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IBD in the elderly population: Results from a population-based study in Western Hungary, 1977–2008☆

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KEYWORDS
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Incidence;
Disease course

Abstract

Background and aims: Limited data are available on the incidence and disease course of IBD in the elderly population. Our aim was to analyze the incidence and disease course of IBD according to the age at diagnosis in the population-based Veszprem province database, which included incident patients diagnosed between January 1, 1977 and December 31, 2008.
Methods: Data of 1420 incident patients were analyzed (UC: 914, age at diagnosis: 38.9 SD15.9 years; CD: 506, age at diagnosis: 31.5 SD13.8 years). Both hospital and outpatient records were collected and comprehensively reviewed.
Results: 106 (11.6%) of UC patients and 21 (4.2%) of CD patients were diagnosed with >60 years of age. In UC, the incidence increased from 1.09 to $10.8/10^5$ in the elderly, while CD increased to $3.04/10^5$ in 2002–2007. In CD, colonic location (elderly: 61.9% vs. pediatric: 24.3%, $p=0.001$, and adults: 36.8%, $p=0.02$) and stenosing disease (elderly: 42.9% vs. pediatric: 14.9%, $p=0.005$, and adults: 19.5%, $p=0.01$) were more frequent in the elderly. A change in disease behavior was absent in the elderly, while in pediatric and adult CD population it was 20.3% ($p=0.037$), 19.8% ($p=0.036$) after 5 years. In UC, extensive disease was more frequent in pediatric patients

☆ Ethical permission: The study protocol was approved by Semmelweis University Regional and Institutional Committee of Science and Research Ethics and the Csolnoky F. Province Hospital Institutional Committee of Science and Research Ethics.

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compared to the elderly ($p=0.003$, OR: 2.73, 95%CI: 1.38–5.41). In addition, pediatric (57.3%, $p<0.001$, OR: 6.58; 95%CI: 3.22–12.9) and adult (39.8%, $p<0.001$, OR: 3.24; 95%CI: 1.91–5.49) patients required more often systemic steroids during follow-up compared to the elderly (17%). Proximal extension at 10 years was 11.6%, but time to extension was not different according to the age at onset.

Conclusions: Elderly patients represent an increasing proportion of the IBD population. Stenosing and colon-only disease were characteristic for elderly CD patients, while the disease course in UC was milder.

1. Introduction

Recent trends indicate a change in the epidemiology of IBD with previously low incidence areas now reporting a progressive rise in the incidence, including some Eastern European countries. In West European and North American countries the figures have stabilized or slightly increased, with even decreasing incidence rates for ulcerative colitis.[1]

Limited data are available on the incidence and disease course of IBD in the elderly population. At least according to published data from North America and Western Europe, it may not be as uncommon as previously suspected. The true incidence in the elderly is difficult to determine because of differences in the populations studied, case definitions of IBD, and potential confusion with other diagnoses such as ischemic colitis or nonsteroidal anti-inflammatory drug (NSAID)-induced colitis. The annual incidence rate in CD in the elderly was $2.5/10^5$, with a higher proportion of colonic disease in France.[2] In a large cohort of 2509 patients from Sweden, the age-adjusted annual incidence was $8/10^5$ person-years for UC at age 65, compared to a peak of $22/10^5$ person-years at age 25.[3] For CD, population-based studies indicate an incidence of $4/10^5$ person-years at age 65 in 1469 patients with CD.[4] Above the age 65, UC affected about twice as many men as women, mainly due to the increasing number of proctitis cases. In UC, a trend toward more distal colonic disease was reported in the elderly. An OMGE survey reported proctitis in 42% of UC patients over the age of 60, compared to 33% in those younger.[5] Disease extension appears to be less common in older patients.

Studies from referral centers have found that the proportion of CD patients with colonic involvement increases with increasing age at diagnosis.[6] Of those diagnosed after the age of 40 years, 48% had isolated colonic involvement compared with 28% and 20% for those diagnosed between age 20 and 40 and before age 20, respectively. In a population-based study from Brittany from 2004, 66% of patients diagnosed at 60 years of age or older had isolated colonic involvement.[2] Furthermore, the proportion of patients with inflammatory (non-stricturing, non-penetrating) behavior was also higher among those diagnosed after the age of 40. Although the overall probabilities for surgery were similar between patients older and younger than 60 years, azathioprine use and the likelihood for hospitalization from a second flare-up were lower in those diagnosed after the age of 60.

The role of age at diagnosis in predicting the disease course was suggested by Beaugerie et al.[7] In CD, an age younger than 40 years (OR: 2.1, 95%CI:1.3–3.6), an initial need for steroid use (OR: 3.1 (95%CI:2.2–4.4), and the presence of perianal disease (OR: 1.8, 95%CI:1.2–2.8) were associated with the development of disabling disease. In another study, terminal ileal location ($p<0.001$), stricturing

