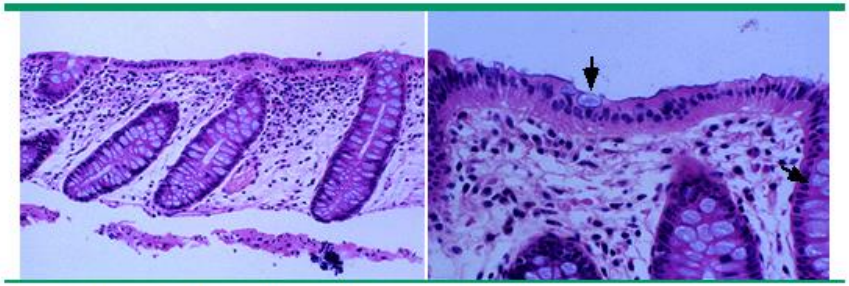
Mikroskopisk kolitt

MidtNorsk vårmøte

Ålesund 17.-18. april 2015

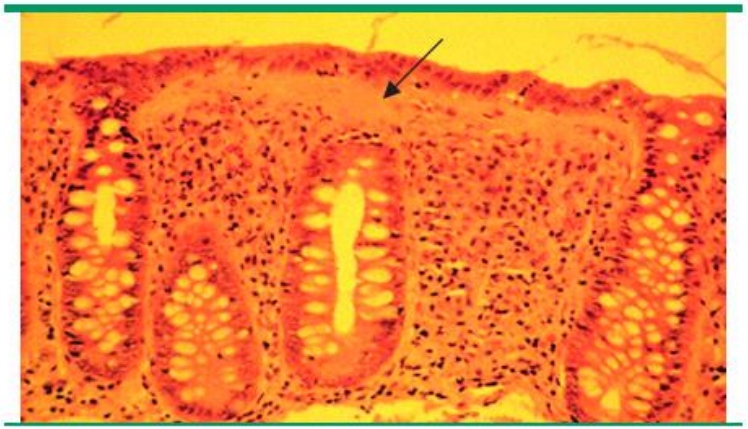
Ragnar Eriksen

Normal colon



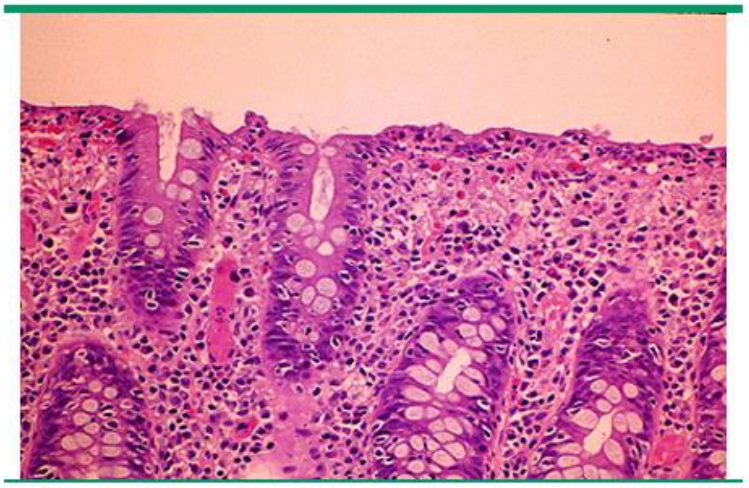
Low (left) and high (right) power views of a biopsy of a normal colon. Low power reveals straight crypts and mild lamina propria mononuclear cell infiltration. High power shows the surface enterocytes with interspersed goblet cells (arrows).
Courtesy of Robert Odze, MD

Collagenous colitis



High power view of a colonic biopsy from a patient with collagenous colitis. There is a thickened subepithelial collagenous band (arrow) associated with increased mononuclear cell infiltration and epithelial degeneration.
Courtesy of Robert Odze, MD.

Lymphocytic colitis



Medium power view of a colonic biopsy from a patient with lymphocytic colitis shows intraepithelial and lamina propria lymphocytic infiltrate.
Courtesy of Robert Odze, MD.

Histologic key features of different forms of microscopic colitis

	LC	CC	MCi or MCnos
IELs	>20 IELs	Normal to slightly increased	5-20 IELs
Subepithelial collagen layer	Normal to slightly thickened	>10 micrometers	5-10 micrometers
Surface epithelium damage	+	++	(+)
Lamina propria inflammation	++	++	+/++

LC: lymphocytic colitis; CC: collagenous colitis; MCi: microscopic colitis incomplete; MCnos: microscopic colitis not otherwise specified; IELs: intraepithelial lymphocytes.

