

Multidisciplinary Inflammatory Bowel Disease Conference: The Impact of the Expert Pathologist on Patient Care

Seo Hyun Kim, MD,^{*}  Anna Buhle, MD,[†] Abra Roberts, MD,[‡] Neha Singh, BS,[§] Adil Mir, MD,[¶] Varun Kesar, MD,[¶] Alicia Lozano, MS,^{||} Wenyan Ji, MA,^{||} Alexandra Hanlon, MS, Ph.D,^{||} and Douglas Grider, MD^{**},^{††},^{‡‡}

From the ^{*}University of California San Diego School of Medicine, San Diego, CA, USA

[†]Carolinas Medical Center, Charlotte, NC, USA

[‡]University of Virginia School of Medicine, Charlottesville, VA, USA

[§]Virginia Tech Carilion School of Medicine, Roanoke, VA, USA

[¶]Division of Gastroenterology, Virginia Tech Carilion School of Medicine, Roanoke, VA, USA

^{||}Center for Biostatistics and Health Data Science, Department of Statistics, Virginia Tech, Roanoke, VA, USA

^{**}Dermatology Section, Department of Internal Medicine, Virginia Tech Carilion School of Medicine, Roanoke, VA, USA

^{††}Department of Basic Science Education, Virginia Tech Carilion School of Medicine, Roanoke, VA, USA

^{‡‡}Dominion Pathology Associates, Roanoke VA, USA

Address correspondence to: Seo Hyun Kim, MD, 200 W Arbor Dr, MC 8425, San Diego, CA 92103 USA, 1 (312) 636 5352, (elinaskim@gmail.com).

Background: Multidisciplinary teams (MDT) aid the diagnosis and management of patients with inflammatory bowel disease (IBD) and improve patient outcomes. The direct impact of a gastrointestinal expert pathologist on MDT care of IBD patients is unknown.

Methods: A retrospective chart review was conducted evaluating all cases (N = 289) discussed at the IBD MDT conference at Carilion Roanoke Memorial Hospital from June 1, 2013, through December 31, 2019. Cases were discussed between 1 and 6 times at the conference. Data collected included demographics, diagnosis before and after conference, reason for diagnostic change, endoscopy findings, medications, surgeries, and clinical follow-up.

Results: Approximately 15% to 42% of patients had a change in diagnosis after the first 3 conferences. The majority of diagnostic changes after the first (84%), second (73%), and third (67%) conferences were due to expert pathologist interpretation. Indeterminate colitis was the most frequently changed diagnosis, and Crohn's disease was the most common new diagnosis after conference. Among patients with a diagnostic change, 28.6% to 38.5% of patients had a change in their IBD medication regimen, and 7.7% to 10.9% had a surgical intervention after the first 2 conferences. Approximately 54.2% to 60% of patients reported clinical improvement or remission within 6 months of the first 3 conferences.

Conclusion: The majority of diagnostic changes made at the multidisciplinary IBD conference were due to histopathologic re-interpretation. A change in diagnosis at times led to significant modifications in medical or surgical management. An expert gastrointestinal pathologist is an essential MDT member for IBD management.

Lay Summary

An expert gastrointestinal pathologist plays a critical role in the diagnosis of patients presented at multidisciplinary team inflammatory bowel disease conferences. Their input at these conferences significantly impacts patients' medical and surgical management and clinical outcomes.

Key Words: Crohn's disease, ulcerative colitis, pathology, multidisciplinary team

Introduction

Inflammatory bowel disease (IBD) includes Crohn's disease (CD) and ulcerative colitis (UC) and often requires extensive diagnostic workup, medical therapies, and surgical procedures throughout the disease course. The complexity of care required to manage IBD can lend itself to misdiagnosis and mismanagement, leading to poorer outcomes for these patients. Multidisciplinary teams (MDTs) composed of experts in the diagnosis and treatment of IBD with complementary expertise were proposed as a better way to manage IBD.¹ The primary goal of MDT is to involve all key professionals in the consideration of complex patient management and/or diagnostic dilemmas to implement

evidence-based and cost-effective care to create an appropriately tailored care plan. Implementation of these multidisciplinary team discussions has been shown to improve patient outcomes.^{1,2}

Several studies have proposed which particular experts should be preferably considered core members of the MDT for the care of IBD patients. Consistent across these proposals are the inclusion of gastroenterologists, surgeons, radiologists, and expert pathologists with specific interest and training in IBD.^{1,3,4} One study highlighted the fundamental role that pathologists play in the diagnosis of IBD and the differentiation from other forms of colitis or enteritis.¹ Although some studies showed that pathologists are

Key Messages**What is already known?**

- A multidisciplinary team (MDT) approach improves outcomes in patients with inflammatory bowel disease (IBD), and an expert gastrointestinal pathologist plays a critical role in diagnosing IBD and discerning its subtypes.

What is new here?

- An expert pathologist plays a critical role in the diagnosis of patients presented at the MDT IBD conference, which significantly impacts patients' medical and surgical management.

How can this study help patient care?

- Consistent incorporation of an expert gastrointestinal pathologist in MDT care of IBD patients can significantly improve the diagnosis, management, and outcomes of patients.

considered an extended or an as needed member of the MDT, other studies favor expert pathologists as core members of the MDT.^{3,4}

The aim of our study was to quantify the impact of an expert gastrointestinal pathologist on the care and outcomes of complex IBD patients within a multidisciplinary team.

Materials and Methods

Patient Cohort

A single-institution retrospective chart review was conducted evaluating all cases discussed at the multidisciplinary IBD conference at Carilion Roanoke Memorial Hospital, (Roanoke, VA, USA) from June 1, 2013, through December 31, 2019. Patients were excluded if they were under the age of 18 years. A total of 289 patient charts were reviewed. Data were collected from available data in the Carilion Clinic electronic medical records system, EPIC, at the time of the study. The patients included in the cohort were all consecutive and followed in serial follow-up IBD conferences as needed. These included both inpatient and outpatient cases. Numerous patients were discussed at more than 1 conference (84 at 2 conferences, 21 at 3 conferences, 8 at 4 conferences, 2 at 5 conferences, 1 at 6 conferences). Cases discussed at more than 1 conference were considered individually and included in separate analyses. The Carilion Clinic Institutional Review Board approved this study.