Notes to Table 1
[a] %,[&] median (IQR).
[b] Elderly vs. pediatric: $p=0.001$, OR: 5.06, 95%CI: 1.81–14.1 and elderly vs. adults: $p=0.02$, OR: 2.79, 95%CI: 1.13–6.88.
[c] Elderly vs. pediatric: $p=0.005$, OR: 4.30, 95%CI: 1.47–12.6, and elderly vs. adults: $p=0.01$, OR: 3.10, 95%CI: 1.26–7.62.
[d] Elderly vs. pediatric: $p=0.037$, OR: 1.25, 95%CI:1.10–1.43, and elderly vs. adults: $p=0.036$, OR: 1.25, 95%CI:1.18–1.32.
[e] $p=0.051$.
[f] Elderly vs. pediatric: $p=0.001$, OR: 0.18, 95%CI:0.06–0.52.
[g] Elderly and adults, pediatric: $p<0.0001$.
[h] n (%),[&] median (IQR).
[i] Low- or high-grade dysplasia.
[j] Elderly vs. pediatric: $p=0.007$, OR: 10.7, 95%CI: 1.30–90.9 and elderly vs. adults: $p=0.006$, OR: 9.9, 95%CI: 1.33–71.4.
[k] Elderly vs. pediatric: $p=0.005$, OR: 2.38, 95%CI: 1.30–4.36 and elderly vs. adults: $p=0.025$, OR: 1.61, 95%CI: 1.06–2.44.
[l] Pediatric vs. elderly: $p=0.003$, OR: 2.73, 95%CI: 1.38–5.41.
[m] Pediatric vs. adult: $p=0.01$, OR: 1.89, 95%CI: 1.15–3.11.
[n] Elderly vs. pediatric: $p=0.07$.
[o] Pediatric vs. elderly: $p=0.001$, OR: 5.05, 95%CI: 1.75–14.5.
[p] Pediatric vs. adult: $p=0.001$, OR: 2.80, 95%CI: 1.50–5.24.
[q] $p=0.007$.
[r] Pediatric vs. elderly: $p<0.001$, OR: 6.58, 95%CI: 3.32–12.9, pediatric vs adult: $p=0.003$, OR: 2.03, 95%CI: 1.25–3.28, adult vs. elderly: $p<0.001$, OR: 3.24, 95%CI: 1.91–5.49.
[s] $p=0.002$.

Table 1 Clinical characteristics of patients with Crohn's disease (A) and ulcerative colitis (B).

(A)

CD		Pediatric *n*=74	Adult *n*=411	Elderly *n*=21
Male/female		46/28	194/217	11/10
Age at presentation (years) [g]		14.5 (13.8–15.2)	32.7 (31.7–33.7)	68.5 (65.4–71.6)
Familial IBD [a]		17.6%	12.4%	9.5%
Location (n)	L1	23	135	8
	L2	18 [b]	151 [b]	13 [b]
	L3	33	122	0
	L4 only	0	3	0
Behavior (n) at diagnosis	B1	46	234	8
	B2	11 [c]	80 [c]	9 [c]
	B3	17	97	4
Behavior change at 5 years [a]				
from B1to B2/B3 or B2 to B3		20.3% [d]	19.8% [d]	0 [d]
Perianal disease [a]		32.4% [e]	25.1%	9.5% [e]
Arthritis [a]		21.6%	28.0%	19.0%
PSC [a]		0	2.0%	4.8%
Ocular [a]		1.4%	5.6%	0
Cutaneous [a]		9.5%	9.7%	4.8%
Steroid use [a]		71.6%	68.6%	57.1%
Azathioprine use [a]		68.9% [f]	42.6%	28.6% [f]
Biological use [a]		9.5%	9.5%	0
Resection at 5 years/reoperation [a]		33.8%/23.5%	30.7%/29.6%	28.6%/16.7%
Smoking habits (n) at diagnosis	no	61	153	10
	ex	0	35	3
	yes	13 [f]	223 [f]	8 [f]

(B)

UC		Pediatric *n*=75	Adult *n*=733	Elderly *n*=106
Male/female		35/40	3289/344	55/51
Age at presentation (years) [g]		15.3 (14.6–16.0)	37.1 (36.2–37.8)	68.7 (67.6–69.9)
Familial IBD [h]		9.3% [j]	8.5% [j]	0.9% [j]
Extent at diagnosis (n)				
	Proctitis	17	193	22
	Left-sided	30 [k]	364 [k]	65 [k]
	Extensive	28 [l,m]	176 [m]	19 [l]
Proximal extension at 5 years		13.3%	8.6%	6.6%
at 10 years		18.7% [n]	13.0%	9.4% [n]
at the end of follow-up		21.3%	16.2%	10.4%
Frequent relapse [h]		9.3%	5.0%	6.6%
Fulminant episode [h]		20.0% [o, p]	8.2% [p]	4.7% [o]
Arthritis [h]		12.0%	14.5%	6.6%
PSC [h]		6.7% [q]	2.7%	0 [q]
Ocular [h]		2.7%	3.3%	0
Cutaneous [h]		5.3%	2.6%	0
Steroid use [h]		57.3% [r]	39.8% [r]	17.0% [r]
Azathioprine use [h]		9.3%	7.8%	2.8%
Colectomy [h]		8.1%	4.1%	1.9%
Dysplasia [h, i]		2.7%	1.8%	1.9%
Cancer [h]		1.3%	2.6%	2.8%
Smoking habits (n) at diagnosis	No	66 [s]	477 [s]	74 [s]
	Ex	1	141	19
	Yes	8	115	13

($p=0.004$), penetrating behavior ($P<0.001$), and age younger than 40 years ($P=0.03$) at diagnosis were independent risk factors for subsequent surgery in a prospective 10-year follow-up study by the IBSEN group.[8] Recently, Peyrin-Biroulet et al.[9] have published a systematic review on the natural history of Crohn's disease in population-based-cohorts. According to the authors' conclusion the impact of changing treatment paradigms with the increased use of immunosuppressants and biological agents on its natural history is poorly understood.

