

World Journal of *Clinical Cases*

World J Clin Cases 2022 October 26; 10(30): 10823-11213



Contents

Thrice Monthly Volume 10 Number 30 October 26, 2022

REVIEW

- 10823** New insights into the interplay between intestinal flora and bile acids in inflammatory bowel disease
Zheng L
- 10840** Role of visfatin in obesity-induced insulin resistance
Abdalla MMI

MINIREVIEWS

- 10852** Hyperthermic intraperitoneal chemotherapy and colorectal cancer: From physiology to surgery
Ammerata G, Filippo R, Laface C, Memeo R, Solaini L, Cavaliere D, Navarra G, Ranieri G, Currò G, Ammendola M
- 10862** New-onset diabetes secondary to acute pancreatitis: An update
Yu XQ, Zhu Q
- 10867** Ketosis-prone diabetes mellitus: A phenotype that hospitalists need to understand
Boike S, Mir M, Rauf I, Jama AB, Sunesara S, Mushtaq H, Khedr A, Nitesh J, Surani S, Khan SA
- 10873** 2022 Monkeypox outbreak: Why is it a public health emergency of international concern? What can we do to control it?
Ren SY, Li J, Gao RD

ORIGINAL ARTICLE

Retrospective Cohort Study

- 10882** Clinical characteristics and prognosis of non-small cell lung cancer patients with liver metastasis: A population-based study
Wang JF, Lu HD, Wang Y, Zhang R, Li X, Wang S

Retrospective Study

- 10896** Prevalence and risk factors for *Candida* esophagitis among human immunodeficiency virus-negative individuals
Chen YH, Jao TM, Shiue YL, Feng IJ, Hsu PI
- 10906** Prognostic impact of number of examined lymph nodes on survival of patients with appendiceal neuroendocrine tumors
Du R, Xiao JW

Observational Study

- 10921** Clinical and epidemiological features of ulcerative colitis patients in Sardinia, Italy: Results from a multicenter study
Magri S, Demurtas M, Onidi MF, Picchio M, Elisei W, Marzo M, Miculan F, Manca R, Dore MP, Quarta Colosso BM, Cicu A, Cugia L, Carta M, Binaghi L, Usai P, Lai M, Chicco F, Fantini MC, Armuzzi A, Mocci G

- 10931** Clinical observation of laparoscopic cholecystectomy combined with endoscopic retrograde cholangiopancreatography or common bile duct lithotripsy

Niu H, Liu F, Tian YB

Prospective Study

- 10939** Patient reported outcome measures in anterior cruciate ligament rupture and reconstruction: The significance of outcome score prediction

Al-Dadah O, Shepstone L, Donnell ST

SYSTEMATIC REVIEWS

- 10956** Body mass index and outcomes of patients with cardiogenic shock: A systematic review and meta-analysis

Tao WX, Qian GY, Li HD, Su F, Wang Z

META-ANALYSIS

- 10967** Impact of being underweight on peri-operative and post-operative outcomes of total knee or hip arthroplasty: A meta-analysis

Ma YP, Shen Q

- 10984** Branched-chain amino acids supplementation has beneficial effects on the progression of liver cirrhosis: A meta-analysis

Du JY, Shu L, Zhou YT, Zhang L

CASE REPORT

- 10997** Wells' syndrome possibly caused by hematologic malignancy, influenza vaccination or ibrutinib: A case report

Šajin M, Luzar B, Zver S

- 11004** Giant cutaneous squamous cell carcinoma of the popliteal fossa skin: A case report

Wang K, Li Z, Chao SW, Wu XW

- 11010** Right time to detect urine iodine during papillary thyroid carcinoma diagnosis and treatment: A case report

Zhang SC, Yan CJ, Li YF, Cui T, Shen MP, Zhang JX

- 11016** Two novel mutations in the *VPS33B* gene in a Chinese patient with arthrogryposis, renal dysfunction and cholestasis syndrome 1: A case report

Yang H, Lin SZ, Guan SH, Wang WQ, Li JY, Yang GD, Zhang SL

- 11023** Effect of electroacupuncture for Pisa syndrome in Parkinson's disease: A case report

Lu WJ, Fan JQ, Yan MY, Mukaeda K, Zhuang LX, Wang LL

- 11031** Neonatal Cri du chat syndrome with atypical facial appearance: A case report

Bai MM, Li W, Meng L, Sang YF, Cui YJ, Feng HY, Zong ZT, Zhang HB

- 11037** Complete colonic duplication presenting as hip fistula in an adult with pelvic malformation: A case report

Cai X, Bi JT, Zheng ZX, Liu YQ

- 11044** Autoimmune encephalitis with posterior reversible encephalopathy syndrome: A case report
Dai SJ, Yu QJ, Zhu XY, Shang QZ, Qu JB, Ai QL
- 11049** Hypophysitis induced by anti-programmed cell death protein 1 immunotherapy in non-small cell lung cancer: Three case reports
Zheng Y, Zhu CY, Lin J, Chen WS, Wang YJ, Fu HY, Zhao Q
- 11059** Different intraoperative decisions for undiagnosed paraganglioma: Two case reports
Kang D, Kim BE, Hong M, Kim J, Jeong S, Lee S
- 11066** Hepatic steatosis with mass effect: A case report
Hu N, Su SJ, Li JY, Zhao H, Liu SF, Wang LS, Gong RZ, Li CT
- 11074** Bone marrow metastatic neuroendocrine carcinoma with unknown primary site: A case report and review of the literature
Shi XB, Deng WX, Jin FX
- 11082** Child with adenylosuccinate lyase deficiency caused by a novel complex heterozygous mutation in the ADSL gene: A case report
Wang XC, Wang T, Liu RH, Jiang Y, Chen DD, Wang XY, Kong QX
- 11090** Recovery of brachial plexus injury after bronchopleural fistula closure surgery based on electrodiagnostic study: A case report and review of literature
Go YI, Kim DS, Kim GW, Won YH, Park SH, Ko MH, Seo JH
- 11101** Severe *Klebsiella pneumoniae* pneumonia complicated by acute intra-abdominal multiple arterial thrombosis and bacterial embolism: A case report
Bao XL, Tang N, Wang YZ
- 11111** Spontaneous bilateral femur neck fracture secondary to grand mal seizure: A case report
Senocak E
- 11116** Favorable response after radiation therapy for intraductal papillary mucinous neoplasms manifesting as acute recurrent pancreatitis: A case report
Harigai A, Kume K, Takahashi N, Omata S, Umezawa R, Jingu K, Masamune A
- 11122** Acute respiratory distress syndrome following multiple wasp stings treated with extracorporeal membrane oxygenation: A case report
Cai ZY, Xu BP, Zhang WH, Peng HW, Xu Q, Yu HB, Chu QG, Zhou SS
- 11128** Morphological and electrophysiological changes of retina after different light damage in three patients: Three case reports
Zhang X, Luo T, Mou YR, Jiang W, Wu Y, Liu H, Ren YM, Long P, Han F
- 11139** Perirectal epidermoid cyst in a patient with sacroccygeal scoliosis and anal sinus: A case report
Ji ZX, Yan S, Gao XC, Lin LF, Li Q, Yao Q, Wang D

