8 (MMP-8)</td>
<td>1.300</td>
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<td><em>B-type natriuretic peptide (BNP)</em></td>
<td>1.471</td>
<td>(0.014)</td>
<td>N-terminal pro-atrial natriuretic peptide (NTpro-ANP)</td>
<td>1.378</td>
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<td><em>E/E’</em></td>
<td>1.459</td>
<td>(0.002)</td>
<td>Highly-sensitive C-reactive protein (hs-CRP)</td>
<td>1.358</td>
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<td>Left ventricular mass indexed to body surface area (LVMI)</td>
<td>1.296</td>
<td>(0.046)</td>
<td>Tumour necrosis factor receptor-1 (TNFR-1)</td>
<td>1.330</td>
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<td>Maximal left atrial volume indexed to body surface area (LAVI_max)</td>
<td>1.237</td>
<td>(0.059)</td>
<td>Cystatin-C</td>
<td>1.778</td>
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<td>Extracellular volume (ECV)</td>
<td>1.519</td>
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<td>1.516</td>
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*Parameters comprising the base prognostic multivariable model
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Parameters comprising the base prognostic multivariable model

Groups

Less than or equal to median Tenascin-C

Above median Tenascin-C

Log-Rank p < 0.0001

Event free survival (%)

Time to event (days)