FIBROGENESIS BIOMARKERS AND RISK FACTORS OF GASTROINTESTINAL TRACT STRICTURES IN CROHN'S DISEASE

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INTRODUCTION

Inflammatory bowel disease (IBD), such as Ulcerative Colitis (UC) or Crohn's Disease (CD) are characterized by chronic inflammation and damage of intestinal tissue, which leads to local expansion of mesenchymal cells and excessive deposition of extracellular matrix components, such as collagen or fibronectin. Inflammatory and fibrotic changes together contribute to progressive bowel wall thickening, stricture development and subsequent obstructing complications. The lifetime risk of stricture formation is about 24,9-50% among patients with CD. A major group of these patients require surgery at least once in the lifetime. Drug development over the last decades has led to better control of the inflammation, however anti- inflammatories do not specifically target or reverse fibrosis. Currently, there are no biomarkers which could be useful in order to stratify patients according to their risk of intestinal strictures development or identify early stages of fibrosis prior to clinical symptoms.

Category	Biomarkers
Extracellular matrix proteins	Collagen, Collagen III, Collagen IV, Fibronectin isoform ED-A, COMP
Growth factors	TGF beta, HGFA
Cytokine antibodies	Anti-TGF beta antibodies, Anti- IL-10 antibodies, Anti GM-CSF antibodies
Antimicrobial antibodies	anti- Saccharomyces cerevisiae antibody (ASCA), anti-zymogen granule membrane glycoprotein 2 (GP2) antibodies, anti- A4-Fla2, anti Fla-X, anti-CBir1, anti- Escherichia coli outer membrane porin C (anti-OmpC), anti-CD associated bacterial sequence (I2), Cathelicidin (LL-37)
Genetic variants	caspase activation recruitment domain (NOD2/CARD15), L-selectin (CD62L), IL12B
Histophathology biomarkers	Mast cell density in the muscularis propria and submucosa, TGFb-activated kinase 1 (TAK1), OGR1 mRNA
Other	miR-19a-3p, miR-19b-3p, a2-Heremans-Schmid glycoprotein (AHSG/fetuin A), elafin, mannan-binding lectin (MBL)

Table 1. Potential biomarkers of fbrogenesis in Crohn's disease

AIM OF THE STUDY

Our study aims to assess the clinical importance of potential biomarkers of gastrointestinal tract fibrosis, as well as to determine the significance of risk factors for stricture formation among patients with CD. By identifying reliable biomarkers, we hope to contribute to the early detection of fibrosis and ultimately improve patient outcomes.

MATERIALS AND METHODS

The study will include a group of 120 patients over 18 years of age with CD, hospitalized in the Department of Gastrointestinal Tract Diseases. The study group will consist of patients with diagnosed stenosis of the gastrointestinal tract, while the control group will include patients without evidence of strictures in the gastrointestinal tract. Diagnosis of gastrointestinal strictures will be confirmed using radiological and/or endoscopic criteria. To meet the radiological criteria, segmental stenosis of the lumen of the gastrointestinal tract in imaging studies is required, with thickening of the wall at the site of the stenosis and widening of the lumen of the gastrointestinal tract in the section prior to the stenosis. The endoscopic criterion is the inability to pass the narrowed section of the gastrointestinal tract with the endoscope without a prior endoscopic dilation of the stenosis. We selected four types of the most promissing potential biomarkers of fibrostenosis: cartilage oligomeric matrix protein COMP, hepatocyte growth factor activator HGFA, antibodies against granulocyte-macrophage colony stimulating factor GM-CSF Ab, isoform ED-A of fibronectin. Peripheral blood samples (5 ml) will be collected from subjects and concentration of candidate biomarkers will be measured in the obtained serum samples by ELISA technique. Subjects will complete questionnaire concerning disease course and risk factors of fibrostenosis.