- 11146** Synchronous gastric cancer complicated with chronic myeloid leukemia (multiple primary cancers): A case report
Zhao YX, Yang Z, Ma LB, Dang JY, Wang HY
- 11155** Giant struma ovarii with pseudo-Meigs's syndrome and raised cancer antigen-125 levels: A case report
Liu Y, Tang GY, Liu L, Sun HM, Zhu HY
- 11162** Longest survival with primary intracranial malignant melanoma: A case report and literature review
Wong TF, Chen YS, Zhang XH, Hu WM, Zhang XS, Lv YC, Huang DC, Deng ML, Chen ZP
- 11172** Spontaneous remission of hepatic myelopathy in a patient with alcoholic cirrhosis: A case report
Chang CY, Liu C, Duan FF, Zhai H, Song SS, Yang S
- 11178** Cauda equina syndrome caused by the application of DuraSeal™ in a microlaminectomy surgery: A case report
Yeh KL, Wu SH, Fuh CS, Huang YH, Chen CS, Wu SS
- 11185** Bioceramics utilization for the repair of internal resorption of the root: A case report
Riyahi AM
- 11190** Fibrous hamartoma of infancy with bone destruction of the tibia: A case report
Qiao YJ, Yang WB, Chang YF, Zhang HQ, Yu XY, Zhou SH, Yang YY, Zhang LD
- 11198** Accidental esophageal intubation *via* a large type C congenital tracheoesophageal fistula: A case report
Hwang SM, Kim MJ, Kim S, Kim S
- 11204** Ventral hernia after high-intensity focused ultrasound ablation for uterine fibroids treatment: A case report
Park JW, Choi HY

LETTER TO THE EDITOR

- 11210** C-Reactive protein role in assessing COVID-19 deceased geriatrics and survivors of severe and critical illness
Nori W

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Rajeev Gurunath Redkar, FRCS, FRCS (Ed), FRCS (Gen Surg), MBBS, MCh, MS, Dean, Professor, Surgeon, Department of Pediatric Surgery, Lilavati Hospital and Research Centre, Mumbai 400050, Maharashtra, India. rajeev.redkar@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJCC as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The WJCC's CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xu Guo*; Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

October 26, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Observational Study

Clinical and epidemiological features of ulcerative colitis patients in Sardinia, Italy: Results from a multicenter study

Salvatore Magrì, Mauro Demurtas, Maria Francesca Onidi, Marcello Picchio, Walter Elisei, Manuela Marzo, Federica Miculan, Roberto Manca, Maria Pina Dore, Bianca Maria Quarta Colosso, Antonio Cicu, Luigi Cugia, Monica Carta, Laura Binaghi, Paolo Usai, Mariantonia Lai, Fabio Chicco, Massimo Claudio Fantini, Alessandro Armuzzi, Giammarco Mocci

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): D, D
Grade E (Poor): 0

P-Reviewer: Ogundipe OA, United States; Osawa S, Japan; Osawa S, Japan; Ogundipe OA, United States

Received: August 9, 2021

Peer-review started: August 9, 2021

First decision: August 29, 2021

Revised: September 6, 2021

Accepted: August 22, 2022

Article in press: August 22, 2022

Published online: October 26, 2022



Salvatore Magrì, Department of Medical Sciences and Public Health, University of Cagliari, Monserrato 09042, Italy

Salvatore Magrì, Endoscopy Unit, Humanitas Istituto Clinico Catanese, Catania 95045, Italy

Mauro Demurtas, Endoscopy Unit, San Martino Hospital, Oristano 09170, Italy

Maria Francesca Onidi, Laura Binaghi, Giammarco Mocci, Gastroenterology Unit, Brotzu Hospital, Cagliari 09121, Italy

Marcello Picchio, Division of General Surgery, Ospedale Civile P Colombo, Velletri 00049, Italy

Walter Elisei, Gastroenterology Unit, San Camillo Forlanini Hospital, Rome 00152, Italy

Manuela Marzo, Internal Medicine and Gastroenterology Department, Cardinale Panico Hospital, Tricase 73039, Italy

Federica Miculan, Department of Surgery, San Martino Hospital, Oristano 09170, Italy

Roberto Manca, Division of Gastroenterology, Santissima Trinità Hospital, Cagliari 09121, Italy

Maria Pina Dore, Dipartimento di Medicina Clinica e Sperimentale, University of Sassari, Sassari 07100, Italy

Bianca Maria Quarta Colosso, Department of Medical Science and Public Health, University of Sassari, Sassari 07100, Italy

Antonio Cicu, Unit of Gastroenterology, ASL Sassari, Sassari 07100, Italy

Luigi Cugia, Monica Carta, Gastroenterology Unit, Santissima Annunziata Hospital, Sassari 07100, Italy

Paolo Usai, Fabio Chicco, Medical Science and Public Health, University of Cagliari, Cagliari 09042, Italy

Mariantonia Lai, Medical Sciences and Public health, Presidio Policlinico of Monserrato, Cagliari, Monserrato 09042, Cagliari, Italy

Massimo Claudio Fantini, Department of Internal Medicine, University of Rome Tor Vergata, Rome 00133, Italy

Alessandro Armuzzi, IBD Unit, Policlinico Universitario Gemelli, Rome 00168, Italy

Corresponding author: Salvatore Magri, MD, Academic Research, Department of Medical Sciences and Public Health, University of Cagliari, Presidio Policlinico of Monserrato, Cagliari, SS 554 km 4500, Monserrato 09042, Italy. salvo10ms@libero.it

Abstract

BACKGROUND

There are little data on the epidemiological and clinical features of adult patients with ulcerative colitis (UC) in the different Italian regions, mainly derived from the absence of a national registry. This prevents correct interpretation of the disease burden.

AIM

To assess the main clinical and epidemiological features of adult patients diagnosed with UC in Sardinia, Italy.

METHODS

We performed a multicenter, observational, cross-sectional study that included adult patients with UC enrolled in seven gastroenterology unit centers in Sardinia. Data were obtained from the patients' medical records and from a questionnaire administered at the inclusion visit.

