Cardiac torsion and strain in fatigued Primary Biliary Cirrhosis patients investigated by 3T cardiac tagging show evidence of accelerated ageing processes

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Introduction: Primary Biliary Cirrhosis (PBC) is an autoimmune liver disease affecting up to 20,000 patients in the UK, mostly affecting females from middle age. A follow-up study [1] of a geographically-defined cohort of 770 PBC patients found that their survival was much poorer than an age- and sex-matched population (standardised mortality ratio for PBC patients was 2.87). Excluding deaths from hepatic causes, the standardised mortality ratio for PBC patients was still 1.73: the balance of the risk was of a cardiac-related death but the mechanism by which the disease could affect cardiac tissue was unclear. 50% of PBC patients suffer systemic fatigue, and in these the risk of cardiac-related death has been shown to be higher than in non-fatigued patients [2]. ^{31}P MRS has been shown to be sensitive to changes in cardiac metabolism in advance of structural abnormalities [3], and our previous work demonstrated that cardiac PCr/ATP ratio was impaired in PBC patients compared to healthy controls, despite no morphological or functional differences being apparent by cine-MRI [4]. We have had the further opportunity to perform cardiac tagging studies on these subjects to examine cardiac strain and torsion.

Methods: 15 proven PBC Stage I-II patients (non-cirrhotic) were recruited and 8 age-, weight- and height-matched female subjects were recruited as controls. Cardiac tagging in the short axis was used to measure circumferential strain and torsion throughout the cardiac cycle. Patient and control subject fatigue severity was assessed by means of a validated questionnaire, the Fatigue Impact Score (FIS), where 0 indicates no fatigue to a maximum of 160. Patients were divided into two groups: those without significant fatigue (defined as FIS < 25) and those with severe fatigue (FIS > 50). All controls had FIS < 25.
MR protocol: (1) Cardiac tagging: Tagged images of the myocardium in the short axis were obtained on a 3T Philips Intera Achieva (Best, NL) with a dedicated 6-channel cardiac coil. A multishot turbo-field echo sequence with TFE factor 9 was used (TR/TE/FA/NEX = 4.9/3.1/10°/1, SENSE factor 2, FOV 350x350mm, voxel size 1.37x 1.37mm with an orthogonal grid with tag spacing of 7mm, fig 1). Two adjacent slices of 10mm thickness were acquired at mid-ventricle with a 2mm gap. *(2) Cardiac morphology:* High resolution, short axis cine-MRI was available for all subjects as reported previously [3] to provide measurements of LV mass, blood pool volumes and diastolic parameters.

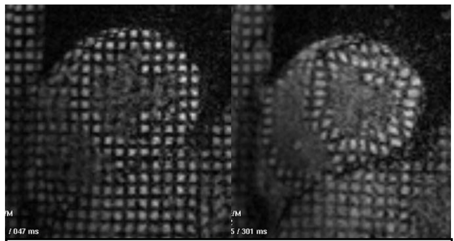
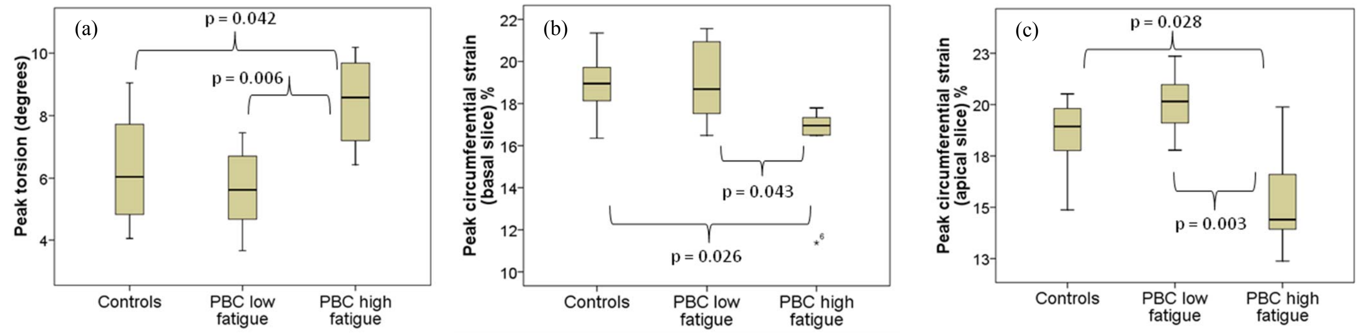


