

was performed in over two-thirds of cases (69.6%; 48/69) and most surgeons either used an SILS approach (46.4%; 32/69) or a laparoscopic approach (40.6%; 28/69). A pursestring was used by the majority (87%; 60/69) at a median height of 4 ± 1.6 cm. The majority of pouches were created using a stapler (85.1%; 57/69) at a median distance of 2.9 ± 1.5 cm from the anal verge. Median operative time was 311 ± 126 min. Under a quarter of abdominal operations were converted (24.6%; 14/57) compared with four cases (5.8%) in the perineal phase. The median length of postoperative stay was 10 ± 6 days and three patients had a re-operation. There were no mortalities. Three patients (4.3%) had an anastomotic leak and two patients (2.9%) had collections. Late morbidity (>1 month) was available in 31 patients and of these seven patients (22.6%) had a stricture.

Conclusions: Transanal minimally invasive proctectomy with ileal pouch anal anastomosis is feasible and safe in patients with UC. It is also associated with relatively low rates of re-operation and anastomotic leakage.

OP018

High-fat diet and inflammation drive intestinal fibrosis enhancing epithelial–mesenchymal transition through the activation of S1P3 signalling

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Background: Epithelial-mesenchymal transition (EMT) is considered to contribute to intestinal fibrosis. However, the mechanisms underlying this process remain largely unknown. Sphingosine-1-phosphate (S1P), a pleiotropic lipid mediator crucially involved in inflammation and cancer, has been identified as a master regulator of fibrosis by activation of sphingosine-1-phosphate receptor 3 (S1P3). Recently S1P has been demonstrated being able to induce EMT in cancer. However, so far no data are available on the functional role of S1P/S1P3 signalling in the gut and its involvement in EMT process associated to intestinal fibrosis. Therefore, our aim was to explore the role of S1P/S1P3 signalling in intestinal fibrosis. **Methods:** Fibroblasts isolated from fibrotic and non-fibrotic biopsies of Crohn's disease patients were analysed before and after S1P and TGF- β stimulation, in the presence or in the absence of S1P3 inhibitors and/or palmitic acid or lipid mixture. S1P levels and S1P3 expression were quantified in cell supernatants and whole tissue. Pro-fibrotic factors were analysed by RT-PCR, whereas collagen deposition by Sirius red. Overexpression of S1P3 was carried out on Caco-2 cells by lentivirus infection. Nine EMT-genes were analysed by RT-PCR. WT and S1P3 ko mice treated with TNBS via enema were fed either a high-fat diet (HFD) or normal diet for up to 12 weeks. Fibrosis and inflammation were quantified by histologic scoring, collagen synthesis, and cytokine expression.

Results: S1P3 expression significantly increased in both whole fibrotic tissue and fibrotic fibroblasts. S1P, TGF- β , and HFD stimulation

augmented on fibrotic fibroblasts S1P3 expression, which was also associated with increased expression of all pro-fibrotic factors analysed. The treatment with specific S1P3 inhibitors reduced proliferation and migration of fibroblasts as well as S1P- and TGF- β -dependent collagen deposition, and pro-fibrotic factors. HFD-fed WT mice exhibited a marked increase of epithelial S1P3 rather baseline displaying a higher accumulation of collagen in the mucosa. In contrast, S1P3 ko mice did not show any changes. Furthermore the combined association of HFD with chronic inflammation resulted in worsening intestinal fibrosis and α -SMA expression from epithelial cells. In vitro a long-HFD stimulation augmented expression of S1P3 on Caco-2 cells, which displayed EMT changes as well as S1P3 overexpressing cells.

Conclusions: Overall, our data demonstrate for the first time that HFD and inflammation cooperate to intestinal fibrosis modulating S1P3 receptor on epithelium, which promotes EMT. These results pave the way for a new specific anti-fibrotic therapy for stricturing complications in CD patients.

OP019

In faecal microbiota transplantation (FMT) for ulcerative colitis, fusobacterium is associated with lack of remission, while metabolic shifts to starch degradation and short-chain fatty acid production are associated with remission (FOCUS study)

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Background: In the FOCUS study, multidonor FMT was effective in the treatment of active ulcerative colitis (UC).¹ Here we characterise the bacterial taxonomic and functional changes associated with outcome.

Methods: A total of 314 fecal and 160 colonic biopsy samples were collected at specific intervals from 70 patients. A total of 113 fecal samples were collected from the 14 individual donors and 21 multidonor batches. DNA and RNA were extracted, RNA converted to cDNA, then 16S rRNA gene sequencing performed using 2x300 bp Illumina MiSeq chemistry. Sequences were analysed using MOTHUR. Shotgun metagenomics was performed on 285 fecal samples using 2x250bp HiSeq 2500 chemistry, with samples analysed using MetaPhlan2 and HUMANN2 for taxonomic and functional inferences, respectively.

Results: Patients: α -Diversity consistently increased following FMT across all datasets (fecal 16S DNA and RNA/cDNA, colonic mucosa 16S DNA and RNA/cDNA, shotgun metagenomics—taxonomic; $p < 0.005$). α -Diversity saturated by Week 4 with trends to greater α -diversity with remission. β -Diversity across all datasets showed FMT significantly shifted global microbial composition ($t = 2.85$, $p = 0.001$, $df=104$; Figure 1), from *Bacteroides* to *Prevotella* dominance.