Conclusion Troponin I elevation observed in ALF/SALF may not represent true myocardial injury and may be better viewed as a marker of metabolic stress. TI is not associated with directly measured haemodynamic abnormalities in ALF patients. Novel serum markers are needed to better reflect cardiovascular compromise in ALF.

P11 RETROSPECTIVE ANALYSIS TO IDENTIFY THE INCIDENCE AND PREVALENCE OF PRE-EXISTING CHRONIC LIVER DISEASE IN PATIENTS PRESENTING WITH HYPERACUTE, ACUTE AND SUB-ACUTE LIVER FAILURE

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V Audimoolam, Y Zen, D Joshi, W Bernal, G Auzinger, C Willars, B Portman, N Heaton, J O'Grady, M Heneghan, K Agarwal, V Aluvihare, A Suddle, J Wendon. *Institute of Liver studies, King's College Hospital, London, UK*

Introduction Liver failure can be classified as hyperacute liver failure (HALF), acute liver failure (ALF), sub-acute liver failure (SALF), acute on chronic liver failure (ACLF) and chronic liver failure. The classification is dependent based upon presentation and the existence of diagnosed or undiagnosed cirrhosis. In individuals presenting with ALF/SALF, liver biopsy is not routinely performed except in exceptional cases because of the increased risk of bleeding due to their coagulopathic state. Hence, the incidence and prevalence of chronic liver disease in patients presenting with ALF/SALF has not been explored.

Method We retrospectively analysed, prospectively collected data from all patients undergoing liver transplantation for ALF/SALF from 2000 to 2010. A single liver histopathologist, blinded to the clinical diagnosis, reviewed the hepatectomy explant specimen. Based on the severity of hepatocyte necrosis, nodular regeneration and chronic inflammatory change four different histopathogical diagnosis were made; ALF, SALF, ACLF and ALF on a background of chronic inflammatory change.

Results A total of 196 patients with a clinical diagnosis of ALF/SALF (152/44, M/F 130:68, a median age 35 (16–69) underwent liver transplantation from 2000 to 2010. 149 patients had both a clinical and histopathological diagnosis in keeping with ALF. Twenty-nine of the 44 SALF patients had a compatible histopathological diagnosis of whom 19 were seronegative one with grade 3–4 siderosis, five autoimmune hepatitis (AIH) and five drug induced (non-paracetamol). Discrepancy between clinical and histopathological findings were observed in 18 patients; three in the ALF group diagnosed histopathologically as SALF (2 Budd Chiari and 1 AIH) and 15 in the SALF group diagnosed histopathologically as ALF (nine sero-neg, four AIH, two drug related). Amongst the clinical ALF group, 11 patients (10 Wilson's, 1 hepatitis B) had evidence of ACLF on histology and five patients (1 HBV, 2 seronegative , 1 Budd Chiari (B. C.) and 1 paracetamol overdose with an h/o excess alcohol) showed evidence of acute liver injury on a background of chronic inflammatory changes without fibrosis or cirrhosis. On comparing the two group's with a clinical diagnosis of ALF/SALF, as expected ALF patients were younger (mean (M) age 31.7 vs 45.3 SALF, $p<0.0001$), had higher INR (M-6.64 vs 4.2, $p<0.0001$) and a lower bilirubin (197 vs 405 $p<0.0001$) Analysis of the survival outcome in patients with a clinical diagnosis of ALF/SALF showed no difference between the two groups—log rank score 0.4, $p=0.5$. INR correlated negatively with survival in the ALF group ($r=-0.244$, $p<0.003$), whereas it was age and creatinine in the SALF group ($r=-0.699$, $p<0.0001$ and $r=-0.341$, $p<0.02$). Survival among ALF/SALF/ACLF was again not significant (log rank score 2.045, $p=0.5$).

Conclusion The incidence and prevalence of acute liver injury on a background of chronic inflammatory change is uncommon. In our HALF/ALF/SALF group, apart from Wilson's and one case of HBV no patient had evidence of cirrhosis. The clinical diagnosis of ALF/SALF using accepted criteria (history+imaging) seems to be accurate in the majority of patients without the recourse to a liver biopsy. However, liver biopsy may still be required to define optimal treatment strategies, for example, lymphoma.

P12 A PRAGMATIC TRAFFIC LIGHT SYSTEM FOR TRIAGE OF LIVER DISEASE: RESULTS IN A COHORT OF 710 SUBJECTS

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N Sheron, S Harris, M Moore, E Williams, M Ledbury, W Mackintosh, L Kramer, N Kapoor, N Johari, A Watts, A Bateman. *University of Southampton, UK*

Introduction At a time when mortality for many diseases is falling, deaths from liver disease have increased fivefold over the last 30 years and have almost doubled over the last 10 years. In order to reduce liver deaths we need to pick up liver disease at a much earlier stage in the community so we need easier more accurate diagnostic methodologies. We used two serum markers and standard tests to develop a simple traffic light diagnostic modality.