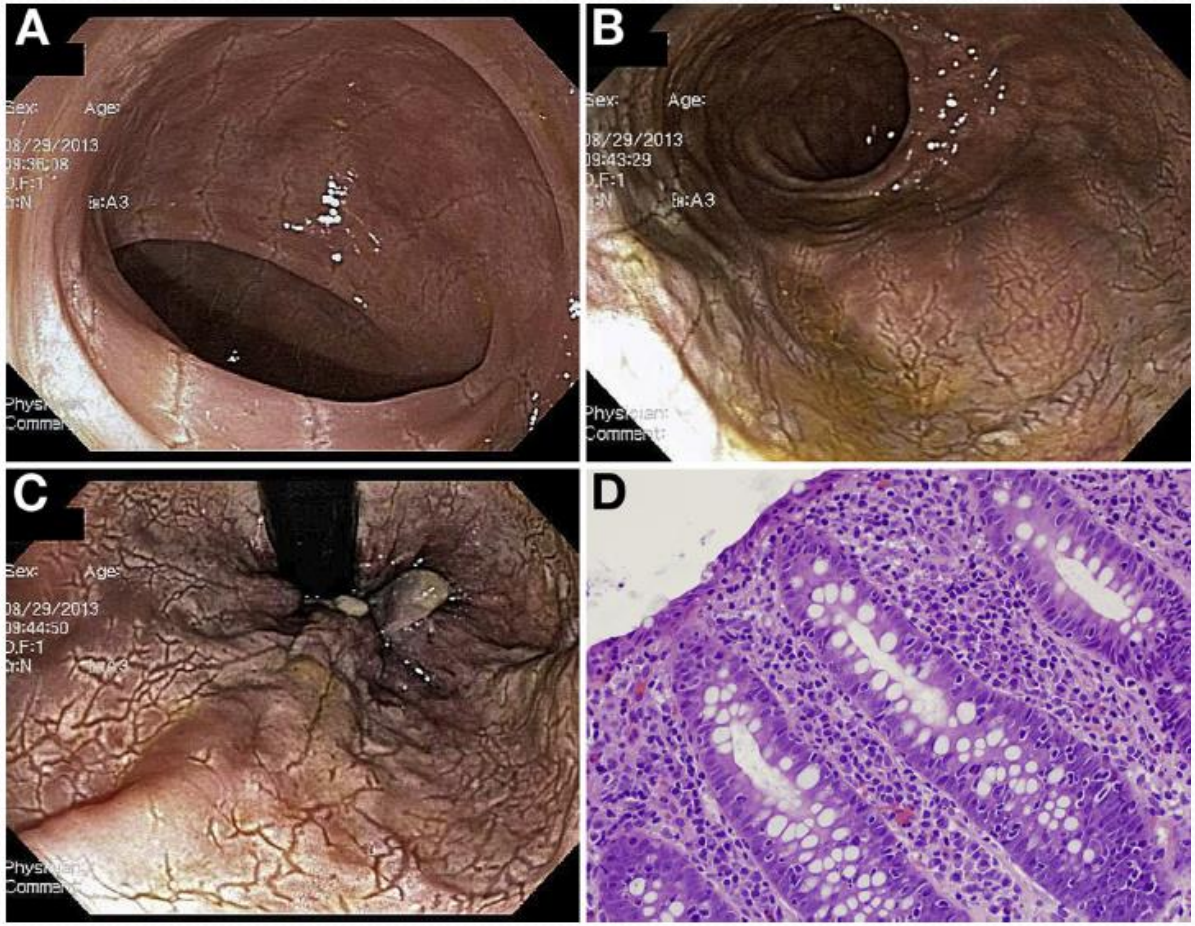
Reproduced from: Münch A, Langner C. Microscopic colitis: Clinical and pathologic perspectives. Clin Gastroenterol Hepatol 2014 (in press).

