High energy phosphate cardiac energetics are abnormal in Primary Biliary Cirrhosis patients in the absence of functional or anatomical abnormalities on structural MRI

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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. 31P MRS has been shown to be sensitive to changes in cardiac metabolism in advance of structural abnormalities [2], and in view of our previous work demonstrating mitochondrial abnormalities in exercising skeletal muscle [3], we speculated that signs of metabolic stress might be present in the phosphorus spectra of PBC patients as a precursor to cardiac damage, even if conventional structural parameters were found to be normal on imaging, as suggested from clinical experience of echocardiography.

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. Phosphorus-31 magnetic resonance spectroscopy was used to measure cardiac high energy phosphate metabolism and high resolution imaging was used to assess cardiac morphology.

Results: Figure 1 shows the PCr/ATP ratio for myocardial tissue in controls and PBC patients. The PCr/ATP ratio is significantly lower for the PBC patients compared to controls (1.64 ± 0.23 vs 1.90 ± 0.10, p < 0.005, Mann-Whitney test). There are no significant differences are found in any left ventricular imaging parameters between the controls and PBC patients – there are no signs of any anatomical or functional abnormality. All the parameters estimated are within the normal range of females of this age group [11].

Conclusion: We have successfully measured high energy phosphate levels in the hearts of primary biliary cirrhosis patients for the first time. It has been shown that there is a metabolic impairment compared to matched controls represented by a mean decrease of 14% in the phosphocreatine/ATP ratio. Our previous work in skeletal muscle leads us to speculate that this change may be mitochondrial in origin. Cardiac morphology from anatomical scanning, however, shows no significant impairment of ejection fraction, LV mass or stroke volume in PBC patients. It appears that a metabolic stress is present in PBC patients that is not explicable by structural disease. This study provides further evidence for primary biliary cirrhosis being a multi-system disease. The cardiac metabolic dysfunction detected here may increase the risk of future functional cardiac mortality: a longitudinal follow-up study will be required to confirm this.