Multidisciplinary IBD Conference

Twice a month, commencing June 1, 2013, the Carilion Clinic IBD MDT met (for a duration of an hour each time) to discuss difficult IBD cases based on a working list available to all participants located in the Carilion Clinic information management system, EPIC. Each conference was 1 hour long. On an average, 5 to 8 cases were discussed in each conference. The responsibility to ensure smooth functioning of the conference was primarily shared by a gastroenterologist with expertise in the field of IBD. A running active list of patients was maintained and shared with all attendees of the conference prior to each session.

Minimum attendance included at least one of each: a gastroenterologist with expertise in inflammatory bowel disease, a colorectal surgeon with interest in inflammatory bowel disease, a radiologist with experience in abdominal imaging, and a fellowship-trained gastrointestinal pathologist. Additionally, interested general gastroenterologists, gastroenterology fellows, internal medicine residents, and Virginia Tech Carilion School of Medicine (VTCOSOM) medical students attended this meeting. Attendance was ensured every time by means of interdisciplinary communication prior to each session, with at least 2 days lead time for the pathologist and radiologist to review the cases to be discussed. Any changes in patient care recommended in the meetings were agreed upon after multidisciplinary discussion and were accepted by the respective physicians responsible for the care of the discussed patient.

Generally, the expert IBD gastroenterologist determined the appropriateness for any case to be discussed at the IBD MDT conference and added cases to the list of patients to discuss every other week. The cases included were from the outpatient inflammatory bowel disease subspecialty clinic, which included referrals to their practice from community gastroenterologists or other endoscopists, and the inpatient gastroenterology team list, as deemed appropriate by the IBD expert gastroenterologist, per clinical complexity. Criteria included discretion based on the clinical experience for any one patient under the care of an expert gastroenterologist, such as how a patient is or is not responding to any particular medical therapy, or a question generated on chart review. Also included were referrals to the expert gastroenterologist after discussion from the referring community practice gastroenterologist, as well as most patients considered for surgical intervention. The exception was surgical emergencies presenting from the emergency department. Rarely, the gastrointestinal pathologist or colorectal surgeon requested a case be reviewed; however, the IBD expert gastroenterologist determined the appropriate of all cases reviewed. The radiologist on the conference never suggested a case for discussion over the study period.

In preparation for the IBD MDT conference, all pertinent past and current histopathology was made available for review by the gastrointestinal pathologist from the patients on the list found in the electronic medical records. Some of the initial biopsy interpretations were from community practice pathologists, especially when the multidisciplinary conference was in infancy. However, in preparation for each IBD MDT conference, each pathology specimen was reviewed by the contributing expert pathologists prior to the conference discussion. All pertinent past and current radiologic studies were reviewed by the radiologist prior to the IBD MDT conference discussion. At the IBD MDT conference, the clinical presentation, endoscopy findings, histopathology, and radiological studies were shown for correlation and discussion by all the active attending participants and placed in the context of the course of the patients' disease, given their current and past medical history.

Based on review of the histopathology in preparation for the IBD MDT conference, the diagnosis might be changed during the conference due to a previously missed microscopic finding, such as a Crohn-like granuloma, aphthous ulcer, increased intraepithelial lymphocytes, or thickened subepithelial collagen plate. Other times, the diagnosis would be clarified by discussion of medication use (eg, NSAIDs,

antibiotics), microbiology studies, or findings noted on radiology not previously considered.

Patients included for repeat review from prior conferences included patients that did not benefit from the proposed changes in diagnosis and/or treatment, those who progressed to more severe disease, or those for whom medical therapy was first attempted but subsequently required surgery. Any change in patient care, including diagnosis or therapy, was determined from multidisciplinary discussions and documented.

Lastly, the severity of colitis or enteritis on each biopsy or surgical resection was also noted if considered to be IBD. The presence or absence of erosion, ulceration, and granulomas were also documented. A "hot-spot" technique, looking for the most active area on any one biopsy, guided the assessment: minimal colitis (neutrophils solely in the lamina propria), mild colitis (cryptitis only), moderate colitis (crypt abscesses with or without cryptitis), and severe colitis (erosions and/or ulcerations).

Data Collected

Baseline demographics including age, sex, and body mass index (BMI) were collected. Social history collected included tobacco use in the last 10 years (yes vs no), pack-year history (in years, if applicable), current alcohol use (yes vs no), alcohol use history (current vs just quit vs never), alcohol use pattern (social use vs history of alcohol use disorder), and illicit drug use (yes vs no). Current immunocompromised state (yes vs no) and the reason for immunocompromise (current immunosuppressive therapy vs history of primary immunodeficiency) were documented. History of sexually transmitted illness (STI, yes vs no) was also collected.

For each patient presented at the IBD conference, their diagnosis immediately before and after the conference was collected. The diagnoses included ulcerative colitis, Crohn's disease, indeterminate colitis, infectious colitis, medication-induced colitis, microscopic colitis, no colitis, nonspecific colitis, or other diagnosis (other). It was documented whether a change in diagnosis occurred (yes vs no) as a result of the multidisciplinary discussion at the IBD conference. A change in severity of colitis (eg, change from mild to moderate colitis) did not count as a change in diagnosis. If a change in diagnosis occurred, the reason for diagnostic change was attributed to either radiographic findings (radiology), histopathology (pathology), or other reasons (other) based on the notes from the multidisciplinary conference.

The preconference endoscopic biopsy report closest to the date of the conference was reviewed, and prominent histopathologic findings were documented per biopsy location (esophagus, stomach, duodenum, jejunum, ileum, ileocecal valve, cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum, anastomosis, and random colon). The histopathologic findings were reviewed by one of 2 histopathologists specializing in gastrointestinal pathology. The presence of mild, moderate, or severe active colitis on histopathology was documented per biopsy location involving the colon. The presence of ulcerations, granulomas, or dysplasia on histopathology was documented per biopsy location involving any portion of the gastrointestinal tract. There were a variable number of locations biopsied per biopsy report per patient. Per biopsy report, the overall severity of colitis for a patient was determined by the highest reported severity of colitis (mild, moderate, or severe) regardless of biopsy location.

Each patient's list of IBD-related medications immediately before and after the conference was collected. These medications or medication categories included aminosalicylates, azathioprine, cyclosporine, hydrocortisone/topical steroids, methotrexate, systemic steroids, biologic agents (eg, infliximab, adalimumab, golimumab, certolizumab, natalizumab/vedolizumab, ustekenumab), and small molecule agents (tofacitinib). After each conference, it was documented whether a patient had an overall change in any of these medications or medication categories and which medications were changed.

