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Association of Age at Diagnosis and Ulcerative Colitis Phenotype

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Abstract

Background—Ulcerative colitis (UC) primarily affects young adults; however, 12% of patients are diagnosed at an advanced age. Previous studies report that older patients are less likely to have pancolitis and more likely to have distal disease location.

Aims—Our objective was to compare UC phenotype by age of diagnosis in a tertiary referral cohort.

Methods—Retrospective database analysis. Demographics, disease extent, and EIM were compared by the following age of diagnosis groups: <17 years, 17–40 years, and >40 years.

Results—A total of 260 patients evaluated between July 1, 2004 and April 19, 2010 were included. Race, smoking history, extraintestinal manifestations of disease, and disease duration were significantly associated with age of diagnosis. As age of diagnosis increased, the proportion of non-white patients increased ($p = 0.04$), former smoking history increased ($p < 0.001$), extraintestinal manifestations of disease decreased ($p < 0.017$), and disease duration decreased ($p < 0.0001$). As age of diagnosis increased, there was a trend for a higher proportion of patients with proctitis and a decreased proportion of patients with pancolitis. Multivariable analysis adjusting for sex, race, smoking history, family history, and disease duration demonstrated that diagnosis at >40 years was associated with a decreased likelihood for pancolitis compared to younger cohorts (OR 0.43, 95% CI 0.24, 0.76).

Conclusions—Diagnosis of ulcerative colitis after age 40 years was associated with decreased disease extent compared to younger age groups, even after adjustment for sex, race, smoking history, family history, and disease duration. Our results suggest that older patients have distinct clinical phenotypes.

Keywords

Ulcerative colitis; Aged; Phenotype; Inflammatory bowel disease

Introduction

Ulcerative colitis (UC) is an idiopathic inflammatory process of the large intestine. The symptoms of UC are chronic, with episodes of flares between periods of disease quiescence. Patients are most often diagnosed with UC in the second or third decade of life; however, studies from Europe and New York report a bimodal age distribution with a second incidence peak occurring later in life [1–5]. Recent studies from the province of Liege have shown that 11% of newly diagnosed UC cases are greater than 60 years old [6]. The data are conflicting on potential differences in disease severity between younger and older patients with UC. An evaluation of a population cohort of newly diagnosed UC patients revealed that patients diagnosed at 65 years or older were more likely to be hospitalized for the first attack of disease and more likely to receive steroids [7]. Conversely, an Italian study found that steroid use was used more frequently in younger patients [8]. However, this study as well as a case–control study of patients from the Mayo Clinic failed to demonstrate a higher rate of colectomy in the elderly [7, 9]. More recent data from the National Inpatient Sample demonstrated that 25% of IBD admissions in 2004 were among patients 65 years and older. Morbidity and mortality were increased in the elderly compared to younger patients [10]. These results are similar to previous work done using the General Practice Research Database which showed the greatest hazard ratio for UC was among patients age 40–59 years [HR 1.79 (1.42–2.27)] [11]. In order to better classify clinical characteristics in patients with UC, the World Congress of Gastroenterology introduced the Montreal Classification system. Using this system, unique subtypes of inflammatory bowel disease are identified based on age of diagnosis, disease extent, and severity [14]. Differences in disease extent between younger and older patients with UC has also been conflicting, as most of the prior studies addressing this topic have not classified patients according to the Montreal Classification system [8, 12, 13]. Therefore, the objective of our study was to compare disease extent in patients with UC based on age at diagnosis using the Montreal Classification System. We hypothesized that patients diagnosed over the age of 40 years were less likely to have extensive colitis disease phenotype.

Methods

In order to evaluate whether age at diagnosis is associated with UC phenotype, we compared differences in UC disease extent among patients diagnosed at young (<17 years), middle (17–40 years), and older (>40 years) age. Our independent variable was age at diagnosis, categorized into these three groups, and our dependent variable was disease extent, which was divided into the following categories: ulcerative proctitis (disease limited to the rectum), left-sided colitis (extent limited to the splenic flexure), or extensive colitis (involvement proximal to the splenic flexure) according to the 2005 Montreal classification system [14]. Accordingly, disease extent was assessed as the maximal extent at any time in the disease course (from diagnosis to time of data extraction). Further, disease extent was defined macroscopically.