RESULTS

Four hundred and forty-two patients with UC were included. The median age at diagnosis was 39 years (interquartile range 28-48). After a median disease duration of 10 years, 53 patients experienced proximal extension of proctitis or left-sided colitis. Seventy-five patients developed extraintestinal manifestations. Nineteen patients (4.3%) developed cancer: two with colorectal cancer and seventeen with extracolonic cancers. Mesalazine (5-ASA) remains the mainstay of treatment for UC. Overall, 95 patients (21.5%) were treated with one or more biologic agents, whereas 15 patients (3.4%) underwent surgery, mostly colectomy.

CONCLUSION

Our results provide important insights into the clinical and epidemiological features of patients with UC, and while waiting for a national Italian registry, present eligible data on the UC population in Sardinia.

Key Words: Inflammatory bowel disease-basic; Inflammatory bowel disease-clinical; Ulcerative colitis; Epidemiology; Natural history; Treatment

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: There are little data on the epidemiological and clinical features of adult ulcerative colitis patients in the different Italian regions, mainly derived from the absence of a national registry. This prevents correct appraisal of the disease burden. A population-based observational study evaluating an entire population in a defined geographic area over an extended period of time is ideal to inform the natural history of a disease and to avoid selection biases associated with referral center cohort studies.

Citation: Magri S, Demurtas M, Onidi MF, Picchio M, Elisei W, Marzo M, Miculan F, Manca R, Dore MP, Quarta Colosso BM, Cicu A, Cugia L, Carta M, Binaghi L, Usai P, Lai M, Chicco F, Fantini MC, Armuzzi A, Mocci G. Clinical and epidemiological features of ulcerative colitis patients in Sardinia, Italy: Results from a multicenter study. *World J Clin Cases* 2022; 10(30): 10921-10930

URL: <https://www.wjgnet.com/2307-8960/full/v10/i30/10921.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i30.10921>

INTRODUCTION

Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative Colitis (UC), are

chronic-relapsing inflammatory diseases of the gastrointestinal tract, mainly affecting the young and middle-aged[1,2].

A considerable variation in the incidence of IBD is observable worldwide, as it increased quickly in Western developed countries during the last 50 years of the 20th century, while newly industrialized nations are documenting the greatest increases in incidence since the years of globalization (2000s)[3].

Currently in Italy, a national disease register for IBD has not yet been developed. This prevents correct interpretation of the disease burden. Based on the disease-specific payment exemptions register, between 150000 and 200000 people are estimated to be affected by IBD, with a prevalence of 100/100000 inhabitants for CD and 121/100000 for UC. Epidemiological data from the European Crohn's and Colitis Organisation's (ECCO) Epidemiological Committee inception cohort showed that the Italian incidence is 10.5/100000 inhabitants per year, indicating lower rates of new diagnosis compared to European ones (> 25/100000), but twofold compared to old Italian data[4-6].

The management of these diseases is arduous, as inflammation often persists even in the absence of gastrointestinal symptoms[7], and this may lead to progressive bowel damage and complications requiring long-term treatments and strict medical follow-up, and in some cases hospitalizations and surgery[8,9]. At the same time, impaired bowel function ultimately leads to a considerable burden not only for patients[10] but also for the healthcare systems[11].

In particular, UC affects mostly young adults around 20-40-years-old with a second peak between 60 years and 80 years, with no differences between sexes[12,13]. Both the clinical presentation and course vary among patients and can range from mostly quiescent to chronic, refractory disease with need of surgery, sometimes complicated by cancer or contributing to cause of death[14].

There are little data on the epidemiological and clinical features of adult UC patients in the different Italian regions, mainly derived from administrative sources such as the Hospital Discharge Register[5, 15,16].

Based on these premises, the aim of this study was to assess the main clinical and epidemiological features of adult patients diagnosed with UC in Sardinia, including location at diagnosis, extraintestinal manifestations, disease progression over time, and treatment.

MATERIALS AND METHODS

Study design and population

We performed a multicenter, observational, cross-sectional study that included adult patients with UC, enrolled between February 2017 and December 2018 in seven Gastroenterology/Endoscopy Units in Sardinia, an Italian region with a population of approximately 1600000 inhabitants. All patients provided written informed consent. The study was approved by the Ethics Board (Prot. PG/2016/17911) and conducted according to the Declaration of Helsinki.

Inclusion and exclusion criteria

We included adult patients (≥ 18 -years-old) with an established diagnosis of UC, based on standard clinical, endoscopic, and histologic criteria. We excluded patients < 18-years-old at the time of enrollment, patients unable to understand the study's questionnaires, or patients previously enrolled in a randomized clinical trial.

Diagnostic criteria

Diagnosis was made at least 3 mo before the study inclusion and the minimum follow-up time was 1 mo. Data were obtained from patients' medical records at each center and from a questionnaire administered at the inclusion visit. The following data were collected: sex, date of birth, lifestyle (smoking habits, alcohol consumption), personal and/or familial history of neoplasia, vaccination status (hepatitis B virus [HBV], human papilloma virus [HPV] and *Streptococcus pneumoniae*), year of diagnosis and age at diagnosis, disease extent both at diagnosis and at study inclusion (according to Montreal classification)[17], extraintestinal manifestations (EIMs), use of UC-related medications (mesalazine [5-ASA], corticosteroids, immunosuppressors, biologic agents), and surgery. Disease extension and regression were defined as a proximal progression or distal regression from the initial extent at diagnosis, respectively, as determined by endoscopy. We also focused on elderly-onset patients, namely patients diagnosed with UC after the age of 60 years.

Statistical analyses

Given an estimated prevalence rate of about 124 cases per 100000 inhabitants for UC in Sardinia[16], we aimed to enroll 400 patients with UC, equivalent to 20% of the UC population in Sardinia. Data were reported on a Microsoft Excel worksheet and analyzed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, United States). Statistics were descriptive: categorical variables are expressed as proportion, while continuous variables are expressed as the median and interquartile range (IQR).

RESULTS

Sex, age at diagnosis, and smoking status

Between February 2017 and December 2018, 442 patients with an established diagnosis of UC were included: 231 (52.3%) were female, with a female-to-male ratio of about 1.1 (Table 1). The median age at diagnosis was 39 years (IQR 28-48). At the time of diagnosis, 4.5% (20/442) of patients were < 16-years-old, 52.7% (233/442) were diagnosed between 17-years-old and 40-years-old, and 42.8% (189/442) at age > 40. About three-quarters of patients were diagnosed between 17-years-old and 49-years-old (23.2% between 17 and 29, 25.5% between 30 and 39, and 23.2% between 40 and 49). In all, 10.9% (48/442) of patients were active smokers and 36.2% (160/442) were former smokers.