Macroscopic Findings in Lymphocytic Colitis

Clinical Gastroenterology and Hepatology 2014;12:e65–e66

Ashish Aggarwal and Debra Helper

Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University Medical Center, Indianapolis, Indiana



Usefulness of colonoscopic examination with indigo carmine in diagnosing microscopic colitis

Authors G. Suzuki[1], M. R. Mellander[1], A. Suzuki[1], C. A. Rubio[2], R. Lambert[3], J. Björk[1], P. T. Schmidt[1]

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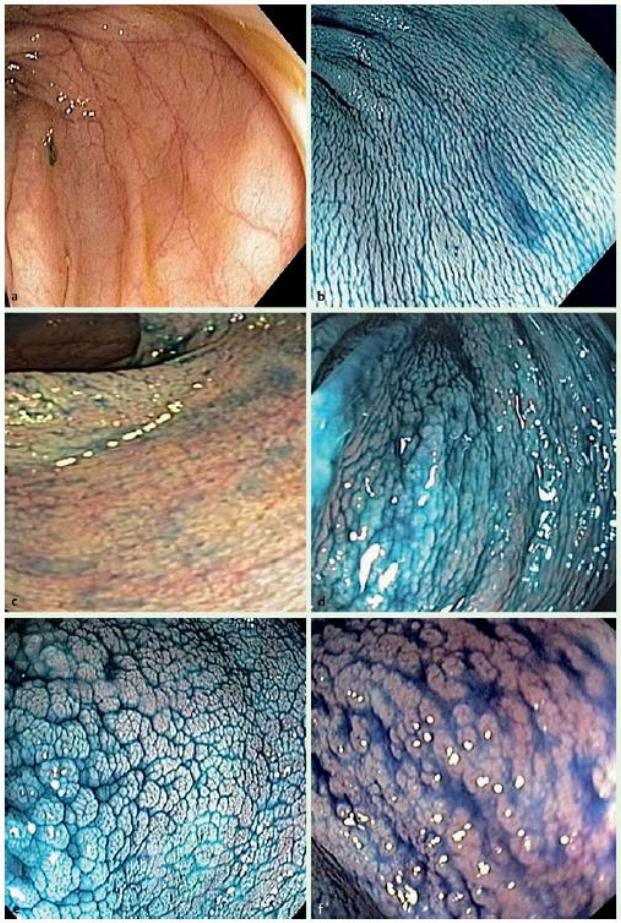


Fig. 1 Microscopic colitis appearances in chromoendoscopy with indigo carmine staining: **a** innominate grooves of normal colon, before staining; **b** innominate grooves of normal colon after staining with indigo carmine. **c**–**f** Indigo carmine staining in cases with microscopic colitis: **c** innominate grooves have disappeared and there is an uneven surface; **d** irregular innominate grooves with nodular surface (small nodules); **e** swollen mosaic pattern; **f** nodular surface (large nodules).

Incidence, Prevalence, and Temporal Trends of Microscopic Colitis: A Systematic Review and Meta-Analysis

Am J Gastroenterol 2015; 110:265–276; doi:10.1038/ajg.2014.431; published online 27 January 2015

Jinlu Tong, MD[1,4], Qinq Zheng, MD[1,4], Chenpeng Zhang, MD[2], Ryan Lo, MD[3], Jun Shen, MD[1] and Zhihua Ran, MD[1]

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Microscopic colitis (MC) has emerged as a leading cause of chronic nonbloody diarrhea.
- ✓ Several studies have reported a considerable variation in the incidence of MC around the world.
- ✓ The trend of MC incidence rate is not clear.

WHAT IS NEW HERE

- ✓ The overall incidence of collagenous colitis and lymphocytic colitis was 4.14 (95% confidence interval (CI) 2.89–5.40) and 4.85 (95% CI 3.45–6.25) per 100,000 person-years at risk, comparable with the incidence of inflammatory bowel disease.
- ✓ Women have a three to four times higher risk of acquiring MC.
- ✓ The incidence rate of MC increased with increasing age.
- ✓ MC incidence rate has become stable in some areas over time.
- ✓ Proton pump inhibitors (PPIs) and selective serotonin reuptake inhibitors (SSRIs) are associated with a significantly increased risk of developing MC.

