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ORIGINAL RESEARCH—CLINICAL

Prevalence of Atherosclerotic Disease in Microscopic Colitis Patients

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BACKGROUND AND AIMS: The preponderance of microscopic colitis (MC) in females may be associated with postmenopausal increased risk of atherosclerosis. The aim of this study was to describe the prevalence of atherosclerotic diseases in adults with MC. **METHODS:** Retrospective observational study of patients with a diagnosis of MC or incomplete MC at our institution from 2008 to 2018. We performed a chart review and extracted data on demographics, comorbidities, medications, diagnosis, imaging, and endoscopy. Data were analyzed descriptively. Logistic regression was used to estimate the unadjusted effects of different variables on MC. **RESULTS:** Of 269 patients, 265 had a MC diagnosis; 236 (89.06%) had collagenous colitis or lymphocytic colitis; and 29 (10.94%) were diagnosed with incomplete MC. Majority were female (79.55%), $\geq$ 65 years (59.11%), and white (88.81%). Majority had the following risk factors for atherosclerosis, smoking (52.04%), hypertension (58.21%), and hyperlipidemia (59.5%). The prevalence of coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease (CVD) was 16.79% (12.32, 21.27), 8.58% (5.23–11.94), and 7.49% (4.33–10.65), respectively. There was no difference in the prevalence of CAD and CVD after adjusting for sex. Females with MC had reduced odds of PAD compared with males. **CONCLUSION:** The prevalence of CAD, PAD, and CVD was 16.79%, 8.58%, and 7.49%, respectively. Similar to the general population, smoking, hypertension, and hyperlipidemia are risk factors for atherosclerosis in MC.

Keywords: Prevalence; Atherosclerosis; Microscopic; Colitis

Introduction

Microscopic colitis (MC) is an inflammatory disease of the colon that manifests as chronic watery, nonbloody diarrhea that severely impairs the quality of life of those affected.[1–3] Diagnosis requires a histological analysis of the colonic mucosa as the colon will appear endoscopically normal or subtly abnormal. There are 2 subtypes of MC: lymphocytic colitis (LC) which will show >20 intraepithelial lymphocytes per 100 epithelial cells, and collagenous colitis (CC) which is characterized by a thickened subepithelial collagen band (>10 microns), with < 20 or > 20 intraepithelial lymphocytes.[1–3] Variant forms which display clinical manifestations of MC but incompletely meet the diagnostic criteria have been reported and are subcategorized as incomplete CC (CCi) and incomplete LC (LCi).[1–4] Thus, incomplete MC (MCi) may represent different stages of disease development.[1,4] The incidence of MC is higher in females but the causes of the preponderance in females are unclear.[1–4] Multiple epidemiological studies have identified risk factors associated with MC, notably smoking, autoimmune conditions (celiac disease [CD], thyroid disorders), and consumption of certain medications (aspirin, non steroidal anti-inflammatory drugs, statins, proton-pump inhibitors), and hormonal therapy.[5–8]

The etiology and pathogenesis of MC is not clearly understood, but it is broadly accepted that a dysregulated immune response to changes in the gut luminal microenvironment results in chronic inflammation.[5–8] There is growing evidence that MC is characterized by a disordered gut microbiome resulting in a relative abundance of proinflammatory bacterial species such as *Proteobacteria, Alistipes,* and *Collinsella* species and reduction of *Faecalibacterium prausnitzii (Ruminococcaceae)*.[9]

Studies have reported that the gut metagenome contributes to adiposity and obesity by regulating host lipid metabolism.[10] The gut microbiota also produces inflammatory molecules such as lipopolysaccharide and peptidoglycan that play a role in metabolic disease and atherosclerosis.[10] Therefore, we hypothesize that the preponderance of MC in females may be associated with postmenopausal increased risk of atherosclerosis and the use of

Abbreviations used in this paper: **CC, collagenous colitis; CD, celiac disease; CCi, incomplete CC; CI, confidence interval; IBS, irritable bowel syndrome; LC, lymphocytic colitis; MACEs, major adverse cardiovascular events; MC, microscopic colitis; MCi, incomplete MC; OR, odds ratio.**

