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Small bowel mucosal healing and deep remission in patients with known small bowel Crohn's disease.

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Background: Mucosal healing (MH) and deep remission (DR) are associated with improved long- and short-term outcomes in Crohn's disease. The vast majority of the available data pertains to colonic MH ***and DR, while the evidence regarding the prevalence and impact of small bowel mucosal healing (SBMH) is scarce.

The aims of the study were to evaluate the prevalence of active inflammation, SBMH and DR in small bowel Crohn's disease (SBCD) patients in clinical remission (CR) or clinically mild disease using biomarkers, video capsule endoscopy (VCE) and magnetic resonance enterography (MRE).

Methods: Patients with known SBCD in CR or with mild symptoms (CDAI<220) for at least 3 months were prospectively recruited and underwent MRE, followed by Agile patency capsule. If patency was ***proven, VCE was performed. The Lewis score (LS) was calculated for each tertile. C-reactive protein (CRP) and fecal calprotectin (FC) were evaluated for their association with clinical activity, MRE and VCE findings. Clinical remission was defined as CDAI < 150. FC >100 µg/g and CRP >5mg/ml were considered abnormal. SBMH was defined as LS< 135; significant SB inflammation was defined as LS >790. Biomarker remission (BR) was defined as a combination of CR (CDAI<150) and normal biomarkers. Deep remission (DR) was defined as a combination of BR and SBMH.

Results: Seventy nine patients were recruited and underwent MRE; 51 with proven patency underwent VCE studies. FC levels were elevated in 47.5% of patients, CRP levels in 29.4% and either biomarker- in 56.5% of the cases. SBMH was observed in 26% of the patients, and MRE did not demonstrate active disease in 23.7% of the patients. In patients with clinica and biomarker remission , SBMH was observed in 47.4% and MRE was normal in 56% of the patients. Deep remission was observed in 22.5% of the patients. The prevalence of deep remission was 50% in patients treated with anti-TNFs, whereas it was 20% in patients treated with thiopurines, 11% in patients not receiving any treatment and 0% in patients treated with 5-aminosalicates (p=0.045 for treated vs not treated with anti-TNFs). There was a significant correlation between normal FC levels and SBMH (r=0.48, p=0.001). CRP did not significantly correlate with SBMH (r=0.54 p=0.1). The combination of both biomarkers did not improve the diagnostic accuracy.

Conclusions: SB inflammation is detected in the majority of CD patients in CR and BR. DR was achieved in 22.5% of the patients in clinical remission and was more frequent in patients ***treated with anti-TNFs. FC was significantly more accurate in prediction of MH than CRP. Our findings emphasize the true inflammatory burden in quiescent patients with SBCD.

UK and DY- equal contribution ; RE and SBH- equal contibution

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Ionizing radiation throughout the duration of immunosuppression therapy in Crohn's disease: should it remain a concern?

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Background: Crohn's disease (CD) patients undergo many radiological studies employing ionizing radiation for diagnosis and management purposes. Our aim was to assess the total radiation exposure of our patients over the years, to estimate risk factors for exposure to high doses and to correlate radiation exposure to immunosuppression.

Methods: The cumulative effective dose of radiation (CEDR) was calculated multiplying the number of imaging studies by the effective dose of each exam. Radiation dose data was collected prospectively.

Results: Four hundred and fifty-one patients with CD (226 female) were followed during 11.0 years (IQR: 6.0-16.0), with 52.1% of the patients being B3-classified patients and 38.6% being steroid dependent. Thirty nine percent of the patients were under combo therapy and 41% had previous abdominal surgery. Sixteen percent were exposed to high radiation dose levels (CEDR>50 mSv) and 4% to CEDR>100 mSv. The mean CEDR between 26-35 years old was 12.539 mSv and a significant dose of radiation (over 50 mSv) was achieved at a median age of 40 (IQR: 29.0-47.0). Abdominal-pelvic computed tomography (CT) scan was the examination that contributed the most for CEDR.

High CEDR (β value; 95% CI) were found for penetrating disease phenotype (22.785, 17.139;28.431), steroid resistance or dependence (8.860, 3.050;14.670), abdominal surgery (18.673, 13.217;24.129), azathioprine (14.739, 6.875; 22.603) and anti-TNF therapy (17.141, 11.564; 22.716). Patients with penetrating phenotype (B3), previous surgery, azathioprine and anti-TNF α therapy were exposed earlier on the course of the disease to CEDR above 50 mSv (p<0.001). The value of CEDR in the patients under immunosuppression mainly increased in the first year of immunosuppression.

Conclusions: Penetrating phenotype, abdominal surgery, steroid resistance or steroid dependence and treatment with anti-TNF α and azathioprine were predictive factors for high CEDR. It was also demonstrated that immunosuppression and anti-TNF α treatment were followed by a sustained increment of radiation exposure.

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Prevalence and risk factors for thromboembolic complications in IBD patients

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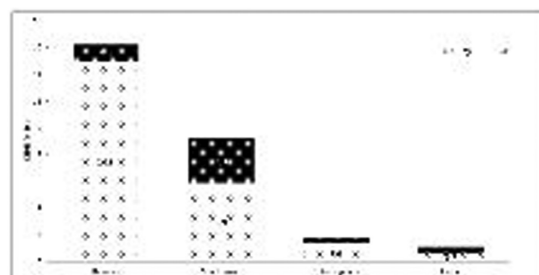
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Background: Inflammatory bowel disease (IBD) patients have an increased risk of venous thromboembolic complications (VTEC) such as deep vein thrombosis (DVT) and pulmonary embolism when compared to the non-IBD population. However, studies assessing VTEC prevalence in IBD as well as analyses of VTEC associated risk factors are scarce. We aimed to assess VTEC prevalence in IBD patients and to identify associated risk factors.