Pertinent surgical history was collected for each patient before and after each conference. These surgeries included partial colectomy, total colectomy, small bowel resection, ostomy creation, ostomy reversal, small or large bowel dilation, and perianal or perivaginal surgery. For each conference in which a patient was discussed, it was documented whether the patient underwent surgery after the conference (yes vs no).

For each time a patient's case was discussed at the conference, it was documented whether the patient achieved clinical response or remission within 6 months after the conference (yes vs no). Clinical response or remission was determined by significant improvement in symptoms or resolution of symptoms, respectively, as documented in the charts.

Statistical Analysis

Descriptive statistics were used to characterize patients with regard to baseline (first conference) demographics and clinical characteristics, including age, sex, BMI, tobacco use, pack year history, alcohol use, alcohol history, social or alcohol use disorder, illicit drugs, immunocompromised state, type of immunocompromise, and history of sexually transmitted illness. Continuous variables were described using means, standard deviations, medians, interquartile ranges, and ranges; categorical variables were described using frequencies and percentages. Data missing for demographic and clinical variables for patients at their first conference (baseline) were evaluated and summarized.

Among those that experienced a change in diagnosis, an indicator combining mild, moderate, and severe chronic active colitis regardless of locations was created based on the highest severity of the chronic active colitis the patient had (mild < moderate < severe). Fourteen indicator variables were created to capture changes in each medication prescribed (yes vs no), as well as an indicator variable for overall changes in medications (ie, any changes in medications, yes vs no) for the overall sample.

For each conference, frequencies and percentages were used to characterize: (1) the changes in diagnosis pre- and postconference (yes vs no); (2) the reason that diagnosis was changed (pathology vs radiology vs other) among patients who had a change in diagnosis; (3) the diagnosis at pre- and postconference; (4) the diagnosis pre- and postconference by the reason the diagnosis was changed (pathology vs radiology vs other) among those that experienced a change in diagnosis; (5) presence of any chronic active colitis regardless of severity and location by the postconference diagnosis among those that experienced a change in diagnosis; (6) preconference endoscopic biopsy findings (ulcerated, granulomas and dysplasia) regardless of region by the postconference diagnosis among those that experienced a change in diagnosis; (7) medications and changes in medications for overall sample and by change

in diagnosis; (8) the reason that diagnosis was changed within patients who changed their diagnosis and their medications in each type of change in medications; (9) the surgical intervention after the conference by change in diagnosis; (10) the specific surgeries performed among those that had a surgery after the conference; and (11) whether patients had a clinical response or remission. Percentages for groups with fewer than 10 patients were generated but not used to make conclusions due to inability to make a reliable inference.

Fisher's exact tests were used to examine differences in (1) the reason that diagnosis was changed by diagnosis pre/postconference; (2) chronic active colitis by diagnosis postconference; (3) ulcerated, granulomas, and dysplasia by diagnosis postconference; (4) changes in medication by changes in diagnosis; and (5) surgical intervention after the conference by changes in diagnosis. All analyses were performed using SAS studio (SAS Institute Inc., Cary, NC) in the Carilion Clinic Sparc environment. Statistical significance was taken at the $P < .05$ level and did not adjust for multiplicity. P values were not generated for conferences with fewer than 10 patients due to inability to make reliable inference.

Results

Demographics

The demographic information and baseline clinical characteristics of the patients were obtained (Table 1). The total number of patients whose chart we reviewed was 289, but only nonmissing values are summarized in Table 1. We summarized the amount of complete vs missing data for all demographic and clinical variables of interest at baseline, and missing data were found to be minimal for the majority of variables (Supplementary Table 1). Over half of patients were female (58%), with a mean age of 46.66 years (SD = 17.39) and a mean BMI of 27.75 (SD = 6.98). Thirty-four percent ($n = 98$) reported tobacco use in the last 10 years, in which smokers reported a mean of 11.78 pack years (SD = 10.9). Less than half of patients reported alcohol use (48.4%), in which 56.1% ($n = 124$) reported current alcohol use and 5.9% ($n = 13$) reported they had just quit alcohol. Among patients with current or recent (just quit) alcohol use, 95.5% ($n = 127$) reported consuming alcohol socially, whereas 4.5% ($n = 6$) had a diagnosis of alcohol use disorder. Nearly 4% of patients ($n = 10$) reported illicit drug use, and 2.4% ($n = 7$) had a history of a sexually transmitted infection. Lastly, over one-third of patients (41.1%) reported an immunocompromised state—the majority (99.1%) from receiving immunosuppressive therapy and the minority (<1%) from having a primary immunodeficiency (Table 1).

The Impact of Pathology in IBD Diagnosis

To investigate the impact of the multidisciplinary conference and an expert gastrointestinal pathologist on IBD diagnosis, we quantified the number of patients who underwent a change in diagnosis after the conference and the reason for the diagnostic change (ie, due to pathology, radiology, or other reasons). The majority of patients were presented only once at the conference, and the number of patients who required repeated presentation decreased with each subsequent conference (Table 2). A total of 289 patients were presented in a conference once, 84 patients were presented twice, 21 patients were presented 3 times, 8 patients were presented 4

Table 1. Summary of demographic and clinical characteristics for patients at their first conference.

Variable		Value
Age (years)	<i>n</i>	289
	Mean	46.66
	SD	17.39
	Median	47.00
	Q1, Q3	32.00, 60.00
	Min, Max	18.00, 87.00
Sex, <i>n</i> (%) ($n = 288$)	Male	121 (42.0%)
	Female	167 (58.0%)
BMI	<i>n</i>	289
	Mean	27.75
	SD	6.98
	Median	27.00
	Q1, Q3	23.00, 31.00
	Min, Max	13.00, 56.00
Tobacco Use (in the last 10 years), <i>n</i> (%) ($n = 285$)	No	187 (65.6%)
	Yes	98 (34.4%)
Pack Year History	<i>n</i>	86
	Mean	11.78
	SD	10.90
	Median	10.00
	Q1, Q3	5.00, 15.00
	Min, Max	0.18, 60.00
Alcohol Use, <i>n</i> (%) ($n = 285$)	No	147 (51.6%)
	Yes	138 (48.4%)
Alcohol history, <i>n</i> (%) ($n = 221$)	Current	124 (56.1%)
	Just quit	13 (5.9%)
	Never	84 (38.0%)
Social or Alcohol use disorder, <i>n</i> (%) ($n = 133$)	Social	127 (95.5%)
	Alcohol Use Disorder	6 (4.5%)
Illicit drugs, <i>n</i> (%) ($n = 287$)	No	277 (96.5%)
	Yes	10 (3.5%)
Immunocompromised, <i>n</i> (%) ($n = 287$)	No	169 (58.9%)
	Yes	118 (41.1%)
Type of immunocompromise, <i>n</i> (%) ($n = 117$)	Immunosuppressive therapy	116 (99.1%)
	Immunodeficiency	1 (0.9%)
History of STI, <i>n</i> (%)	No	282 (97.6%)
	Yes	7 (2.4%)

times, 2 patients were presented 5 times, and 1 patient was presented 6 times (Table 2).