Aim To develop a simple one-step traffic light diagnostic modality that could be used to triage liver disease of all aetiologies in the community.

Method Subjects were out-patients or in-patients at Southampton University Hospitals Trust between 2003 and 2009. Serum fibrosis markers hyaluronic acid and collagen P3NP were combined with FBC, INR and LFTs in a test cohort (n=119) with a firm diagnosis of the stage of fibrosis. On the basis of the test data, a simple clinical traffic light algorithm was created using HA, P3NP, INR, Albumin, and platelets. An evaluation cohort of 591 subjects, of whom 278 had independent staging of fibrosis, was used to AUROC validate the model and compare a modified binary logistic model—in the abstract data sets are combined.

Results

Abstract P12 Table 1 Original traffic light all subjects with staged fibrosis n=39

	Green	Amber	Red	
No fibrosis	31	26	20	77
Progressive fibrosis	22	48	109	179
Cirrhosis	2	4	135	141
	55	78	264	397

Survival in all subjects n=710.

Conclusion The traffic light system detected 98% of subjects with cirrhosis and 88% of subjects with progressive fibrosis, in the latter mortality over 5 years was not increased. We envisage this system being used to inform subjects about the need to moderate high risk behaviour, and triage subjects with severe disease to secondary care. Repeat testing at 5-year intervals in increased risk groups should have the potential to pick up most cases of significant liver disease before a fatal presentation to hospital. The traffic light system has been applied to the detection of liver disease in a community sample of 10 000 in the ALDES study funded by NIHR.

P13 ALLO- AND AUTO-ANTIBODY RESPONSES IN ALCOHOLIC LIVER DISEASE AS BIOMARKERS OF PROGNOSIS

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I Patanwala, J Palmer, E Henderson, C Day, D Jones. *Institute of Cellular Medicine, Newcastle University, UK*

Introduction Alcoholic liver disease (ALD) frequently has a poor prognosis and in many populations, including in the UK, its impact is growing as a result of alcohol consumption patterns. Whereas abstinence from alcohol is clearly the optimum approach to treatment, patients need to survive the initial episode of liver disease in order to benefit. Although the trigger for ALD is self-evident, the

process by which alcohol gives rise to liver injury remains unclear, precluding the informed targeting of interventions based on ameliorating pathogenic processes. Furthermore, we lack reliable biomarkers to identify patients at particular risk of poor outcome at the outset of a liver disease episode in order to target therapy. Several studies have identified the presence, in sub-sets of ALD patients, of antibodies reactive with adduct-modified self-proteins such as malondialdehyde (MDA)-adducted albumin (MDA-HSA) and self-antigens such as cytochrome P450 2E1 (Cyp2E1, arising, it is thought as a consequence of an "altered-self" mechanism). To date, however, the biological significance of these antibodies and the implications that they hold for prognosis and treatment are unclear.
Aim In this study we set out, in a serial cohort of 38 ALD patients (all cirrhotic and all continuing to consume alcohol), to address the biological significance of auto- and allo-antibody responses.
Method Patients were fully phenotyped with regard to their antibody, clinical, biochemical and histological status. Clinical follow-up was then undertaken for 5 years.
Results The presence of both MDA-HSA and Cyp2E1 reactive antibody was significantly associated with risk of death during follow-up (Cyp2E1 AUC for prediction of death during follow-up 0.78 (95% CI 0.64 to 0.93), p=0.01; MDA 0.73 (0.55–0.92, p=0.05). An optimal composite measure based on reactivity to both antigens was highly predictive of risk of death during follow-up (auc 0.83 (0.7–0.96, p=0.005)). Interestingly amongst baseline biochemical parameters only bilirubin was (weakly) predictive of death during follow-up (auc 0.74 (0.62–0.92), all other biochemical parameters p=ns). Individual histological parameters were similarly not predictive of death during follow-up.
Conclusion Antibody reactivity with allo- and auto-antigens in ALD is a predictor of poor outcome and the optimal composite risk measure warrants prospective validation in outcome series. It is unclear at present whether the association with antibody reactivity results from a pathogenetic process (immune-mediated damage driving liver injury) or occurs as a consequence of enhanced injury (increased liver damage enhancing reactivity to these antigens). Further work in this area is warranted.