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Table 1. Demographic and Clinical Characteristics of Patients With Microscopic Colitis at Loyola University Medical Center, 2008–2018

Variable	N	Summary statistic
Sex, n (%)	269	
Female		214 (79.55)
Male		55 (20.45)
Age (y), n (%)	269	
65[a]		159 (59.11)
49–64		80 (29.74)
34–48		20 (7.43)
19–33		10 (3.72)
Age (y), n (%)	269	
> 50		235 (87.36)
< 50		34 (12.64)
Race, n (%)	268	
Asian		4 (1.49)
Black		10 (3.73)
Latino		14 (5.22)
Native American		2 (0.75)
White		238 (88.81)
Hormonal therapy, n (%)	269	
Multiple		1 (0.37)
Oral contraceptives		20 (7.43)
Hormone replacement therapy		16 (5.95)
IUD/Hormone secreting/ Other		5 (1.86)
No hormonal therapy		227 (84.39)
Hormonal therapy, n (%)	269	
Yes		42 (15.61)
No		227 (84.39)
Smoking, n (%)	269	
Yes		140 (52.04)
No		129 (47.96)
History of diarrhea, n (%)	269	
Yes		241 (89.59)
No		28 (10.41)
Positive stool for pathogens, n (%)	269	
Yes		18 (6.69)
No		251 (93.31)
Alcohol use, n (%)	269	
Yes		148 (55.02)
No		121 (44.98)
Diabetes, n (%)	269	
Yes		53 (19.70)
No		216 (80.30)
HLD, n (%)	269	
Yes		160 (59.48)
No		109 (40.52)
CAD, n (%)	269	
Yes		68 (25.28)
No		201 (74.72)
HTN, n (%)	269	
Yes		155 (57.62)
No		114 (42.38)
IBS, n (%)	269	
Yes		28 (10.41)
No		241 (89.59)
Thyroid disease, n (%)	269	
Yes		66 (24.54)
No		203 (75.46)
Celiac disease, n (%)	269	
Yes		12 (4.46)
No		257 (95.54)
Autoimmune disease, n (%)[a]	269	
Yes1		31 (11.52)
No		238 (88.48)
Probiotics, n (%)	269	
Yes		76 (28.25)
No		193 (71.75)
NSAIDs, n (%)	269	
Yes		125 (46.47)
No		144 (53.53)
Anticonvulsants, n (%)	269	
Yes		17 (6.32)
No		252 (93.68)
Statins, n (%)	269	
Yes		143 (53.16)
No		126 (46.84)
PPI, n (%)	269	
Yes		111 (41.26)
No		158 (58.74)
SSRIs, n (%)	269	
Yes		96 (35.69)
No		173 (64.31)
Tricyclic antidepressants, n (%)	269	
Yes		26 (9.67)
No		243 (90.33)
Aspirin, n (%)	269	
Yes		130 (48.33)
No		139 (51.67)
Beta-blocker, n (%)	269	
Yes		99 (36.80)
No		170 (63.20)
Plavix, n (%)	269	
Yes		33 (12.27)
No		236 (87.73)
H2 blocker, n (%)	269	
Yes		62 (23.05)
No		207 (76.95)
Antidiabetic, n (%)	269	
Yes		52 (19.33)
No		217 (80.67)
Microscopic colitis, n (%)	265	
Incomplete colitis (LCi/ CCi)		29 (10.94)
Lymphocytic colitis (LC)		100 (37.74)
Collagenous colitis (CC)		136 (51.32)
Coronary artery disease, n (%)	268	
Yes		45 (16.79)
No		223 (83.21)
PAD, n (%)	268	
Yes		23 (8.58)
No		245 (91.42)
Thromboembolic disease, n (%)	266	
Yes		6 (2.26)
No		260 (97.74)

Table 1. Continued

Variable	N	Summary statistic
CVD, n (%)	267	
Yes		20 (7.49)
No		247 (92.51)
Hypertension, n (%)	268	
Yes		156 (58.21)
No		112 (41.79)
BMI, mean (SD)	266	27.69 (6.46)
Systolic blood pressure (mmHg), mean (SD)	267	129.29 (17.79)