After the first conference, 42% of patients had a change in diagnosis; and among these, 84% of the patient diagnosis changes were due to pathology, 11.8% were due to radiology, and 4.2% were due to other (medication or other clinical history, other laboratory finding). After the second conference, 31.7% of the patients had changes in their diagnosis, among

which 73.1% were due to pathology, 23.1% were due to radiology, and 3.8% were due to other. After the third and fourth conferences, approximately 15% of the patients had changes in diagnosis, where the majority were due to pathology. After the fifth and sixth conference, no patients had changes in diagnosis (Table 2).

Each patient presented at the multidisciplinary conference had a presenting diagnosis of ulcerative colitis, Crohn's disease, indeterminate colitis, microscopic colitis, infectious colitis, no colitis, or other. Crohn's disease was the most common presenting diagnosis at all conferences, followed by indeterminate colitis, then ulcerative colitis (Supplementary Table 2).

To investigate which specific initial diagnoses that the multidisciplinary conference and the pathologist played a role in changing, we analyzed the distribution of initial diagnoses that changed after the conference and their

respective reason for change (Table 3). Regardless of the reason for diagnostic change, at the first conference, indeterminate colitis ($n = 35$, 29.4%) was the most common presenting diagnosis that was changed, followed by Crohn's disease ($n = 30$, 25.2%), ulcerative colitis ($n = 22$, 18.5%), and no colitis ($n = 20$, 16.8%). At the second conference, Crohn's disease ($n = 9$, 34.6%) was the most common presenting diagnosis that was changed, followed by indeterminate colitis ($n = 7$, 26.9%) and ulcerative colitis ($n = 4$, 15.4%). At the third conference, the 3 patients who had a diagnostic change had a presenting diagnosis of ulcerative colitis ($n = 1$, 33.3%), indeterminate colitis, or infectious colitis. At the fourth conference, the one patient who had a diagnostic change had presented with indeterminate colitis ($n = 1$, 100.0%; Table 3).

For each conference, no significant associations were found between diagnosis before conference, and the reason

Table 2. Summary of change in diagnosis and the reason that diagnosis was changed.

Conference Number	Change in Diagnosis				
	Yes				No
	Total	Pathology	Radiology	Other	
First (N = 289)	119 (42.0%)	100 (84.0%)	14 (11.8%)	5 (4.2%)	164 (58.0%)
Second (N = 84)	26 (31.7%)	19 (73.1%)	6 (23.1%)	1 (3.8%)	56 (68.3%)
Third (N = 21)	3 (15.8%)	2 (66.7%)	1 (33.3%)	0	16 (84.2%)
Fourth (N = 8)	1 (14.3%)	1 (100.0%)	0	0	6 (85.7%)
Fifth (N = 2)	0	0	0	0	2 (100.0%)
Sixth (N = 1)	0	0	0	0	1 (100.0%)

Table 3. Summary of diagnosis before conference by the reason that diagnosis was changed among patients who had changes in their diagnosis.

Conference Number	Diagnosis before Conference	Reason of Change in Diagnosis				P*
		Overall	Pathology	Radiology	Other	
First (N = 119)	Ulcerative colitis	22 (18.5%)	22 (22.0%)	0	0	0.373
	Crohn's disease	30 (25.2%)	22 (22.0%)	6 (42.9%)	2 (40.0%)	
	Infectious colitis	1 (0.8%)	1 (1.0%)	0	0	
	Indeterminate colitis	35 (29.4%)	30 (30.0%)	3 (21.4%)	2 (40.0%)	
	Microscopic colitis (collagenous or lymphocytic)	2 (1.7%)	1 (1.0%)	1 (7.1%)	0	
	No colitis	20 (16.8%)	16 (16.0%)	3 (21.4%)	1 (20.0%)	
	Other	6 (5.0%)	5 (5.0%)	1 (7.1%)	0	
	Nonspecific colitis	3 (2.5%)	3 (3.0%)	0	0	
Second (N = 26)	Ulcerative colitis	4 (15.4%)	3 (15.8%)	1 (16.7%)	0	0.804
	Crohn's disease	9 (34.6%)	4 (21.1%)	4 (66.7%)	1 (100.0%)	
	Infectious colitis	1 (3.8%)	1 (5.3%)	0	0	
	Indeterminate colitis	7 (26.9%)	6 (31.6%)	1 (16.7%)	0	
	No colitis	2 (7.7%)	2 (10.5%)	0	0	
	Other	1 (3.8%)	1 (5.3%)	0	0	
	Nonspecific colitis	2 (7.7%)	2 (10.5%)	0	0	
Third (N = 3)	Ulcerative colitis	1 (33.3%)	1 (50.0%)	0	0	—
	Infectious colitis	1 (33.3%)	1 (50.0%)	0	0	
	Indeterminate colitis	1 (33.3%)	0	1 (100.0%)	0	
Fourth (N = 1)	Indeterminate colitis	1 (100.0%)	1 (100.0%)	0	0	—

*P values were not generated for conferences with fewer than 10 patients due to inability to make reliable inference (as denoted with “—”).

that diagnosis was changed at an alpha level of 0.05. The distribution shows that pathology was the most common reason for diagnostic change for the large majority of presenting diagnoses (Table 3). Among those who had a change in diagnosis due to pathology after the first conference, 30.0% ($n = 30$) had presented with indeterminate colitis, 22.0% ($n = 22$) had presented with Crohn's disease, 22.0% ($n = 22$) had presented with ulcerative colitis, and 16% ($n = 16$) had presented with no colitis. Among those who had a change in diagnosis due to pathology after the second conference, 31.6% ($n = 6$) had presented with indeterminate colitis, 21.1% ($n = 4$) had presented with Crohn's disease, 15.8% ($n = 3$) had presented with ulcerative colitis, and 10.5% ($n = 2$) had presented with no colitis. Overall, indeterminate colitis was the most commonly changed diagnosis due to pathology, followed by Crohn's disease, then ulcerative colitis (Table 3). Distributions for the third ($N = 3$) and fourth ($N = 1$) conferences were included, but neither P values nor descriptive observations were made because they each contained fewer than 10 patients, rendering us unable to make a reliable inference (Table 3).

