1 (MMP3), Collagenase 3 (MMP13), Kallikrein-6 (KLK6), Cathepsin D (CTSD) and Cathepsin E (CTSE) had increased activity whilst Meprin A subunit alpha (MEP1A), Cathepsin B (CTSB) and Granzyme A (GZMA) had reduced activity in HCC compared to controls.

Conclusions Urinary CE-MS analysis identified eight proteases specific to HCC. These proteases could be associated with the development of HCC. Recent cancer research revealed that most of the proteases associated with cancer are involved in the degradation of the extracellular matrix and are also involved in the growth and spreading of cancer in the body.

P175 URINARY ANALYSIS OF HEPATOCELLULAR CARCINOMA PATIENTS USING SOLID PHASE MICROEXTRACTION

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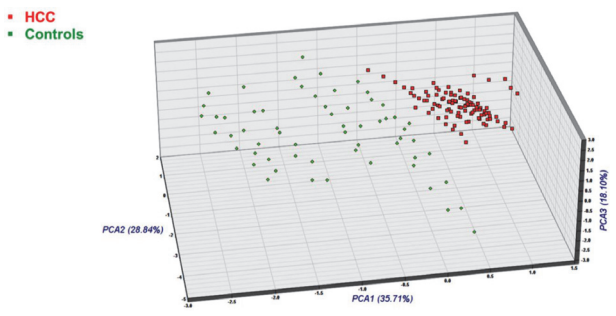
Introduction Solid phase microextraction (SPME) is an analytical method for preconcentration of volatile organic compounds (VOCs) commonly used in analysis of biological samples. We applied SPME to study the urinary signatures of VOCs in hepatocellular carcinoma (HCC) patients.

Methods Ethical approval was granted by Coventry and Warwickshire research ethics committee (09/H1211/38). We conducted a prospective recruitment between January to June 2019. Male to female ratio was 5:1 and mean age was 72 years (range 42 to 94). HCC cases were diagnosed as per EASL recommendations for 2018. Controls included patients that were suspected of cancer but had negative investigations. We collected 5 mls of urine from 31 HCC cases and 18 controls. The urine samples were left to freeze within 2 hours to – 80°C. Analysis of these samples was then completed at the end of study recruitment. Prior to analysis samples were left to thaw in a water bath at 50°C for 1 h. Urine was then placed into a Falcon conical centrifuge tube 50-mL with a modified cap with two slots to allow two solid phase microextraction tabs to be inserted to absorb gases from the head space of the samples. The tabs were then analysed using an array of eight metal oxide gas sensors. Responses from the gas sensors (1 to 8) to the urinary vapours were captured over a period of 180 seconds. The responses were digitized and stored by a computer software. The method of principal components analysis (PCA) was then employed to visualize these data.



Abstract P175 Figure 1

Results Data from the eight gas sensor responses were then demonstrated on a PCA plot, which made no assumptions about separation between classes. This visually showed that responses from the urinary VOCs of HCC patients were clearly differentiated from controls as shown in the plot below. This gives the impression that HCC has a potential urinary specific chemical signature. Urinary VOCs signature could potentially be used in the diagnosis of HCC.

Conclusions Application of SPME urinary VOCs analysis in HCC patients has future potential as a diagnostic method. This will require further validation from other interested research groups.

P176 TSPAN6: A NOVEL PLAYER IN THE MICROENVIRONMENT OF PRIMARY LIVER CANCERS

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Introduction Tetraspanins, a large family of membrane proteins, have been implicated in the regulation of the tumour microenvironment of a number of cancers. TSPAN6 has previously been shown to modulate the immune microenvironment in breast cancers via indirect interactions with tumour-infiltrating B cells; however, TSPAN6 has not been studied within the context of primary liver cancers, nor the human liver in general.

Methods TSPAN6 mRNA expression was quantified in normal, chronically diseased and primary liver cancer tissues. The distribution and cellular localisation of TSPAN6 protein expression was explored utilising immunohistochemistry and multi-colour immunofluorescence. In addition, hepatocellular carcinoma (HCC) tumour samples were histologically scored on intensity and proportion of positivity for TSPAN6 and Kaplan-Meier curves were generated for patients with negative/low expression vs. positive TSPAN6 tumour expression.

Results Transcriptional expression of TSPAN6 was comparable between normal and chronically diseased liver tissues, but was increased in primary liver cancer tissues, compared to matched distal tissues. TSPAN6 was strongly expressed in biliary epithelial cells, and to a lesser degree in hepatocytes within normal tissues and showed increased expression in the diseased state. In chronically diseased tissues, a strong association with the fibrotic septa was observed and we show that TSPAN6 strongly co-localised with cytokeratin 7, a marker of intermediary cells in the ductular reaction. TSPAN6-expressing cells were also in close association with aggregates of $CD20^+$ B cells within diseased tissues. Primary liver cancer tumours showed variable expression of TSPAN6 and preliminary analysis in HCC tumours suggested a correlation between positive tumour TSPAN6 expression and better overall patient survival, over a 5 year period.

Conclusions In this study, we have described, for the first time, the expression of TSPAN6 in human liver tissues. Chronically diseased liver tissues showed increased protein expression of TSPAN6 compared to normal tissues, and its expression was largely associated with the fibrotic septa and

was in close proximity to B cell rich areas. TSPAN6 expression was highly variable between primary liver cancer tumour tissues, but increased expression was linked to higher patient survival. Our preliminary data suggest that TSPAN6 could play a role in the tumour microenvironment of primary liver cancers and further investigation is warranted.