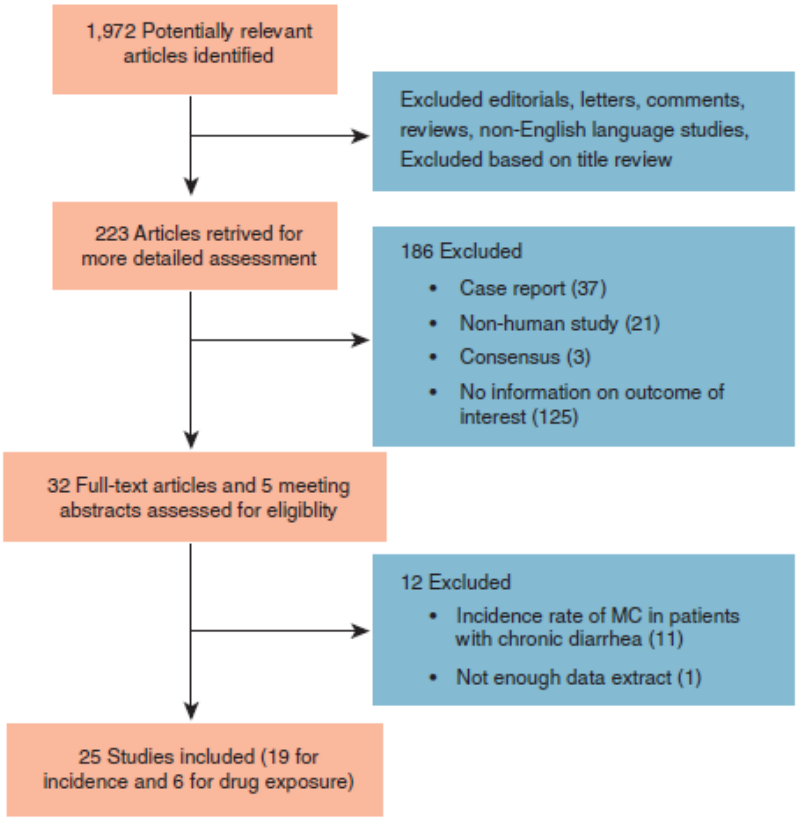


Figure 1. Flow diagram for selection of studies included in the systematic review and meta-analysis. MC, microscopic colitis.

The epidemiology of microscopic colitis: a 10-year pathology-based nationwide Danish cohort study

Scandinavian Journal of Gastroenterology. 2015; 50: 393–398

OLE K. BONDERUP[1], TATJANA WIGH[2], GUNNAR L. NIELSEN[3], LARS PEDERSEN[4] & MORTEN FENGER-GRØN[4,5]

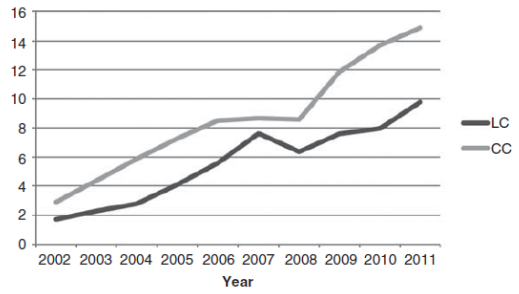
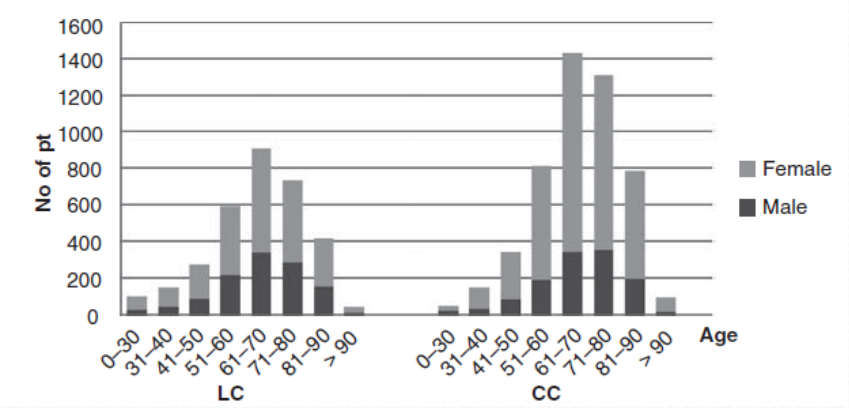
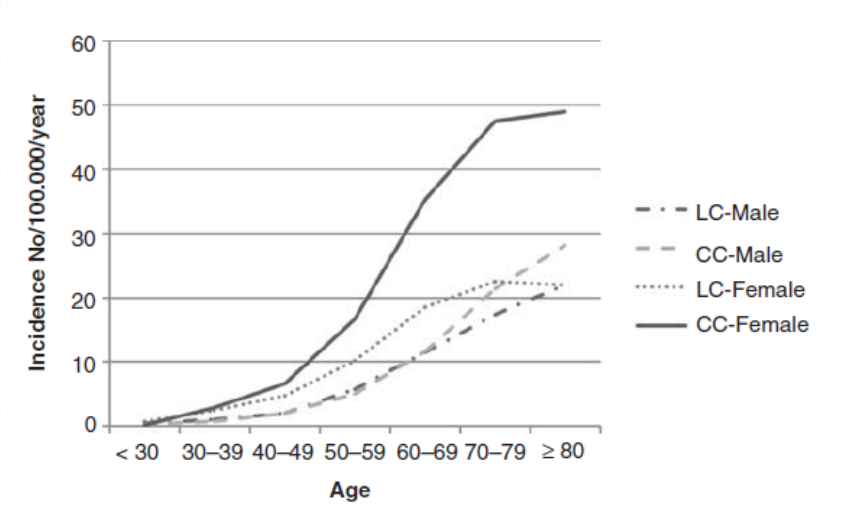


Figure 1. Incident cases of LC and CC reported in the Danish Pathology Register from 2002 to 2011. Abbreviations: CC = Collagenous colitis; LC = Lymphocytic colitis.

