PTU-044 TO STENT OR NOT TO STENT IN MALIGNANT LARGE BOWEL OBSTRUCTION

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Introduction Self expanding metallic stents (SEMS) can resolve obstruction due to colorectal cancer (CRC), enabling subsequent elective rather than emergency surgery. This study compared the outcomes after stenting and subsequent elective surgery versus emergency surgery (ES) for obstructing CRC.

Methods Prospectively collected data from a consecutive series of 153 patients with large bowel obstruction secondary to CRC, presenting to a single NHS Trust from April 2010 to March 2017, were retrospectively analysed. Of these, 41 (26.8%) had stenting as a bridge to surgery (SBTS) followed by elective surgery and 112 (73.2%) had ES. Primary outcomes were mortality rates after surgery at 30 days, 90 days and 1 year. Secondary outcomes were the rates of stoma formation and anastomotic leak (both clinical and radiological).

Results Thirty-day mortality was 7.3% with SBTS and 12.5% with ES. Ninety-day mortality was 7.3% with SBTS and 17.9% with ES. One-year mortality was 19.5% with SBTS and 32.1% with ES. The anastomotic leak rate was 7.1% with SBTS and 14.0% with ES. The rate of stoma formation was 39.0% with SBTS and 33.0% with ES. With cancers proximal to the splenic flexure excluded, stoma rates were 38.5% with SBTS and 54.2% with ES.

Conclusions Without adjustment for confounding variables superiority of SBTS over ES cannot be inferred. But these results suggest SBTS can be a safe alternative to ES and may offer advantages in respect of stoma and leak rates.

PTU-045 URINARY VOC AND FAECAL MICROBIOME CHARACTERISATION OF COLORECTAL CANCER PATIENTS, THEIR FIRST-DEGREE RELATIVES AND SPOUSES

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Introduction Colorectal cancer (CRC) is the one of the commonest causes of cancer worldwide, and, subsequently, there has been a drive in recent years to identify a non-invasive CRC biomarker. Volatile organic compounds (VOC) detection in various bodily substances, by means such as mass spectrometry and electronic nose, have gained particular interest. CRC patients have been shown to be distinguishable from healthy controls using urinary VOC detection in several studies, including two published by the research group at UHCW and the University of Warwick.^{1 2} There has also been significant research into the role that the intestinal microbiome plays in health and disease in humans.

The aim of this study was to characterise the urinary VOC and stool microbiome profiles of CRC patients, their spouses and first degree relatives with the goal of determining whether environmental and genetic controls could be distinguished from the CRC subjects using urinary VOC and faecal microbiome profiling.

Methods 56 CRC subjects, 45 spouses and 37 relatives were recruited. Sample analysis was performed using an LC-FAIMS-MS apparatus to detect urinary VOCs, whilst an Illumina Miseq platform was used for 16 s RNA sequencing. Urinary data was processed and analysed using a 5-fold cross-validation with sparse logistics regression and random Forrest statistical classifiers. Microbiome data was analysed using standardised uPARSE and QIIME pathways. Comparisons were also made between pre-treatment and post-treatment CRC samples (n=23) to determine if there was any change in VOC or microbiome profiles after treatment.

Results The urinary VOC profiles of CRC subjects could be distinguished from both sets of healthy controls using both classifiers. Achieved sensitivities were 63%–69%, specificities 64%–69% and AUC 0.71–0.72. No statistically significant differences could be found in the urinary VOC profiles of pre-operative and post-operative samples.

Microbiome analysis revealed over 1300 operational taxonomic units (OTUs), with a similarity of >93% between CRC samples and control groups, with significantly different bacterial abundances identified in 82 OTUs, mainly Clostridiales. Pre-treatment and post-treatment sample analysis revealed differences of 17 (3%) and 22 (4%) OTUs at 3 and 6 months respectively, again principally Clostridiales.

Conclusions This study provides further validity of the use of urinary VOCs as a non-invasive biomarker for CRC detection, demonstrated here against genetic and environmental controls. The LC-FAIMS-MS technology is a variant of the previously utilised FAIMS, although exact chemical identification is not possible due to a lack of a validated database. Microbiome analysis showed broadly similar bacterial profiles between the various groups, will subtle differences in some families, such as clostridiales, and a restricted CRC profile, compared to the healthy controls.

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PTU-046 NOVEL LACTOFERRIN-LOADED ALGINATE MICROGELS DISPLAY ANTI-CLOSTRIDIUM DIFFICILE DEFENCE PROPERTIES IN VITRO

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Introduction We previously reported that some forms of bovine lactoferrin (bLf) are effective in substantially delaying *C. difficile* growth and preventing production of toxins in a human *in vitro* gut model of *C. difficile* infection (CDI). The aim of the present study was to develop lactoferrin-loaded alginate microparticles coated with high molecular weight chitosan for enhanced protein stability, and to subsequently evaluate their anti-*C. difficile* defence properties *in vitro*.