BMI, body mass index; IUD, intrauterine device; HLD, hyperlipidemia; HTN, hypertension; NSAIDs, non steroidal anti-inflammatory drugs; PPI, proton pump inhibitor; SD, standard deviation; SSRI, selective serotonin reuptake inhibitor.
[a]Autoimmune disease other than celiac and thyroid disease.

medications to treat risk factors for atherosclerotic disease. The aim of this study was to describe the prevalence and risk factors for atherosclerotic diseases such as coronary artery disease (CAD), peripheral arterial disease (PAD), and cerebrovascular disease (CVD) in adults with MC in order to estimate the disease burden attributable to atherosclerosis in patients with MC.

Methods

We performed a natural language search of the pathology records at our institution from 2008 to 2018 using the search terms lymphocytic colitis and collagenous colitis. The total sample (n = 269) included patients with either a diagnosis of MC or MCi (CCi/LCi). Histological descriptions were based on hematoxylin and eosin staining, and special stains were used in borderline cases (CD3 immunohistochemical staining for LC and trichrome stain for CC). We used the original pathology reports generated by expert gastrointestinal pathologists with knowledge of MC during the study period. We retrospectively performed a chart review and extracted data on demographics, comorbidities, medication, diagnosis, imaging, endoscopy, cardiac catheterization, electrocardiogram, echocardiography, ankle brachial index, treatment, and outcomes for the total sample. Diagnosis of irritable bowel syndrome (IBS) was based on Rome IV criteria, CD was diagnosed by positive celiac serology and duodenal biopsies, thyroid and autoimmune disease were diagnosed by thyroid function tests and autoimmune serology. The study was approved by the institutional review board of Loyola University Medical Center, Maywood, Illinois.

Statistical analysis

Frequencies and percentages are reported for categorical variables. Means and standard deviations are reported for numerical variables. Frequencies and column percentages are reported to describe the bivariate relationships between categorical variables and MC diagnosis. Stratified means and standard deviations are reported for numerical variables. Univariable binary logistic regression models were used to estimate the unadjusted effects of demographics and clinical characteristics on MC diagnosis. Wald 95% confidence intervals (CIs) are reported for each odds ratio (OR) estimate, and a Type III Wald chi-square P value is reported for the overall effect of each predictor. Fisher's exact test P values are provided where expected frequencies were < 5, and precise, reliable odds ratios could not be estimated.

Results

A total of 269 unique patients were studied, 265 of these patients had a valid, non-missing MC diagnosis. Two hundred and thirty-six patients (89.06%) were diagnosed as CC or LC, and 29 (10.94%) were diagnosed with MCi. Majority were female (79.55%), $\geq$ 65 years (59.11%), and white (88.81%). Majority had the following risk factors for atherosclerosis, smoking (52.04%), hypertension (58.21%), and hyperlipidemia (59.5%). The mean body mass index was 27.7, and the mean systolic blood pressure was 129.2 mmHg (Table 1). The prevalence of CAD, PAD, and CVD was 16.79% (12.32–21.27), 8.58% (5.23–11.94), and 7.49% (4.33–10.65), respectively (Table 2). The prevalence of IBS, CD, thyroid disease, and other autoimmune diseases was 10.41% (6.76–14.06), 4.46% (1.99–6.93), 24.54% (19.39–29.68), and 11.52% (7.71–15.34), respectively. We assessed the unadjusted effects of demographic and clinical characteristics on the diagnosis of MC to determine if any demographic or clinical variables were significantly associated with MC compared to MCi (Table 3). Patients 50 years or older had higher odds of MC relative to MCi compared to patients younger than 50 years (OR 4.65, 95% CI 1.94–11.15, $P < .01$). Patients on aspirin had higher odds of having MC relative to MCi compared to patients who are not on aspirin (OR 2.72, 95% CI 1.16, 6.37, $P = .02$). Patients on beta-blockers had higher odds of MC relative to MCi compared to patients not taking beta-blockers (OR 3.01, 95% CI 1.11, 8.17, $P = .03$). The study population was analyzed to describe the bivariate associations of age and sex on various disease outcomes (Tables 4 and 5). There was a significant association between age and CAD ($P = .02$) and a trend toward statistical significance for PAD ($P = .05$). There was no statistically significant difference in the odds

