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Alimentary Tract

Disease patterns in late-onset ulcerative colitis: Results from the IG-IBD "AGED study"

Walter Fries[a,*], Anna Viola[a,1], Natalia Manetti[b], Iris Frankovic[c], Daniela Pugliese[d], Rita Monterubbianesi[e], Giuseppe Scalisi[f], Annalisa Aratari[g], Laura Cantoro[h], Maria Cappello[i], Leonardo Samperi[j], Simone Saibeni[k], Giovanni Casella[l], Giammarco Mocci[m], Matilde Rea[n], Federica Furfaro[o], Antonella Contaldo[p], Andrea Magarotto[q], Francesca Calella[s], Francesco Manguso[t], Gaetano Inserra[j], Antonino C. Privitera[u], Mariabeatrice Principi[p], Fabiana Castiglione[n], Flavio Caprioli[q,r], Sandro Ardizzone[v], Silvio Danese[w,x], Claudio Papi[g], Fabrizio Bossa[f], Anna Kohn[e], Alessandro Armuzzi[d], Renata D'Incà[c], Vito Annese[b], Angela Alibrandi[y], Stefanos Bonovas[w], Gionata Fiorino[w], on behalf of the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD)

[a] *Clinical Unit for Chronic Bowel Disorders, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy*
[b] *Gastroenterology Unit, University Hospital Careggi, Florence, Italy*
[c] *Gastroenterology Unit, Department of Surgical, Oncological, and Gastroenterological Sciences, University of Padua, Padua, Italy*
[d] *IBD Unit Complesso Integrato Columbus, Fondazione Policlinico Gemelli Università Cattolica, Rome, Italy*
[e] *Gastroenterology Unit, A.O. San Camillo Forlanini, Rome, Italy*
[f] *Div. of Gastroenterology, IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Foggia, Italy*
[g] *Gastroenterology Unit, San Filippo Neri Hospital, Rome, Italy*
[h] *Gastroenterology Unit, Campus BioMedico, University of Rome, Rome, Italy*
[i] *UOC Gastroenterologia ed Epatologia, A.O.U. Policlinico, Palermo, Italy*
[j] *Internal Medicine, Department of Medical and Pediatric Sciences, University of Catania, Catania, Italy*
[k] *U.O. Gastroenterologia, Ospedale di Rho, ASST Rhodense, Italy*
[l] *Dipartimento di Medicina Ospedale Desio, Dipartimento di Medicina, Desio, MB, Italy*
[m] *SC Gastroenterologia Ospedale "Brotzu", Cagliari, Italy*
[n] *Gastroenterology, "Federico II" University, Naples, Italy*
[o] *Gastroenterology and IBD-Unit, Luigi Sacco University Hospital, Milan, Italy*
[p] *Gastroenterology Section (D.E.T.O.), University of Bari, Bari, Italy*
[q] *Gastroenterology and Endoscopy Unit, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico, Milan, Italy*
[r] *Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy*
[s] *Gastroenterology, Ospedale San Giuseppe, Azienda USL11, Empoli, Firenze, Italy*
[t] *UOSC of Gastroenterology and Endoscopy, AORN "A. Cardarelli", Naples, Italy*
[u] *IBD Unit Azienda Ospedaliera per l'Emergenza "Cannizzaro", Catania, Italy*
[v] *Gastroenterology and Digestive Endoscopy, ASST Fatebenefratelli Sacco, University of Milan, Milan, Italy*
[w] *IBD Center, Department of Gastroenterology, Humanitas Research Hospital, Rozzano, Milan, Italy*
[x] *Department of Biomedical Sciences, Humanitas University, Rozzano, Milan, Italy*
[y] *Department of Economics, University of Messina, Messina, Italy*

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ABSTRACT

Background: Late-onset UC represents an important issue for the near future, but its outcomes and relative therapeutic strategies are yet poorly studied.
Aim: To better define the natural history of late-onset ulcerative colitis.

* Corresponding author at: IBD-UNIT, Clinical Division for Chronic Bowel Disorders, Dept. of Clinical and Experimental Medicine, Via Consolare Valeria 1, 98125 Messina, Italy.
E-mail address: fwalter@unime.it (W. Fries).
[1] Anna Viola shares first authorship with Walter Fries.

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Methods: In a multicenter retrospective study, we investigated the disease presentation and course in the first 3 years in 1091 UC patients divided into 3 age-groups: diagnosis ≥65 years, 40–64 years, and <40 years. Disease patterns, medical and surgical therapies, and risk factors for disease outcomes were analyzed.
Results: Chronic active or relapsing disease accounts for 44% of patients with late-onset UC. Across all age-groups, these disease patterns require 3–6 times more steroids than remitting disease, but immunomodulators and, to a lesser extent, biologics are less frequently prescribed in the elderly. Advanced age, concomitant diseases and related therapies were found to be inversely associated with the use of immunomodulators or biologics, but not with surgery.
Conclusions: The conclusion that late-onset UC follows a mild course may apply only to a subset of patients. an important percentage of elderly patients present with more aggressive disease. Since steroid use and surgery rates did not differ in this subgroup, lower use of immunosuppressive therapy and biologics may reflect concerns in prescribing these therapies in the elderly.