Design and Setting

This was a cross-sectional study of adults with UC evaluated at the University of Maryland Inflammatory Bowel Disease Program between July 1, 2004 and April 16, 2010. Clinical information for each patient evaluated at the University of Maryland IBD Program is stored in a hard copy medical chart as well as a password-protected, HIPAA-compliant, IRB-approved Microsoft Access® database.

Identification of Subjects

Patients were identified from the University of Maryland IBD Database. Patients included in the study were those who had a diagnosis of UC confirmed in the record using standard clinical, endoscopic, radiographic, and pathological criteria [15]. To be included in this study, we required that the patient record had enough information to formulate a disease phenotype according to the Montreal classification. Patients with a diagnosis of Crohn's disease or other forms of IBD were excluded from the analysis.

Variable Definitions

The outcome variable of UC disease extent was categorized according to the Montreal classification system. Categories include proctitis, left-sided colitis, and extensive or pancolitis. The maximal extent of disease at any time point from the time of diagnosis to the most recent clinical evaluation was used for disease extent. Family history of IBD consisted of first or second degree relative with IBD. Extraintestinal manifestations (EIM) included arthritis of small and large joints, erythema nodosum, pyoderma gangrenosum, aphthous ulcers, ankylosing spondylitis, sacroileitis, iritis, episcleritis, uveitis, and primary sclerosing cholangitis. Disease duration was measured in years from both time of symptom onset and from time of diagnosis.

Data Analysis

We compared the unadjusted association between the categorical study and outcome variables using the Chi-squared test and Fisher's exact test. Study and outcome variables were collapsed into dichotomous categories as age >40 (yes or no) and extensive disease extent (yes or no) respectively. We performed stratified analyses to test for effect modification using the Breslow-Day test for homogeneity ($p < 0.05$). If effect modification was not present, we tested for confounding. We suspected confounding if the Mantel-Haenszel OR differed by 10% from the OR computed from the unadjusted association between age at diagnosis and disease behavior. A logistic regression analysis was used to determine the likelihood of pancolonic or extensive disease extent in patients diagnosed at >40 years of age. Potential confounding variables were added to the logistic model in a stepwise fashion. Only those variables that were significant ($p < 0.05$), that changed the odds ratio by 10%, or that were clinically important were included in the final model. All analyses were performed using SAS® v.9.2 (Cary, NC).

This study was approved on December 10, 2009 by the University of Maryland Institutional Review Board with a waiver of consent from participants.

Results

A total of 260 patients evaluated between July 1, 2004 and April 19, 2010 were included. Fifty-one percent of patients were male and 78% were Caucasian. The average duration of disease was 9.9 years from the time of diagnosis. Mean age at diagnosis was 29.9 years. Twenty (7.7%) were diagnosed under age 17, 160 (61.5%) were diagnosed between 17 and 40 years of age, and 80 (30.8%) were diagnosed over age 40. Complete demographic information for the study population is shown in Table 1. There was a trend towards a higher proportion of patients with a positive family history of IBD in patients diagnosed under 17 years (55%) compared to the other age groups (see Table 1). Eighty, 71, and 41% of patients diagnosed at <17, 17–40, >40 years of age, respectively, were never smokers ($p < 0.001$). Mean disease duration from time of diagnosis was 15.4, 10.3, and 7.6 years in patients diagnosed at <17, 17–40, and >40 years, respectively ($p < 0.001$). EIM were more common in patients diagnosed >40 years compared to other age groups (Table 1).

Association Between Age at Diagnosis and Disease Extent

As displayed in Fig. 1, there was a trend towards a decreased proportion of patients with pancolitis as age of diagnosis increased. Eighty, 66, and 51% of patients had pancolitis for age of diagnosis <17 years, 17–40 years, and >40 years, respectively ($p = 0.10$). An unadjusted analysis demonstrated that the age of diagnosis over 40 years was a protective factor for pancolonic disease extent (OR 0.51, 95% CI 0.30, 0.88). Logistic regression analysis demonstrated that even after adjusting for sex, race, family history, and disease duration, patients diagnosed at age >40 years were less likely to develop pancolitis compared to patients diagnosed <40 (OR 0.43, 95% CI 0.24, 0.76) (Table 2). White race was also found to be a significant risk factor for pancolitis after adjustment for age of diagnosis, sex, family history, smoking history, and disease duration (OR 1.95, 95% CI 1.05, 3.62).