P14 MYCOPHENOLATE MOFETIL IN PATIENTS WITH AUTOIMMUNE HEPATITIS INTOLERANT TO AZATHIOPRINE

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D Jothimani, D Jothimani, U Warshow, A Barnardo, M Cramp, J Mitchell, T Cross. *Southwest Liver Unit, Derriford Hospital, Plymouth, UK*

Introduction Autoimmune hepatitis (AIH) is an immune mediated necroinflammatory condition of the liver. The majority of patients respond to the standard treatment combination of prednisolone and azathioprine. Twenty percent of patients either don't respond, or are intolerant to azathioprine. Several case series supports the use of mycophenolate mofetil (MMF) as a second line agent in refractory AIH. Its role is unclear in patients intolerant to azathioprine.
Aim To evaluate the efficacy and tolerability of MMF for the management of AIH.
Method A retrospective case note review from January 2000 to March 2010 in patients diagnosed with AIH (immune profile and liver biopsy). Patients on MMF were identified and evaluated. Treatment response to MMF was defined as a biochemical remission within 4 weeks of treatment commencement and treatment failure as either a non-response or relapse while on standard therapy.
Results 117 patients with autoimmune hepatitis were identified. 20/117 (17%) received MMF. The median age was 56 years (18–79 years) with male/female, 1:7. Three patients had overlap syndrome with autoimmune cholangitis, PSC and PBC, and six had cirrhosis. All patients were commenced on prednisolone for induction at a median dose of 30 mg (7.5–40 mg) and azathioprine within 3 months for remission. Azathioprine was discontinued due to intolerance following its adverse events, such as leucopenia, nausea and diarrhoea in 18 patients within 4 months (0–24 months). Two patients were true non-responders to azathioprine. All these patients were commenced on MMF at a median dose of 1 g twice daily in addition to low dose maintenance prednisolone. At a median follow-up of 47 months (5–83 months), MMF was well tolerated and 14/19 patients (one lost to follow-up) remained in remission including five patients with cirrhosis. Intolerance to MMF was seen in three patients (skin rash, hair loss) and poor response in two patients.
Conclusion Our case series supports the use of MMF as a second-line agent in AIH patients intolerant to azathioprine. It was well tolerated in patients including those with cirrhosis.

P15 NON-INVASIVE ASSESSMENT OF HEPATIC FIBROSIS IN PRIOR NON-RESPONDERS TO HEPATITIS C VIRUS TREATMENT—A COMPARISON OF EIGHT MARKER PANELS OF LIVER FIBROSIS

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[1]S Tanwar, [2]E Ellis, [3]C Herold, [1]W Rosenberg. *[1]Centre for Hepatology, University College London, London, UK; [2]University of Southampton, Southampton, UK; [3]University of Erlangen, Erlangen, Germany*

Introduction The detection of advancing fibrosis in patients who have previously failed standard therapy for hepatitis C virus (HCV) is important both for ascertaining prognosis and stratifying patients for further treatment with emerging therapies. Whilst liver biopsy remains the reference standard, non-invasive markers of liver fibrosis may be able to reduce the need for liver biopsy in this group of patients.
Method 80 previous non-responders to pegylated interferon and ribavirin (46 male, 34 female, age 24–98 years, mean 48.9) were recruited from five centres. Serum was taken at the time of liver biopsy. Seven tests of liver fibrosis and simple biochemical markers were compared. These were: Hyaluronic acid (HA); Indirect tests: APRI, Forn's, Fib-4; Tests including HA: SHASTA, Hepascore, Fibrometer and ELF test. Area under receiver operating characteristic curves (AUROC) were plotted for minimal fibrosis (F0–1 vs F2–6), mild fibrosis (F0–2 vs F3–6), moderate fibrosis (F0–3 vs F4–6), and severe fibrosis/cirrhosis (F0–4 vs F5–6).
Results AUROCs (and asymptotic 95% confidence intervals) are presented for each test for minimal, mild and severe fibrosis.

Abstract P15 Table 1 Results

Test	F0–1 vs F2–6 n=26 n=54	F0–2 vs F3–6 n=35 n=45	F0–4 vs F5–6 n=57 n=23
ELF	0.802 0.705–0.900	0.851 0.770–0.932	0.859 0.765–0.953
Hepascore	0.777 0.674–0.880	0.757 0.653–0.861	0.859 0.766–0.925
Fibrometer	0.775 0.669–0.876	0.740 0.632–0.849	0.808 0.698–0.917
SHASTA	0.652 0.532–0.772	0.654 0.535–0.773	0.806 0.691–0.921
HA	0.668 0.551–0.785	0.710 0.597–0.822	0.769 0.637–0.902
FIB-4	0.714 0.597–0.832	0.768 0.666–0.869	0.814 0.704–0.924
Forns	0.717 0.597–0.837	0.763 0.660–0.866	0.813 0.701–0.925
APRI	0.654 0.529–0.780	0.674 0.557–0.791	0.764 0.650–0.878

ELF was best at detecting lesser degrees of fibrosis and was better than the indirect marker panels either with or without HA. ELF and