Elderly and adult-onset Inflammatory Bowel Disease: 20 years report

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Research Article

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Abstract

Background

Cases of IBD diagnosed after the age of 65 are increasing, due to either an ageing population or a greater awareness of this condition in older patients. This study aims to compare natural history, therapeutical approach, disease and therapy-related complications in elderly and adult patients.

Methods

Patients referring to the IBD-outpatient clinic of the Gastroenterology Unit (Spedali Civili Brescia) that received a diagnosis of IBD after the age of 65 between January 2000 and August 2021 were enrolled and matched 1:1 by disease, sex and year of diagnosis with a patient who received diagnosis between 40 and 64 years of age.

Results

A total of 154 elderly patients (45 Crohn's disease and 109 Ulcerative colitis) were matched with 154 adults.

In Crohn's disease, abdominal pain and diarrhea were more frequent amongst adults; while symptoms at UC presentation were similar. Extraintestinal manifestations were more frequently reported amongst adults (p 0.03). Despite a similar number of relapses in both cohorts, the elderly were more frequently hospitalized.

In CD, the number of patients who faced a surgical approach was similar for both cohorts, but mean time to surgery was significantly lower in the elderly (4.7 vs 28.9 months, p0.03). On the contrary, UC elderly patients faced surgery more frequently (17% vs 8%, p0.07), but mean time from diagnosis was similar. Biological therapy was more common for adults (p<0.05), with a larger use of anti-integrin, despite anti-TNFalfa in elderly-UC patients (70% vs 7%). Intestinal complications and systemic infections were higher amongst the elderly.

Conclusions

Elderly and adult-onset IBD seem to have similar presentation and clinical behavior. However, the elderly present more IBD-related hospitalizations and complications.

Introduction

The incidence of inflammatory bowel disease (IBD) is increasing worldwide with an ageing population causing it to be a rising problem.

Moreover, because mortality from IBD is only slightly increased, its prevalence amongst older people is expected to increase.
Data on natural history and therapeutic strategies in the elderly are controversial and derive mostly from observational studies, as old people are often excluded from clinical trials.  

There is no uniformity surrounding the age that defines elderly-onset IBD, with some studies indicating over 50, others over 60 and others 65.

Additionally, there are two different groups of elderly affected by IBD: individuals with elderly-onset IBD and patients diagnosed with IBD at an earlier age who have become old.

In research studies, these two different sets of populations have not always been evaluated separately. Thus, a distinction is important to better define the characteristics of elderly-onset IBD.

Therefore, the aim of this study was to compare disease presentation, clinical course, therapeutic approach and disease- and therapy-related complications between elderly-onset IBD (EO-IBD) and adult-onset IBD (AO-IBD) over a prolonged follow up period.

**Methods**

From January 2000 to August 2021, patients with an established diagnosis of IBD (UC or CD) were identified using the clinical database of the IBD outpatient clinic of the Gastroenterology Unit of Spedali Civili Brescia (Italy).

Age at diagnosis was used to categorize patient into elderly-onset and adult-onset IBD groups.

Patients receiving IBD diagnosis after the age of 65 were enrolled and defined as elderly-onset IBD (case group). Each patient was matched 1:1 according to diagnosis (UC or CD), sex and year of diagnosis, with a patient who received a diagnosis of IBD between 40 and 64 years (adult-onset IBD; control group).

The initial diagnosis of IBD was confirmed by clinical, biochemical, radiological, endoscopic and histologic assessment.

Demographic information, clinical characteristics at disease onset, comorbidity, disease course, medical and surgical history, disease- and therapy-related complications were all analyzed.

Patients without a follow-up visit within the final year of data collection were contacted by telephone and invited to a follow-up visit.

Statistical analysis was conducted using the statistical software package Graphpad 9.0.

Descriptive variables were reported as numbers and percentages for categorical variables; while mean/standard deviation or median/interquartile ranges were used for continuous variables. Categorical data were compared between cohorts using two-sided Fisher's exact test or Pearson's chi-square test, as appropriate.
Paired t-test was used to compare continuous variables with a normal distribution between cohorts. P-value $\leq 0.05$ was considered significant.

Ethical Committee of Spedali Civili Hospital in Brescia granted ethical approval for this study.

**Results**

**Demographic information and risk factors at the time of IBD diagnosis**

Between January 2000 and August 2021, a total of 154 patients were identified as elderly-onset IBD. Amongst them, 45 were elderly-onset CD and 109 elderly-onset UC. Each patient in this cohort was matched for year of diagnosis, diagnosis (CD or UC) and gender with a patient diagnosed with IBD from 40 to 64 years (adult-onset IBD). Therefore, a total of 308 patients were included in this study.

