Digestive and Liver Disease 51 (2019) 346–351

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Alimentary Tract

Management of ulcerative colitis in a real-life setting: An Italian multicenter, prospective, observational AIGO study

Maria Lia Scribano[a,*], Claudio Papi[b], Francesco Costa[c], Aurora Bortoli[d], Francesco Bortoluzzi[e], Elisabetta Buscarini[f], Maria Cappello[g], Luigi Caserta[h], Claudio Cortelezzi[i], Antonio Ferronato[j], Francesco Manguso[k], Silvia Mazzuoli[l], Nicoletta Orzes[m], Anna Kohn[a], on behalf of AIGO IBD Study Group[1]

[a] Gastroenterology Unit, AO San Camillo-Forlanini, Rome, Italy
[b] Gastroenterology Unit, San Filippo Neri Hospital, Rome, Italy
[c] Gastroenterology Unit, AOUP, Pisa, Italy
[d] Gastroenterology Unit, UAO G Salvini, Rho, Italy
[e] Gastroenterology Unit, Ulss 3 Serenissima, Venice, Italy
[f] Gastroenterology Unit, Maggiore Hospital, Crema, Italy
[g] Gastroenterology and Hepatology Section, DIBIMIS, University of Palermo, Palermo, Italy
[h] Gastroenterology Unit, San Martino Hospital, Genoa, Italy
[i] Gastroenterology Unit, ASST Settelaghi, Varese, Italy
[j] Endoscopy Unit, PO Alto Vicentino, ULSS 7 Pedemontana, Vicenza, Italy
[k] Gastroenterology Unit, Cardarelli Hospital, Naples, Italy
[l] Gastroenterology Unit, San Nicola Pellegrino Hospital, Trani, Italy
[m] Gastroenterology Unit, PO Gorizia-Pordenone, Gorizia, Italy

ARTICLE INFO

Article history:
Received 16 April 2018
Received in revised form 4 July 2018
Accepted 4 August 2018
Available online 16 August 2018

Keywords:
Clinical practice
Management
Real-life
Ulcerative colitis

ABSTRACT

Background: No data are available on the variability in the clinical management of ulcerative colitis (UC) patients by Italian gastroenterologists. Therefore, improving the standards of UC care as provided by the National Welfare Clinical Path (PDTA), in accordance with the European Crohn's and Colitis Organization (ECCO) guidelines for UC, is not easy.
Aims: To assess the management of UC by Italian gastroenterologists in a real-life setting taking into account its variability.
Methods: This prospective, cross-sectional, observational study included IBD-specialized gastroenterologists (GSIBDs) and general gastroenterologists (GGs) working in Italian public hospital units. Consecutive patients with an UC flare were enrolled and the medical treatment evaluated. For each center, the physician in charge of the study (16 GSIBDs and 10 GGs) was administered two electronic questionnaires.
Results: Among 26 units, 573 UC patients were enrolled. Good adherence to the European guidelines was reported; GSIBDs reported greater adherence than GGs with a higher prescription of rectal and combination therapy in mild to moderate distal disease and a higher rate of hospitalization in severe UC.
Conclusion: The management of UC by Italian gastroenterologists in clinical practice is good according to the ECCO consensus recommendations, though some discrepancies are present between GSIBDs and GGs.

1. Introduction

Ulcerative colitis (UC) is a chronic relapsing inflammatory bowel disease (IBD) with steadily increasing incidence in Italy and other southern European countries [1]. Despite several medical treatment options being available, the disease still impacts quality of life and the working capability of patients [2–4]. UC carries a substantial economic burden for the national health care system, as the disease often occurs at a young age and has the potential to cause lifelong ill health [5]. In light of all these aspects, UC and Crohn's disease were recently included in the National Chronicity Plan issued by the Italian Ministry of Health. This plan identifies the wide variation in the clinical management of patients as a critical issue. The

* Corresponding author at: Gastroenterology Unit, AO San Camillo-Forlanini, Circonvallazione Gianicolense 87, 00152 Rome, Italy.
E-mail address: marialiascribano@virgilio.it (M.L. Scribano).
[1] See Appendix A.

https://doi.org/10.1016/j.dld.2018.08.006
1590-8658/

aim of the plan is to propose and favor the application of IBD health care standards as defined by the recently published National Welfare Clinical Path (PDTA). The PDTA refers to the European Crohn's and Colitis Organization (ECCO) consensus document [6,7] for the medical management of UC.