We conclude that there has been a continuous increase in the number of patients fulfilling the histopathological MC criteria recorded in the nationwide Danish Pathology Register from 2002 to 2011. The risk of MC increased with increasing age, but the mean age at the time of diagnosis was stable in the observation period. CC was more frequently diagnosed than LC. Although MC was more frequent among women, the overall female/male ratio was unchanged. A simultaneous increase in the number of analyzed colonic biopsies could indicate that an increased awareness of the disease contributes to this observed increase. However, continuous epidemiological studies are important to disclose a possible real increase in the incidence of MC.

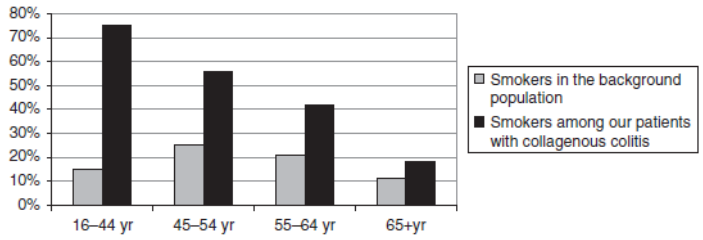

1600
1400
1200
1000
800
600
400
200
0
No of pt
0–30
31–40
41–50
51–60
61–70
71–80
81–90
> 90
LC
CC
Age
Female
Male


60
50
40
30
20
10
0
Incidence No/100.000/year
< 30
30–39
40–49
50–59
60–69
70–79
≥ 80
Age
LC-Male
CC-Male
LC-Female
CC-Female

Is smoking a risk factor for collagenous colitis?

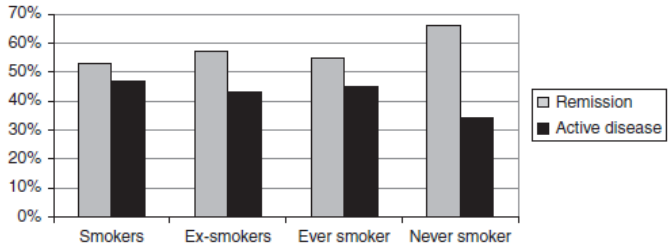
LINA VIGREN[1], KLAS SJÖBERG[1], CECILIA BENONI[1,5], CURT TYSK[2,5], JOHAN BOHR[2,5], ANDERS KILANDER[3,5], LASSE LARSSON[3], MAGNUS STRÖM[4,5] & HENRIK HJORTSWANG[4,5]

Scandinavian Journal of Gastroenterology. 2011; 46: 1334–1339



p-values: 16–44 years < 0.001; 45–54 = 0.0048; 55–64 = 0.0020; 65+ = 0.12

Figure 1. Daily smokers in the control group compared with smokers among patients with collagenous colitis.



Ever smoked = current smokers and ex-smokers

Figure 2. Disease activity in patients with collagenous colitis in relation to smoking habits.

Celiac disease and other autoimmune diseases in patients with collagenous colitis

Scandinavian Journal of Gastroenterology. 2013; 48: 944–950

LINA VIGREN[1,5], CURT TYSK[2,5], MAGNUS STRÖM[3,5], ANDERS F KILANDER[4,5], HENRIK HJORTSWANG[3,5], JOHAN BOHR[2,5], CECILIA BENONI[1,5], LASSE LARSON[4] & KLAS SJÖBERG[1,5]