The two cohorts were therefore homogeneous for disease, gender and length of follow-up.

Demographic data and patient characteristics’ at IBD diagnosis stage are reported in Table 1 for CD and UC. Patients with adult-onset CD were more likely to be current smokers compared to elderly onset-CD (46% vs 14%; $p = 0.0013$), while no differences were found between elderly and adult-onset UC. There were no differences for family history of IBD between the cohorts.
### Table 1
patients’ characteristics at diagnosis

<table>
<thead>
<tr>
<th></th>
<th>CD</th>
<th>UC</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Elderly (≥ 65 yrs)</td>
<td>Adults (40–64 years)</td>
</tr>
<tr>
<td>N pts</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Mean age (yrs) (SD)</td>
<td>71.3 (4.7)</td>
<td>48.6 (6.6)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>18 (40)</td>
<td>18 (40)</td>
</tr>
<tr>
<td>Mean length follow up (yrs) (SD)</td>
<td>7.3 (5.1)</td>
<td>8.1 (5.7)</td>
</tr>
<tr>
<td>Misdiagnosis, N (%)</td>
<td>23 (52.3)</td>
<td>19 (43.2)</td>
</tr>
<tr>
<td>Diarrhea, N (%)</td>
<td>18 (40)</td>
<td>27 (61.4)</td>
</tr>
<tr>
<td>Weight loss, N (%)</td>
<td>14 (31.1)</td>
<td>9 (20.5)</td>
</tr>
<tr>
<td>Proctorrhagia, N (%)</td>
<td>6 (13.3)</td>
<td>8 (18.2)</td>
</tr>
<tr>
<td>Abdominal pain, N (%)</td>
<td>22 (48.9)</td>
<td>31 (70.5)</td>
</tr>
<tr>
<td>Mortality, N (%)</td>
<td>11 (24.4)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>CIRS com</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3 (6.7)</td>
<td>25 (59.1)</td>
</tr>
<tr>
<td>2</td>
<td>8 (17.8)</td>
<td>15 (34.1)</td>
</tr>
<tr>
<td>≥ 3</td>
<td>34 (75.6)</td>
<td>3 (6.8)</td>
</tr>
<tr>
<td>Median CIRS sev, (SD)</td>
<td>1.6 (0.3)</td>
<td>1.3 (0.1)</td>
</tr>
</tbody>
</table>

### Clinical Characteristics At The Time Of IBD Diagnosis

Disease presentation and symptoms severity at the time of diagnosis were compared between elderly and adult cohorts. Mean times from first symptoms to IBD diagnosis were similar within the cohorts, but much longer for CD than for UC.
In Crohn's disease, abdominal pain was more frequent in adult-onset CD than in elderly-onset CD (70% vs 49%, p 0.05), while there were no differences for proctorrhagia, extra-intestinal manifestations, weight-loss, fever or anemia.

Although not significant, abdominal pain was more frequent in adult-onset UC than in elderly-onset UC (24% vs 14%, p 0.08). No differences were present for diarrhea, proctorrhagia, abdominal pain, extra-intestinal manifestations, fever or anemia.

Associated diverticulosis was significantly more frequent amongst elderly-onset IBD, both for CD (57% vs 13% p < 0.00001) and UC (58% vs 18% p < 0.0001).

At the time of diagnosis, elderly-onset IBD were more likely to have comorbidities than adult-onset IBD. That is, 76% of elderly-onset CD had a CIRS comorbidity index ≥ 3 vs 7% of adults (p < 0.0001), while for UC patients it was 66% vs 17%, p < 0.0001.

**Disease Course And Treatment**

Disease course and treatment are summarized in Table 2.
Table 2
disease course, surgery and biological therapy