No data are available on the variability in the clinical management of UC by Italian physicians; therefore, it is difficult to outline the actions to promote educational efforts by scientific societies in order to support Health Ministry governance and improve adherence to the European consensus guidelines.

In most cases in Italy, UC patients are under the care of gastroenterologists in public hospital centers, both general gastroenterologists (GGs) and gastroenterologists specialized in inflammatory bowel disease (GSIBDs). A previous nationwide survey in Spain [8] based on a questionnaire filled out by gastroenterologists on the management of mild to moderate UC indicated that, despite good agreement between GGs and GSIBDs, GGs have some shortcomings in specific aspects of UC management and lower adherence to European ECCO guidelines.

One of the main limitations of this study was that the survey responses may not reflect the actual decision-making in clinical practice. Also, in European countries, adherence to guidelines is variable, with national differences in the clinical management of UC [9–13]. In order to assess this issue in Italy in a real-life setting, we performed a cross-sectional, prospective study of the management of UC by gastroenterologists working in Italian public hospital centers. We enrolled consecutive patients with an UC flare defined clinically by the Truelove and Witts severity index [14] and evaluated the clinical management and medical procedures prescribed in that specific clinical setting. Finally, we evaluated whether a difference exists in the clinical approach between GSIBDs and GGs.

2. Materials and methods

This prospective, cross-sectional, observational study included Italian hospital gastroenterologists involved in IBD care and working in public Gastroenterology (GI) units across Italy who were recruited by an announcement on the website of the Italian Association of Hospital Gastroenterologists and Endoscopists (AIGO). At baseline, each physician in charge of the study at their center completed an electronic questionnaire (QA; Supplementary Appendix 1) addressing the hospital facilities and personal clinical experience in IBD management. The hospital data included information on the availability of an emergency department, GI ward, and organized IBD outpatient clinic. The questionnaire also requested the IBD activity, as indicated by the number of IBD patients in follow-up at the center: less than 200, between 200 and 500, or more than 500 patients. The physician data included the years of specialization in GI, self-identification as GG or GSIBD, years of clinical activity with IBD patients, percentage of IBD patients in clinical practice for those without an IBD outpatient clinic, percentage of UC patients followed at the center, and hours per week dedicated to IBD outpatient activity.

2.1. Patients

From June 2014 to July 2015, consecutive outpatients with a flare-up of active UC were recruited with an upward limit of 30 patients per physician. All diagnoses were established by commonly accepted clinical, endoscopic, and histological criteria [6]. The Truelove and Witts severity index was used to assess clinical disease activity [14]. According to the Montreal Classification, UC was classified into proctitis, left-sided, and extensive colitis [15]. Patients were included in the study regardless of the degree of clinical activity, extent of disease, and previous/concomitant medical treatment. Patients with previous colectomy were excluded. Each patient provided written, informed consent to participate in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

At enrollment, demographic and clinical details were collected and recorded using an electronic questionnaire (QB; Supplementary Appendix 2). The demographic data included age at enrollment and gender. Clinical data included year of symptom onset, year of diagnosis, disease extent, disease activity, concomitant specific therapies, and previous treatment with systemic steroids, immunosuppressants (IMMs), and anti-TNFα agents. All diagnostic procedures required by the physician to assess the current relapse were recorded. In the second part of the questionnaire (QB; Supplementary Appendix 2), the physician recorded the specific treatment prescribed for the patient (i.e., drug, dosage, length of treatment, and route of administration) and any request for hospital admission.

2.2. Statistical analysis

Data were analyzed using StatsDirect statistical software (version 1.9.8) and Epistat (Epistat Services, 1991). Categorical variables were summarized as frequencies and percentages, and continuous variables were summarized as medians and interquartile ranges. Chi-squared and Kruskal–Wallis tests were used where appropriate. A p-value less than 0.05 was considered significant.

3. Results

3.1. Characteristics of the gastroenterologists and hospital units

Twenty-six gastroenterologists from different regions in the North (n = 10), Centre (n = 11), and South of Italy (n = 5) were involved in the study. Approximately two-thirds (n = 16, 61%) identified themselves as GSIBDs. Most of the GSIBDs had at least 10 years of experience and organized outpatient clinic activity. Only 39% of the gastroenterologists were GGs (Table 1), working in GI centers with less IBD activity and an organized IBD outpatient clinic limited to less than half of the centers. Very few centers had a GI ward, regardless of IBD activity.