Abstract

Background and aims. Collagenous colitis (CC) is associated with autoimmune disorders. The aim of the present study was to investigate the relationship between CC and autoimmune disorders in a Swedish multicenter study. ***Methods.*** Patients with CC answered questionnaires about demographic data and disease activity. The patient's files were scrutinized for information about autoimmune diseases. ***Results.*** A total number of 116 CC patients were included; 92 women, 24 men, median age 62 years (IQR 55–73). In total, 30.2% had one or more autoimmune disorder. Most common were celiac disease (CeD; 12.9%) and autoimmune thyroid disease (ATD, 10.3%), but they also had Sjögren's syndrome (3.4%), diabetes mellitus (1.7%) and conditions in skin and joints (6.0%). Patients with associated autoimmune disease had more often nocturnal stools. The majority of the patients with associated CeD or ATD got these diagnoses before the colitis diagnosis. ***Conclusion.*** Autoimmune disorders occurred in one-third of these patients, especially CeD. In classic inflammatory bowel disease (IBD), liver disease is described in contrast to CC where no cases occurred. Instead, CeD was prevalent, a condition not reported in classic IBD. Patients with an associated autoimmune disease had more symptoms. Patients with CC and CeD had an earlier onset of their colitis. The majority of the patients with both CC and CeD were smokers. Associated autoimmune disease should be contemplated in the follow-up of these patients.

Microscopic Colitis or Functional Bowel Disease With Diarrhea: A French Prospective Multicenter Study

Am J Gastroenterol advance online publication, 8 July 2014; doi:10.1038/ajg.2014.182

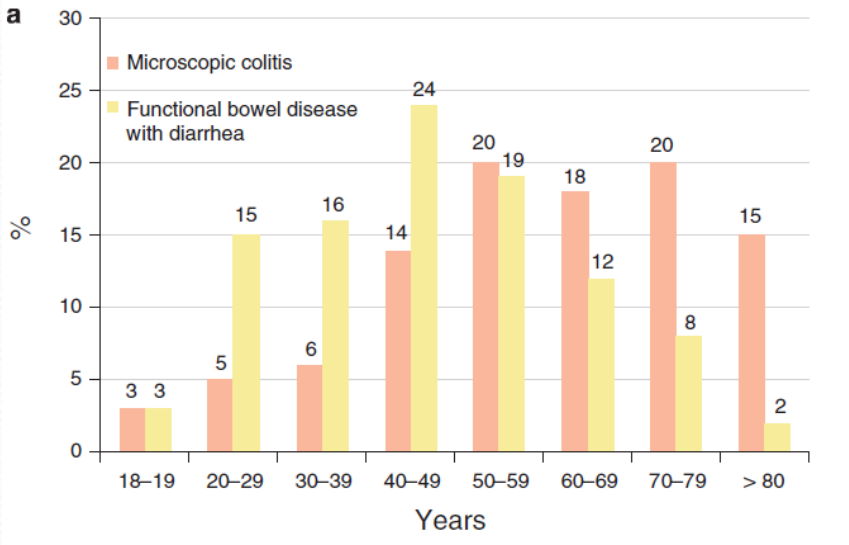


Figure 2. Age distribution of microscopic colitis (MC) and functional bowel disorder with diarrhea (FBD-D). Age distribution at the time of diagnosis (**a**) in patients with microscopic colitis and functional bowel disease with diarrhea and (**b**) in patients with collagenous and lymphocytic colitis.

Table 8. New drugs recently introduced (less than 3 months before the onset of diarrhea) in patients with MC and FBD-D depending on the duration of diarrhea, (a) less than 12 months and (b) more than 12 months

(a)		
	Diarrhea duration ≤12 months	
	New drug introduced (%)	No drug (%)
MC	58 (62)	36 (38)
FBD-D	37 (27)	100 (73)
	<0.0001	
(b)		
	Diarrhea duration >12 months	
MC	11 (30)	26 (70)
FBD-D	30 (22)	107 (78)
	NS	

FBD-D, functional bowel disorder with diarrhea; MC, microscopic colitis; NS, not significant.

Age >50 years, the presence of nocturnal stools, weight loss, the introduction of a new drug, and the presence of a known autoimmune disease increase the probability of MC and thus the indication for colonoscopy with biopsies.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Microscopic colitis (MC) is a common cause of chronic non-bloody diarrhea of rising incidence.
- ✓ Clinical presentation of MC and functional bowel disorder with diarrhea (FBD-D) may be similar.
- ✓ Some drugs and autoimmune diseases are associated with MC.

WHAT IS NEW HERE

- ✓ Age at onset greater than 50 years, recent diarrhea, nocturnal stools, weight loss, new drug intake, and presence of autoimmune diseases help to predict MC rather than FBD-D.
- ✓ Proton pump inhibitors and anti-parkinson agents are the most frequently incriminated drug classes.
- ✓ The identification of predictive factors of MC helps to decide whether colonoscopy with biopsies is indicated.
- ✓ The absence of recent drug intake or autoimmune disease, observed in a third of patients, does not exclude the diagnosis of MC.

