occurs in 20%–40% of adult patients harbouring the common m.3243A>G mutation, usually with a hypertrophic phenotype. Pathogenetic mechanisms are unclear yet no detailed study of myocardial structure, function and bioenergetics has been performed in m.3243A>G mutation carriers to identify early markers of cardiac involvement.

**Methods** Cardiac MRI was performed in 20 adult patients (10 males, mean age 35.2±13.1 years) harbouring the m.3243A>G mutation, without clinical evidence of cardiac involvement on routine ECG and echocardiographic screening, and 20 age- and gender-matched healthy controls (10 males, 38.4±14.2 years): (1) phosphorus-31 magnetic resonance spectroscopy, (2) cine imaging (5), cardiac tagging, and (4) late gadolinium enhancement (LGE) imaging on a Philips Intera Achieva 3 Tesla scanner. Clinical disease burden was determined using: (1) the Newcastle Mitochondrial Disease Adult Scale (NMDAS), a 29-domain validated scoring system with a single cardiac domain, and (2) urinary mutation load, the best predictor of overall clinical outcome in m.3243A>G mutation carriers.

**Results** Compared to control subjects and following Bonferroni correction for multiple comparisons, patients had increased left ventricular mass index (LVMI), LV mass to end-diastolic volume ratio (M/V ratio), LV radial wall thicknesses (all p<0.01), peak torsion and torsion to endocardial circumferential strain ratio (both M/V ratio), phosphocreatine (PCr)/adenosine triphosphate (ATP) ratio was significantly decreased (p<0.0001) and correlated with increased LVMI (r=-0.59, p<0.01). These findings are consistent with a reduction in contractile function in the subendocardium compared to the subepicardium, and similar to those reported in familial hypertrophic cardiomyopathy, but there were no differences in diastolic function in our study. Nine patients had diabetes mellitus and 3 had treated hypertension. Among patients, there was no correlation of LVMI or M/V ratio with age, blood pressures, fasting blood glucose or HbA1C but there were no differences in diastolic function in our study. Nine patients had diabetes mellitus and 3 had treated hypertension.

**Conclusions** Concentric remodelling and subendocardial dysfunction are prevalent in m.3243A>G mutation carriers without clinical cardiac disease. Assessment of myocardial deformation may be useful in monitoring disease progression or response to early intervention. Patients with higher urinary mutation loads and disease burden may be at increased risk of cardiac involvement.

**073 EVALUATION OF CLINICAL MARKERS OF EARLY DISEASE EXPRESSION AND THE ABILITY TO PREDICT GENOTYPE IN FAMILIES WITH HCM AND MUTATIONS IN CARDIAC MYOSIN BINDING PROTEIN C**

doi:10.1136/heartjnl-2012-301877b.73

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**Introduction** Familial evaluation for the presence of left ventricular hypertrophy (LVH) is an important part of management in hypertrophic cardiomyopathy. However due to incomplete penetrance, the presence of LVH does not reliably identify all mutation carriers, with consequences for cascade screening. Previous studies in small genotyped populations have suggested that reduced myocardial tissue Doppler velocities in unaffected relatives may predate the development of LVH and may therefore be useful in identifying at risk relatives. The value of such techniques in a large cohort of genotyped relatives remains unknown however. This study sought to prospectively evaluate ECG and Echo markers of early disease expression in a large genotyped cohort of families with mutations in myosin binding protein C (MYBPC3).

**Methods** Relatives of index cases with HCM related to mutations in MYBPC3 (4 insertion/deletion, 7 missense, 4 nonsense, 5 intronic, 2 double heterozygotes) were evaluated. Clinical examination, ECG and transthoracic Echo (operator blinded to genetic status) were performed and combined with genetic predictive testing. The clinical value of ECG and Echo derived indices in predicting genotype were assessed.

**Results** Of 95 relatives, 40 did not carry the family mutation (Group 1, 22 males, 38.5±16.7 years), 59 were unaffected mutation carriers (Group 2, 17 males, 37.4±16.8 years) and 16 were clinically affected and excluded from the study. ECG evidence of left atrial enlargement (21 vs 5%, p<0.01) and non-pathological Q waves (64 vs 28%, p<0.001) were more common in group 2 than group 1. S wave amplitude in lead V2 was greater in group 2 than group 1 (16.6±7.9 vs 12.4±8.2 mV, p<0.02) and also lead V3 (12.7±6.9 vs 9.5±6.1 mV, p=0.02). ECG criteria for left ventricular hypertrophy were specific