Predictors of Surgical Intervention in Patients with Inflammatory Bowel Disease

Thesis

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By
Ahmed Elkattary Mohamed Elkattary
M.B.B.Ch

Under supervision of
Prof. Dr. Khaled Hamdy Abd El Megeed
Professor of Internal Medicine, Hepatology and Gastroenterology
Faculty of Medicine, Ain Shams University

Prof. Dr. Shereen Abou Bakr Saleh
Assistant Professor of Hepatology and Gastroenterology
Faculty of Medicine, Ain Shams University

Dr. Christina Alphonse Anwar
Lecturer of Internal Medicine, Hepatology and Gastroenterology
Faculty of Medicine, Ain Shams University

Ain Shams University
Faculty of Medicine
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Ahmed Elkattary

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List of Abbreviations

Abb.	Full term
ANCA	Anti Neutrophilic Cytoplasmic Antibody
ASCA	Anti *Saccharomyces Cerevisiae* Antibodies
C. Difficile	Clostridium Difficile
CBC	Complete Blood Count
CD	Crohn's Disease
CDAI	Crohn's Disease Activity Index
CRC	ColoRectal Carcinoma
CRP	C Reactive Protein
EEN	Exclusive enteral nutrition
ESR	Erythrocyte Sedimentation Rate
HBI	Harvey-Bradshaw Index
IBD	Inflammatory Bowel Diseases
IBS	Irritable Bowel Syndrome
IL	InterLeukin
MSCs	Mesenchymal Stem Cells
NO	Nitric Oxide
NOD gene	Nodulation gene
PPD	purified protein derivative
TBMT	Thiopurine-S-methyltransferase
TNF	Tumor Necrosis Factor
TYK2	Tyrosine kinase 2
UC	Ulcerative Colitis
UCEI	Ulverative Colitis Endoscopic Index of Severity
WCE	Wirless Capsule Endoscopy

ABSTRACT

Background: Inflammatory bowel disease (IBD) is comprised of two major disorders: Ulcerative Colitis and Crohn's disease. Ulcerative Colitis affects the colon, where as Crohn's disease can involve any component of the gastrointestinal tract from the mouth to the perianal area. These disorders have somewhat different pathologic and clinical characteristics, but with substantial overlap; their pathogenesis remains poorly understood.

Objective: To determine & detect different predictors that help us to characterize patients with high probability of undergoing surgical intervention for inflammatory bowel diseases.

Patients and Methods: The present study was designed to detect & identify possible factors that can be used to predict surgical intervention in patients with IBD. The present study was a case control study that was conducted on 80 patients with inflammatory bowel disease (either controlled by medical treatment or needed surgical intervention as a part of disease control) who were recruited form Ain-Shams university hospitals and El Quabbary general hospital in Alexandria.

Results: In the current study, there was no statistically significant difference between surgical and medical patients in terms of extraintestinal manifestations ($p = 0.25$). On the contrary, there were statistically significant differences between surgical and medical patients in terms of perianal disease ($p < 0.001$) and granuloma ($p = 0.012$). Surgical patients were more likely to have perianal disease and granulomas. Peri-anal disease was negative predictor of surgical treatment. In the present study, there were statistically significant differences between surgical and medical patients in terms of CDAI for CD ($p < 0.001$) and Mayo score for UC ($p < 0.001$). Surgical patients were more likely to have higher scores. CDAI and Mayo score were negative predictors of surgical treatment. **Conclusion:** Surgical treatment is a common outcome in IBD. Certain clinical features and the extent of disease are risk factors for surgical intervention. Our study indicates that smoking, Chron's disease, perianal disease, granulomas, higher severity scores, higher stool Calprotectin level, CRP, and ESR were associated with higher risks of surgical intervention. In addition, smoking, peri-anal disease, CDAI, Mayo score, Stool Calprotectin level, and CRP level were predictors of surgical treatment.