Methods Different forms of bLf (iron-depleted; apo-bLf, iron-saturated; holo-bLf, and manganese-saturated; Mn-bLf) and BSA-FITC were encapsulated in calcium-alginate and chitosan-coated alginate particles. Microgel particles were fabricated using the emulsification/internal gelation method. Protein encapsulation efficiency was confirmed by fluorescence microscopy imaging of BSA-FITC-loaded hydrogel particles. *In vitro* release studies conducted in pH-simulated gastrointestinal conditions were employed to investigate protein-loading efficiency and release rate of encapsulated protein. The various encapsulated bLf forms were evaluated for their influence on intestinal epithelial barrier function and cell viability alone, and in combination with purified whole *C. difficile* toxins A and B or bacterial supernatant samples of the epidemic 027 *C. difficile* strain. Enterocyte viability and epithelial permeability were assessed using trypan blue exclusion, MTT cytotoxicity assay and changes in *trans*-epithelial electrical resistance (TEER) in Caco-2 cells, respectively.

Results Alginate microparticles are suitable for encapsulation and pH-triggered release of metal-bound bLf proteins. The application of bLf (5 mg/mL) delivered from alginate microparticles to human intestinal epithelial cells (hIECs) significantly reduced the cytotoxic effect of toxin A and bacterial supernatant samples on Caco-2 cells, as illustrated by increased TEER values and enhanced Caco-2 cell viability. Pre-treatment of Vero cell monolayers with all forms of encapsulated bLf followed by exposure to toxin B or bacterial supernatant induced a fall in mitochondrial enzyme activity.

Conclusions Our results are the first to suggest that alginate-bLf microparticles show protective effects against *C. difficile* toxin-mediated mucosal damage and impairment of barrier function in hIECs. The future potential of lactoferrin-loaded alginate microparticles in the treatment and prevention of CDI deserves further investigation in preclinical studies.

PTU-047 HIGH PREVALENCE OF CLOSTRIDIUM DIFFICILE RIBOTYPE 078 IN IBD OUTPATIENTS

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Background and Objectives Point prevalence studies have reported higher carriage rates of *C. difficile* in IBD patients compared with the general population, but longitudinal prospective data are lacking. The objectives of this observational study were to investigate and molecularly characterise isolates of *C. difficile*, collected prospectively on a monthly basis over a one-year period among IBD outpatients and healthy controls (HC).

Methods At enrolment, recruited participants had established diagnoses of UC (n=16) and Crohn's disease (n=6) and reported no recent hospitalisation or exposure to antibiotics. PCR ribotype and toxin status (cytotoxigenic culture) were determined for all +ive stool cultures. All participants underwent a monthly telephone interview to identify potential risk factors for *C. difficile* acquisition (changes in medications, exposure to antibiotics, clinic attendances, hospitalisation) and

to assess for disease activity (Harvey-Bradshaw Index and Simple Clinical Activity Colitis Index).

Results Two patients underwent physician-initiated laboratory testing of *C. difficile* during the sample collection phase, although no participants developed or were treated for *C. difficile* infection. *C. difficile* was cultured from 29/223 samples (13%) representing 16/22 patients and 1 of 5 HC with concurrent antibiotic exposure in 6/29 visits (20%). Of the toxin +ive isolates (n=25; 078, 005, 302 and 015), 72% (n=21) were PCR ribotype 078. Toxigenic negative ribotypes included 023, 026 and 656. Of those toxin +ive isolates, 9 samples (36%) were associated with relapsing IBD of which 7/9 were ribotype 078. Multiple stool specimens also tested +ive for different ribotypes in 3 patients with UC, all of whom were taking regular immunosuppressants. WGS studies of the 078 isolates revealed marked genetic similarity, with only 3 of the 21 isolates varying by 1 or more nucleotides when compared to the 078 reference genome, suggesting there may have been a common source for cross-transmission.

Conclusions The high prevalence of PCR ribotype 078 in this IBD outpatient cohort is consistent with the recent emergence of this strain in the community. These results reinforce the importance of testing all in-and outpatients with an apparent flare or relapsing IBD for carriage of toxigenic *C. difficile* to inform optimal management strategies. Future research is needed to understand the predominance of 078 isolates in IBD, particularly in the context of clinical relapse.

PTU-048 SERUM TRACE METAL CONCENTRATIONS IN CLOSTRIDIUM DIFFICILE INFECTION AND THEIR RELATIONSHIP TO DISEASE SEVERITY

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Introduction Trace metals play a central role in host-pathogen interactions, impacting both microbial growth/pathogenicity and antimicrobial host immune defences. The main objective of this study was to determine the relationship between serum trace metal concentrations and severity of *C. difficile* infection (CDI).

Methods We analysed biobanked serum samples previously collected from a single-centre prospective observational study in which we recruited consecutive hospitalised patients ≥18 years with symptomatic toxin-positive *C. difficile* diarrhoea. Severe *C. difficile* was defined as WCC ≥15×10⁹/L or an increase in serum creatinine ≥1.5 above baseline, or pseudomembranous colitis, megacolon, need for colectomy or septic shock requiring ICU admission. Selected trace metal (iron, selenium, zinc, cadmium, cobalt, copper, magnesium, manganese, nickel and lead) concentrations in sera were determined by inductively-coupled mass spectrometry (ICP-MS). Mean biometal concentrations were compared between mild and severe CDI cases using Mann-Whitney test. Univariate and multivariate regression analyses were used to identify clinical and biochemical factors associated with risk of severe CDI.

Results A total of 224 serum samples derived from 149 patients [n=65 male; mean age (S.D.) 65.7 years (16.4); n=84