Disease extent

Disease extent at the time of diagnosis was proctitis [E1] in 81 (18.3%) patients, left-sided colitis [E2] in 178 (40.3%), and extensive colitis [E3] in 176 (39.8%). Data were not available for 7 patients (1.6%). After a median disease duration of 10 years (IQR 3-15.5), 53 patients (12%) experienced proximal extension of proctitis or left-sided colitis: 13 (24.5%) patients from E1 to E2, 12 (22.7%) from E1 to E3, and 28 (52.3%) from E2 to E3. In 28 patients (6.3%), there was a regression of disease extent after a median disease duration of 10.5 years (IQR 7-16.75): 10 patients (35.7%) from E2 to E1, 8 (28.6%) from E3 to E1, and 10 (35.7%) from E3 to E2.

EIMs, malignancies, and vaccinations

Seventy-five patients (16.3%) developed EIMs, the most frequent being articular (50/72, 69.4%), followed by hepatobiliary (11/72, 15.3%, of which 6 patients with primary sclerosing cholangitis), cutaneous (9/72, 12.5%) and ocular (5/72, 6.9%); in 3 patients (4.2%) there was a combination of articular and ocular manifestations. After UC diagnosis, 19 patients (4.3%) developed cancer: 2 with colorectal cancer (CRC) and 17 with extracolonic cancers (5 breast, 4 skin, 2 prostate, 2 thyroid, 1 pancreas, 1 stomach, 1 gastric MALT lymphoma, 1 multiple myeloma). In the study population, patients' self-reported vaccination rates were 30.3% (134/442) for HBV, 2% (9/442) for HPV, and 1.6% (7/442) for *S. pneumoniae*.

Medical and surgical treatment

Details on medical therapy are shown in Table 2. Twenty-eight patients (6.3%) received no UC treatment at the inclusion visit. The most common therapy at inclusion visit was 5-ASA: 368 (86.6%) of patients were taking it at baseline, whereas 46 (10%) withdrew it. No data were available for 17 patients. Nine percent of patients started with corticosteroids, either systemic or with low bioavailability, whereas 51.7% were exposed to one or more courses of steroids during their disease course. Azathioprine was used by 40 (9%) patients; 69 (15.6%) withdrew it during their disease course, mainly for adverse events.

Overall, 95 patients (21.5%) were treated with one or more biologic agents: 72 patients (75.8%) were treated with one biologic agent, 17 (17.9%) with two and 6 (6.3%) with three. At study inclusion, infliximab was the most common anti-tumor necrosis factor alpha (TNF α) biologic used, (55/442, 12.4%), followed by adalimumab (12/442, 2.7%) and golimumab (5, 1.1%); while vedolizumab (VDZ) was used in 11 (2.5%) patients. Nine of the eleven patients with VDZ were previously treated with anti-TNF α , while two were naïve to any biologic.

Eleven patients (2.5%) were treated with a combination therapy of immunosuppressant drug plus biologic: ten in association with anti-TNF α agents, one with VDZ. None of the patients was treated with a combination of biologics.

A total of 15 patients (3.4%) had a resection performed. Of these, 13 patients (87%) underwent colectomy, while 2 (13%) underwent hemicolectomy for CRC. The median time between diagnosis and surgery was 5 years (IQR 2-20). The vast majority of patient who underwent surgery were with extensive colitis at diagnosis (12 patients, 80%) compared with 3 patients (20%) with left-sided colitis.

Elderly-onset UC

Fifty-one patients (11.5%) were diagnosed with UC after the age of 60 years. Among them, 31 (60.8%) were male. Disease extent at diagnosis was E1 in 7 patients (13.7%), E2 in 24 (47.1%), and E3 in 20 (37.2%); data were not present in 1 patient. After a median follow-up time of 4 years (IQR 1-6), there was a proximal extension of disease in 3 patients (5.9%).

Three patients (5.9%) developed EIMs (two articular and one erythema nodosum). Four patients (7.8%) had a history of neoplasia (two with skin cancer, one with prostate cancer, one with breast cancer).

The most common therapy at the time of inclusion visit was 5-ASA, used by 368 (83.2%) of patients. Four patients (7.8%) were taking corticosteroids, while 50.1% received one or more courses of steroids after the diagnosis, either systemic or with low bioavailability. Two patients (3.9%) were under treatment with azathioprine, while three patients withdrew it during their disease course (two for adverse events and one for disease remission). Four patients (7.8%) were under treatment with biologic

Table 1 Clinical and demographical characteristics of patients with ulcerative colitis

Characteristics	n = 442, n (%)
Female, n (%)	231 (52)
Age at diagnosis, yr (IQR)	39 (28-48)
Smoking status	
Active	48 (10.9)
Former	160 (36.2)
Never	234 (52.9)
Disease extent at diagnosis	
E1, proctitis	81 (18.3)
E2, left-sided colitis	178 (40.3)
E3, extensive colitis	176 (39.8)
Uncertain extent	7 (1.6)
Disease extent	53 (12)
E1 to E2	13 (25)
E2 to E3	28 (52.3)
E1 to E3	12 (22.7)
Extraintestinal manifestations	75 (16)
Articular	50 (69.4)
Hepatobiliary	11 (15.2)
Cutaneous	9 (12.5)
Ocular	5 (6.9)
Previous surgery	15 (3.4)
Colectomy	13 (87)
Hemicolectomy	2 (13)
Malignancies	19 (4)
Colorectal cancer	2 (11)
Breast	5 (26)
Skin	4 (21)
Prostate	2 (11)
Thyroid	2 (11)
Pancreas	1 (5)
Stomach	1 (5)
Multiple myeloma	1 (5)
MALT lymphoma	1 (5)
Self-reported vaccination status	
HBV	134 (30.3)
HPV	9 (2)
<i>Streptococcus pneumoniae</i>	7 (1.6)

HBV: Hepatitis B virus; HPV: Human papilloma virus.

agent: three with infliximab and one with VDZ. No one underwent colectomy.

Table 2 Medical treatment in patients with ulcerative colitis

Medical therapy	Current users, n (%)	Former users, n (%)	Never used, n (%)
Mesalazine, n = 425	368 (86.6)	46 (10.8)	11 (2.6)
Corticosteroids	41 (9.1)	228 (51.7)	173 (39.2)
Thiopurines	40 (9)	69 (15.6)	333 (75.4)
Methotrexate	5 (1.1)	4 (1)	432 (97.9)
Infliximab	55 (12.4)	22 (5.0)	365 (82.6)
Adalimumab	12 (2.7)	6 (1.4)	424 (95.9)
Golimumab	5 (1.1)	11 (2.5)	426 (96.4)
Vedolizumab	11 (2.5)	1 (0.2)	430 (97.3)

DISCUSSION

In this study, we summarized the main characteristics and natural history of UC in a large population study of a single Italian region, Sardinia, including demographic data, disease extension, EIMs, malignancies, vaccinations, and medical and surgical treatment.