P177 IDENTIFYING MISSED OPPORTUNITIES FOR TRANSPLANT ASSESSMENT: A REVIEW OF REFERRALS TO A LIVER TRANSPLANT CENTRE

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Introduction Liver transplant (LT) has revolutionised management of chronic liver disease. In an era of ever-increasing demand, promoting equity of timely access needs to be a priority. Markers of disease severity including MELD and nutritional status correlate well with waiting list mortality. These variables deteriorate with referral delay. Through analysis of patients referred to a LT unit over a two-year period we sought to establish characteristics that could be used as markers to represent a 'late' referral.

Methods Referrals for liver transplantation for chronic liver disease (CLD) between 1 April 2017- 31 March 2019 were reviewed. Electronic patient records were interrogated to establish patient demographics, severity of disease at referral and assessment outcome.

Results In this period 371 patient with CLD were referred for LT assessment. Of these, 64% were male and 50% had alcohol related liver disease. Median UKELD at referral was 54 (range 42–72), 58 (16%) UKELD > 60 at referral.

150/371 (40.4%) were listed for transplantation of whom 26 (17%) died on the waiting list. In addition, 19 (5%) of patients died prior to completion of their assessment and 17.9% were not listed because they required further optimisation of clinical status due to frailty or malnutrition. Other patients were declined listing because of medical/surgical contraindications (31.2%), alcohol concerns (9%) and were considered too early (36.1%). In total therefore 144 patients (39%) were unable to access LT because of the advanced nature of their disease.

281 patients (76%) had ascites at referral, 64 (22.8%) had undergone > 5 paracentesis (LVP) procedures prior to referral, 27 (9.6%) had undergone > 10 LVP. A smaller proportion of patients in the >10 LVP group were listed compared with the <10 group (26% vs 35%). A greater proportion of patients in the >10 LVP group died during the study follow-up period compared with <10 group (37% vs 32%).

Conclusion In this heterogenous population, identifying markers of 'late referral' is challenging. A potential surrogate marker identified by this study is number of LVP prior to transplant assessment referral. There are unavoidable late referrals due to late presentation, non-attendance or substance concerns. Failure to recognise the significance of recurrent LVP procedures may represent missed opportunities for earlier referral. It is likely that the reasons behind these later referrals are multi-factorial and further work is needed to identify and improve these modifiable risk factors.

P178 GOOD CLINICAL OUTCOMES FOLLOWING DIRECT INTRAHEPATIC PORTOCAVAL SHUNT (DIPS) FOR BUDD CHIARI SYNDROME

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Introduction Budd Chiari syndrome (BCS) is a rare but potentially life-threatening condition. Recanalization using TIPSS or hepatic venous stenting is key to relieving hepatic congestion. These procedures are impossible in complete HV occlusion. Direct intrahepatic portocaval shunt (DIPS) is a new procedure where a stent is placed directly from the inferior vena cava, often through the caudate lobe, to the portal vein and therefore bypassing the thrombosed HVs. We report our experience in using DIPS for recanalization in BCS.

Methods Single centre retrospective analysis from May 2015 to January 2019 comparing outcomes following a DIPS insertion compared to our centre's previously published data.

Results 14 patients were referred for a DIPS procedure. M:F ratio 8:6; age 40.5±13.2; follow up 23.1±15.0 months. HV-BCS type in all. Aetiology: myeloproliferative neoplasm (MPN) in 7, all JAK2+ve with mutation load 17.3±10.2%; PNH, 1; idiopathic, 6 (all –ve following next generation sequencing). Pre-DIPS: MELD 13.1±3.2, UKELD 49.1±13.35, BCS-TIPS PI score 4.45±1.1. Post DIPS portal pressure gradient was 6.9±2.2 mmHg. Clinical indication: variceal bleeding and ascites (n=1) or ascites (n=13). Multidisciplinary consensus to undertake a DIPS insertion as a first line procedure was reached in 13 patients, in 1 patient a TIPSS insertion was initially attempted, when this failed a rescue DIPS was performed. One DIPS insertion (7%) was not successful, this patient is now on the waiting list for transplantation. In all remaining patients, successful stent placement was achieved, and none required escalation to transplantation. Ascites resolution was seen in 7 out of 11 patients at follow up (64%). 2 patients developed hepatic encephalopathy post DIPS (14%). Primary patency rates at 6 months, 1 year, and 2 years were 83%, 83%, 58% respectively. Secondary patency was 100%. Transplant free survival 100% to date. The outcomes are comparable to a previously reported series from the same institution, with similar BCS-TIPS PI but slightly lower MELD.

Conclusion Our data demonstrates that with technical excellence, multidisciplinary management, and careful patient selection, DIPS results in very good clinical outcomes in patients unsuitable for standard TIPSS. The outcomes are comparable to standard TIPSS from our historic data. We strongly recommend early referral of all patients with BCS to multidisciplinary teams in centres that offer advanced interventional radiology and liver transplantation.

P179 NHS BISCUIT CULTURE – NAFLD PREVALENCE AND THE USE OF FIBROSCAN

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