3.2. Population baseline characteristics

The demographic and clinical characteristics of the patients are reported in Table 2. No significant differences were observed regarding patient gender and age, or disease duration. The large majority of patients had a flare of mild to moderate activity (n = 485, 85%). At enrollment, nearly all patients were on maintenance treatment with different drugs. The vast majority were receiving oral aminosalicylates at a daily dose of 400 mg–4.8 g, with more than 90% of patients receiving a daily dose of more than 1.2 g. Most patients underwent endoscopy at relapse before treatment adjustment. Very few patients underwent computed tomography (CT) or magnetic resonance imaging (MRI), but 1 out of 5 underwent intestinal ultrasound (Table 2).

The characteristics of patients enrolled by GGs and GSIBDs were similar; however, a significantly lower rate of proctitis was noted by the GSIBDs. At enrollment, more patients in the GSIBDs group were on rectal or combined oral and rectal therapy with aminosalicylates and anti-TNFα agents. In addition, more patients in the GGs group underwent endoscopy before treatment adjustment (Table 2).

Table 1
Characteristics of the physicians and GI hospital units.

	All gastroenterologists (%) n = 26	General gastroenterologists (%) n = 10	IBD specialized gastroenterologists (%) n = 16
IBD clinical experience ≥10 years	17 (65)	6 (60)	11 (69)
IBD activity (hours/week) mean (range)	12.5 (2–32)	7 (2–14)	15.8 (5–32)
GI ward	7 (27)	2 (20)	5 (31)
Emergency department	16 (61)	2 (20)	14 (87)
IBD outpatient clinic	17 (65)	4 (40)	13 (81)
Number of IBD pts in follow-up			
<200	7 (27)	7 (70)	0
200–500	9 (35)	3 (30)	6 (37)
>500	10 (38)	0	10 (63)

GI, Gastroenterology; IBD, inflammatory bowel disease; pts, patients.

Table 2
Characteristics of the patients.

	All gastroenterologists n = 26	General gastroenterologists n = 10	IBD specialized gastroenterologists n = 16	*p Value*
Patients	573	189	384	
Females: n (%)	248 (43.4)	84 (44.4)	164 (42.7)	
Age: median (IQR)	49 (18–87)	48.5 (18–85)	48.5 (18–87)	
Disease duration (years): median (IQR)	7.5 (0.5–44)	7.0 (0.5–41)	7.5 (0.5–44)	
Disease extension — n (%)				
Proctitis	61 (10.6)	28 (14.8)	33 (0.9)	**0,03**
Left sided colitis	274 (47.8)	89 (47.1)	185 (48.2)	0,87
Extensive colitis	234 (40.8)	72 (38.1)	162 (42.2)	0,39
NR	3 (0.7)	0	3 (0.8)	
Disease activity — n (%)				
Mild to moderate	485 (84.6)	157 (83.1)	328 (85.4)	0,54
Severe	85 (14.8)	31 (16.4)	54 (14.1)	0,51
NR	3 (0.5)	1 (0.5)	2 (0.5)	
Treatment at enrollment — n (%)				
Aminosalycilates	484 (84.5)	154 (81)	330 (85.9)	0,20
— Oral monotherapy	219 (38.2)	88 (47)	131 (34.1)	**0,005**
— Rectal	171 (29.8)	41 (22)	130 (33.8)	**0,004**
— Oral + rectal	149 (26.0)	35 (18)	114 (29.7)	**0,005**
Steroids				
— Oral	105 (18.3)	27 (15)	78 (20.3)	0,10
— Rectal	57 (9.9)	16 (8)	41 (10.7)	0,49
Immunosuppressants	79 (13.8)	20 (11)	59 (15.4)	0,15
Anti-TNFα	11 (1.9)	0	11 (2.9)	**0,042**
No treatment	48 (8.4)	20 (11)	28 (7.3)	0,23
Incomplete data	6.4 (6–8)	4 (3–5)	2.4 (2–4)	
Endoscopy performed before treatment adjustment — n (%)	456 (79.6)	161 (85.2)	293 (76.3)	**0,018**
Plain abdominal X-ray — n (%)	87 (14.3)	25 (13.2)	62 (16.1)	0,42
Abdominal ultrasound — n (%)	128 (22.4)	39 (20.6)	89 (23.2)	0,56
CT scan/MRI — n (%)	41 (7.2)	9 (4.7)	32 (8.3)	0,16

Significance of bold values is $p < 0.05$.
IBD, inflammatory bowel disease; NR, not reported; anti-TNFα, anti-tumor necrosis factor antibody alpha; CT, computed tomography; MRI, magnetic resonance imaging.