<table>
<thead>
<tr>
<th></th>
<th>CD</th>
<th>UC</th>
<th>P value</th>
<th>CD</th>
<th>UC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Elderly (≥ 65 yrs)</td>
<td>Adults (40–64 years)</td>
<td>P value</td>
<td>Elderly (≥ 65 yrs)</td>
<td>Adults (40–64 years)</td>
<td>P value</td>
</tr>
<tr>
<td>N pts</td>
<td>45</td>
<td>45</td>
<td></td>
<td>109</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>EIM, N (%)</td>
<td>13 (28.9)</td>
<td>24 (53.3)</td>
<td>0.03</td>
<td>9 (8.3)</td>
<td>21 (19.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Median time to first relapse, months (SD)</td>
<td>10.4 (11.6)</td>
<td>19.9 (29.9)</td>
<td>0.17</td>
<td>21.9 (30.7)</td>
<td>25.4 (40.4)</td>
<td>0.57</td>
</tr>
<tr>
<td>Relapse, N (%)</td>
<td></td>
<td></td>
<td>0.08</td>
<td></td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>0</td>
<td>22 (48.9)</td>
<td>18 (40)</td>
<td></td>
<td>42 (38.5)</td>
<td>39 (35.8)</td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>17 (37.8)</td>
<td>12 (26.7)</td>
<td></td>
<td>50 (45.9)</td>
<td>49 (45)</td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>6 (13.3)</td>
<td>15 (33.3)</td>
<td></td>
<td>17 (15.6)</td>
<td>21 (19.3)</td>
<td></td>
</tr>
<tr>
<td>Surgery, N (%)</td>
<td>18 (40)</td>
<td>22 (48.9)</td>
<td>0.52</td>
<td>19 (17.4)</td>
<td>9 (8.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>Mean time to surgery, months (SD)</td>
<td>4.7 (12.2)</td>
<td>28.9 (40.1)</td>
<td>0.03</td>
<td>23.3 (35.5)</td>
<td>25.3 (22.4)</td>
<td>0.88</td>
</tr>
<tr>
<td>Biological therapy, N (%)</td>
<td>5 (11.4)</td>
<td>18 (40)</td>
<td>0.003</td>
<td>10 (9.2)</td>
<td>28 (25.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>Anti-TNFα, N (%)</td>
<td>2 (4.5)</td>
<td>16 (35.6)</td>
<td></td>
<td>3 (30)</td>
<td>26 (92.9)</td>
<td></td>
</tr>
<tr>
<td>Anti-integrin, N (%)</td>
<td>3 (6.8)</td>
<td>2 (4.4)</td>
<td></td>
<td>7 (70)</td>
<td>2 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Intestinal complications, N (%)</td>
<td>21 (47.7)</td>
<td>23 (51.1)</td>
<td>0.83</td>
<td>22 (20.4)</td>
<td>10 (9.2)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Disease course and the therapeutic approach during the follow-up period were compared for the elderly and adult cohorts. Adult patients were found to have developed extra-intestinal manifestations significatively more frequently than elderly patients (29% vs 53%, p 0.03 for CD; 9% vs 20%, p 0.03 for UC).

Median time to first relapse did not differ between the two groups.

There was no difference in frequency of surgery for CD. However, Kaplan-Meyer analysis for mean time to surgery demonstrated that it occurred significatively earlier in the elderly (4.7 vs 28.9 months, p 0.03) (Fig. 1).

Although not significant, surgery was more frequent amongst elderly-UC than adult-UC (17% vs 9%, p 0.07), while there was no difference between cohorts for time to surgery.
Therapy for the induction of remission at the time of diagnosis of IBD was similar for elderly- and adult-onset CD and UC. In both groups, steroids was the most prescribed therapy at the time of diagnosis of CD, while 5-ASA was the most frequently prescribed at UC diagnosis.

No difference in terms of 5-ASA and immunosuppressant use for maintenance was present between groups.

Biological therapy was used more in adult than in elderly-onset IBD (11% vs 40%, p 0.003 for CD; 9% vs 26%, p 0.002 for UC).

### Hospitalizations And Complications

Hospitalizations and therapy-related complications are summarized in Table 3.

<table>
<thead>
<tr>
<th></th>
<th>Elderly (≥ 65 yrs)</th>
<th>Adults (40–64 years)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N pts</td>
<td>154</td>
<td>154</td>
<td></td>
</tr>
<tr>
<td>Adverse reactions, N (%)</td>
<td>10 (6.5)</td>
<td>20 (13)</td>
<td>0.08</td>
</tr>
<tr>
<td>Drug-related complications, N (%)</td>
<td>47 (30.5)</td>
<td>40 (26)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hospitalizations, N (%)</td>
<td>96 (62.3)</td>
<td>71 (46.1)</td>
<td>0.006</td>
</tr>
<tr>
<td>Infections + biological therapies</td>
<td>17 (54.8)</td>
<td>20 (37.7)</td>
<td>0.73</td>
</tr>
<tr>
<td>Infections no biological therapy</td>
<td>38 (30.9)</td>
<td>19 (18.8)</td>
<td>0.008</td>
</tr>
<tr>
<td>Biological therapy start before 2016</td>
<td>1 (0.7)</td>
<td>21 (13.6)</td>
<td>0.006</td>
</tr>
<tr>
<td>Biological therapy start post-2016</td>
<td>14 (9.1)</td>
<td>25 (16.2)</td>
<td></td>
</tr>
</tbody>
</table>

IBD-related hospitalizations were more common amongst the elderly; 62% vs 46% of adults (p 0.006) had at least one IBD-related hospitalization during the follow-up period (Fig. 2).

