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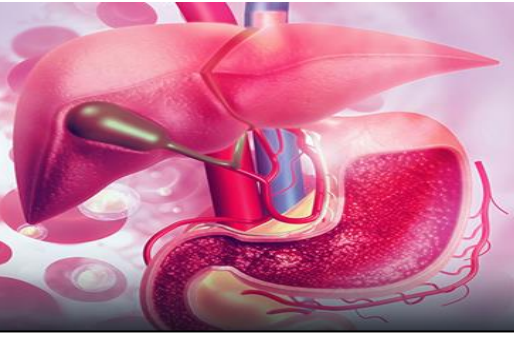

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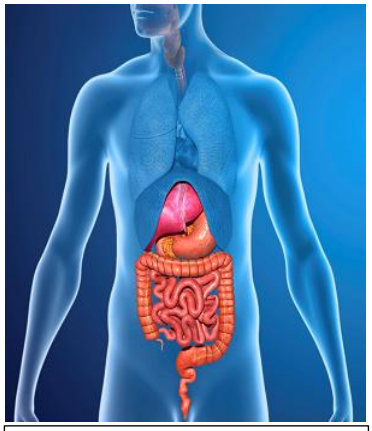
Relationship between Endoscopic healing and biologic treatment failure in patients with ulcerative colitis



Gastrointestinal disease

INTRODUCTION- Chronic ulcerative colitis (UC) is a remitting and relapsing disease that can progress from mild inflammation without symptoms to extensive inflammation of the colon. It can cause systemic symptoms, frequent bloody stools, dysfunctional colonic motility, tissue damage and possible permanent fibrosis, and even require surgery.[1] Endoscopic healing (EH) has been highlighted as a long-term target of UC treatment by the International Organisation for the Study of Inflammatory Bowel Disease (IOIBD) through its Selecting Therapeutic Targets in IBD (STRIDE)-II effort. EH, which was also known as endoscopic improvement in clinical trials, was characterized by a Mayo endoscopic sub-score of 0 or 1. It was linked to a lower chance of developing colon cancer, hospitalisation, surgery, and clinical recurrence. Over the past ten years, a growing number of individuals with ulcerative colitis (UC) have been treated with biologics. There was still little study on the relationship between endoscopic healing (EH) and unsuccessful biologic treatments.[2] The purpose of this study was to investigate the relationship between EH and biologic treatment failure connected to loss of response (LOR) throughout the therapy's maintenance phase.

METHODS- A retrospective observational study was conducted among 52 patients with established diagnosis of UC who started anti-tumor necrosis factor (TNF)-alpha agents (infliximab (IFX), adalimumab (ADA), golimumab (GLM), vedolizumab (VDZ), and ustekinumab (UST). A two-item patient-reported outcome (PRO2) measure, taken from the Mayo score, was used to assess clinical activity. A score of 0 for both rectal bleeding and stool frequency indicated a PRO2-based clinical remission. A rectal bleeding score of 0 and a stool frequency score of 0 were considered indicators of symptomatic remission. LOR, as determined by physicians' descriptions in patient records, was defined as disease deterioration following the main response to biologic therapies. Biologic therapy failure was described as stopping biologic treatments or increasing the dosage of other medications, such as topical 5-aminosalicylic acid (5-ASA) or corticosteroids for ulcerative colitis (UC) caused by LOR to biologic therapies. Using the Mayo endoscopic sub-score (MES), endoscopic severity was assessed. EH was defined as MES 0 or 1, and MES 0 was the definition of total EH. The existence of EH and one of the following four factors such as disease extent, concurrent thiopurines, biologic agent type, and starting disease activity were included as explanatory variables in sensitivity analyses.

