Posters

Clinical hepatology

P01 UDCA RESPONSE CRITERIA IDENTIFY A SUB-GROUP OF PBC PATIENTS WITH AN INHERENTLY GOOD PROGNOSIS RATHER THAN A SPECIFIC DISEASE RESPONSE

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Introduction Recent follow-up cohort studies have identified biochemical parameters in UDCA-treated patients which identify "responders" with survival identical to normal control populations, in contrast to "non-responders" who have survival indistinguishable from that predicted by the Mayo Risk Score for untreated patients. The most widely accepted criteria for UDCA "response", proposed by Corpechot, consist of alkaline phosphatase (ALP) <3× uln, alanine transaminase (ALT) <2× uln and bilirubin <1× uln. However, Bilirubin and ALP levels are independent predictors of outcome in PBC irrespective of UDCA treatment. ALT, in addition, is a biomarker for overlap syndrome, a prognostic feature itself.
Aim UDCA response criteria identify a group of patients with an inherently low risk rather than UDCA response per se.
Method In a comprehensive cohort of patients, geographically defined in 1999 followed up for 10 years, a group of patients (n=94) not treated with UDCA were identified. This cohort, matched prospectively to individual community case controls, represents an opportunity to study the natural history of non-UDCA treated PBC.
Results In the whole cohort (including UDCA treated patients), survival was significantly better in the UDCA-responding patients (defined using the Corpechot criteria) than in the non-UDCA-treated patients ($p<0.05$ log-rank test) although as in other studies survival was not the same as in age and sex match controls ($p<0.05$). Of the 94 non-UDCA receiving patients, 80 and 14 had, after 1 year of follow-up, biological features which, if they had received UDCA, would have been compatible with UDCA-response and UDCA-non response, respectively. Un-transplanted survival was significantly better in the non-UDCA patients meeting response criteria (58/80 (72%) at 10 years follow-up) than in non-UDCA treated patients meeting non-response criteria (5/14 (36%), $p=0.01$; χ^2 9.4, $p<0.01$ log-rank test). The magnitude of this effect was similar to that associated with UDCA response in other series. The absence of UDCA treatment precludes, of course, this being a phenomenon of actual UDCA response.
Conclusion UDCA response criteria identify a group of patients who, at the time of criterion measurement, have a good prognosis. It does not appear to matter whether attainment of these parameters is a natural feature of untreated disease or a consequence of treatment. These criteria therefore have an important role in identifying high and low risk patients, and a sub-group of PBC patients with poor prognosis for whom additional therapies should be sought. They do not, however, provide specific information about the actions of UDCA.

P02 IMPAIRED SUBENDOCARDIAL MYOFIBRE FUNCTION IN PRIMARY BILIARY CIRRHOSIS

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Introduction A follow-up study[1] 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 1.73: the balance of the risk was of a cardiac-related death 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]
Method 15 proven PBC stage I–II patients were recruited (age: 48±6 y) and 8 age, weight and height- matched female subjects were recruited as controls (age: 52±11 y). MRI short axis cardiac tagging was used to measure circumferential strain and torsion throughout the cardiac cycle.[3] 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.
Results In fatigued PBC patients, cardiac torsion was increased and circumferential strain significantly decreased compared to controls and non-fatigued PBC patients, indicating impaired subendocardial myofibre function, which is characteristic of advanced ageing.[3] Anatomical MRI showed no morphological or functional alteration in the hearts of either group of PBC patients compared to controls.

Abstract P02 Table 1 Results

	Control	PBC non-fatigued	PBC fatigued
Torsion to endocardial strain ratio	0.46±0.14	0.44±0.12	0.70±0.13*
Peak torsion	6.3±1.9	5.6±1.4	7.9±1.4*
Peak endocardial circumferential strain	18.9±1.6	19.0±2.0	16.5±2.4*

*p <0.05 by ANOVA.

Conclusion In PBC patients with severe fatigue we have found changes in the relationship between 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.

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REFERENCES

1. **Prince M,** Chetwynd A, Newman W, *et al*. Survival and symptom progression in a geographically based cohort of patients with primary biliary cirrhosis: Follow-up for up to 28 years. *Gastroenterology* 2002;**123**:1044–51.
2. **Jones DEJ.** Pathogenesis of primary biliary cirrhosis. *J Hepatology* 2003;**39**:639.
3. **Lumens J,** Delhaas T, Arts T, *et al*. Impaired subendocardial contractile myofiber function in asymptomatic aged humans, as detected using MRI. *Am J Physiol Heart Circ Physiol*. 2006;**291**:H1573–H1579.

P03 THE USE OF BRUM1 RESEQUENCING MICROARRAY TO IDENTIFY MUTATIONS IN PATIENTS WITH NEONATAL CHOLESTASIS

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Introduction Neonatal cholestasis is the presenting clinical feature of serious and potentially life limiting liver diseases such as progressive familial intrahepatic cholestasis (PFIC), arthrogryposis-renal-cholestasis (ARC) syndrome and Niemann Pick C (NPC) disease. A single rapid molecular test to confirm the diagnosis would reduce the delay from molecular genetic investigation at multiple diagnostic centres thus facilitating optimal clinical management and counselling. We have designed a resequencing microarray (BRUM1) capable of simultaneously sequencing multiple genes associated with neonatal cholestasis.