Intestinal complications (such as strictures, fistulas and abscess) were similar for elderly- and adult-onset CD (48% vs 51%, p 0.83), but were higher for elderly UC patients (20% vs 9%, p = 0.02). Systemic infections occurred equally amongst both elderly and adult patients. However, subgroup analysis of patients without biological therapy, revealed it to be more prevalent amongst older patients (31% vs 19%, p = 0.008).

Drug-related complications did not differ between the two groups (31% vs 26%, p = 0.45)
Although biological therapy is still significantly less used in the elderly, this trend has changed over the last five years. Before 2016, only one elderly IBD patient was treated with biological drugs compared to 14 patients after 2016. This trend is not repeated for adults (21 before 2016 and 25 after).

Unexpectedly, adverse drug reactions were more common amongst adult-onset IBD (7% vs 13%, p = 0.08). However, most of adverse drug reactions encountered were caused by antiTNFα agents, which were seldom used among elderly patients.

**Discussion**

Incidence and prevalence of IBD in elderly patients is rising worldwide.

Considering the frailty of this population, clinical management of older people affected by IBD necessitates the balancing risk of disease with treatment-related complications.

This prospective-retrospective observational study (parallel cohort study) compared elderly- and adult-onset IBD, evaluating clinical features at the moment of diagnosis, natural history, IBD-related hospitalizations, therapeutic strategies, and complications related to the disease or to therapy during a mean follow up period of 21 years.

Our findings lead us to make some recommendations that may assist the clinical management of IBD in the elderly.

Regarding risk factors for the development of IBD, we did not find any difference in terms of family history of IBD. It has been suggested that genetic factors may influence the development of early-onset IBD, but such studies encompassed a pediatric or young control group, while this control group was composed of adult patients, with IBD onset between 40 and 64 years.

Therefore, we observed no difference in term of genetic predisposition or risk factors. As shown in other studies, clinical features of elderly-onset IBD are generally similar to those of adult patients, although some differences may arise.

There was no difference for symptoms that lead to a diagnosis of IBD, except for abdominal pain, which was more common amongst adults, both for UC and CD, respectively. This unreported abdominal pain in the elderly might be due to decreased intestinal motility or better ability to tolerate pain.

The clinical course for elderly-onset IBD was evaluated considering time to first relapse post disease onset, number of relapses, number of IBD-related hospitalizations, need for surgery and mean time to surgery post follow-up.

Time to first relapse was similar regardless of the initial therapy used to induce remission. Moreover, frequency of disease flares did not differ either, which might suggest that disease behavior was similar in both cohorts, both for CD and UC. Although elderly-onset IBD course is often thought to be milder
severity $^{22,5,23}$ results are controversial with some population-based studies suggesting that elderly-onset IBD may have a course similar to adult-onset IBD $^{6,7}$, as this study found.

Other studies evaluating the clinical course of IBD in the elderly have yielded conflicting results. Some suggest that the natural history of elderly-onset IBD is less aggressive than for younger patients $^{17,8,24,19,25}$, while others found a similar clinical course $^{26,10}$. This heterogeneity could be, in part, due to a lack of uniformity surrounding the age defining elderly-onset IBD and the age of the control group in different studies $^{27}$. In the present study, like other authors $^{28}$, we defined elderly-onset IBD as after the age of 65, which is the conventional threshold defining geriatric age, but several other ages have been used in other studies, for example over 50 years $^{19}$, over 60 years $^{3,8,29}$ and over 70 years $^{30}$.

In accordance with previous studies $^{3,8,5}$ we found that, for CD, the need for surgery did not differ between EO-CD and AO-CD, while time to surgery was significantly shorter for elderly patients.

Due to biological therapy use being significantly more frequent in adults, it is possible that the lack of usage of these drugs in the elderly could give rise to an earlier necessity for surgery. On the other hand, it might imply a longer asymptomatic phase of the disease, which gives rise to surgery earlier following diagnosis. Similarly to other authors $^{8,10,31}$, we did not find any differences in terms of surgery for UC. Time to surgery did not differ in UC for either cohort, which might support a recommendation not to delay surgery in the elderly. In fact, it has been shown that in the elderly UC complications and mortality are higher when surgery is delayed $^{32}$.