RESULTS- The study results showed that 52 individuals had follow-up colonoscopies and 53 biologic treatments throughout a 12-week period. Out of all patients, only 32 (60.4%) had colonoscopies within a year of beginning biologic drugs. However, all patients had them within two years. The mean duration between the start of medication and the subsequent colonoscopy was 58 weeks (IQR: 42.0–103.0 weeks). Thirty-three patients (62.3%) obtained EH in less than two years. In all, 69.8% of the patients were treated with TNF-alpha medications, followed by 7.2% with VDZ and 8.1% with UST. PRO2-based clinical remission and symptomatic remission were observed in a notably higher proportion of EH patients than in those without (PRO2-based clinical

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remission, 78.8 vs. 0.0%; symptomatic remission, 100.0 vs. 70.0%). Even though none of the patients without EH were in PRO2-based clinical remission, 30% of them were in symptomatic remission. Of the 33 individuals who had endoscopic haemorrhage (EH), 26 had full EH (Mayo endoscopic sub-score [MES] 0, 78.8%). All patients who achieved EH continued on biologic therapy without LOR for the median follow-up period of 110 weeks following colonoscopies. Conversely, 8 out of 20 patients who did not reach EH had LOR, which led them to stop using biologic medicines (relative risk=3.75, 95% CI 2.23–5.51, p<0.001). 33 weeks (IQR, 12.0–69.0 weeks) was the median amount of time between a colonoscopy and the end of medication. Patients who obtained EH within two years had a considerably decreased probability of biologic therapy failure, according to the Kaplan-Meier estimator (p<0.001, log-rank test; Figure 1). Patients who obtained EH within a year were at a considerably decreased probability of failing their biologic therapy (p<0.05, log-rank test). Compared to patients without biologic therapy failure, a notably reduced proportion of patients (50.0 vs. 84.4%, p=0.048) experienced extensive colitis. Compared to individuals without biologic therapy failure, a statistically reduced proportion of patients (0.0 vs. 17.8%) got ADA treatment. Patients with biologic therapy failure had substantially lower proportions of patients in PRO2-based clinical remission and symptomatic remission at the time of colonoscopy than did patients without such failure. However, at the time of the colonoscopy, 50% of the patients who had failed biologic therapy were symptom-free. The median duration from colonoscopy to medication termination among patients who had failed biologic therapy was numerically shorter in those who did not have symptomatic remission than in those who did (64.0 vs. 102 weeks, p=0.34). Regardless of the severity of the disease, concurrent medications, biologic agent type, or initial disease activity, a Cox regression analysis revealed EH as an independent factor linked to a decreased risk of biologic treatment failure (Hazard Ratio= 0.0324, 95% CI 0.0002–0.3126, p<0.001).

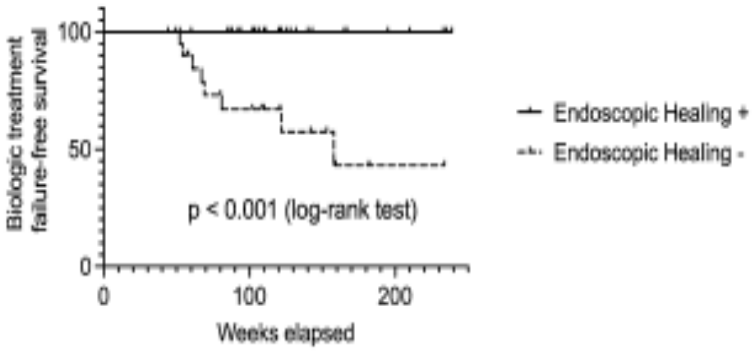

Figure 1. Assessment of the effect of endoscopic healing in patients with ulcerative colitis within two years after biologic initiation on treatment failure by Kaplan-Meier survival analysis

DISCUSSION-The current study showed that in UC patients, EH was an independent predictor associated with a decreased risk of biologic therapy failure related to LOR.[2] Similar to this study, Yzet C et al. showed that in patients with CD, full endoscopic healing was linked to better long-term results than partial endoscopic healing, as well as fewer surgeries and hospital stays and a generally lower probability of treatment failure.[3]

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CONCLUSION-The current study concluded that EH as an independent predictor linked to a lower chance of biologic therapy failure related to LOR in UC patients. It was advised to have a follow-up colonoscopy within 1-2 years after starting biologic therapy in order to modify treatment for any mucosal inflammation that may stay and maintain a longer state of clinical remission.