Methods: Data from patients enrolled in the Swiss IBD Cohort Study (SIBDCS) were analyzed. Since 2006 the SIBDCS collects data on a large sample of IBD patients from hospitals and private practices across Switzerland.

Results: A total of 90/2284 (3.94%) IBD patients suffered from VTEC. Of these, 45/1324 (3.4% overall; 2.42% with DVT, 1.51% with PE) had CD, and 45/960 (4.7% overall; 3.23% with DVT, 2.40% with PE) presented with UC.

In CD patients, median disease duration was 12 years in the VTEC group compared to 8 years in the CD group without VTEC (p=0.001). IBD-related intestinal surgery was more often performed in CD patients with VTEC compared to patients without VTEC (53.3% vs. 35.8%, p=0.016). No differences among the two groups were observed for perianal surgery (26.7% vs. 19.2%, p=0.216) or for disease location (p=0.596). UC-related intestinal surgery was more frequently encountered in the VTEC group compared to the one without VTEC (22.2% vs. 5.0%, p<0.001). Perianal surgery was not identified as risk factor for VTEC in CD patients (VTEC prevalence 4.4% in CD patients having undergone perianal surgery vs. 2.0% VTEC prevalence in CD patients not having undergone perianal surgery, p=0.240). UC patients with VTEC were found to suffer more frequently from pancolitis when compared to UC patients without VTEC (53.3% vs 40.3%, p=0.003). IBD treatment, including immunomodulators and anti-TNF agents, was used in similar frequencies in CD and UC patients with and without VTEC. Ciclosporin use was more prevalent in UC patients group with VTEC (15.6% vs. 6.0%, p=0.021). Logistic regression modeling found no significant association of VTEC with the following factors: age, gender, use of oral contraception, body mass index, smoking status, age at time of IBD diagnosis, and IBD family history.

Conclusions: IBD is associated with an important number of VTEC. VTEC were more prevalent in UC patients compared to CD patients. Intestinal surgery is a risk factor for VTEC in both UC and CD patients. Disease duration was identified as risk factor for VTEC in CD patients whereas pancolitis was significantly associated with VTEC in UC patients.

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Serological Antibodies for the Prediction of Post-operative Recurrent Crohn's Disease. Results from the POCER study

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Background: Disease recurrence after Crohn's disease resection occurs in up to up to 80% of patients, with two thirds ultimately requiring further surgery. Although clinical risk factors help in assessing the risk of relapse, a test that identifies patients at higher risk of recurrence would be clinically valuable. We investigated the value of serological antimicrobial antibodies to predict disease recurrence after surgery in a large prospective cohort of patients.

Methods: 171 patients had 525 samples tested peri-operatively, and 6, 12 and 18 months post-operatively as part of a structured study ("POCER") designed to diminish post-operative recurrence. Two-thirds of patients underwent colonoscopy at 6 months and all underwent colonoscopy at 18 months post-operatively. Serologic markers (ANCA, pANCA, ASCA IgA/IgG, anti-OmpC, anti-CBir1, anti-A4-Fla2, anti-Fla-X) were tested at each time point. Univariate analysis was performed for each (positive/negative) at all time points for endoscopic recurrence (Rutgeert's score ≥i2). Antibody titre was investigated using quartile sum score (QSS) method (range 7-28) and logistic regression analysis.

Results: Patients with recurrence at 18 months were more likely to be positive for anti-Fla-X than those without recurrence, when measured at baseline (64% v 45%; P=0.049), 6 months (65% v 43%, P=0.021) and 18 months (53% v 33%, P=0.038) post operatively. Patients negative for anti-Fla-X at 6 months had a lower risk of recurrence at 18 months (OR 0.38, 95%CI 0.17-0.84, P=0.018), when adjusted for age, gender, disease behaviour and smoking. A negative ANCA titre at 6 months was associated with recurrence at 6 months (ANCA -ve v +ve: recurrence 87% v 13%, P=0.002). Adjusted for baseline characteristics (age, gender disease location, smoking, pANCA) the total antibody titre for all antibodies combined was not predictive of endoscopic recurrence at 6 or 18 months.

Conclusions: The presence of the serological antibody anti-Fla-X identifies patients at higher risk of developing early disease recurrence, while the presence of positive ANCA predicts patients at lower risk of post-operative recurrence. Fla-X is an immunogenic bacterial antigen, arising from subunits of bacterial flagella (flagellin) from Clostridium subphylum cluster XIVa. Serologic screening of patients prior to surgery may assist in selecting patients at elevated risk of post-operative recurrence. The role of Fla-X in relation to microbiota that may be linked to recurrence requires evaluation.

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Patient-reported outcomes in biologic and thiopurine treatment of IBD measured as HRQoL and symptoms

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Background: Biological and thiopurine drugs are these days considered to be first line long-term treatment for severe or 5-ASA non-responding cases of IBD. Treatment strategies can be either single or combination therapy. The monitoring of these treatments tend to vary depending on which treatment strategy is chosen. Patients with biological treatment as either mono- or combination therapy tend to be more frequently monitored, but the frequency and extent of monitoring varies between different IBD clinics. At Danderyd Hospital,