Less prognostic factors are available in UC. One of the important predictive factors for colectomy is disease extent, identified by previous studies and also in a recent 10-year population-based inception cohort study.[10] In the same study, an age at the time of diagnosis greater than 50-years was associated with a reduced hazard ratio (0.28) for subsequent colectomy. In addition, one-fifth (69/288) of patients with proctitis or left-sided colitis had progressed to extensive colitis. In contrast, pediatric UC was more aggressive. Disease course was characterized by disease extension in 49% of patients during a 6.5-year population-based study.[11] The cumulative rate of colectomy was 8% at 1 year and 20% at 5 years.

Since the influence of age at onset on the presentation, clinical course, and surgical requirements is understudied in population-based incidence cohorts, the aim of this study was to analyze the time-trends in the incidence according to the age at diagnosis, and association between age at diagnosis, disease phenotype and course of IBD in the population-based Veszprem province database, including incident patients diagnosed between January 1, 1977 and December 31, 2008.

2. Materials and methods

A well-characterized Hungarian cohort of 1420 incident cases with inflammatory bowel diseases diagnosed between January 1, 1977 and December 31, 2008 were included. In total, 914 ulcerative colitis (UC, male/female: 479/435, age at diagnosis: 38.9 years, SD: 15.9 years) and 506 Crohn's disease (CD, male/female: 251/255, age at diagnosis: 31.5 years, SD 13.8 years) patients were diagnosed during the follow-up period. Patients with indeterminate colitis at diagnosis were excluded from the analysis. The clinical data of all patients are summarized in Table 1. The rate of Gypsies is below the Hungarian average (2.5%), while few people of Jewish ethnicity live in the province. The ratio of urban/rural residence was also relative stable (55% urban). The source of age- and gender-specific demographic data of the province for the statistical analysis was the Hungarian Central Statistical Office (KSH).

IBD patient data were collected every year from the seven general hospitals and gastroenterology outpatient units (Internal Medicine Departments, Surgery Departments, Pediatric Departments, and Outpatient Units), each staffed by at least one gastroenterologist or internist with special interest in gastroenterology, as well as family physicians. The majority of patients (76% of UC and 94% of CD patients) were monitored at the Csolnoky F. Province Hospital in Veszprem. This hospital also serves as a secondary referral centre for IBD patients in that province. Data collection was prospective since 1985, while prior to that, data were only in Veszprem collected prospectively. In other sites throughout the province, data for this period (1974–1985) were collected retrospectively in 1985. Both inpatients and outpatients permanently residing in the investigated area were included in the study. Most patients were followed up regularly. Diagnoses (based on hospitalization records, out-patient visits, endoscopic, radiological and histological evidence) generated in each hospital and outpatient unit were reviewed thoroughly, using the Lennard–Jones criteria.[12] The provincial IBD register data were centralized in Veszprem. The disease phenotype was assessed by a questionnaire completed by the clinician at the time of diagnosis, and updated yearly, as necessary. A more detailed description of our data collection method, case ascertainment, geographical and socioeconomic background of the province and the Veszprem Province IBD Group was published in our previous epidemiological studies.,[13,14] Moreover, due to Hungarian health authority regulations, a follow-up visit is obligatory for IBD patients at a specialized gastroenterology centre every six months. Otherwise, the conditions of the health insurance policy change and they forfeit their ongoing subsidized therapy. Consequently, the relationship between IBD patients and specialists is a close one.

Age, age at onset, the presence of familial IBD, presence of extra-intestinal manifestations (EIM); arthritis: peripheral and axial; ocular manifestations: conjunctivitis, uveitis, iridocyclitis; skin lesions: erythema nodosum, pyoderma gangrenosum; and hepatic manifestations: primary sclerosing cholangitis (PSC), frequency of flare-ups (frequent flare-up: >1/year,[15,16]) were recorded. The disease phenotype (age at onset, duration, location, and behavior) was determined according to the Montreal Classification[17] (non-inflammatory behavior: either stricturing or penetrating disease). Perianal disease and behavior change during follow-up was also registered. Medical therapy was registered in details (e.g., steroid and/or immunosuppressive/biological use, azathioprine intolerance as defined by the ECCO [European Crohn's and Colitis Organisation] Consensus Report[15]), need for surgery/reoperation (resections in CD and colectomy in UC), colonoscopic surveillance (at least 2 colonoscopies/5 years after a disease duration of 10 years) and smoking habits, were investigated by reviewing the medical charts and completing a questionnaire. Only patients with a confirmed diagnosis for more than 1 year were enrolled.

The study was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics and the Csolnoky F. Province Hospital Institutional Committee of Science and Research Ethics.

2.1. Statistical analysis

Variables were tested for normality by Shapiro Wilk's W test. Wilcoxon rank sum test, χ^2-test and χ^2-test with Yates correction and logistic regression were used to test differences in disease phenotype between subgroups of UC and CD patients for dichotomous variables. Odds ratios (OR) were calculated. Kaplan–Meier survival curves were plotted for analysis with LogRank and Breslow tests to determine probability of change in disease extent in UC and behavior

in CD. Additionally, Cox-regression analysis was used to assess the association between categorical clinical variables and surgical requirements. Variables with a p value<0.2 in univariate analysis were included in the multivariate testing. A p value of <0.05 was considered as significant. Results for continuous variables are expressed as median (lower and upper quartile) unless otherwise stated. For the statistical analysis SPSS15.0 (SPSS Inc, Chicago, IL, USA) was used.