Keywords: Inflammatory bowel disease, ulcerative colitis

INTRODUCTION

Inflammatory bowel disease (IBD) is comprised of two major disorders: Ulcerative Colitis and Crohn's disease. Ulcerative Colitis affects the colon, where as Crohn's disease can involve any component of the gastrointestinal tract from the mouth to the perianal area. These disorders have somewhat different pathologic and clinical characteristics, but with substantial overlap; their pathogenesis remains poorly understood ***(Gomollón et al., 2019).***

Although IBD incidence is increasing globally, the precise etiology remains unclear and a cure for IBD has yet to be discovered. The most accepted hypothesis of IBD pathogenesis is that complex interactions between genetics, environmental factors, and the host immune system lead to aberrant immune responses and chronic intestinal inflammation. ***(Nishida et al., 2018).***

Crohn's disease is an idiopathic chronic transluminal inflammatory disorder of the gastrointestinal tract which is increasing in prevalence for unknown reasons. The three major phenotypes of the disease are inflammatory, stricturing, and penetrating ***(Lightner, 2020).***

Regardless of phenotype or anatomic location (small bowel, ileocolic, colonic, perianal), medical management consistently includes the use of glucocorticoids (e.g., prednisone), immunomodulators (6-mercaptopurine, methotrexate, azathioprine), or biologics (infliximab,

adalimumab, certolizumab pegol, vedolizumab, ustekinumab) ***(Lightner, 2020).***

Ulcerative colitis (UC), another idiopathic chronic inflammatory disease of the gastrointestinal tract, is limited to the colon and rectum. Similar to CD, its incidence continues to increase for unknown reasons and its controversial biologics are actually reducing the need for hospitalizations and proctocolectomy ***(Lightner, 2020).***

Despite the introduction of biologics, up to 60–80% with CD still require an intestinal resection and 20% with UC will undergo a proctocolectomy for medically refractory disease. While some studies suggest the rates of surgery are decreasing in the era of biologics, these figures still represent a significant proportion of IBD patients requiring major abdominopelvic surgery. And these patients are now coming to the operating room exposed to both systemic and gut-selective biologics, with worsened disease severity and a compromised health status ***(Lightner, 2020).***

Thus, it is imperative to characterize patients with high probability of undergoing surgical intervention for IBD. Previous reports indicated that a high relapse rate, need for admission, extraintestinal manifestations, development of penetrating disease, multiple admissions for flares, early age at diagnosis, smoking, extensive ulceration of the mucosa, high titers of serum antibodies, and mutations of the *NOD2* gene are significant predictors for surgical intervention for IBD ***(Yarur et al., 2011).***

AIM OF THE WORK

This study aims to determine & detect different predictors that help us to characterize patients with high probability of undergoing surgical intervention for inflammatory bowel diseases.

Chapter 1

INFLAMMATORY BOWEL DISEASES

A) Definitions & Types of IBD:

Inflammatory bowel disease (IBD) is comprised of two major disorders: Ulcerative Colitis and Crohn's disease. Ulcerative Colitis affects the colon, where as Crohn's disease can involve any component of the gastrointestinal tract from the mouth to the perianal area. These disorders have somewhat different pathologic and clinical characteristics, but with substantial overlap; their pathogenesis remains poorly understood ***(Gomollón et al., 2019).***

Ulcerative Colitis is a chronic inflammatory condition characterized by relapsing and remitting episodes of inflammation limited to the mucosal layer of the colon. It almost invariably involves the rectum, and the extent often involves more proximal portions of the colon in a continuous fashion ***(Gomollón et al., 2019).***

Crohn's disease is characterized by transmural inflammation and by skip areas of involvement (ie, segments of normal-appearing bowel interrupted by areas of disease). The transmural inflammatory nature of Crohn's disease may lead to fibrosis and strictures and to obstructive clinical presentations that are not typically seen in patients with Ulcerative Colitis. Transmural inflammation may also result in sinus tracts, giving

rise to microperforations and fistula formation ***(Gomollón et al., 2019).***

B) Epidemiology Of IBD

- ***Geographic and time trends:***

In the past decade, inflammatory bowel disease has emerged as a public health challenge worldwide. In North America and Europe, over 1.5 million and 2 million people suffer from the disease, respectively ***(Ng et al., 2017).***

Since the 1950s, the incidence and prevalence of inflammatory bowel disease steadily increased in the countries of North America, Europe, and Australia. During this time, more than two-thirds of studies reported that incidence rates were increasing significantly in the western world ***(Ng et al., 2017).***

Now, newer epidemiological studies suggest that incidence might be rising rapidly in South America, eastern Europe, Asia, and Africa. Additionally, an increase in disease incidence among ethnicities and nationalities in whom inflammatory bowel diseases were previously uncommon ***(Ng et al., 2017).***