Table 2. Prevalence of Atherosclerotic Diseases and Non-Atherosclerotic Diseases Among Patients With Microscopic Colitis

Atherosclerotic disease	Prevalence (95% CI)
Coronary artery disease	16.79 (12.32, 21.27)
Peripheral artery disease	8.58 (5.23, 11.94)
Cerebrovascular disease	7.49 (4.33, 10.65)
Non-atherosclerotic disease	
Irritable bowel syndrome	10.41 (6.76, 14.06)
Celiac disease	4.46 (1.99, 6.93)
Thyroid disease	24.54 (19.39, 29.68)
Other autoimmune disease	11.52 (7.71, 15.34)

Table 3. Unadjusted Effects of Demographics and Clinical Characteristics on Microscopic Colitis Diagnosis

Variable	Microscopic colitis diagnosis		OR (95% CI)	*P*
	Colitis (CC/LC) (%)	Incomplete colitis (CCi/LCi) (%)		
	236 (89.06)	29 (10.94)	-	-
Sex				
Female	191 (80.93)	22 (75.86)	1.35 (0.54, 3.36)	.52
Male (REF)	45 (19.07)	7 (24.14)		
Age (y)				
>50	212 (89.83)	19 (65.52)	4.65 (1.94, 11.15)	<.01[a]
<50	24 (10.17)	10 (34.48)		
Race				
Non-white	25 (10.59)	4 (14.29)	0.71 (0.23, 2.21)	.56
White (REF)	211 (89.41)	24 (85.71)		
Hormonal therapy				
Yes	35 (14.83)	7 (24.14)	0.55 (0.22, 1.38)	.20
No (REF)	201 (85.17)	22 (75.86)		
Smoking				
Yes	127 (53.81)	11 (37.93)	1.91 (0.86, 4.21)	.11
No (REF)	109 (46.19)	18 (62.07)		
History of diarrhea				
Yes	211 (89.41)	26 (89.66)	0.97 (0.27, 3.45)	.97
No (REF)	25 (10.59)	3 (10.34)		
Positive stool for pathogens				
Yes	17 (7.20)	1 (3.45)	2.17 (0.28, 16.96)	.46
No (REF)	219 (92.80)	28 (96.55)		
Alcohol use				
Yes	134 (56.78)	12 (41.38)	1.86 (0.85, 4.07)	.12
No (REF)	102 (43.22)	17 (58.62)		
Diabetes				
Yes	44 (18.64)	6 (20.69)	0.88 (0.34, 2.29)	.79
No (REF)	192 (81.36)	23 (79.31)		
HLD				
Yes	144 (61.02)	13 (44.83)	1.93 (0.89, 4.19)	.10
No (REF)	92 (38.98)	16 (55.17)		
CAD				
Yes	61 (25.85)	4 (13.79)	2.18 (0.73, 6.51)	.16
No (REF)	175 (74.15)	25 (86.21)		
HTN				
Yes	137 (58.05)	14 (48.28)	1.48 (0.68, 3.21)	.32
No (REF)	99 (41.95)	15 (51.72)		
IBS				
Yes	28 (11.86)	0 (0.00)	-	.05[b]
No (REF)	208 (88.14)	29 (100.00)		
Thyroid disease				
Yes	63 (26.69)	3 (10.34)	3.15 (0.92, 10.78)	.07
No (REF)	173 (73.31)	26 (89.66)		
Celiac disease				
Yes	12 (5.08)	0 (0.00)	-	.37[b]
No (REF)	224 (94.92)	29 (100.00)		
Autoimmune disease				
Yes	27 (11.44)	4 (13.79)	0.81 (0.26, 2.50)	.71
No (REF)	209 (88.56)	25 (86.21)		
Probiotics				
Yes	67 (28.39)	8 (27.59)	1.04 (0.44, 2.46)	.93
No (REF)	169 (71.61)	21 (72.41)		
NSAIDs				
Yes	107 (45.34)	16 (55.17)	0.67 (0.31, 1.46)	.32
No (REF)	129 (54.66)	13 (44.83)		
Anticonvulsants				
Yes	14 (5.93)	2 (6.90)	0.85 (0.18, 3.95)	.84
No (REF)	222 (94.07)	27 (93.10)		