Discussion

Increasing age at diagnosis was associated with a decreased likelihood for extensive or pancolonic disease extent in patients with UC in a tertiary care referral cohort. Patients diagnosed less than 17 years of age were more likely to have a positive family history of IBD and patients diagnosed over age 40 were more likely to have EIM. Patients diagnosed at older ages were also more likely to be former smokers than other age groups. Age at diagnosis over age 40 was associated with less extensive colitis after adjusting for sex, race, family history, smoking history, and disease duration. Caucasian race was found to be associated with a higher likelihood of pancolitis after adjusting for the same variables.

Our findings are consistent with results previously published which demonstrated that later age of diagnosis was associated with less extensive disease [8, 12, 13, 16]. In a retrospective review of 93 patients with ulcerative colitis, proctitis was found to be more common among patients with ulcerative colitis diagnosed after age 50 ($p = 0.077$) [13]. Similarly, Riegler et al. found a trend towards more limited forms of colitis among patients diagnosed at age 50 years or older. Patients in this study were outpatients from 17 different gastroenterologic centers in Italy. However, only 12% of patients in this cohort had pancolitis compared to the 62% in our study [8]. This large difference may in part be explained by the fact that our patients were from a tertiary referral program and thus were more likely to have pancolitis. Similarly, an evaluation of a tertiary referral population in Korea showed a lower proportion of patients with pancolitis in patients diagnosed at age 40 years or older [16].

In contrast to our findings, a retrospective study from Greece by Triantafillidis et al. [17] found no difference in UC disease extent by age of diagnosis. Fifty-one (12%) patients were diagnosed after age 60, while 362 were diagnosed prior to age 60. Eighty-four percent of patients in the older age group had disease limited to the rectum and/or sigmoid, which was not significantly different from patients in the younger group. Despite the similarity in disease extent between the two age groups, they found that those diagnosed over age 60 were significantly less likely to undergo surgical intervention for their disease compared to younger patients. This may have been due to medical comorbidities in the elderly affecting their surgical candidacy. Comorbidities and disease duration were not accounted for in this analysis. None of the above studies used multivariate logistic regression analysis to adjust for confounding factors such as disease duration.

Our results also differ from those published in a recent study by Ha et al. [18] which also utilized the Montreal classification system to categorize disease extent by age of diagnosis. This retrospective study did not find a difference in disease extent or severity when comparing patients diagnosed between 18 and 30 years of age to patients diagnosed at age 50 or over. Although disease extent was defined according to the Montreal classification, the time point at which disease extent was determined was the time of diagnosis. Our analysis

differed in that disease extent was determined based on the maximal disease extent from time of diagnosis to data extraction. For example, if a patient had pancolonic disease at any time in the disease course, they were classified as having pancolonic disease extent. This may account for the differences in our findings. This is an important difference as disease extent has been shown to progress or regress over time [19]. In addition, we evaluated patients at the cut points used in the Montreal classification for Crohn's disease (<17 years of age at diagnosis, 17–40 years of age at diagnosis, and >40 years of age at diagnosis).

The predilection for pancolitis among Caucasian subjects in our study contrasts with findings from a previous study by Flasar et al. which did not identify a significant difference in UC disease extent between racial or ethnic groups [20]. While our sample size was slightly larger (260 subjects compared to 197 subjects) the proportion of non-white patients in both studies was similar. The race variable definition varied slightly, with patient self-report being the sole method of race data collection for our study, while in the other study race was defined either by patient self-report or in some cases by provider report.

Our study has several strengths. First, we characterized patient's disease extent using the Montreal classification. Second, we included patients in all age ranges in our analyses. Third, we performed adjusted analyses to minimize confounding factors. Our study is limited by the fact that follow-up is variable depending on the age of diagnosis. Due to the dynamic progression of UC disease extent, some suggest that the phenotypic presentation of UC is not established until several years after diagnosis [21]. Since disease duration decreased significantly with age at diagnosis in our study population, it is possible that over time older patients will develop more extensive disease extent; however, disease duration was adjusted for in the logistic regression analysis and did not decrease the association between age at diagnosis and disease extent. Our patients were from a tertiary referral program and in general have more severe disease. Thus, our findings of decreased disease extent in patients diagnosed at older ages may not be generalizable to patients in the community with mild to moderate disease.