Endoscopic healing within two years was associated with a lower incidence of LOR-related biological therapy failure in individuals with Ulcerative colitis.

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Evaluation of adipose tissue lipolysis biomarkers in gastrointestinal cancer

INTRODUCTION- Adipocytes are specialized storage cells that safely store fatty acids (FAs) as triacylglycerol (TAG) in lipid droplet (LD) organelles. The basic process of hydrolyzing TAG to FAs for internal or systemic energy usage, known as adipocyte lipolysis.[1] Insulin resistance and inflammation were two systemic changes that have been linked to various metabolic changes of the adipose tissue in cancer. Studies on human cancer have recently looked into the metabolism of adipose tissue, finding altered browning patterns, heightened fibrosis, and inflammatory infiltration of the subcutaneous adipose tissue (SAT). Additionally, increased lipolysis—particularly in experimental models—was linked to the emergence of the cachexia phenotype. Furthermore, nothing was known about the potential effects of cachexia caused by cancer diseases on the expression of genes and proteins in adipose tissue. In order to understand the complicated pathophysiology of adipose tissue atrophy/loss in cancer, this element seems to be very important. Due to the fact that gastrointestinal cancers were known to be frequently linked to altered body composition and poor nutritional status, this study aimed to examine the variations in the primary molecular markers of lipolysis in SAT according to the type of gastrointestinal cancer in patients at the time of initial diagnosis. Next, the study examined variations based on the existence of cachexia.[2]

METHODS-A total of 23 patients enrolled in this cohort study. Recent cancer diagnosis (within 4 weeks), no anticancer therapy prior to surgery, age ≥18, and capacity for informed permission were the inclusion criteria.

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Participants receiving elective abdominal surgery for benign diseases served as the control group in this study. The functional assessment of anorexia/cachexia treatment (FAACT) anorexia/cachexia subscale (A/CS) score was used in the study to determine if anorexia was present. In order to further evaluate inflammatory and nutritional indicators, such as serum C-reactive protein (CRP) and albumin. Blood samples from fasting subjects in EDTA tubes was collected. The samples were then centrifuged using normal laboratory procedures. Patients with gastric, pancreatic, and colorectal cancer at the time of initial diagnosis were included in this study, along with controls who had benign conditions. Following the collection of SAT and extraction of total RNA, qRT-PCR was used to assess ATGL, HSL, PPARα, and MCP1. A Western blot was used to assess PLIN1, PLIN5, and CGI-58.

RESULTS- The current study results showed that mean age of cancer patients upon presentation was 72.1 ± 11.6 years, with 12 women (52%). The two most common comorbidities were diabetes (30%) and hypertension (61%). Nine controls, or 60% of the group, were female, and their mean age was 58.1 ± 13.9 years ($p = 0.002$). Patients with GI cancer exhibited increased expression of HSL and ATGL compared to controls ($p \leq 0.008$), as well as a tendency towards increased PPARα ($p = 0.055$). It was discovered that GI cancer patients with cachexia ($p = 0.033$) and those without cachexia ($p = 0.017$) had an overexpression of ATGL compared to controls. In comparison to controls, HSL was greater in patients with cachexia ($p = 0.020$) and those without it ($p = 0.021$). In comparison to controls, ATGL was increased in gastric cancer ($p = 0.014$), and greater HSL was discovered in pancreatic cancer ($p = 0.033$) and gastric cancer ($p = 0.008$). At the protein level, an increased CGI-58 in gastric cancer compared to controls ($p = 0.027$), in cachectic compared to controls ($p = 0.029$), and in cancer against controls ($p = 0.019$) was observed (Figure 1).