3. Results

3.1. Incidence of IBD in the elderly population

In total, 914 ulcerative colitis (male/female: 479/435, age at diagnosis: 38.9 years, SD15.9 years) and 506 Crohn's disease (male/female: 251/255, age at diagnosis: 31.5 years, SD13.8 years) patients were diagnosed during the follow-up period. One-hundred-six (11.6%) of the UC patients and 21 (4.2%) of the CD patients were diagnosed when above the age of 60 years, while 74 CD and 75 UC patients were pediatric cases (0–18 years at diagnosis). The clinical data of all patients is summarized in Table 1. The age distribution of all IBD cases is presented in Fig. 1.

The incidence in UC and CD in the pediatric, adult (19–60 years at diagnosis; CD: 411, UC:733) and elderly (>60 years at diagnosis) population is presented in Fig. 2. In the adult population, the total gender-adjusted incidence in UC and CD increased from 2.44 (95%CI: 1.08–5.54) and 1.18 (95%CI: 0.37–3.41) in 1977–1981 to 17.2 (95%CI: 12.5–23.6) and 13.8 (95%CI: 9.7–19.7) in 2002–2007. Similarly, UC increased in the elderly from 1.09 (95%CI: 0.13–9.01) to 10.8 (95%CI: 5.4–21.5); however, CD was virtually absent until the 1990 s in the elderly population. The incidence increased to 3.04 (95%CI: 0.88–10.5) in 2002–2007.

3.2. Clinical phenotype at diagnosis and change of disease behavior and location in the elderly

The clinical characteristics and disease course of the elderly population was compared to the pediatric and adult cohorts.

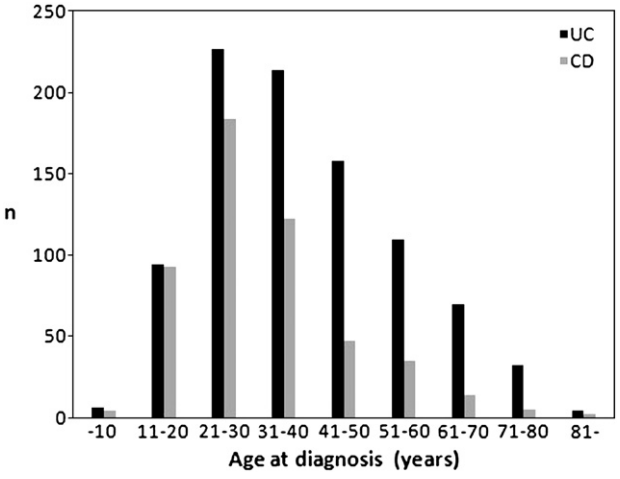

Figure 1 Distribution of patients with inflammatory bowel diseases according to the age at diagnosis, 1977–2008.

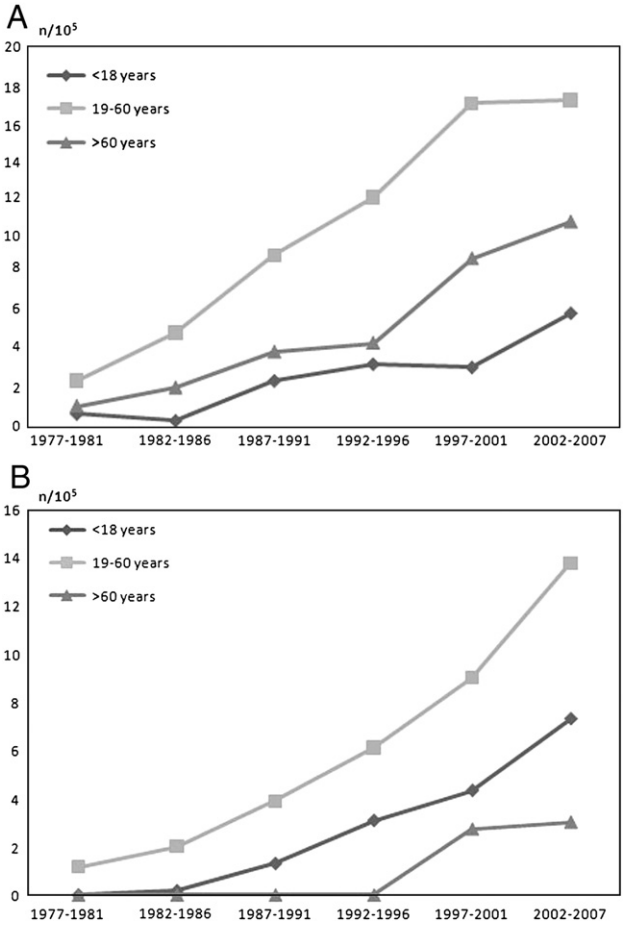

Figure 2 Sex-adjusted incidence of ulcerative colitis (A) and Crohn's disease (B) according to the different age groups in Veszprem Province between 1977 and 2007.