After each multidisciplinary conference, new diagnoses included ulcerative colitis, Crohn's disease, indeterminate colitis, infectious colitis, medication-induced colitis, microscopic colitis, no colitis, or other (Table 4). To study the distribution of newly diagnosed illnesses after the multidisciplinary conference, we isolated the patients who had a change in diagnosis and analyzed the distribution of their diagnoses after conference and the reason for diagnostic change.

The most common new diagnosis was Crohn's disease for all conferences (Table 4). For each conference, no significant

associations were found between diagnosis after conference and the reason that diagnosis was changed at an alpha level of 0.05. However, distribution shows that the large majority of new diagnoses after conference were made due to histopathological interpretation (Table 4).

Among those given a new diagnosis due to pathology after the first conference, 31.0% ($n = 31$) were newly diagnosed with Crohn's disease, 14.0% ($n = 14$) were newly diagnosed with indeterminate colitis, 10.0% ($n = 10$) were newly diagnosed with ulcerative colitis, and 17.0% ($n = 17$) were newly diagnosed with no colitis. Among those given a new diagnosis due to pathology after the second conference, 42.1% ($n = 8$) were newly diagnosed with Crohn's disease, 15.8% ($n = 3$) were newly diagnosed with ulcerative colitis, and 5.3% ($n = 1$) were newly diagnosed with no colitis (Table 4). Distributions for the third ($N = 3$) and fourth ($N = 1$) conferences are included, but neither P values nor descriptive observations were made, as they each contained fewer than 10 patients, rendering us unable to make a reliable inference (Table 4). A breakdown of the diagnoses pre- and postconference of the 289 cases presented at the MDT IBD conference are included in Supplementary Table 3.

The distribution of the severity of colitis (ie, mild, moderate, severe, or none), which was determined by pathologic interpretation of endoscopic biopsies done before each conference, was analyzed in the patients who had a diagnostic change after conference. No significant associations were found between diagnosis after conference and severity of chronic active colitis at an alpha level of 0.05 (Supplementary Table 4). However, distribution shows that for patients newly diagnosed with Crohn's disease after conference, 12 (42.9%) had mild colitis, 9 (32.1%) had moderate colitis, and 7 (25%)

Table 4. Summary of diagnosis after conference by the reason that diagnosis was changed among patients who had changes in their diagnosis.

Conference Number	Diagnosis after Conference	Reason of Change in Diagnosis				P^*
		Overall	Pathology	Radiology	Other	
First (N = 119)	Ulcerative colitis	10 (8.4%)	10 (10.0%)	0	0	0.535
	Crohn's disease	34 (28.6%)	31 (31.0%)	2 (14.3%)	1 (20.0%)	
	Infectious colitis	7 (5.9%)	5 (5.0%)	2 (14.3%)	0	
	Medication-induced colitis	5 (4.2%)	5 (5.0%)	0	0	
	Indeterminate colitis	18 (15.1%)	14 (14.0%)	2 (14.3%)	2 (40.0%)	
	Microscopic colitis (collagenous or lymphocytic)	2 (1.7%)	2 (2.0%)	0	0	
	No colitis	20 (16.8%)	17 (17.0%)	2 (14.3%)	1 (20.0%)	
	Other	21 (17.6%)	14 (14.0%)	6 (42.9%)	1 (20.0%)	
	Crohn's disease and Medication-induced colitis	1 (0.8%)	1 (1.0%)	0	0	
	Nonspecific colitis	1 (0.8%)	1 (1.0%)	0	0	
Second (N = 26)	Ulcerative colitis	3 (11.5%)	3 (15.8%)	0	0	0.441
	Crohn's disease	11 (42.3%)	8 (42.1%)	3 (50.0%)	0	
	Infectious colitis	1 (3.8%)	1 (5.3%)	0	0	
	Medication-induced colitis	2 (7.7%)	2 (10.5%)	0	0	
	Indeterminate colitis	3 (11.5%)	1 (5.3%)	2 (33.3%)	0	
	No colitis	2 (7.7%)	1 (5.3%)	1 (16.7%)	0	
	Other	4 (15.4%)	3 (15.8%)	0	1 (100.0%)	
Third (N = 3)	Crohn's disease	2 (66.7%)	1 (50.0%)	1 (100.0%)	0	—
	Indeterminate colitis	1 (33.3%)	1 (50.0%)	0	0	
Fourth (N = 1)	Crohn's disease	1 (100.0%)	1 (100.0%)	0	0	—

* P values were not generated for conferences with fewer than 10 patients due to inability to make reliable inference (as denoted with "—").

had severe colitis for the first conference; 3 (50.0%) had moderate colitis, and 3 (50.0%) had severe colitis for the second conference; 1 (50.0%) had moderate colitis, and 1 (50.0%) had severe colitis for the third conference (Supplementary Table 4). For patients newly diagnosed with ulcerative colitis after conference, 2 (22.2%) had mild colitis, 5 (55.6%) had moderate colitis, and 2 (22.2%) had severe colitis for the first conference; 1 (33.3%) had mild colitis, and 2 (66.7%) had moderate colitis for the second conference (Supplementary Table 4).

The presence of ulcerations (Supplementary Table 5), granulomas (Supplementary Table 6), and dysplasia (Supplementary Table 7), as determined by pathologic interpretation of endoscopic biopsies, was reviewed in patients who had a diagnostic change after conference. The majority of patients who had a diagnostic change did not have dysplasia, but 1 patient newly diagnosed with Crohn's disease after the first conference did have dysplasia (Supplementary Table 7). Two other patients newly diagnosed with no colitis ($n = 1$) and other diagnosis ($n = 1$) also had dysplasia (Supplementary Table 7).

The Impact of Pathology on IBD Management and Clinical Outcomes

To study the impact of the multidisciplinary IBD conference and diagnostic change on IBD medication management, the distribution of medication changes made after each conference was analyzed (Table 5). Overall, the percentage of patients who had a change in at least 1 IBD medication after each conference was 34.3% ($n = 99$) for the first conference, 34.5% ($n = 29$) for the second conference, and 23.8% ($n = 5$) for the third conference. A total of 2 patients after the fourth conference ($N = 8$) and 1 patient after the fifth conference ($N = 2$) had a change in at least 1 IBD medication. The 1 patient presented at the sixth conference did not have a change in medication (Table 5).