Fig 1 : Tagged images at *(left)* end diastole and (*right)* end systole

Analysis: The Cardiac Image Modelling package (University of Auckland) was used to analyse the tagging data by aligning a mesh on the tags between the endo- and epi-cardial contours. Circumferential strain and the rotation of the two planes was calculated throughout the cardiac cycle. Torsion between the two planes (taken as the circumferential-longitudinal shear angle) was then calculated according to the method in [5], so as to account for the radius of the ventricle.

Results: It is found that the peak torsion achieved during systole is significantly higher in the PBC patients with high fatigue (8.4 ± 1.5°, fig 2a) compared to both the control group (6.3 ± 1.9°, p = 0.04) and those PBC patients without fatigue (5.6 ± 1.4°, p = 0.006). In addition, the maximal circumferential strain achieved during the cardiac cycle is lower in fatigued PBC patients than in controls or non-fatigued patients: this is true in both slices acquired (figs 2b and 2c). However, parameters derived from cine imaging show no morphological or functional alteration in the hearts of either group of PBC patients compared to controls [3]. This pattern of increased torsion and decreased circumferential strain has been previously observed in a study of healthy ageing [6] where a mean age difference between groups of 22 years and 69 years old gave rise to a mean difference in torsion of 1.4°. In addition for the PBC group as a whole, the residual torsion at 150% end-systolic time was found to be significantly greater compared to controls (fig 2d), and the maximum rate of recoil lower (fig 2e). This suggests that the PBC hearts are subtly less efficient at diastolic relaxation, though this is not reflected in cine-MRI blood pool measurements. Delayed release of torsion at 150% end-systolic time has also been previously identified to be elevated in aged, but otherwise healthy controls [6].



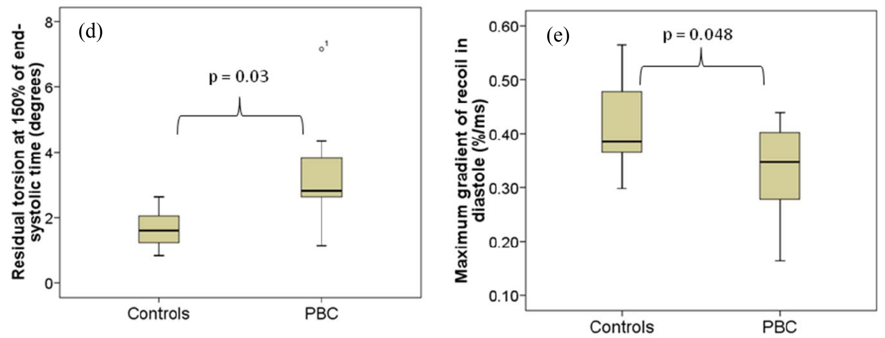


Fig 2: Results of the cardiac tagging analysis showing, for the control and PBC patients with and without significant fatigue, (a) peak torsion at end-systole, (b) the peak circumferential strain in the basal slice and (c) in the apical slice. (d) Residual torsion at 150% of end-systolic time and (e) maximum diastolic recoil rate for controls and PBC patients.

Conclusion: This study has applied cardiac tagging to study myocardial motion in the hearts of PBC patients for the first time. In those PBC patients with severe fatigue we have found changes in peak torsion and circumferential strain indicating that these patients may have suffered effective ageing of their hearts. This is in alignment with previous findings that PBC patients with substantial fatigue had a greater risk of cardiac-related death. For the PBC group as a whole we have identified delayed release of torsion in diastole which is also consistent with an advanced ageing process.

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