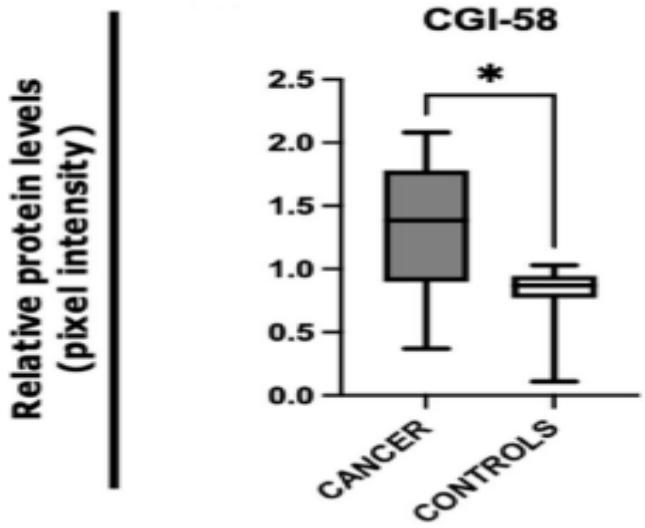

Figure 1. Patients with gastrointestinal cancers had greater levels of CG158 expression in comparison with controls

DISCUSSION- The current study showed that cancer patients had significantly greater levels of HSL mRNA and ATGL.[2] Similar to this, Agustsson T et al. reported that increased expression and function of adipocyte HSL mostly determined the mechanisms of increased lipolysis in cancer cachexia.[3]

CONCLUSION-The current study concluded that gene and protein expression of lipolysis of SAT were discovered to be regulated in a cohort of gastrointestinal cancer patients, and the elevation of the biomarkers evaluated was considerably greater in patients with gastric and pancreatic cancers. This information appears to be useful not only in understanding the pathophysiology of cancer-related nutritional and metabolic changes, but also in developing anti-catabolic therapies that should be implemented as soon as possible to enhance the patient's prognosis and quality of life.

This study identified important molecular changes associated with adipose tissue lipolysis throughout the early stages of cancer illness.

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Association between Body Mass Index and Gastro Esophageal Reflux Disease symptoms

INTRODUCTION- The term "gastro esophageal reflux disease" (GERD) refers to a group of symptoms that can include reflux of stomach contents into the oesophagus, which can cause a wide range of extra-oesophageal manifestations, including asthma, arrhythmias, recurrent aspiration pneumonia, and uncomfortable symptoms like dysphagia, heartburn, and regurgitation.[1] One potential risk factor for the occurrence and intensity of GERD symptoms has been shown to be the body mass index (BMI). A number of health problems have been connected to BMI, an indicator that evaluates body fat by taking a person's height and weight into account. There were numerous studies done on how it affects and how severe GERD is. Given the rising global incidence of GERD, it's critical to understand the relationship between BMI and symptoms of the GERD.[2] The aim of the study was to determine the relationship between GERD symptoms and BMI.

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METHODS-This was a descriptive cohort study. The study involved a total of 185 patients who were diagnosed with GERD. Age, gender, and socioeconomic level were among the key demographic data that was collected. The participants' medical histories, including any pre-existing conditions, medication usage, and the duration of their GERD symptoms, were documented. The standard formula, which divides weight in kilogram by height in metres squared, was used to compute BMI. Using validated questionnaires, the frequency and severity of symptoms such chest pain, regurgitation, and heartburn were assessed to ascertain the severity of GERD symptoms. The World Health Organisation (WHO) used different BMI classifications to assign participants to underweight, normal weight, overweight, and obese categories. The appropriate inferential statistical tests were used to assess the association between BMI and the intensity of GERD symptoms. The level of significance was established at $p<0.05$.

RESULTS- The study results showed that patients' ages varied from 18 to 30 (24.32%), 31 to 45 (32.43%), 46 to 60 (27.03%), and 61 years or more (16.22%). The patients' most common medical disorders were hypertension (18.92%), diabetes mellitus (13.51%), and prior gastrointestinal (GI) illnesses (21.62%). The other medical disorders were asthma (8.11%) and cardiovascular problems (10.81%). Proton pump inhibitors (32.43%), antacids (21.62%), and H2 blockers (16.22%) were the most often utilised drugs by patients. The majority of patients (29.73%) reported having GERD symptoms for more than three years, followed by 1-3 years (24.32%), 6 months to one year (18.92%), and less than six months (27.03%). 37.84% patients reported having severe symptoms, 24.32% reported having moderate symptoms, and 10.81% reported having mild symptoms. Moreover, 27.03% of patients did not exhibit any symptoms of GERD. By BMI, 24.32% of patients were normal weight, 5.41% were underweight, and the majority of patients (40.54%) were either overweight or obese (29.73%). These variables may also be important for the intervention's effectiveness and provide vital data for assessing how GERD affects individuals with the different BMI ranges shown in Table 1.