Disease extent in UC is an important feature because it is an indicator of severity of disease, as well as the type of treatment needed. Patients with initial diagnosis of pancolitis appear to have a worse disease course and need a more aggressive treatment, both medical and surgical, while distal UC is associated with a better prognosis[18]. In our cohort, diagnosis of proctitis was made in 18.3% of patients, left-sided colitis in 40.3%, and extensive colitis in 39.8%. The overall rate of extension was 12% after a median follow-up of 10 years, which was significantly lower than in others that reported highest rates [19,20]. This feature could be explained in different ways. First, a possible explanation is linked to the time of UC diagnosis that in our cohort was 39 years, substantially comparable with European data[4], but earlier than the North American countries, where the highest rate of UC extension is reported[21]. If the diagnosis is significantly delayed, as well as the start of therapy, patients are predisposed to a major risk of disease extension and an aggressive course. Moreover, we can speculate that Sardinia, a region geographically isolated from European continent, has a selected population, less pre-disposing to develop a more aggressive disease due to genetic or environmental factors. Among the latter, diet plays an important role in IBD pathogenesis, by modulating the gut microbiota, and consequently, it could have an impact on IBD course[22]. In particular, if several lines of evidence point to aspects of the typical Western diet that may promote the development of IBD and its course, less is known about the beneficial role of Mediterranean diet (Md), more frequently adopted in Southern Europe, particularly in Sardinia. Md is characterized by a high intake of fruits and vegetables, olive oil and oily fish, grains and nuts[23]. Chicco *et al*[24] conducted an observational study in a Sardinian population of IBD patients showing a spontaneous improvement of disease activity and inflammatory markers in patients that adopted a Md. Further prospective studies are needed in this setting.

EIMs are common in IBD and adversely impact patient's quality of life and can even be life-threatening. The real prevalence and burden of EIMs have not been fully evaluated yet stands around 15%-50% since prospective studies are lacking[25]. The analysis of clinical characteristics revealed that 16.3% of our populations experienced EIMs, the most was frequent articular (69.4%), followed by hepatobiliary (15.2%), cutaneous (12.5%), and ocular (6.9%).

5-ASA remains the mainstay of treatment for UC. In our cohort, we observed that almost all patients received 5-ASA, while only 10% were formerly used, mainly because of the concomitant treatment with immunomodulators or biologics. However more recent publications have demonstrated no benefit to concomitant 5-ASA in UC patients escalated to anti-TNF α or VDZ[26]. Despite the increasing therapeutic armamentarium available, clinics still prescribe 5-ASA even when it fails or in step-up therapy. One of the reasons could be the role of 5-ASA in CRC prevention. American guidelines suggest that 5-ASA therapy may be stopped in patients that achieved long remission or are treated with biologics[27]. Instead ECCO guidelines emphasize the role of 5ASA in CRC prevention suggesting a withdrawal only in low-risk patients (limited disease extent, a history of remission for several years, no previous requirement of systemic corticosteroids)[28]. Considering also the burden on healthcare budgets and albeit rare potential adverse effects, there is a need to consider withdrawing 5-ASA in a subset of patients.

Regarding biological therapy we observed that 21% of patients were exposed to one or more biologics, a proportion significantly higher than the European population[29]. This trend might follow a top-down approach with rapid escalation as the result of the "era of mucosal healing" as a treatment goal[30]. However, the majority of participating centers were tertiary biologic-prescribing IBD hospitals with greater propensity to use biologics. The impact of this more aggressive therapeutic approach on the

disease course needs to be further evaluated. Another important finding seen in this study is that the majority of patients did not receive combination therapy with an anti-TNF α or VDZ and an immunomodulatory drug.

Population-based cohorts of patients diagnosed after the introduction of biologics in Europe and North America have reported surgery rates of 3%-6% in UC[13,31]. These numbers are comparable to the surgery rates observed in the present cohort. Recent studies have shown a reduced rate of colectomy in UC assuming that this trend is strongly linked to use of biologic agents that positively influence the disease course[32]. It remains to be proven if current IBD treatment strategy can influence the course in the long term.

CRC has always garnered special attention in IBD. Population-based data from our cohort demonstrate only two cases of CRC. This finding seems to be in line with the results of an Italian study conducted by Taborelli *et al*[33], which showed that CRC risk among both UC and CD patients was similar to that expected in the general population. These data could be explained by several factors as diet, chemoprevention or colonoscopy surveillance. Differently, we observed a higher rate of extraintestinal tumors. However, it is difficult to establish whether there is an influence of the natural history of intestinal disease or is the result of unrelated factors.

Patients with IBD are vulnerable to infections because of the immunological disorder caused by the disease itself or to the immunosuppression induced by the treatment[34]. Thus, the determination of vaccination status is important to limit under-immunization. Despite the current practice recommendations for routine vaccination in IBD[35,36], our findings demonstrate significant deficiencies in self-reported vaccination uptake with a low rate of adherence to vaccination schedules, in particular for *S. Pneumoniae* and HPV. Inadequate counseling, deficiencies in physicians' knowledge about vaccinations and uncertainties about vaccination indications in IBD patients have been implicated as an important contributor to poor uptake of vaccination[37]. This suggests that more attention needs to be given to vaccination counseling. A structured review of vaccination status at time of diagnosis, prior the initiation of immunosuppressive therapy and an annual review represent an optimal strategy in this setting. By contrast, in our study, the rate of self-reported vaccination for HBV was 30.3%, higher than that reported in others[38,39]. These data are clearly due to the vaccination campaign introduced in Italy in 1991 that makes vaccination mandatory for all people born since 1979 rather than through intervention by gastroenterologists.

Our study had some limitations that need to be taken into consideration. These include the heterogeneity of the participating centers in terms of health care of which they are part. In addition, few centers have contributed to the collection of the majority of data making potentially skewed the data collection. Moreover, the study may be limited by the retrospective data collection. Although we controlled for many potential confounders, unmeasurable variables might alter data extractions.

CONCLUSION

In conclusion, although a national IBD registry is not yet available, this is one of the first studies conducted in Italy that provides important insights on the clinical and epidemiological features of patients with UC as well as the management and its natural history. Our data seem in line with Italian and European data. While waiting for a national registry, our results present eligible features of UC population in Sardinia considering that the number of patients enrolled represents about 20% of the population.

ARTICLE HIGHLIGHTS

Research background

There are little data on the epidemiological and clinical features of patients with adult ulcerative colitis (UC) in Italy.

Research motivation

This population-based observational study evaluated an entire population in a defined geographic area over an extended period of time. This is ideal to inform the natural history of disease and also to avoid selection biases associated with referral center cohort studies.

Research objectives

To describe the characteristics of patients at the time of UC diagnosis and to register the use of immunosuppressive treatments and biological drugs, surgeries, and malignancies after diagnosis of UC.