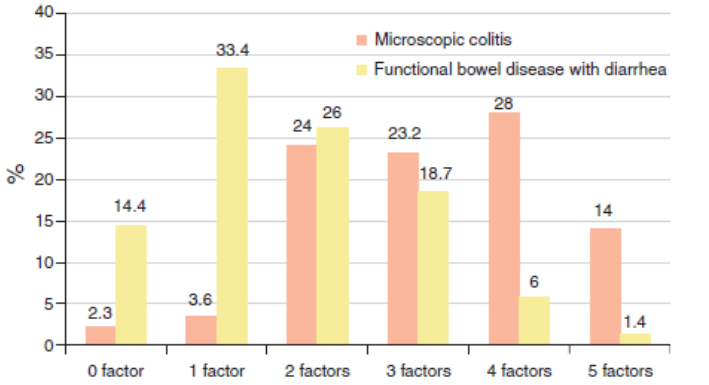


Table 9. Independent predictive factors of microscopic colitis in logistic regression analysis

Variables	OR (95% CI)	*P*
Presence of autoimmune disease	4.0 (2.1–7.7)	<0.0001
Drug introduced in the three months before onset diarrhea	3.7 (2.1–6.6)	<0.0001
Age >50 years	3.4 (1.9–6.2)	<0.0001
Loss of weight	2.2 (1.2–3.8)	0.008
Diarrhea for less than 12 months	2.0 (1.1–3.5)	0.024

CI, confidence interval; OR, odds ratio.

Scoring System to Identify Patients With Microscopic Colitis

Published in Gastroenterology
Journal Scan / Research · February 13, 2015

- **TAKE-HOME MESSAGE**
- In this retrospective study, researchers evaluated data from 476 patients with chronic diarrhea to develop a diagnostic scoring system for microscopic colitis (MC). MC was significantly associated with age ≥50 years, female sex, weight loss, absence of abdominal pain, and use of proton pump inibitors or nonsteroidal anti-inflammatory drugs. The scoring system developed had 90.5% sensitivity and 45.3% specificity.
- "Researchers suggest that the scoring system for MC may provide cost savings by reducing the need for colonic biopsies in patients unlikely to have MC." – Mukund Venu, MD

Development and Validation of a Scoring System to Identify Patients With Microscopic Colitis

John S. Kane,* Olorunda Rotimi,‡ Simon M. Everett,* Shairoz Samji,* Flurina Michelotti,* and Alexander C. Ford*,§

Leeds Gastroenterology Institute, St James's University Hospital, Leeds; ‡Department of Histopathology, St James's University Hospital, Leeds; and §Leeds Institute of Biomedical and Clinical Sciences, University of Leeds, Leeds, United Kingdom

Clinical Gastroenterology and Hepatology 2015;

In the derivation cohort, 85 patients were diagnosed with MC on the basis of histologic analysis. Age ≥50 years, female sex, use of proton pump inhibitors or nonsteroidal anti-inflammatory drugs, weight loss, and absence of abdominal pain were significantly associated with MC. We created a scoring system for diagnosis of MC, with scores ranging from −8 to +38; scores ≥8 were used to identify the presence of MC. This cutoff value identified patients with MC in the validation cohort (74 patients, 16.1%) with 90.5% sensitivity and 45.3% specificity (area under the receiver operating characteristic curve value, 0.76). Because of its ability to exclude MC and therefore avoid the need for routine collection of colonic biopsies, this scoring system reduced the cost of evaluation by >£7000/patient.

We collected data on risk factors for MC to create a scoring system that identifies patients with MC with more than 90% sensitivity. This system can also reduce costs by identifying patients who are unlikely to have MC who do not require biopsy analysis.

Table 2. Item Scores Within the Diagnostic Scoring System

Item	OR	95% CI	Regression coefficient	Used within the scoring system	Item score
Female gender	1.94	1.14–3.30	0.662	Yes	+4
Age ≥50 y	6.98	3.40–14.3	1.944	Yes	+13
Current PPI use	2.47	1.46–4.16	0.903	Yes	+6
Current NSAID use	5.28	2.44–11.4	1.664	Yes	+11
Weight loss present	1.89	1.11–3.24	0.639	Yes	+4
Abdominal pain present	0.28	0.16–0.47	−1.283	Yes	−8
Celiac disease present	2.35	0.85–6.51	0.854	No	N/A
Nocturnal diarrhea present	1.17	0.54–2.53	0.155	No	N/A

The European Microscopic Colitis Group (EMCG)

In comparison with other inflammatory bowel diseases (IBD), our knowledge about MC remains limited. More research is needed to investigate the aetiology and pathophysiology of MC, but above all more clinical studies are needed to improve the medical care of MC patients.