1. Introduction

The natural history of the late-onset ulcerative colitis (UC), i.e., diagnosed at or above 65 years of age, is not well-defined. Disease course, response to therapy, prognosis, and outcomes comparing populations with late- and early-onset of disease have been investigated in several studies with conflicting results [1–4].

Epidemiological studies have shown that late-onset is observed in 8–11% of all UC patients[1,2,4,5]; thus, together with the rise of the overall incidence of UC, a large population of elderly patients should be expected to be diagnosed in the upcoming decades. No trial data, on treatment-specific issues, are currently available for the elderly patients [6], regarding response to treatments or harm. The only available data come from observational studies. Based on these studies, late-onset UC seems to be characterized by a milder disease-course, better response to steroids [7], lower rates of disease progression, and lesser need for immunomodulators (IMM) or biologics (BIO) [1,8]. However, the less frequent use of IMM or BIO in the elderly, as compared to younger populations, may also reflect safety concerns limiting their prescription by the physicians. Currently, frequent severe infections and less favorable outcomes have been reported in elderly patients treated with anti-TNF treatments [9,10], as well as frequent adverse events in patients on thiopurines, e.g., skin cancer or lymphoproliferative diseases [11,12]. It is also well-documented that elderly UC patients have more disease-related hospitalizations as compared to younger patients [13,14], and higher post-surgical morbidity and mortality [15–19].

The aim of the Assessment of IBD in Geriatric patients and Evolution of Disease (AGED)-study was to assess the differences in disease severity and extension at UC onset in 3 different age-groups (i.e., diagnosis ≥65 years, 40–64 years, and <40 years of age), and to compare the disease-course and patterns in the first 3 years following diagnosis.

2. Methods

The AGED-study is a multicenter retrospective cohort study conducted by the Italian Group for the study of IBD (IG-IBD) in 20 referral centers across Italy. Consecutive subjects diagnosed with UC between 2005 and 2010, according to established endoscopic and histological criteria [20], were included. Patients were categorized into three age-groups: (a) diagnosis ≥65 years, (b) 40–64 years, and (c) diagnosis <40 years of age. The following data were analyzed: time to diagnosis (defined as the time interval between symptom-onset and definite diagnosis), smoking status (current, never, and ex-smokers), haemoglobin and C-reactive protein (CRP) levels at diagnosis, extension of disease at diagnosis according to the Montreal classification [21] and severity of disease according to the endoscopic Mayo subscore [22] at onset and during the follow-up. In addition, data on previous and/or concomitant extra-intestinal manifestations (EIM) and concomitant diseases, expressed as the Charlson Comorbidity Index (CCI) [23], were collected. In the follow-up period, therapy with mesalazine (5-ASA), steroids (systemic or low bioavailability steroids; LBS), IMM therapy (thiopurines or methotrexate), BIO (anti-TNFs), and colonic surgery rates were reviewed. Response to steroids in the first year was defined as no further prescription of steroids, or therapy with IMM, BIO, or surgery in the subsequent 12 months, after the first course of steroids. Response to IMM was defined as no further prescription of steroids, BIO or UC-related surgery after initiation of therapy with IMM or no discontinuation of IMM due to adverse effects. Moreover, the disease pattern was categorized, at the end of the observation period, as follows:

- *Pattern 1*: disease onset and subsequent mild or no activity,
- *Pattern 2*: relapsing behavior (more than one flare per year, with remission time >3 months),
- *Pattern 3*: chronically active disease, defined as no remission lasting more than 3 months.

Assessment of the disease patterns was performed according to Henriksen et al. [24], excluding patients colectomized within the first year, or patients lost to follow-up after the first year.

Data regarding the disease-onset and response to steroids, were analyzed and compared among the 3 study-groups, whereas the follow-up data over 3 years were analyzed by disease pattern and compared between *pattern 1* and pooled *patterns 2 and 3*.

The study protocol was approved by the IG-IBD scientific committee and subsequently by the local ethics committee of the coordinating center (Messina, Protocol no. 02/2013; February 25th, 2013). Data were collected and handled anonymously according to the national law on data protection.

2.1. Statistical methods

Descriptive statistics are presented as means ± standard deviations (SD), medians and ranges, or percentages when appropriate. Variables were non-normally distributed; thus, non-parametric tests (the Pearson's chi-squared; the Fisher's exact; and the Kruskal–Wallis rank test) were used for the statistical evaluations. Logistic regression analysis was carried out to identify risk factors for immunosuppression, or colonic surgery. We followed a standard approach for model selection. In the univariable analysis, a criterion of P less than or equal to 0.05 was used to identify candidate predictors. Then, we fitted multivariable models and used backwards selection procedure to eliminate those variables not sig-