Research methods

Consecutive patients with UC in ambulatory follow-up, at the time of the visit, were invited, after obtaining informed consent, to fill out a questionnaire concerning the natural history of their chronic disease object of the study.

Research results

Four hundred and forty-two patients were included in the study. A high proportion of patients were treated with one or more biologics. 5-ASA remains the mainstay of UC treatment. Left-sided colitis is the most frequent location.

Research conclusions

This is one of the first large-scale nationwide, observational studies to investigate the epidemiological characteristics of UC in Italy. Sardinia, a region geographically isolated from the European continent. This selected population is less likely to develop aggressive disease due to genetic or environmental factors.

Research perspectives

Correct and objective mapping of the epidemiological and clinical characteristics of patients with UC, but in general with inflammatory bowel disease, cannot be separated from the presence of a national registry that compiles national data. It is desirable that this happens in Italy.

FOOTNOTES

Author contributions: Magri S and Mocci G performed the study design, data capture, and data validation; Magri S, Demurtas M, and Picchio M performed the statistical analyses; Magri S drafted the manuscript; Magri S, Demurtas M, Onidi MF, Picchio M, Elisei W, Marzo M, Miculan F, Manca R, Dore MP, Quarta Colosso BM, Cicu A, Cugia L, Pisanu R, Carta M, Binaghi L, Usai P, Lai M, Chicco F, Fantini MC, Cabras F, Armuzzi A, and Mocci G performed the data capture and revised the manuscript; Mocci G approved the final version of the manuscript.

Institutional review board statement: The research project has been approved by the Ethics Board (Prot. PG/2016/17911).

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: Italy

ORCID number: Salvatore Magri 0000-0001-5635-069X; Mauro Demurtas 0000-0002-2237-1246; Maria Francesca Onidi 0000-0002-1233-7618; Marcello Picchio 0000-0001-5070-8240; Walter Elisei 0000-0003-4951-0194; Manuela Marzo 0000-0001-6337-4411; Federica Miculan 0000-0002-5353-9822; Roberto Manca 0000-0002-7086-1004; Maria Pina Dore 0000-0001-7305-3531; Bianca Maria Quarta Colosso 0000-0002-8594-0434; Antonio Cicu 0000-0002-2259-8571; Luigi Cugia 0000-0002-9577-808X; Monica Carta 0000-0001-7999-3794; Laura Binaghi 0000-0003-0002-4574; Paolo Usai 0000-0003-0734-3279; Mariantonia Lai 0000-0002-9565-401X; Fabio Chicco 0000-0003-0662-3180; Massimo Claudio Fantini 0000-0003-2870-3827; Alessandro Armuzzi 0000000315720118; Giammarco Mocci 0000-0002-9263-7409.