3.3. Treatment by disease severity

3.3.1. Mild-moderate colitis

Almost all patients (92%) with mild-moderate left-sided or extensive colitis were on maintenance therapy at the time of the flare; the vast majority (83%) were receiving oral aminosalicylates and a few patients developed clinical relapse while on oral steroids (14%) or IMMs (14%). The prescribed therapy and the therapy at enrollment are reported in Table 3. In most cases (n = 380, 86%), the dose of oral aminosalicylates was increased to >2 g/d, with an average of 3.6 g/d (range 1.2–4.8 g/d). Approximately two-thirds of the patients (n = 258, 60%) received rectal therapy in association with oral aminosalicylates. Rectal steroids were prescribed in 1 out of 4 patients (N = 103, 24%), and in the majority of cases rectal steroids were prescribed in combination with topical aminosalicylates (79%). Beclomethasone dipropionate (BDP) was the preferred rectal steroid (n = 63, 62%) and was indicated as an oral formulation to 66 out of 166 (40%) patients treated with oral steroids. Combination treatment with oral and rectal aminosalicylates (≥1 g) was prescribed more frequently by GSIBDs for left-sided and extensive colitis and anti-TNFα agents for left-sided colitis (Table 3).

3.3.2. Severe colitis

Eighty-five patients (14.8%) had an acute severe attack of UC according to the Truelove and Witts criteria. Almost all patients (97%) were on treatment at the time of the flare, mostly with oral aminosalicylates (85%), a small number with IMMs (15%). Thirty-three patients were on oral steroids at an average dose of 28 mg/d of methylprednisolone equivalent (range 4–52 mg).

Forty-one patients were hospitalized (48%) and managed with intravenous (i.v.) steroids at an average dose of 60 mg/d (range 50–70 mg) (n = 29, 71%) and anti-TNFα agents (n = 24, 58%). Eight patients received anti-TNFα agents as first line treatment. The patients who were not hospitalized and were managed on an outpatient basis (n = 44) were prescribed steroids (n = 31, 70%), mainly

Table 3
Treatments at enrollment and prescribed for mild to moderate flare of UC according to disease extension.

Mild to moderate activity	All Gastroenterologists Patients n = 485		General gastroenterologists Patients n = 157		IBD specialized gastroenterologists Patients n = 327		*p Value*
Proctitis — n (%)	*At enrollment* N = 57	Prescribed	*At enrollment* N = 25(15.9)	Prescribed	*At enrollment* N = 32(9.8)	Prescribed	
Aminosalicylates							
Any dosage	*20*	45 (79)	*6*	15 (60)	*14*	30 (91)	**0,005**
Rectal ≥1 g	*11*	35 (61)	*5*	11 (44)	*6*	24 (75)	**0,034**
Combo oral/rectal ≥1 g	*14*	28 (49)	*5*	9 (36)	*9*	19 (59)	0,13
Steroids							
Rectal	*4*	22 (39)	*2*	12 (44)	*2*	12 (36)	0,59
Oral	*8*	10 (17)	*9*	7 (28)	*0*	3 (0.9)	0,087
Anti-TNFα	0	6 (10)	0	6 (24)	0	0	**0,012**
Left-sided colitis — n (%)	N = 241		N = 76 (48.4)		N = 165 (50.5)		
Aminosalicylates							
Oral	*207*	223 (92)	*64*	68 (89)	*143*	155 (94)	0,13
Rectal any dosage	*69*	194 (80.5)	*15*	55 (72)	*54*	139 (84)	**0,046**
Rectal ≥1 g	*63*	173 (72)	*12*	46 (60.5)	*51*	127 (77)	**0,013**
Combo oral/rectal ≥1 g	*51*	166 (69)	*7*	45 (59)	*44*	121 (73)	**0,040**
Steroids							
Rectal	*27*	64 (27)	*7*	24 (32)	*20*	40 (24)	0,29
Oral	*21*	88 (36)	*2*	27 (35.5)	*19*	61(37)	0,94
IMMs	*27*	35 (14)	*5*	7 (9)	*22*	28 (17)	0,74
Anti-TNFα	*0*	37 (15)	*0*	3 (4)	*0*	34 (21)	**0,0017**
Extensive colitis — n (%)	N = 187		N = 57 (36.3)		N = 130 (40)		
Aminosalicylates							
Oral	*149*	158 (84)	*44*	44 (77)	*105*	114 (88)	0,10
Rectal any dosage	*51*	107 (57)	*14*	28 (49)	*37*	79 (61)	0,18
Rectal ≥1 g	*47*	99 (53)	*13*	24 (42)	*34*	75 (58)	0,070
Combo oral/rectal ≥1 g	*40*	92 (49)	*10*	21 (37)	*30*	71 (55)	**0,037**
Steroids							
Rectal	*10*	39 (21)	*3*	15 (26)	*7*	24 (18)	0,30
Oral	*41*	78 (42)	*12*	23 (40)	*29*	55 (42)	0,92
IMMs	*33*	45 (24)	*9*	10 (17.5)	*24*	35 (27)	0,23
Anti-TNFα	*6*	43 (23)	*0*	9 (16)	*6*	34 (26)	0,17