In the elderly CD population, a greater number of patients presented with pure colonic location (elderly:61.9% vs. pediatric:24.3%, $p=0.001$, OR:5.06, 95%CI: 1.81–14.1, and adults:36.8% $p=0.02$, OR:2.79, 95%CI: 1.13–6.88) and stenosing disease (elderly: 42.9% vs. pediatric: 14.9%, $p=0.005$, OR:4.30, 95%CI: 1.47–12.6, and adults 19.5%, $p=0.01$,OR: 3.10, 95% CI: 1.26–7.62) (Table 1).

The rate of change in disease behavior (from B1 to B2/B3 or from B2 to B3) was 0% in the elderly CD population at 5 years, while in the pediatric population, it was 20.3% ($p=0.037$, OR:1.25, 95%CI: 1.10–1.43) and 37.3%, and 19.8% ($p=0.036$, OR: 1.25, 95%CI: 1.18–1.32) and 27.8% in the adult CD population, at 5 and 10 years, respectively. Similar results were found in a Kaplan–Meier analysis (Fig. 3). Smoking at the time of diagnosis (54.4% vs. 14.3%, $p<0.001$) and during follow-up (39.8% vs. 14.3%, $p=0.02$) was more common in the adult population compared to the elderly patients. In a logistic regression analysis, perianal disease (Coefficient: 1.61, $p<0.001$, OR: 5.00, 95%CI: 2.73–9.17), non-colon disease location at diagnosis (Coefficient: 0.84, $p=0.005$, OR: 2.31, 95%CI: 1.28–4.16) but not age at onset ($p=0.3$) were factors associated with disease behavior change at 5 years. In the same analysis, smoking at the

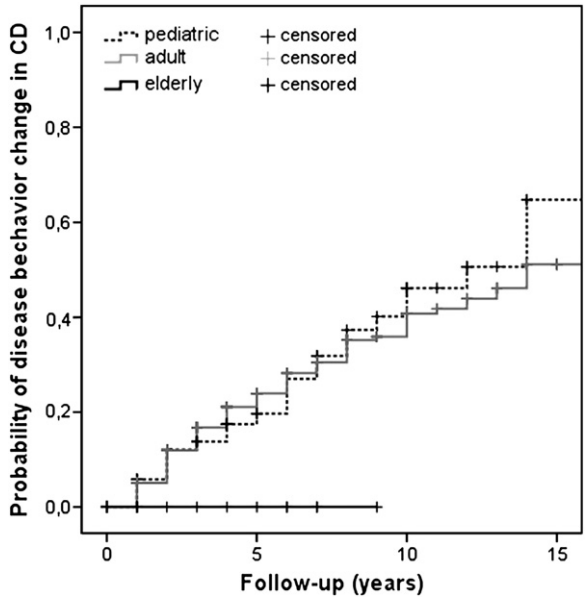

Figure 3 Disease behavior change in patients with Crohn's disease according to the age at onset. $p_{Logrank}=0.05, p_{Breslow}=0.07$ between adult vs. elderly. $p_{Logrank}=0.06, p_{Breslow}=0.08$ between pediatric vs. elderly.

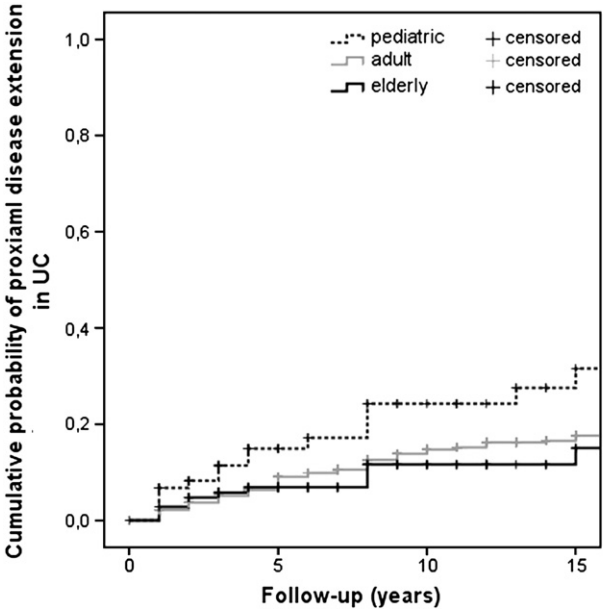

Figure 4 Proximal disease extension in patients with ulcerative colitis according to the age at onset. pLogRank = 0.073, pBreslow = 0.057.

time of diagnosis was close to being significant (Coefficient: 0.53, $p=0.06$, OR: 1.69, 95%CI: 0.98–2.93).

In UC, left-sided disease at diagnosis was more frequent in the elderly (proctitis: 20.7%, left-sided: 61.3%, extensive: 17.9%, $OR_{elderly.vs.pediatric}$: 2.38, 95%CI: 1.30–4.36, $p=0.005$; $OR_{elderly.vs.adults}$: 1.61, 95%CI: 1.06–2.44, $p=0.025$) compared to pediatric and adult patients (pediatric: 22.7%, 40.0% and 37.3%; adults: 26.3%, 49.7% and 24.0%,). In contrast, extensive disease was more frequent in the pediatric patients compared to the elderly ($p=0.003$, OR: 2.73, 95% CI: 1.38–5.41). Proximal extension at 5 and 10 years was observed in 6.6% and 9.4% of elderly patients, while in the pediatric patients it was 13.3% and 18.7%, and 8.6% and 13.0% in the adult patients ($p=$NS), respectively. Similarly, the time to proximal extension was not different in a Kaplan–Meier analysis ($p_{LogRank}=0.073$, $p_{Breslow}=0.057$) (Fig. 4).