S-Editor: Chang KL

L-Editor: Filipodia

P-Editor: Chang KL

REFERENCES

- 1 **Lamb CA**, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, Hayee B, Lomer MCE, Parkes GC, Selinger C, Barrett KJ, Davies RJ, Bennett C, Gittens S, Dunlop MG, Faiz O, Fraser A, Garrick V, Johnston PD, Parkes M, Sanderson J, Terry H; IBD guidelines eDelphi consensus group, Gaya DR, Iqbal TH, Taylor SA, Smith M, Brookes M, Hansen R, Hawthorne AB. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019; **68**: s1-s106 [PMID: [31562236](#) DOI: [10.1136/gutjnl-2019-318484](#)]
- 2 **Loftus EV Jr**, Schoenfeld P, Sandborn WJ. The epidemiology and natural history of Crohn's disease in population-based patient cohorts from North America: a systematic review. *Aliment Pharmacol Ther* 2002; **16**: 51-60 [PMID: [11856078](#) DOI: [10.1046/j.1365-2036.2002.01140.x](#)]
- 3 **Kaplan GG**, Ng SC. Understanding and Preventing the Global Increase of Inflammatory Bowel Disease. *Gastroenterology* 2017; **152**: 313-321.e2 [PMID: [27793607](#) DOI: [10.1053/j.gastro.2016.10.020](#)]
- 4 **Burisch J**, Pedersen N, Čuković-Čavka S, Brinar M, Kaimakliotis I, Duricova D, Shonová O, Vind I, Avnstrøm S, Thorsgaard N, Andersen V, Krabbe S, Dahlerup JF, Salupere R, Nielsen KR, Olsen J, Manninen P, Collin P, Tsianos EV, Katsanos KH, Ladefoged K, Lakatos L, Björnsson E, Ragnarsson G, Bailey Y, Odes S, Schwartz D, Martinato M, Lupinacci G, Milla M, De Padova A, D'Inca R, Beltrami M, Kupcinskas L, Kiudelis G, Turcan S, Tighineanu O, Mihu I, Magro F, Barros LF, Goldis A, Lazar D, Belousova E, Nikulina I, Hernandez V, Martinez-Ares D, Almer S, Zhulina Y, Halfvarson J, Arebi N, Sebastian S, Lakatos PL, Langholz E, Munkholm P; EpiCom-group. East-West gradient in the incidence of inflammatory bowel disease in Europe: the ECCO-EpiCom inception cohort. *Gut* 2014; **63**: 588-597 [PMID: [23604131](#) DOI: [10.1136/gutjnl-2013-304636](#)]
- 5 **Di Domenicantonio R**, Cappai G, Arcà M, Agabiti N, Kohn A, Vernia P, Biancone L, Armuzzi A, Papi C, Davoli M. Occurrence of inflammatory bowel disease in central Italy: a study based on health information systems. *Dig Liver Dis* 2014; **46**: 777-782 [PMID: [24890621](#) DOI: [10.1016/j.dld.2014.04.014](#)]
- 6 **Tragnone A**, Corrao G, Miglio F, Caprilli R, Lanfranchi GA. Incidence of inflammatory bowel disease in Italy: a nationwide population-based study. Gruppo Italiano per lo Studio del Colon e del Retto (GISC). *Int J Epidemiol* 1996; **25**: 1044-1052 [PMID: [8921493](#) DOI: [10.1093/ije/25.5.1044](#)]
- 7 **Cellier C**, Sahnoud T, Froguel E, Adenis A, Belaiche J, Bretagne JF, Florent C, Bouvry M, Mary JY, Modigliani R. Correlations between clinical activity, endoscopic severity, and biological parameters in colonic or ileocolonic Crohn's disease. A prospective multicentre study of 121 cases. The Groupe d'Etudes Thérapeutiques des Affections Inflammatoires Digestives. *Gut* 1994; **35**: 231-235 [PMID: [7508411](#) DOI: [10.1136/gut.35.2.231](#)]
- 8 **Burisch J**, Munkholm P. The epidemiology of inflammatory bowel disease. *Scand J Gastroenterol* 2015; **50**: 942-951 [PMID: [25687629](#) DOI: [10.3109/00365521.2015.1014407](#)]
- 9 **Fumery M**, Singh S, Dulai PS, Gower-Rousseau C, Peyrin-Biroulet L, Sandborn WJ. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. *Clin Gastroenterol Hepatol* 2018; **16**: 343-356.e3 [PMID: [28625817](#) DOI: [10.1016/j.cgh.2017.06.016](#)]
- 10 **Pariente B**, Cosnes J, Danese S, Sandborn WJ, Lewin M, Fletcher JG, Chowers Y, D'Haens G, Feagan BG, Hibi T, Hommes DW, Irvine EJ, Kamm MA, Loftus EV Jr, Louis E, Michetti P, Munkholm P, Oresland T, Panés J, Peyrin-Biroulet L, Reinisch W, Sands BE, Schoelmerich J, Schreiber S, Tilg H, Travis S, van Assche G, Vecchi M, Mary JY, Colombel JF, Lémann M. Development of the Crohn's disease digestive damage score, the Lémann score. *Inflamm Bowel Dis* 2011; **17**: 1415-1422 [PMID: [21560202](#) DOI: [10.1002/ibd.21506](#)]
- 11 **Sonnenberg A**. Time trends of mortality from Crohn's disease and ulcerative colitis. *Int J Epidemiol* 2007; **36**: 890-899 [PMID: [17420164](#) DOI: [10.1093/ije/dym034](#)]
- 12 **Danese S**, Fiocchi C. Ulcerative colitis. *N Engl J Med* 2011; **365**: 1713-1725 [PMID: [22047562](#) DOI: [10.1056/NEJMr1102942](#)]
- 13 **Burisch J**, Katsanos KH, Christodoulou DK, Barros L, Magro F, Pedersen N, Kjeldsen J, Vegh Z, Lakatos PL, Eriksson C, Halfvarson J, Fumery M, Gower-Rousseau C, Brinar M, Cukovic-Cavka S, Nikulina I, Belousova E, Myers S, Sebastian S, Kiudelis G, Kupcinskas L, Schwartz D, Odes S, Kaimakliotis IP, Valpiani D, D'Inca R, Salupere R, Chetcuti Zammit S, Ellul P, Duricova D, Bortlik M, Goldis A, Kievit HAL, Toca A, Turcan S, Midjord J, Nielsen KR, Andersen KW, Andersen V, Misra R, Arebi N, Oksanen P, Collin P, de Castro L, Hernandez V, Langholz E, Munkholm P; Epi-IBD Group. Natural Disease Course of Ulcerative Colitis During the First Five Years of Follow-up in a European Population-based Inception Cohort-An Epi-IBD Study. *J Crohns Colitis* 2019; **13**: 198-208 [PMID: [30289522](#) DOI: [10.1093/ecco-jcc/jjy154](#)]
- 14 **Kaplan GG**, Seow CH, Ghosh S, Molodecky N, Rezaie A, Moran GW, Proulx MC, Hubbard J, MacLean A, Buie D, Panaccione R. Decreasing colectomy rates for ulcerative colitis: a population-based time trend study. *Am J Gastroenterol* 2012; **107**: 1879-1887 [PMID: [23165448](#) DOI: [10.1038/ajg.2012.333](#)]
- 15 **Valpiani D**, Manzi I, Mercuriali M, Giuliani O, Ravaioli A, Colamartini A, Bucci L, Falcini F, Ricci E. A model of an inflammatory bowel disease population-based registry: The Forlì experience (1993-2013). *Dig Liver Dis* 2018; **50**: 32-36 [PMID: [28988755](#) DOI: [10.1016/j.dld.2017.09.120](#)]
- 16 **Macaluso FS**, Mocci G, Orlando A, Scondotto S, Fantaci G, Antonelli A, Leone S, Previtali E, Cabras F, Cottone M. Prevalence and incidence of inflammatory bowel disease in two Italian islands, Sicily and Sardinia: A report based on health information systems. *Dig Liver Dis* 2019; **51**: 1270-1274 [PMID: [31176630](#) DOI: [10.1016/j.dld.2019.05.017](#)]
- 17 **Satsangi J**, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut* 2006; **55**: 749-753 [PMID: [16698746](#) DOI: [10.1136/gut.2005.082909](#)]
- 18 **Burisch J**, Jess T, Martinato M, Lakatos PL; ECCO -EpiCom. The burden of inflammatory bowel disease in Europe. *J Crohns Colitis* 2013; **7**: 322-337 [PMID: [23395397](#) DOI: [10.1016/j.crohns.2013.01.010](#)]
- 19 **Solberg IC**, Lygren I, Jahnsen J, Aadland E, Høie O, Cvancarova M, Bernklev T, Henriksen M, Sauar J, Vatn MH, Moum B; IBSEN Study Group. Clinical course during the first 10 years of ulcerative colitis: results from a population-based inception cohort (IBSEN Study). *Scand J Gastroenterol* 2009; **44**: 431-440 [PMID: [19101844](#) DOI: [10.1080/00365520802600961](#)]