Our study demonstrates that patients diagnosed with UC over the age of 40 are less likely to develop pancolitis after adjusting for sex, race, family history, and disease duration. Larger epidemiologic studies are needed to confirm our findings and to examine if disease extent in elderly patients with UC (>60 years of age at diagnosis) differs from that of patients diagnosed at age 40–59 years. These studies should ideally be cohort studies at the time of diagnosis to allow for equal follow-up time among the groups for disease extent to “evolve”. We suspect that older patients have a different form of UC characterized by limited colonic involvement. If confirmed, our findings will be important to guide treatment for clinicians and should prompt investigation into differences in pathogenesis of UC in different age groups. Furthermore, the diagnosis of IBD may not be considered early in older patients with lower gastrointestinal symptoms because of a decreased clinical suspicion among clinicians. Characterizing disease phenotypes in older patients with IBD may make clinicians more aware that UC can occur in this population.

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Abbreviations

EIM	Extraintestinal manifestations
IBD	Inflammatory bowel disease

UC Ulcerative colitis

References

1. Loftus CG, Loftus EV Jr, Harmsen WS, et al. Update on the incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota, 1940–2000. *Inflamm Bowel Dis*. 2006; 13:254–261. [PubMed: 17206702]
2. Lapidus A, Bernell O, Hellers G, Persson PG, Lofberg R. Incidence of Crohn's disease in Stockholm County 1955–1989. *Gut*. 1997; 41:480–486. [PubMed: 9391246]
3. Stowe SP, Redmond SR, Stormont JM, et al. An epidemiologic study of inflammatory bowel disease in Rochester, New York. Hospital incidence. *Gastroenterology*. 1990; 98:104–110. [PubMed: 2293567]
4. Cottone M, Cipolla C, Orlando A, Oliva L, Aiala R, Puleo A. Epidemiology of Crohn's disease in Sicily: a hospital incidence study from 1987 to 1989. 'The Sicilian Study Group of Inflammatory Bowel Disease'. *Eur J Epidemiol*. 1991; 7:636–640. [PubMed: 1783057]
5. Sonnenberg A. Age distribution of IBD hospitalization. *Inflamm Bowel Dis*. 2010; 16:452–457. [PubMed: 19714765]
6. Piront P, Louis E, Latour P, Plomteux O, Belaiche J. Epidemiology of inflammatory bowel diseases in the elderly in the province of Liege. *Gastroenterol Clin Biol*. 2002; 26:157–161. [PubMed: 11938067]
7. Jones HW, Hoare AM. Does ulcerative colitis behave differently in the elderly? *Age Ageing*. 1988; 17:410–414. [PubMed: 3239501]
8. Riegler G, Tartaglione MT, Carratu R, et al. Age-related clinical severity at diagnosis in 1705 patients with ulcerative colitis: a study by GISC (Italian Colon-Rectum Study Group). *Dig Dis Sci*. 2000; 45:462–465. [PubMed: 10749318]
9. Tremaine WJ, Timmons LJ, Loftus EV Jr, et al. Age at onset of inflammatory bowel disease and the risk of surgery for non-neoplastic bowel disease. *Aliment Pharmacol Ther*. 2007; 25:1435–1441. [PubMed: 17539983]
10. Ananthakrishnan AN, McGinley EL, Binion DG. Inflammatory bowel disease in the elderly is associated with worse outcomes: a national study of hospitalizations. *Inflamm Bowel Dis*. 2008; 15:182–189. [PubMed: 18668678]
11. Card T, Hubbard R, Logan RF. Mortality in inflammatory bowel disease: a population-based cohort study. *Gastroenterology*. 2003; 125:1583–1590. [PubMed: 14724808]
12. Gupta S, Saverymuttu SH, Keshavarzian A, Hodgson HJ. Is the pattern of inflammatory bowel disease different in the elderly? *Age Ageing*. 1985; 14:366–370. [PubMed: 4072825]
13. Zimmerman J, Gavish D, Rachmilewitz D. Early and late onset ulcerative colitis: distinct clinical features. *J Clin Gastroenterol*. 1985; 7:492–498. [PubMed: 4086743]
14. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut*. 2006; 55:749–753. [PubMed: 16698746]
15. Lennard-Jones JE. Classification of inflammatory bowel disease. *Scand J Gastroenterol Suppl*. 1989; 170:2–6. discussion 16–9. [PubMed: 2617184]
16. Lee JH, Cheon JH, Moon CM, et al. Do patients with ulcerative colitis diagnosed at a young age have more severe disease activity than patients diagnosed when older? *Digestion*. 2010; 81:237–243. [PubMed: 20110709]
17. Triantafyllidis JK, Emmanouilidis A, Pomonis E, et al. Ulcerative colitis in the elderly: clinical patterns and outcome in 51 Greek patients. *J Gastroenterol*. 2001; 36:312–316. [PubMed: 11388393]
18. Ha CY, Newberry RD, Stone CD, Ciorba MA. Patients with late-adult-onset ulcerative colitis have better outcomes than those with early onset disease. *Clin Gastroenterol Hepatol*. 2010; 8:682–687. e1. [PubMed: 20363368]