Significantly more pediatric UC patients had at least one fulminant episode[18] during follow-up (pediatric: 20%, adult: 8.2% and elderly: 4.7%, $p=0.001$). In a logistic regression analysis, the age at diagnosis (Coefficient: −0.784, $p=0.004$, OR: 0.46, 95%CI: 0.27–0.77) and disease location at the time of diagnosis (Coefficient: 1.024, $p<0.001$, OR: 2.78, 95%CI: 1.93–4.02) were independent predictors of fulminant episodes.

3.3. Need for immunosuppression, surgery, and dysplasia/colorectal cancer in IBD in the elderly

The need for azathioprine was more common in the pediatric and adult CD populations (68.9%, 42.6% vs. 28.6%, $p<0.001$). Similarly, the use of anti-TNF agents was absent in the elderly population, while in the other two patient groups it was 9.5%. In a logistic regression analysis, the age at diagnosis, presence of perianal disease, and disease behavior at diagnosis were independent predictors for the need for immunosuppression during follow-up (Table 2).

Surgical resection rates in CD were 33.8%,30.7% and 28.6% after 5 years in the pediatric, adult and elderly populations ($p=$NS), respectively. However, if we analyzed the risk for surgery in a Kaplan–Meier analysis, in patients with non-stricturing–non-penetrating (B1) disease at diagnosis, age at onset was significantly associated with time to surgery (Fig. 5.). Similarly, age at onset (Hazard ratio (HR):0.41, 95%CI: 0.21–0.79, $p=0.007$), but not smoking at diagnosis ($p=0.08$) or perianal disease ($p=0.19$), was significant predictor for time to surgery in patients with B1 disease in a Cox-regression analysis using the enter method.

In UC, significantly more pediatric (57.3%, $p<0.001$, OR: 6.58; 95%CI: 3.22–12.9) and adult (39.8%, $p<0.001$, OR: 3.24; 95%CI: 1.91–5.49) patients required systemic steroids during follow-up compared to the elderly (17%) population. In a logistic regression analysis, the age at diagnosis

Table 2 Logistic regression: Predictive factors for need for azathioprine therapy in Crohn's disease.

Factor	Coefficient	*P* value	OR	95% CI
Advanced age at diagnosis	−1.012	<0.001	0.36	0.25–0.59
Perianal disease	0.476	0.04	1.61	1.02–2.54
Disease behavior at diagnosis	0.288	0.02	1.33	1.05–1.69
Location	0.177	0.13	1.19	0.95–1.51
Smoking	0.213	0.25	1.24	0.85–1.80

The coefficient is equivalent to the natural log of the OR; *p* value: level of significance.
OR: odds ratio; 95% CI: 95% confidence interval.

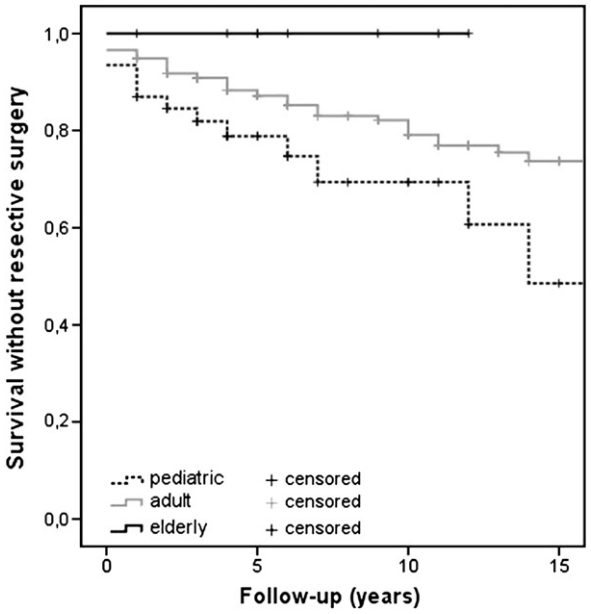

Figure 5 Survival without resective surgery in patients with non-stenosing non-penetrating Crohn's disease behavior at diagnosis, according to the age at onset. $p_{Logrank} = 0.032$, $p_{Breslow} = 0.046$.

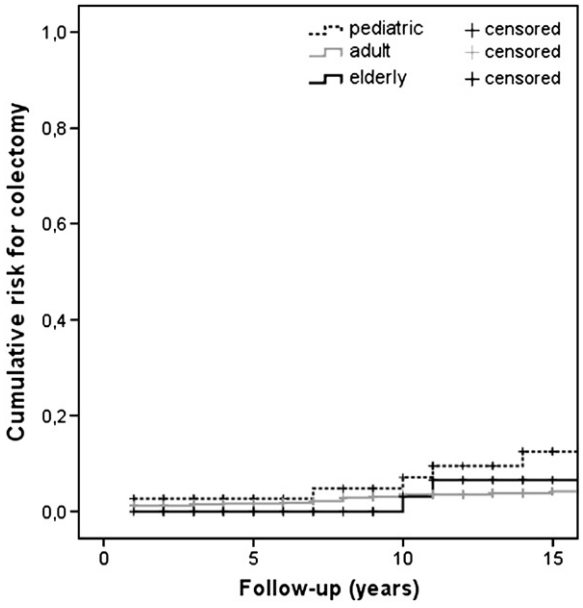

Figure 6 Cumulative probability of colectomy in patients with ulcerative colitis according to the age at onset. pLogRank = 0.073, pBreslow = 0.057.