Table 5. Summary of overall change in medication by changes in diagnosis for all patients.

Conference Number	Change in Medication	Change in Diagnosis			<i>P</i>
		Overall	No	Yes	
First (N = 289)	No	190 (65.7%)	102 (62.2%)	85 (71.4%)	0.127
	Yes	99 (34.3%)	62 (37.8%)	34 (28.6%)	
Second (N = 84)	No	55 (65.5%)	37 (66.1%)	16 (61.5%)	0.805
	Yes	29 (34.5%)	19 (33.9%)	10 (38.5%)	
Third (N = 21)	No	16 (76.2%)	13 (81.3%)	1 (33.3%)	0.155
	Yes	5 (23.8%)	3 (18.8%)	2 (66.7%)	
Fourth (N = 8)	No	6 (75.0%)	5 (83.3%)	0	—
	Yes	2 (25.0%)	1 (16.7%)	1 (100.0%)	
Fifth (N = 2)	No	1 (50.0%)	1 (50.0%)	0	—
	Yes	1 (50.0%)	1 (50.0%)	0	
Sixth (N = 1)	No	1 (100.0%)	1 (100.0%)	0	—

^a*P* values were not generated for conferences with fewer than 10 patients due to inability to make reliable inference (as denoted with “—”).

Among the patients who had a change in diagnosis, the percentage of patients who had a change in at least one IBD medication after each conference was 28.6% ($n = 34$) for the first conference and 38.5% ($n = 10$) for the second conference. After the third conference, 2 out of 3 patients who had a diagnostic change also had a change in medication. After the fourth conference, the 1 patient who had a diagnostic change also had a change in medication. Of the 2 patients presented at the conference for the fifth time, 1 patient had a change in IBD medication but no change in diagnosis. The 1 patient presented at the conference for the sixth time did not have a change in diagnosis nor change in medication after conference. For each conference, no significant associations were found between change in medications and change in diagnosis at an alpha level of 0.05, which indicates the change rates are not different between the patients who had changes in their diagnosis vs those who did not (Table 5). The list of specific IBD medications reviewed and the rate of change for each medication after conference are included (Supplementary Table 8).

For patients who had a diagnostic change and a change in medication after conference, the large majority of diagnostic changes were due to pathology (Supplementary Table 9). After the first conference, 82.4% ($n = 28$) of patients who had a change in diagnosis and IBD medication were attributed to pathology. After the second conference, 80.0% ($n = 8$) of patients who had a change in diagnosis and IBD medication were attributed to pathology. After the third and fourth conferences, 100.0% ($n = 2$, $n = 1$, respectively) of patients who had a change in diagnosis and IBD medication were attributed to pathology (Supplementary Table 9).

To investigate the effects of a multidisciplinary conference and diagnostic change on surgical intervention, the distribution of patients who underwent surgery after each conference was analyzed (Table 6). Overall, the percentage of patients who had surgery after each conference was 17.0% ($n = 49$) for the first conference, 20.2% ($n = 17$) for the second conference, and 19.0% ($n = 4$) for the third conference. No patients underwent surgery after the fourth, fifth, or sixth conferences (Table 6). Among the patients who had a change in diagnosis, the percentage of patients who had surgery after the conference was 10.9% ($n = 13$) for the first conference and 7.7% ($n = 2$) for the second conference. One out of 3 patients with a change in diagnosis after the third conference had surgery after conference (Table 6). A significant association was found for first conference ($P = .016$) at an alpha level of 0.05, which indicates a different distribution of whether surgery was done among patients who had changes in their diagnosis vs not. A significant association at an alpha level of 0.05 was not found for subsequent conferences (Table 6).

Among those who had surgery done after conference, partial colectomy was the most common type of surgery performed (Supplementary Table 10). A total of 29 (63.0%) patients had partial colectomy after the first conference, and 8 (53.3%) patients had partial colectomy after the second conference. Other types of surgeries included total colectomy, small bowel resection, ostomy creation or reversal, small or large bowel dilation, and perianal or perivaginal surgery (Supplementary Table 10).

To study the impact of the multidisciplinary conference on the patients' clinical response, we reviewed whether each patient had an improvement or resolution in symptoms within 6 months after each conference (Table 7). The percentage of

Table 6. summary of surgeries or procedures done after conference by change in diagnosis.

Conference Number	Surgery Done After Conference	Change in Diagnosis			P*
		Overall	No	Yes	
First (N = 289)	No	240 (83.0%)	128 (78.0%)	106 (89.1%)	0.016
	Yes	49 (17.0%)	36 (22.0%)	13 (10.9%)	
Second (N = 84)	No	67 (79.8%)	41 (73.2%)	24 (92.3%)	0.077
	Yes	17 (20.2%)	15 (26.8%)	2 (7.7%)	
Third (N = 21)	No	17 (81.0%)	13 (81.3%)	2 (66.7%)	0.530
	Yes	4 (19.0%)	3 (18.8%)	1 (33.3%)	
Fourth (N = 8)	No	8 (100.0%)	6 (100.0%)	1 (100.0%)	—
Fifth (N = 2)	No	2 (100.0%)	2 (100.0%)	0	—
Sixth (N = 1)	No	1 (100.0%)	1 (100.0%)	0	—

*P values were not generated for conferences with fewer than 10 patients due to inability to make reliable inference (as denoted with “—”).

patients who had clinical response or remission after each conference was 54.2% ($n = 135$) for the first conference, 57.9% ($n = 44$) for the second conference, 60.0% ($n = 12$) for the third conference, 50.0% ($n = 4$) for the fourth conference, and 100.0% ($n = 2$) for the fifth conference. The 1 patient presented at the sixth conference did not have clinical response within 6 months (Table 7).