Table 3. Continued

Variable	Microscopic colitis diagnosis: Colitis (CC/LC) (%)	Incomplete colitis (CCi/LCi) (%)	OR (95% CI)	P
Statins				
Yes	129 (54.66)	11 (37.93)	1.97 (0.89, 4.36)	.09
No (REF)	107 (45.34)	18 (62.07)		
PPI				
Yes	95 (40.25)	13 (44.83)	0.83 (0.38, 1.80)	.64
No (REF)	141 (59.75)	16 (55.17)		
No (REF)	135 (57.20)	16 (55.17)		
SSRIs				
Yes	86 (36.44)	8 (27.59)	1.50 (0.64, 3.54)	.35
No (REF)	150 (63.56)	21 (72.41)		
Tricyclic antidepressants				
Yes	23 (9.75)	2 (6.90)	1.46 (0.33, 6.53)	.62
No (REF)	213 (90.25)	27 (93.10)		
Aspirin				
Yes	120 (50.85)	8 (27.59)	2.72 (1.16, 6.37)	.02[a]
No (REF)	116 (49.15)	21 (72.41)		
Beta-blocker				
Yes	91 (38.56)	5 (17.24)	3.01 (1.11, 8.17)	.03[a]
No (REF)	145 (61.44)	24 (82.76)		
Plavix				
Yes	30 (12.71)	2 (6.90)	1.97 (0.44, 8.69)	.37
No (REF)	206 (87.29)	27 (93.10)		
H2 blocker				
Yes	54 (22.88)	7 (24.14)	0.93 (0.38, 2.30)	.88
No (REF)	182 (77.12)	22 (75.86)		
Antidiabetic				
Yes	46 (19.49)	3 (10.34)	2.10 (0.61, 7.23)	0.24
No (REF)	190 (80.51)	26 (89.66)		
Coronary artery disease				
Yes	41 (17.45)	4 (13.79)	1.32 (0.44, 4.00)	.62
No (REF)	194 (82.55)	25 (86.21)		
PAD				
Yes	20 (8.51)	3 (10.34)	0.81 (0.22, 2.90)	.74
No (REF)	215 (91.49)	26 (89.66)		
Thromboembolic disease				
Yes	6 (2.58)	0 (0.00)	-	.99[b]
No (REF)	227 (97.42)	29 (100.00)		
CVD				
Yes	18 (7.69)	2 (6.90)	1.12 (0.25, 5.12)	.88
No (REF)	216 (92.31)	27 (93.10)		
Hypertension				
Yes	135 (57.45)	17 (58.62)	0.95 (0.44, 2.08)	.90
No (REF)	100 (42.55)	12 (41.38)		

	n	Mean (SD)	N	Mean (SD)		
BMI	233	27.49 (6.45)	29	28.67 (6.12)	0.97 (0.92, 1.03)	.35
Systolic blood pressure (mmHg)	234	128.92 (18.23)	29	131.62 (14.75)	0.99 (0.97, 1.01)	.44

BMI, body mass index; IUD, intrauterine device; HLD, hyperlipidemia; HTN, hypertension; NSAIDs, non steroidal anti-inflammatory drugs; PPI, proton pump inhibitor; SD, standard deviation; SSRI, selective serotonin reuptake inhibitor.
[a]Significant at $\alpha < 0.05$.
[b]Fisher's exact test *P* value.

of CVD, IBS, CD, thyroid disease, and other autoimmune diseases in females compared to males. The odds of PAD were 72% reduced for females compared to males ($P = .01$). The odds of thyroid disease were higher for females compared to males ($P = .01$). There was a trend toward a statistically significant difference in the odds of other autoimmune diseases in females compared to males ($P = .06$).