Keep microscopic colitis in mind!

Information for gastroenterologists and pathologists

D. Aust (Dresden), **S. Miehlke** (Hamburg)

An initiative of the

EMCG
EUROPEAN MICROSCOPIC COLITIS GROUP

- Microscopic colitis is a chronic inflammatory bowel disease whose incidence is increasing.
- The guiding symptom is watery, non-bloody diarrhoea which occurs almost daily.
- It mainly affects women in the second half of their lives.
- The endoscopic findings are generally unremarkable.
- Histological findings based on stepped biopsies of the colon (two each from the ascending, transverse and descending/sigmoid colon) are crucial in making a reliable diagnosis.
- It is vital to differentiate this disease diagnostically from irritable bowel syndrome.

Requirements of gastroenterologists:

- Stepped biopsies from the different colon sections in separate labelled vessels
- Accompanying information about clinical symptoms and medication

Differential diagnosis irritable bowel syndrome – microscopic colitis

	Irritable bowel syndrome	Microscopic colitis
First occurrence of disease	Commonly younger than 50 years of age	Commonly older than 50 years of age
Stool consistency	Soft – **variable** – hard	Watery/soft
Abdominal pain/discomfort	Obligatory	Variable
Nocturnal diarrhoea	Very rare	Possible
Feeling of incomplete bowel evacuation	Common	No
Weight loss	Rare	Common
Faecal incontinence	Rare	Common
Feeling of fullness/bloating	Common	Rare
Accompanying autoimmune disease	No	Yes

Checklist

When should microscopic colitis be considered?

- Intermittent or persistent, also nocturnal watery diarrhoea for several weeks (stool frequency ≥ 3/day)
- Commonly over 50 years of age
- Predominantly women
- Accompanying abdominal pain
- Faecal incontinence complaints
- Smokers
- Concurrent medication (PPI (lanzoprazole), SSRI (sertraline), NSAID, acarbose, ranitidine and ticlopidine)
- Concurrent autoimmune diseases (rheumatism, thyroid disease, diabetes, coeliac disease)

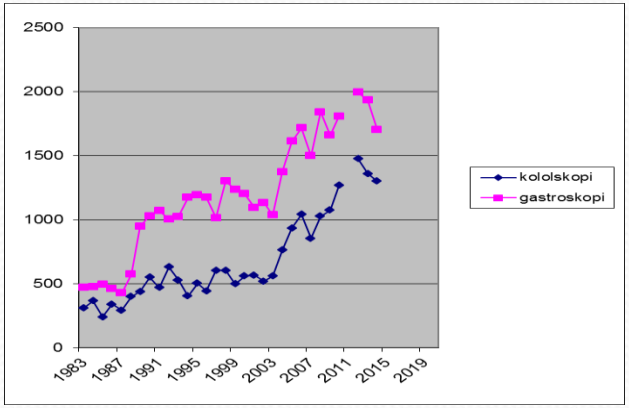
Further diagnostic investigation with colonoscopy and biopsies in the complete colon for histopathological assessment are required to make a diagnosis or to exclude *microscopic colitis*.

Koloskopi i Ålesund 2014

Gastroskopi:
1702, hvorav 70 % polikliniske og 30 % innlagte
(95 % diagnostiske og 5 % terapeutiske)
Endoskopisk hemostase: 24 pasienter

Koloskopi:
1301, hvorav 86 % polikliniske og 14% innlagte
(75 % diagnostiske og 25 % terapeutiske)
Polypektomi: 223 pasienter

- IBS-diagnose gitt etter koloskopi: 18%
  - K 58.9: 8,5%
  - K 58.0: 9%



2014	16-19 år	20-44 år	45-66 år	67-79 år	80-89 år	Sum
K58.0	5	48	49	17	1	120
K58.9	6	52	41	12	2	113
Totalsum	11	100	90	29	3	233

- Diagnose ikke korrigert etter histologisvar

Konklusjon

- Bruk av scoringssystem kan skille pas med MC fra IBS-D med sensitivitet 90%/ spesifisitet < 50%
- Kan potensielt spare belastningen på skopilab og patologi-lab, og bidra til å redusere presset på ventelister til koloskopi
- Pas med IBS trenger konsultasjon/ IBS-skole mer enn endoskopisk utredning