Discussion

Inflammatory bowel disease is a complex disease that can be easily misdiagnosed and mismanaged. It is well-established that a gastrointestinal expert pathologist plays a critical role in diagnosing IBD by discerning its subtypes, Crohn's disease and ulcerative colitis, distinguishing it from the less specific indeterminate colitis, as well as from its histological mimics such as medication-induced colitis, infectious colitis, and microscopic colitis.^{5,6} Several studies have shown that a multidisciplinary team approach is effective in improving IBD diagnosis, management, and patient outcomes.^{7,8} Many institutions across the United States have therefore implemented the use of a multidisciplinary team in managing IBD. However, there is no clear guideline regarding how multidisciplinary teams should be structured,⁹ and the teams do not consistently include a gastrointestinal expert pathologist as a core member. For instance, the multidisciplinary IBD team studied by Hartford et al only includes a pathologist in the multidisciplinary discussion 32% of the time, and the team investigated by Ferman et al includes a gastroenterologist, colorectal surgeon, radiologist, IBD nurse, psychologists, and dieticians, but not a pathologist. Although the inclusion of a pathologist in multidisciplinary IBD care has been proposed by many, there is no study to date that quantifies or characterizes the direct impact that a pathologist has in contributing to multidisciplinary IBD care.

Our study shows that a large percentage of patients had a change in diagnosis after the multidisciplinary conference (up to 42%), consistent with literature that a multidisciplinary team approach has a significant benefit in determining accurate

Table 7. Summary of clinical response or remission for all patients.

Conference Number	Clinical Response or Remission	
	No	Yes
First (N = 289)	114 (45.8%)	135 (54.2%)
Second (N = 84)	32 (42.1%)	44 (57.9%)
Third (N = 21)	8 (40.0%)	12 (60.0%)
Fourth (N = 8)	4 (50.0%)	4 (50.0%)
Fifth (N = 2)	0	2 (100.0%)
Sixth (N = 1)	1 (100.0%)	0

IBD diagnosis.⁸ Importantly, the large majority of these diagnostic changes (eg, 100 out of 119 patients [84%] presented at the first conference) were attributed to histopathologic evaluation by a gastrointestinal expert pathologist, revealing the substantial impact that a pathologist has in influencing IBD diagnosis in a multidisciplinary discussion.

Crohn's disease was the most common presenting diagnosis discussed at the conference, consistent with findings from other studies.^{7,8} Indeterminate colitis, ulcerative colitis, and Crohn's disease were consistently among the most common presenting diagnoses that changed after the conference—expectedly so, given the complex nature of these illnesses and the difficulty to clinically distinguish among the 3 in complex cases. Recently in 2022, indeterminate colitis has been considered to be IBD in which the histology, radiology, clinical history, and other laboratory studies do not allow differentiation of UC from Crohn's disease. However, in previous years, the term *indeterminate colitis* was considered to include all cases with histologic, radiologic, and endoscopic evidence of chronic IBD confined to the colon but without fulfillment of diagnostic criteria for UC or CD—which is how indeterminate colitis was defined in our study given our review of cases from years 2013 to 2019.¹⁰

Indeterminate colitis was used when a diagnosis of IBD was appropriate, but neither ulcerative colitis nor Crohn's disease could be determined from the histopathology found on colonic biopsies or from the histopathology of resection specimens.¹⁰ The distinction of Crohn's disease from ulcerative colitis was often clarified at the IBD MDT conference when colonoscopy findings, histopathology, and radiologic studies were correlated through discussion in an interdisciplinary manner, as reflected in our data. The diagnostic difficulties were shown to be best resolved by clinicopathologic correlation. However, sometimes review of the pathology in any particular case would reveal a diagnostic feature missed, such as small Crohn-like granulomas in the lamina propria, cryptocytic granuloma misinterpreted as a Crohn-like granuloma, missed basal plasmacytosis, or missed focal crypt distortion.

Nonspecific colitis was the term used when the etiology of colitis could not be determined on histopathologic examination.¹¹ This was distinct from when the diagnosis was thought to be IBD of uncertain phenotype. Thus, nonspecific colitis would include cases of unrecognized IBD, as well as infectious colitis, drug reaction, nonspecified immune reaction, and microscopic colitis, among a few.

The diagnosis of infectious colitis was made in the context of an acute colitis without classic histopathologic features of chronic colitis in the appropriate clinical context.¹² In all cases, ancillary laboratory studies were reviewed.

Among the initial diagnoses that were changed after review by an expert pathologist, indeterminate colitis was the most common. This highlights the role that histopathologic evaluation plays in changing indeterminate colitis, usually a temporary diagnosis, to the eventual established diagnosis. Based on review of our data, it was observed that indeterminate colitis was most frequently changed to Crohn's disease after the conference at our institution. In the study by Notteghem et al, 54% of patients with indeterminate colitis were classified as UC, and 33% were considered to have CD after 1-year follow-up.¹³ In contrary, the study by Wells et al revealed that 40% of IC patients were reclassified to CD, and 24% were reclassified to UC.¹⁴

Medication-induced colitis and microscopic colitis are also diagnoses that can be missed and usually require histopathologic evaluation for accurate identification. In this study, 5 cases of medication-induced colitis were newly diagnosed after the first conference, all due to pathology. A total of 4 cases of microscopic colitis (2 after the first conference and 2 after the second conference) were newly diagnosed, again all due to pathology. Medication-induced colitis can mimic IBD, as its effects are often nonspecific and may appear as any combination of ulceration, inflammation, and stricture formation endoscopically.⁶ Microscopic colitis is challenging to evaluate histologically and can be missed in one-third of cases in the initial examination.¹⁵

A significant percentage of patients (approximately 24% to 35%) underwent a change in IBD medication after being discussed at the multidisciplinary conference; this is consistent with previous literature that multidisciplinary teams lead to changes in medication management.⁸ More importantly, we show that a diagnostic change led to a change in medication approximately 29% to 39% of the time after the conference. Since the majority of diagnostic changes in patients who had both a change in diagnosis and change in medication were due to pathology (approximately 80% to 82%), this suggests that pathologists have a direct and significant impact in influencing medication management of IBD patients. Although a change in medication did not show a statistically significant association with a change in diagnosis, this may be due to the fact that the variable course of IBD with its relapsing and remitting nature at times led to a change in medication without a change in diagnosis.

Additionally, a significant percentage of patients (approximately 17% to 20%) underwent surgery after being discussed at the multidisciplinary conference, where partial colectomy was the most common surgical intervention. Interestingly, a larger percentage of patients were recommended surgery if they did not have a diagnostic change than if they did have a diagnostic change after the first and second conferences; and this difference was statistically significant for the first conference. This may be explained by the fact that each patient case is presented at the conference with a specific goal in mind, for example, to determine the most optimal surgical intervention or to determine the most accurate diagnosis. Therefore, patients whose cases were being discussed for determination of the best surgical intervention may not have had a dilemma surrounding their diagnosis to begin with. Such selection bias may have influenced the said data. Nevertheless, we show that a diagnostic change led to surgical intervention in approximately 8% to 11% of patients with diagnostic change after the conference, which is still clinically significant.