Table 4. Comparison of Atherosclerotic, Autoimmune, and Other Diseases by Age

Outcome	Age (y)		OR (95% CI)	*P*
	> 50	< 50		
	235 (87.36)	34 (12.64)	-	-
CAD				
Yes	44 (18.80)	1 (2.94)	-	.02[a,b]
No	190 (81.20)	33 (97.06)		
PAD				
Yes	23 (9.83)	0 (0.00)	-	.05[b]
No	211 (90.17)	34 (100.00)		
Thromboembolic disease				
Yes	6 (2.59)	0 (0.00)	-	.99[b]
No	226 (97.41)	34 (100.00)		
CVD				
Yes	19 (8.15)	1 (2.94)	-	.49[b]
No	214 (91.85)	33 (97.06)		
IBS				
Yes	22 (9.36)	6 (17.65)	0.48 (0.18, 1.29)	.15
No	213 (90.64)	28 (82.35)		
Celiac disease				
Yes	11 (4.68)	1 (2.94)	1.62 (0.20, 12.96)	.65
No	224 (95.32)	33 (97.06)		
Thyroid disease				
Yes	61 (25.96)	5 (14.71)	2.03 (0.75, 5.49)	.16
No	174 (74.04)	29 (85.29)		
Autoimmune disease[c]				
Yes	26 (11.06)	5 (14.71)	0.72 (0.26, 2.03)	.54
No	209 (88.94)	29 (85.29)		

[a]Significant at $\alpha = 0.05$ level.
[b]Fisher's exact test *P* value.
[c]Autoimmune disease other than celiac and thyroid disease.

Discussion

Atherosclerosis is a process that is largely driven by chronic inflammation. Endothelial cells of arteries modulate immune responses to perform structural, metabolic, and signaling functions to maintain the homeostasis of the vessel wall.[11,12] As a consequence of long-standing pathologic inflammation, the endothelium activates inflammatory mediators which alter the normal protective behavior of vascular cells.[11,12] Numerous studies have established traditional risk factors (tobacco smoking, hypercholesterolemia, and hypertension) which exacerbate the dysregulation of the vascular immune systems. Consequently, the arterial walls inappropriately proliferate via the accumulation of cholesterol and the recruitment of macrophages to the arterial wall, contributing to cardiovascular diseases and thrombotic complications.[11–13] Bacteria have also been implicated as a causative agent of atherosclerosis.[14]

In murine models, gut microbiota has been shown to metabolize dietary lipid phosphatidylcholine to trimethylamine, which promotes atherosclerosis and inflammation. In humans, levels of choline, trimethylamine N-oxide, and betaine have been found to predict cardiovascular disease.[10] A study using shotgun sequencing of the gut metagenome demonstrated that the genus *Collinsella* was enriched in patients with symptomatic atherosclerosis, compared to healthy controls.[10] We hypothesized a potential association between atherosclerotic diseases and MC. However, our results showed that the majority of our MC patients did not have significant atherosclerotic diseases. The prevalence was 16.79%, 8.58%, and 7.49% for CAD, PAD, and CVD, respectively. This was determined despite our MC patients sharing many traditional risk factors for atherosclerosis such as age, smoking, hypertension, and hyperlipidemia. However, our study has several noteworthy observations and implications. Our study is the first to describe the prevalence and risk factors of atherosclerotic disease in MC. Second, although our study population had more females than males, there was no difference in the prevalence of CAD and CVD after adjusting for sex. Interestingly and contrary to our hypothesis, females had reduced odds of PAD compared with males. Third, our results differ from prior studies on the prevalence of IBS, CD, thyroid disease, and other autoimmune diseases in MC patients.[15–17]

We observed a lower prevalence of IBS and CD compared to prior studies,[15,16] and a higher prevalence of thyroid disease compared to a prior study.[17] Fourth, the pathologic inflammation involved in MC may exhibit a slower temporal progression in the vascular system compared to inflammatory bowel disease.[13]