(Coefficient: −0.930, $p<0.001$, OR: 0.39, 95%CI: 0.28–0.56) and disease location at diagnosis (Coefficient: 1.028, $p<0.001$, OR: 2.80, 95%CI: 2.25–3.47) were independent predictors of need for systemic steroids.

The rate of colectomy due to non-malignant disease was low in all three groups (pediatric: 8.1%; adults: 4.1%, and elderly: 1.9%). The difference between the pediatric and elderly patients was approaching the level of significance ($p = 0.06$). Similarly, in a Kaplan–Meier analysis age at onset was also not a significant determinant of time to colectomy (Fig. 6).

UC-associated dysplasia and cancer were diagnosed in 1.9% and 2.5%, respectively, of UC patients during follow-up; however, we did not find any difference among the various age groups. In contrast, the time to development of UC-associated dysplasia and/or cancer was shorter in the elderly group in a Kaplan–Meier analysis ($p_{LogRank} = 0.032$, $p_{Breslow} = 0.002$, Fig. 7). However, the difference was not significant if cancer cases were analyzed separately (data not shown).

4. Discussion

In the present study, we assessed the time-trends in the incidence of IBD according to the age at diagnosis, and the association between age at diagnosis, disease phenotype, and course of disease in the population-based Veszprem province database, including incident patients diagnosed between 1977 and 2008. The present study has shown that elderly patients represent an increasing proportion of the IBD population. Reviews from population-based samples of patients, including the Olmsted County IBD Database also demonstrated approximately 10% of their cohort as being geriatric.[19] Similarly, in the present study, encompassing a Hungary cohort, we observed a sharp increase in UC (from 1.09/10^5 in 1977–1981 to 10.8/10^5 in 2002–2007) and CD to 3.04/10^5 in 2002–2007. Interestingly, both UC (males: 14.1/10^5 and in females: 8.7/10^5 in 2002–2007) and CD (males: 4.2/10^5 and females: 2.3/10^5 in 2002–2007) was relatively more frequent in elderly males at any time point. In concordance with some previous reports regarding the elderly population,[4] UC affected about twice as many men

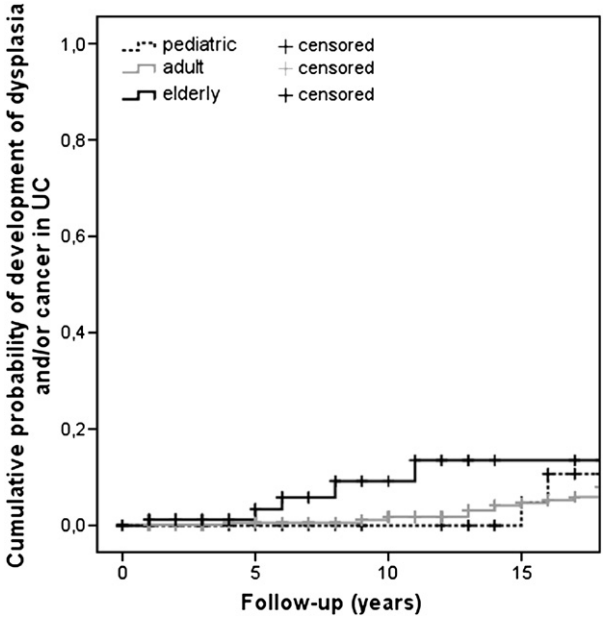

Figure 7 Development of colitis associated dysplasia/cancer in patients with ulcerative colitis according to the age at onset $p_{Logrank} = 0.032$, $p_{Breslow} = 0.002$.

as women throughout the follow-up period (incidence in males/females 1977–1982:1.7/10^5 vs. 0.6/10^5; in 2002–2007: 14.1/10^5 vs. 8.7/10^5).

The clinical characteristics and disease course of the elderly population was compared to other age groups. Age at diagnosis is of interest as a criterion that is available at diagnosis and may separate different disease patterns. Although a better prognosis for CD has been reported in older patients,[2,5,7,20] conflicting data have been obtained regarding the outcomes of late-onset CD. Of note, most studies of older CD patients were conducted in referral centers and were, therefore, open to bias related to greater disease severity. One of the exceptions is a population-based study from Brittany from 2004, where 66% of patients diagnosed at 60 years of age or older had isolated colonic involvement.[2,5] In the same study, the proportion of patients with inflammatory (non-stricturing, non-penetrating) behavior was higher among those diagnosed after the age of 40. Although the overall probabilities for surgery were similar between patients older and younger than 60 years, azathioprine use and the likelihood for hospitalization from a second flare-up were lower in those diagnosed after the age of 60.

Similarly, in the present study, there were more patients with pure colonic location in the CD cohort. However, somewhat unexpected and in contrast to previous reports, we found a significantly higher proportion of stenosing disease in the elderly population at the time of diagnosis. Moreover, a change in disease behavior (from B1 to B2/B3 or from B2 to B3) was significantly less common in the elderly CD (0%) population compared to the pediatric (20.3%, $p=0.037$) and adult (19.8%, $p=0.036$) patients at 5 years. However, significance was lost after adjustment for confounding variables, and in a logistic regression analysis, perianal disease, disease location at diagnosis, smoking at diagnosis but not age at onset were all factors associated with a change in disease behavior at 5 years.