Despite a similar clinical course and number of relapses, EO-IBD were more likely to be hospitalized due to IBD relapse. As geriatric patients tend to have functional impairment and increased numbers of comorbidities, they might need hospitalization more frequently, due to their frailty, independent of the severity of the relapse. In our study, comorbidities were significatively more frequent amongst elderly (CIRS), which might explain the higher number of IBD-related hospitalizations. This finding is consistent with what has previously been described by Nguyen et al., regarding the annual cost of IBD-related hospitalizations, which are significatively higher in EO-IBD than AO-IBD $^{12}$.

The therapeutic strategy for the induction of remission at the time of diagnosis was similar for both groups, while maintenance therapy was different with biological/anti-TNFα used almost exclusively in adult patients. This result is consistent with previous studies $^{26,13}$; and might reflect physician concern with adverse effects and the risk of infection in the elderly $^{14,1,15,16}$. Compared to younger patients, elderly patients have immunodeficiency, higher cancer risk, detrimental polypharmacy and altered drug metabolism. This might raise concerns for clinicians regarding the use of immunosuppressing agents, biological therapies and standard dose therapy $^{33}$.

A study suggested that elderly patients hospitalized with IBD were less likely to receive immunomodulators and/or biological agents during hospitalization or before admission compared with younger IBD patients. $^{34}$
Indeed, little is known about the safety of biological agents in elderly IBD patients, as most trials exclude IBD patients over 60 years. Some studies have reported that ageing is a risk factor for serious infections in IBD patients receiving biological drugs. We found that, in the subgroup of IBD patients with no biological therapy, infections were significantly more frequent among elderly-onset IBD than adult-onset IBD.

Old age itself is related to an increased risk of serious infection among patients with IBD.

Moreover, biological therapy is related to an increased risk of infection in the elderly, compared to older or younger patients not receiving such therapies. Therefore, the infection risk in this population needs to be taken into account when biological therapy is prescribed in elderly-onset IBD, and all the precautions to minimize risks, such as appropriate vaccination, need to be implemented.

Biological therapy has been also associated with risk of malignancy, and older age is an independent risk factor for the development of cancer. Thus, concerns have been raised surrounding biological therapy for older patients, in particular those with a history of cancer.

However, newer and more selective biological therapies have been approved recently. Due to its gut-selective anti-inflammatory action, vedolizumab is considered to be safe both for the risk of cancer onset/recurrence and for non-intestinal infections.

Real-life studies for ustekinumab also show promising results in this age group.

Overall, the results of our study suggest that elderly-onset IBD could have a clinical presentation and a natural history similar to adult-onset IBD. There are some peculiarities in the clinical presentation and natural history of the disease, but, all in all, natural history of elderly-onset IBD does not appear to be less aggressive than adult-onset IBD. On the other hand, patients’ characteristics are different: elderly patients are more likely to present comorbidities and poly-pharmacotherapy, they are more prone to medical complications and have increased susceptibility to infections and steroid-related side-effects. All these factors have to be considered when treating elderly-onset IBD. In particular, the management of elderly-onset IBD requires the evaluation of the disease burden, balancing safety and efficacy of treatment. Further studies encompassing elderly-onset IBD subjects are needed to understand the natural history of the disease, while randomized controlled trials, including elderly IBD patients, are required to achieve the best management of IBD in this growing segment of the population.

**Abbreviations**

IBD: inflammatory bowel disease

CD: Crohn's disease

UC: Ulcerative colitis
CIRS: cumulative illness rating scale
AO: adult onset
EO: elderly onset

**Declarations**

**Ethics approval and consent to participate**

Ethical approval for this study was granted by the Brescia Province Ethics Committee, Spedali Civili of Brescia (10/12/2016). Written informed consent was obtained from all patients. All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

**Consent for publication**

Not applicable.

**Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author, on reasonable request.

**Competing interest**

The authors declare that they have no competing interests.

**Funding**

No funding was received for this study.

**Authors’ Contributions**

Study design and idea: CP, IZ, FL, CR
Data acquisition: CP, IZ
Analysis of data: CP, IZ
Writing of manuscript: CP, IZ, FL, CR
Revision of manuscript: CP, IZ, FL, CR

All authors have read and approved the manuscript in its current state.

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Not applicable.

References


**Figures**

![Figure 1](image)

**Figure 1**

Time to surgery (Crohn's disease) $p = 0.03$
Figure 2

IBD-related hospitalizations