Variable	Number of Patients(n=185)	Percentage (%)
Duration of GERD Symptoms		
Less than 6 months	50	27.03%
6 months to 1 year	35	18.92%
1-3 years	45	24.32%
More than 3 years	55	29.73%
GERD Symptoms		
Mild	20	10.81%
Moderate	45	24.32%
Severe	70	37.84%
None	50	27.03%
BMI Category		
Underweight	10	5.41%
Normal	45	24.32%
Overweight	75	40.54%
Obese	55	29.73%

Table 1. Duration of GERD, GERD symptoms and BMI Category

DISCUSSION- The study revealed that most of the participants utilized proton pump inhibitors (32.43%), antacids (21.62%), and H2 blockers (16.22%).[2] Similar to this, Zaterka et al. showed that despite certain safety concerns, proton pump inhibitors remain the first choice for people with GERD or NERD because of strong data supporting their effectiveness. Prescription of proton pump inhibitors for patients with clear indications, with appropriate dosage and adverse event monitoring, was advised, as with any medical intervention.[3]

CONCLUSION- The current study highlighted the symptoms, medical history, and demographics of GERD patients. These results underlined the importance of controlling GERD, particularly in individuals with comorbidities and chronic symptoms, and support earlier study. The significant percentage of obesity and overweight among individuals highlighted the need of controlling weight when treating GERD.

The high incidence of severe symptoms in individuals who were overweight or obese indicated that the intensity of symptoms increased with elevated BMI and highlighted the need of controlling weight in the management of GERD.

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A rare case report of lupus enteritis manifesting as colorectal involvement

INTRODUCTION- An autoimmune condition with systemic inflammatory symptoms is called systemic lupus erythematosus (SLE). Most often detected problems include skin, kidney, and central nervous system involvement along with haematological abnormalities. In 40–60% of SLE patients, gastrointestinal involvement was a common complaint.[1] Dental ulcers, protein-losing enteropathy, intestinal pseudo-obstruction, autoimmune pancreatitis, hepatic damage, lupus enteritis (LE), and a variety of additional problems can be indicative of SLE's effect on the digestive system. Among the conditions that affect the gastrointestinal (GI) system in SLE were appendicitis, colitis, gastritis, and enteritis. Vomiting, diarrhoea, nausea, lack of appetite, and stomach discomfort make up around half of the GI symptoms associated with SLE. A potentially harmful consequence that affects people with active SLE was LE. It happens to people who were really sick and probably won't get better. The majority of small intestine-related LE cases in SLE occur after the condition has been diagnosed. As a result, it might be challenging to determine whether colorectal LE was linked to SLE.[2] The purpose of this case report was

to describe a 35-year-old woman who had minimal intestinal involvement but full colorectum involvement. She showed signs of improvement and disease activity following high-dose corticosteroid treatment.