- 20 **Meucci G**, Vecchi M, Astegiano M, Beretta L, Cesari P, Dizioli P, Ferraris L, Panelli MR, Prada A, Sostegni R, de Franchis R. The natural history of ulcerative proctitis: a multicenter, retrospective study. Gruppo di Studio per le Malattie Infiammatorie Intestinali (GSMII). *Am J Gastroenterol* 2000; **95**: 469-473 [PMID: [10685752](#) DOI: [10.1111/j.1572-0241.2000.t01-1-01770.x](#)]
- 21 **Roda G**, Narula N, Pinotti R, Skamnelos A, Katsanos KH, Ungaro R, Burisch J, Torres J, Colombel JF. Systematic review with meta-analysis: proximal disease extension in limited ulcerative colitis. *Aliment Pharmacol Ther* 2017; **45**: 1481-1492 [PMID: [28449361](#) DOI: [10.1111/apt.14063](#)]
- 22 **Durchein F**, Petritsch W, Hammer HF. Diet therapy for inflammatory bowel diseases: The established and the new. *World J Gastroenterol* 2016; **22**: 2179-2194 [PMID: [26900283](#) DOI: [10.3748/wjg.v22.i7.2179](#)]
- 23 **Kelder T**, Stroeve JH, Bijlsma S, Radonjic M, Roeselers G. Correlation network analysis reveals relationships between diet-induced changes in human gut microbiota and metabolic health. *Nutr Diabetes* 2014; **4**: e122 [PMID: [24979151](#) DOI: [10.1038/nutd.2014.18](#)]
- 24 **Chicco F**, Magri S, Cingolani A, Paduano D, Pesenti M, Zara F, Tumbarello F, Urru E, Melis A, Casula L, Fantini MC, Usai P. Multidimensional Impact of Mediterranean Diet on IBD Patients. *Inflamm Bowel Dis* 2021; **27**: 1-9 [PMID: [32440680](#) DOI: [10.1093/ibd/izaa097](#)]
- 25 **Ott C**, Schölmerich J. Extraintestinal manifestations and complications in IBD. *Nat Rev Gastroenterol Hepatol* 2013; **10**: 585-595 [PMID: [23835489](#) DOI: [10.1038/nrgastro.2013.117](#)]
- 26 **Ungaro RC**, Limketkai BN, Jensen CB, Allin KH, Agrawal M, Ullman T, Colombel JF, Jess T. Stopping 5-aminosalicylates in patients with ulcerative colitis starting biologic therapy does not increase the risk of adverse clinical outcomes: analysis of two nationwide population-based cohorts. *Gut* 2019; **68**: 977-984 [PMID: [30420398](#) DOI: [10.1136/gutjnl-2018-317021](#)]
- 27 **Feuerstein JD**, Isaacs KL, Schneider Y, Siddique SM, Falck-Ytter Y, Singh S; AGA Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology* 2020; **158**: 1450-1461 [PMID: [31945371](#) DOI: [10.1053/j.gastro.2020.01.006](#)]
- 28 **Doherty G**, Katsanos KH, Burisch J, Allez M, Papamichael K, Stallmach A, Mao R, Berset IP, Gisbert JP, Sebastian S, Kierkus J, Lopetuso L, Szymanska E, Louis E. European Crohn's and Colitis Organisation Topical Review on Treatment Withdrawal ['Exit Strategies'] in Inflammatory Bowel Disease. *J Crohns Colitis* 2018; **12**: 17-31 [PMID: [28981623](#) DOI: [10.1093/ecco-jcc/jjx101](#)]
- 29 **Vegh Z**, Burisch J, Pedersen N, Kaimakiotis I, Duricova D, Bortlik M, Vinding KK, Avnstrøm S, Olsen J, Nielsen KR, Katsanos KH, Tsianos EV, Lakatos L, Schwartz D, Odes S, D'Inca R, Beltrami M, Kiudelis G, Kupcinskis L, Jucov A, Turcan S, Barros LF, Magro F, Lazar D, Goldis A, de Castro L, Hernandez V, Niewiadomski O, Bell S, Langholz E, Munkholm P, Lakatos PL; EpiCom-group. Treatment Steps, Surgery, and Hospitalization Rates During the First Year of Follow-up in Patients with Inflammatory Bowel Diseases from the 2011 ECCO-Epicom Inception Cohort. *J Crohns Colitis* 2015; **9**: 747-753 [PMID: [26055976](#) DOI: [10.1093/ecco-jcc/jjv099](#)]
- 30 **Neurath MF**, Travis SP. Mucosal healing in inflammatory bowel diseases: a systematic review. *Gut* 2012; **61**: 1619-1635 [PMID: [22842618](#) DOI: [10.1136/gutjnl-2012-302830](#)]
- 31 **Targownik LE**, Singh H, Nugent Z, Bernstein CN. The epidemiology of colectomy in ulcerative colitis: results from a population-based cohort. *Am J Gastroenterol* 2012; **107**: 1228-1235 [PMID: [22613902](#) DOI: [10.1038/ajg.2012.127](#)]
- 32 **Reich KM**, Chang HJ, Rezaie A, Wang H, Goodman KJ, Kaplan GG, Svenson LW, Lees G, Fedorak RN, Kroeker KI. The incidence rate of colectomy for medically refractory ulcerative colitis has declined in parallel with increasing anti-TNF use: a time-trend study. *Aliment Pharmacol Ther* 2014; **40**: 629-638 [PMID: [25039715](#) DOI: [10.1111/apt.12873](#)]
- 33 **Taborelli M**, Sozzi M, Del Zotto S, Toffolutti F, Montico M, Zanier L, Serraino D. Risk of intestinal and extra-intestinal cancers in patients with inflammatory bowel diseases: A population-based cohort study in northeastern Italy. *PLoS One* 2020; **15**: e0235142 [PMID: [32574216](#) DOI: [10.1371/journal.pone.0235142](#)]
- 34 **Rahier JF**, Magro F, Abreu C, Armuzzi A, Ben-Horin S, Chowers Y, Cottone M, de Ridder L, Doherty G, Ehehalt R, Esteve M, Katsanos K, Lees CW, Macmahon E, Moreels T, Reinisch W, Tilg H, Tremblay L, Veereman-Wauters G, Vigeat N, Yazdanpanah Y, Eliakim R, Colombel JF; European Crohn's and Colitis Organisation (ECCO). Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2014; **8**: 443-468 [PMID: [24613021](#) DOI: [10.1016/j.crohns.2013.12.013](#)]
- 35 **Mazzola G**, Macaluso FS, Adamoli L, Renna S, Cascio A, Orlando A. Diagnostic and vaccine strategies to prevent infections in patients with inflammatory bowel disease. *J Infect* 2017; **74**: 433-441 [PMID: [28263759](#) DOI: [10.1016/j.jinf.2017.02.009](#)]
- 36 **Desalermos AP**, Farraye FA, Wasan SK. Vaccinating the inflammatory bowel disease patient. *Expert Rev Gastroenterol Hepatol* 2015; **9**: 91-102 [PMID: [25160668](#) DOI: [10.1586/17474124.2014.934672](#)]
- 37 **Malhi G**, Rumman A, Thanabalan R, Croitoru K, Silverberg MS, Hillary Steinhart A, Nguyen GC. Vaccination in inflammatory bowel disease patients: attitudes, knowledge, and uptake. *J Crohns Colitis* 2015; **9**: 439-444 [PMID: [25908717](#) DOI: [10.1093/ecco-jcc/jjv064](#)]
- 38 **Papa A**, Felice C, Marzo M, Andrisani G, Armuzzi A, Covino M, Mocci G, Pugliese D, De Vitis I, Gasbarrini A, Rapaccini GL, Guidi L. Prevalence and natural history of hepatitis B and C infections in a large population of IBD patients treated with anti-tumor necrosis factor- α agents. *J Crohns Colitis* 2013; **7**: 113-119 [PMID: [22464811](#) DOI: [10.1016/j.crohns.2012.03.001](#)]
- 39 **Fabris P**, Baldo V, Baldovin T, Bellotto E, Rassu M, Trivello R, Tramatin A, Tositti G, Floreani A. Changing epidemiology of HCV and HBV infections in Northern Italy: a survey in the general population. *J Clin Gastroenterol* 2008; **42**: 527-532 [PMID: [18277889](#) DOI: [10.1097/MCG.0b013e318030e3ab](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