19. Moum B, Ekbom A, Vatn MH, Elgjo K. Change in the extent of colonoscopic and histological involvement in ulcerative colitis over time. *Am J Gastroenterol.* 1999; 94:1564–1569. [PubMed: 10364026]
20. Flasar MH, Quezada S, Bijpuria P, Cross RK. Racial differences in disease extent and severity in patients with ulcerative colitis: a retrospective cohort study. *Dig Dis Sci.* 2008; 53:2754–2760. [PubMed: 18273704]
21. Van Limbergen J, Russell RK, Drummond HE, et al. Definition of characteristics of childhood-onset inflammatory bowel disease. *Gastroenterology.* 2008; 135:1114–1122. [PubMed: 18725221]

Fig. 1. Disease extent by age at diagnosis in adults with ulcerative colitis evaluated at the University of Maryland Inflammatory Bowel Disease Program between July 1, 2004 and April 16, 2010

Baseline characteristics of patients with ulcerative colitis evaluated at the University of Maryland IBD Program from July 2004 to April 2010 by age of diagnosis

Table 1

Variable	Overall (n = 260) n, %	<17 years (n = 20) n, %	17–40 years (n = 160) n, %	>40 years (n = 80) n, %	p value ^a
Sex					
Male	128 (51)	7 (35)	78 (49)	47 (59)	0.12
Female	132 (49)	13 (65)	82 (51)	33 (41)	
Race					
White	202 (78)	18 (90)	116 (73)	68 (85)	0.04
Non-white	58 (22)	2 (10)	44 (28)	12 (15)	
Family history					
Yes	72 (28)	11 (55)	42 (26)	19 (24)	0.08
No	185 (71)	9 (45)	116 (73)	60 (75)	
Unknown	3 (1)	0 (0)	2 (1)	1 (1)	
Smoking					
Current	13 (5)	3 (15)	7 (4)	3 (4)	<0.001
Former	84 (32)	1 (5)	39 (25)	44 (55)	
Never	163 (63)	16 (80)	114 (71)	33 (41)	
Location					
Proctitis	20 (8)	0 (0)	13 (8)	7 (9)	0.08
Left-sided colitis	78 (30)	4 (20)	42 (26)	32 (40)	
Pancolitis	162 (62)	16 (80)	105 (66)	41 (51)	
EIM					
Yes	52 (20)	1 (5)	28 (18)	23 (29)	0.03
No	208 (80)	19 (95)	132 (82)	57 (71)	
Disease duration since diagnosis (mean ± SD)	9.9 ± 7.6	15.4 ± 10.7	10.3 ± 7.5	7.6 ± 6.2	<0.001 ^b
Disease duration since symptoms (mean ± SD)	11.2 ± 8.1	15.5 ± 10.4	11.2 ± 7.7	10.0 ± 8.1	<0.001 ^b

^a Chi-squared, Fischer's exact test

^b ANOVA test

Table 2

Logistic regression of association between age of diagnosis >40 and pancolitis after adjusting for sex, race, and family history

Characteristic	OR (95% CI)
Age of diagnosis	
40 years	0.43 (0.24, 0.76)
<40 years	1 (reference)
Sex	
Male	1.49 (0.88, 2.52)
Female	1 (reference)
Race	
White	1.95 (1.05, 3.62)
Other	1 (reference)
Family history	
Yes	0.84 (0.47, 1.51)
No or unknown	1 (reference)
Disease duration	
10 years	0.84 (0.49, 1.43)
<10 years	1 (reference)