CASE PRESENTATION- A 35-year-old woman arrived at the hospital complaining of vomiting and inexplicable stomach pain. Following her lupus nephritis diagnosis, the patient took her medicine consistently for five years. Up until two months before LE started, she had taken her prescription irregularly. Upon physical examination, the patient exhibited pressing and distributed abdominal discomfort without rebound tenderness. A high antinuclear antibody titer (ANA 1:100) and lower titers of C3 and C4 were found in laboratory testing. In accordance with the European League Against Rheumatism/ American College of Rheumatology (EULAR/ACR) classification criteria, which improved the combined sensitivity and specificity of the SLE diagnosis by adding antinuclear antibodies to the entry criterion, the kidney biopsy score for class IV lupus nephritis (diffuse proliferative glomerulonephritis) on the International Society of Nephrology (ISN) was 10, the lower complement C3 and C4 scores were 4, and the overall score was 14 (≥10). It was easy to diagnose SLE. Reduction in complement C3 level was a sensitive marker of active SLE. The day following hospitalisation, a computed tomography (CT) scan of the abdomen was done using contrast enhancement. With the target sign, also known as the doughnut sign, on the CT scan, there was a clear and dramatic edema of the whole colon and rectum, and the thickened intestinal wall extended between the rectum and ascending colon by 4 to 13 mm. Localised ischemia and congestive alterations were seen in the same intestine. The ischemic section of the intestinal wall was partially discontinuous, and showed gas shadows of a discontinuous mucosal line. Along with mesenteric fat attenuation, bilateral ureter-hydronephrosis, and ascites, the mesenteric arteries were thickened and enlarged, exhibiting the comb sign. The patient was treated with hydroxychloroquine (100 mg), 100 mL of 0.9% sodium chloride, 10 mg of methylprednisolone sodium succinate, and nutritional assistance. Seven days prior to release, a follow-up CT scan was carried out, and no abnormal finding were found (Figure 1). She had methylprednisolone and hydroxychloroquine medication for one week, and after that, her SLE symptoms and disease activity considerably improved.

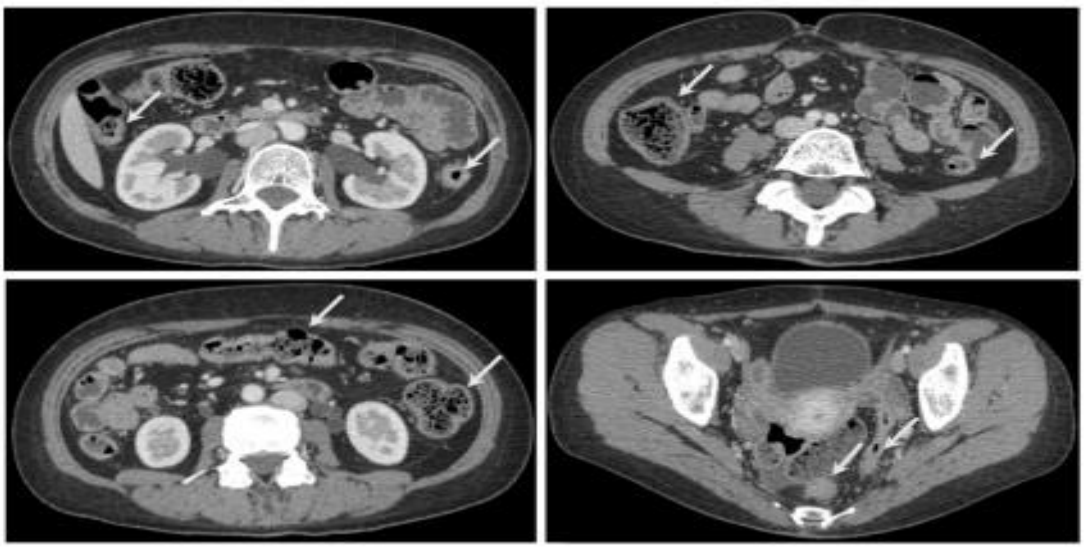

Figure 1. After one week of therapy, patients contrast-enhanced computed tomography scan revealing normal colon (white arrows)

DISCUSSION- This case report showed that after receiving high-dose corticosteroid therapy, patient showed improvement in her symptoms and disease activity.[2] Similar to this, Zhou JB et al. showed that corticosteroid medication has been used successfully as the first line of treatment, decreasing the need for surgery. Hydroxychloroquine may lessen the incidence of lupus flares and organ damage.[3]

CONCLUSION-The current study concluded that although colorectal LE without small intestine involvement was extremely rare, early detection and good corticosteroid treatment eliminated the need for surgical management. Physicians should be aware that colorectal LE without small intestine involvement can indicate a lupus flare.

High-dose methylprednisolone and hydroxychloroquine can be used as a combination treatment for general manifestation and specific harmful element as the first line treatment for colon and rectum LE associated with SLE.

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