The culmination of proper IBD diagnosis and medical and surgical management through a multidisciplinary discussion led to good patient outcomes. Approximately 54% to 60% of patients presented at our multidisciplinary conference had a good clinical response or clinical remission within 6 months of the conference. It is evident that histopathologic evaluation by a gastrointestinal expert pathologist in the setting of a multidisciplinary team plays a crucial role in IBD diagnosis, management, and patient outcomes.

The multidisciplinary conference also served an important role in elucidating microscopic findings not seen initially. Those histologic features included the following: not seeing epithelioid granulomas, over-calling germinal center cells in a lymphoid aggregate-epithelioid granulomas, over-calling a cryptolytic granuloma as an epithelioid Crohn-like granuloma, missing a thickened subepithelial collagen plate or increased intraepithelial lymphocytes, not recognizing small aphthous ulcerations or deep fissuring ulceration, and under-calling neutrophilic infiltrates in the terminal ileum.

Limitations of this study include its retrospective cohort study design and the study population being from a single institution. The observational study design has opportunity for selection bias, and not all eligible patients may have been referred for discussion at the MDT meeting. Although the STROBE guidelines for observational studies were not formally followed, we referred to its systematic checklist for observational studies so as to conduct the study in an organized fashion. Data collection was performed using a consistent method, but the possibility of errors in the chart and missingness of data cannot be excluded. There was no control group as it is challenging to construct, and thus improvement over standard practice cannot be estimated.

Furthermore, data regarding concomitant use of medications like NSAIDs were not collected, although discussed at each conference. Capsule endoscopy findings were also not collected, which were at times used to diagnose small-bowel Crohn's disease at the conference. Lastly, we were not able to assess for endoscopic remission or response to therapy, as not all patients had a repeat endoscopy postconference.

This study solely focuses on the contribution of a gastrointestinal-pathology trained pathologist to the multidisciplinary team assembled to discuss the best care for patients with challenging IBD problems or potential mimics of IBD. Hence, the focus was on the most appropriate working diagnosis and implicated management thereof. Although the diagnosis in some cases could be made on histopathology alone, most cases presented at the conference benefitted from the contributions of each participant. The diagnosis was confirmed or determined by clinical-pathologic correlation. Each case was reviewed individually in depth to establish the diagnosis and modify any therapy as appropriate based on said review.

It would be beneficial for future studies to prospectively investigate the impact of including an expert gastrointestinal pathologist on IBD diagnosis, management, and patient outcomes. Future studies should continue to examine the most effective organization and membership of a multidisciplinary team to optimize outcomes of IBD patients. In addition, the future of IBD management might include assessment of disease resolution based on histopathology (histologic remission), not just endoscopic findings (endoscopic remission) and/or clinical symptomatology (clinical remission). If such ever became standard, an IBD MDT conference and the

standard inclusion of an expert pathologist with gastrointestinal pathology expertise would become even more important to IBD patient care.

Supplementary Data

Supplementary data is available at *Inflammatory Bowel Diseases* online.

Funding

Research reported in this publication was supported in part by the National Center For Advancing Translational Sciences of the National Institutes of Health under award number UL1TR003015. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Conflicts of Interest

The authors have no financial disclosures or conflicts of interest to disclose.

References

1. Ricci C, Lanzarotto F, Lanzini A. The multidisciplinary team for management of inflammatory bowel diseases. *Dig Liver Dis*. 2008 Jul;40(Suppl 2):S285-S288.
2. Mawdsley JE, Irving PM, Makins RJ, Rampton DS. Optimizing quality of outpatient care for patients with inflammatory bowel disease: the importance of specialist clinics. *Eur J Gastroenterol Hepatol*. 2006 Mar;18(3):249-253.
3. Morar P, Read J, Arora S, et al. Defining the optimal design of the inflammatory bowel disease multidisciplinary team: results from a multicentre qualitative expert-based study. *Frontline Gastroenterol*. 2015 Oct;6(4):290-297.
4. Lee CK, Melmed GY. Multidisciplinary team-based approaches to IBD management: how might "one-stop shopping" work for complex IBD care? *Am J Gastroenterol*. 2017 Jun;112(6):825-827.
5. Woodman I, Schofield JB, Haboubi N. The histopathological mimics of inflammatory bowel disease: a critical appraisal. *Tech Coloproctol*. 2015;19(12):717-727.
6. Schofield JB, Haboubi N. Histopathological mimics of inflammatory bowel disease. *Inflamm Bowel Dis*. 2020 Jul;26(7):994-1009.
7. Ferman M, Lim AH, Hossain M, Siow GW, Andrews JM. Multidisciplinary team meetings appear to be effective in inflammatory bowel disease management: an audit of process and outcomes. *Intern Med J*. 2018;48(9):1102-1108.
8. Hartford LB, Allen LJ, Lennox H, Jairath V, Van Koughnett JAM. The impact of multidisciplinary conferences on treatment plans for patients with inflammatory bowel disease in a tertiary Canadian centre. *J Can Assoc Gastroenterol*. 2021 Dec;4(6):284-289.
9. Iyer NG, Chua MLK. Multidisciplinary team meetings - challenges of implementation science. *Nat Rev Clin Oncol*. 2019 Apr;16(4):205-206.
10. Geboes K, De Hertogh G. Indeterminate colitis. *Inflamm Bowel Dis*. 2003 Sep;9(5):324-331.
11. Emara M, Salama R, Hamed E, et al. Non-specific colitis among patients with colitis: frequency and relation to inflammatory bowel disease, a prospective study. *J Coloproctol*. 2019;39(04):319-325.
12. Surawicz C. Histopathology of infectious colitis. *Can J Gastroenterol Hepatol*. 1989;3(291797):1-5.
13. Nottoghem B, Salomez JL, Gower-Rousseau C, et al. What is the prognosis in unclassified colitis? results of a cohort study of 104 patients in the Northern-Pas-de-Calais region. *Gastroenterol Clin Biol*. 1993;17(11):811-815.
14. Wells AD, McMillan I, Price AB, Ritchie JK, Nicholls RJ. Natural history of indeterminate colitis. *Br J Surg*. 1991 Feb;78(2):179-181.
15. Olesen M, Eriksson S, Bohr J, Järnerot G, Tysk C. Lymphocytic colitis: a retrospective clinical study of 199 Swedish patients. *Gut*. 2004 Apr;53(4):536-541.