Table 5. Comparison of Atherosclerotic and Non-Atherosclerotic Disease by Sex

Outcome	Sex		OR (95% CI)	*P*
	Female	Male		
	214 (79.55)	55 (20.45)	-	-
CAD				
Yes	33 (15.42)	12 (22.22)	0.64 (0.30, 1.34)	.23
No	181 (84.58)	42 (77.78)		
PAD				
Yes	13 (6.07)	10 (18.52)	0.28 (0.12, 0.69)	.01[a]
No	201 (93.93)	44 (81.48)		
Thromboembolic disease				
Yes	6 (2.83)	0 (0.00)	-	.60[b]
No	206 (97.17)	54 (100.00)		
CVD				
Yes	16 (7.51)	4 (7.41)	1.02 (0.33, 3.17)	.98
No	197 (92.49)	50 (92.59)		
IBS				
Yes	24 (11.21)	4 (7.27)	1.61 (0.53, 4.85)	.40
No	190 (88.79)	51 (92.73)		
Celiac disease				
Yes	10 (4.67)	2 (3.64)	1.30 (0.28, 6.11)	.74
No	204 (95.33)	53 (96.36)		
Thyroid disease				
Yes	61 (28.50)	5 (9.09)	3.99 (1.52, 10.48)	.01[a]
No	153 (71.50)	50 (90.91)		
Other autoimmune disease[c]				
Yes	29 (13.55)	2 (3.64)	4.15 (0.96, 17.98)	.06
No	185 (86.45)	53 (96.36)		

[a]Significant at $\alpha = 0.05$ level.
[b]Fisher's exact test *P* value.
[c]Autoimmune disease other than celiac and thyroid disease.

Fifth, our study showed that age ≥50, aspirin, and beta-blockers (which can all be indicators of atherosclerotic events) were significantly associated with higher odds in MC compared to MCi. If we accept that MC is a more advanced stage than MCi, this suggests that a different phase of inflammation in MC may play a role in the manifestation of atherosclerosis. Last, our findings may alternatively imply that chronic inflammation in MC is mostly confined to the colonic tract and not systematically involved as was hypothesized. It is unclear at this stage if the prevalence of atherosclerotic diseases observed is over or underrepresented in our study population compared to age- and sex-matched controls. The results of this study will form a baseline for future studies.

A similar hypothesis was tested in a recently published matched-cohort study that investigated the risk of having major adverse cardiovascular events (MACEs) in Swedish MC patients.[18] Forss et al showed that MC patients had a higher overall risk of MACEs compared to reference individuals matched on age, sex, calendar year, and county (hazard ratio 1.27 (95% CI 1.21–1.33).[18] The study was notable for risk-stratifying the different components of MACEs defined as ischemic heart disease, congestive heart failure, and stroke.[18] However, it must be noted that risk factors for MACEs in general are largely determined by the inherent characteristics of the investigated cohort. For instance, congestive heart failure is not always due to ischemia but can also be from alcohol or substance use, arrhythmia, amyloidosis, and viral infections; similarly, stroke events can be induced by hypertension, coagulopathy, and cardiac arrhythmias.

In contrast, our study exclusively determined the prevalence and risk factors of atherosclerotic disease in MC patients in the United States without assessing MACEs. Moreover, the etiologies of cardiovascular complications in a Swedish population may differ from the US population with regard to different risk factors (diet, lifestyles, genetics).[19] A study conducted in Sweden using coronary computed tomography angiography found atherosclerosis in 42.1% of the participants without known CAD or symptoms, and significant stenosis (≥50%) in 5.2% of participants.[20] Taken together, our results imply a moderate burden of atherosclerosis in MC patients; the study by Forss et al is timely and showed that MC patients are at increased risk of MACEs compared to the general population but not mortality. However, it is unclear if the higher risk of MACEs is predominantly due to atherosclerotic disease.

The strengths of our study include a detailed review and analysis of 265 histologically confirmed unique patients with verifiable source data, such as imaging, endoscopy,

cardiac catheterization, electrocardiogram, echocardiography, and ankle brachial index. Limitations include the single-center retrospective design with the risk of selection bias and confounding. Multivariable logistic regression with adjustment for confounders was not performed due to sample size limitations.

Conclusion

The prevalence of CAD, PAD, and CVD in MC patients was 16.79%, 8.58%, and 7.49%, respectively. Similar to the general population, smoking, hypertension, and hyperlipidemia were risk factors for atherosclerosis in MC. Further studies will compare the prevalence of CAD, PAD, and CVD and the risk of MACEs in our study population with age- and sex-matched controls from the US general population, proper selection of control subjects such as patients with noninflammatory chronic diarrhea due to other etiologies will strengthen the quality of the future studies.

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