In concordance with an earlier French study,[2] the need for resective surgery was not different amongst the various age groups in CD. How can we explain this? First, there were differences in the proportion of patients with an already complicated disease phenotype at diagnosis (elderly patients B2 or B3: 61.9%, pediatric: 37.8%, adult: 43.1%). Second, the role of medical strategy as a disease modifying factor was suggested first in the pediatric population. In a population-based, incident pediatric CD cohort from France collected between 1988 and 2002,[21] stricturing behavior at diagnosis (HR:2.54) and treatment with corticosteroids (HR:2.98) were associated with increased risk for surgery, whereas treatment with azathioprine (HR:0.51) was associated with a decreased risk in multivariate Cox models. Similarly, in a previous paper, our group has also shown that early AZA/biological therapy reduced the risk for first operation in CD, in both, smokers and non-smokers in a referral adult CD population.[22] A possible limitation of the present study is that the medical strategy has changed during the last decades. Early aggressive administration of immunosuppressants was started systematically only in the mid 1990s, while biologicals became available only in the late 1990s. Nonetheless, the lesser and later use of azathioprine and biologicals might have lead to higher surgical rates in adults and elderly patients. This is supported by the lower risk for resective surgery in a Kaplan–Meier analysis in patients diagnosed between 2002 and 2008 compared to patients diagnosed between 1977 and 2001 (data not shown), and earlier use of azathioprine (total AZA exposure since diagnosis: 44.0% in the first cohort diagnosed between 1977 and 2001 vs. 48% in patients diagnosed between 2002 and 2008). In addition, the probability for a change in disease behavior at 5-years in patients with non-stenosing, non-penetrating (B1) behavior at diagnosis was significantly less in those diagnosed between 2002 and 2008 (14.7%, OR: 0.49, 95%CI: 0.27–0.87, $p=0.013$) compared to those diagnosed between 1977 and 2001 (26.2%). In contrast, the need for systemic steroids did not affect the risk for surgery at 5 years (without steroids: 33.3%, with steroids: 30%). However, if we analyzed the risk for surgery, in patients with non-stricturing–non-penetrating (B1) disease at diagnosis, only the age at diagnosis was significantly associated with time to surgery in a Kaplan–Meier and in a Cox-regression analysis.

Previous studies examining the natural history of UC in elderly patients have yielded conflicting results; some studies suggested that late-onset UC is less aggressive with fewer colectomies,[10,23,24] whereas other studies indicated that disease course and prognosis (including cumulative admission rates, relapse, and surgery rates) were not different between young patients and patients diagnosed above the age of 40 years.[25] In the present study, left-sided disease was predominant in the elderly patients, yet in contrast to some previous reports,[5] we did not notice an extensive increase in the percentage of proctitis cases in the elderly. Of note, the rate of proctitis at diagnosis, in the UC cohort, increased from 15.5% to 28.6% in patients diagnosed before and after 1990 ($p<0.001$), while the rate of extensive colitis remained the same (23.5–27%). Similarly, proximal extension at 5 and 10-years was not significantly different between elderly patients and adults; however, there was a tendency for a higher rate of disease extension at 10 years in patients with a pediatric onset (9.4% vs. 18.7%, $p=0.08$).

The disease course in pediatric UC patients was more aggressive with significantly more patients having at least one fulminant episode during follow-up ($p=0.001$). Similarly, more pediatric ($p<0.001$) and adult ($p<0.001$) patients required systemic steroids during follow-up compared to the elderly population, and age at diagnosis was independently associated with the need for systemic steroid therapy in a logistic regression analysis. Somewhat contradictory, the rate of colectomy due to non-malignant disease was low in all three groups (pediatric: 8.1%; adults: 4.1%; elderly: 1.9%). The difference between pediatric and elderly patients was approaching the level of significance ($p=0.06$).

An important point is the risk of UC-associated dysplasia and cancer. In the present study, UC-associated dysplasia and cancer was diagnosed in 1.9% and 2.5%, respectively, of UC patients during follow-up, but we did not find any difference among the different age groups. In contrast, the time to development of UC-associated dysplasia and/or cancer was shorter in the elderly, supporting the idea that not only the risk for developing sporadic colon polyps increases with age, but acquired genetic mutations already present at the time of diagnosis of UC in the elderly patients, in parallel with the chronic inflammation observed in UC, may lead to the earlier development of UC-associated dysplasia and/or cancer in patients diagnosed above the age of 60 years. Of note, due to

the low absolute number of dysplasia/cancer cases, the statistical power of the present study is low. However, since the incidence of UC in the elderly is relatively high, if confirmed, this may impact the suggested surveillance strategies in elderly patients with UC.

In conclusion, elderly patients represent an increasing proportion of the IBD population. Stenosing and colon-only disease was characteristic for elderly CD patients, with the absence of change in disease behavior and a lower risk for surgery in patients with inflammatory disease. Still, the absolute risk for resective surgery did not vary. In UC, left-sided location and not proctitis was predominant in this elderly population. The disease course in the elderly was milder, with fewer fulminant episodes, less systemic steroid exposure, and a trend for fewer colectomies. On the contrary, although the absolute risk was low, UC-associated dysplasia and/or cancer developed quicker in the elderly patients.

Conflicts of interest

The authors disclose no conflicts.

Acknowledgments

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