Significance of bold values is p < 0.05.
UC, ulcerative colitis; IBD, inflammatory bowel disease; anti-TNFα, anti-tumor necrosis factor antibody alpha; IMM, immunosuppressants.

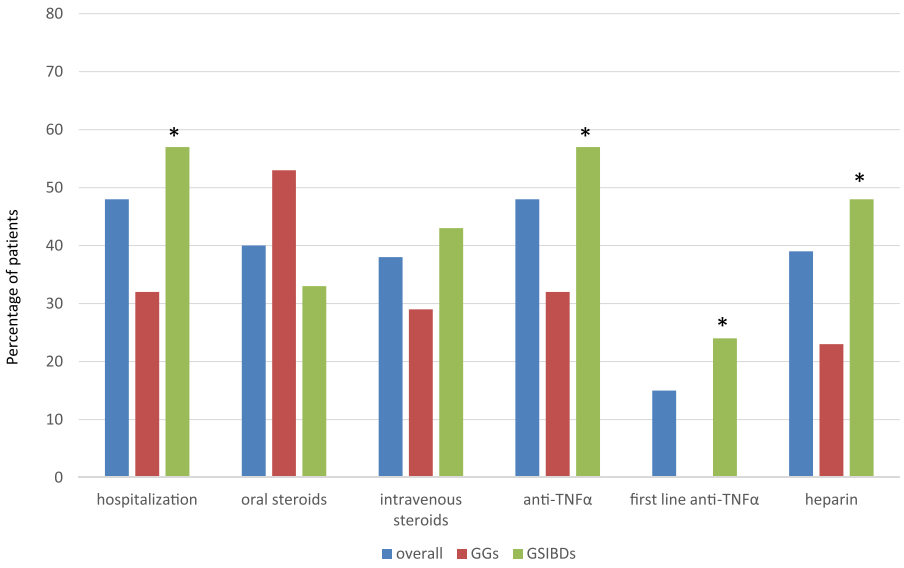

Fig. 1. Acute severe colitis: management and drug prescription.
GGs, general gastroenterologists; GSIBDs, inflammatory bowel disease specialized gastroenterologists; *$p < 0.05$.

oral at an average dose of 50 mg/d (range 10–65 mg) (n = 27). Anti-TNFα agents (n = 17, 38%) were prescribed in five patients as first line treatment. The prescription of subcutaneous low molecular weight heparin for thromboembolic prophylaxis was limited to 58% of the hospitalized patients. More patients were hospitalized by GSIBDs (57% vs. 32%; p = 0.045) and prescribed heparin (48% vs. 23%; p = 0.036) and anti-TNFα agents as second (57% vs. 32%; p < 0.045) and first line treatment (24% vs. 0%; p = 0.008; Fig. 1).

3.4. Treatment related to proctitis

A minority of patients had mild to moderate active proctitis (Table 3). Topical aminosalicylates were prescribed for the majority of these patients at the same rate as suppositories or enema. Nevertheless, less than two-thirds of patients were prescribed 1 g or more of aminosalicylates, and only 1 out of 2 in combination with oral aminosalicylates. Rectal steroids were prescribed almost exclusively with rectal aminosalicylates, mainly (91%) as BDP. GSIBDs prescribed significantly more rectal aminosalicylates, whereas GGs prescribed more anti-TNFα agents (Table 3).

4. Discussion

To the best of our knowledge, this is the first prospective study to provide a detailed description of UC management in clinical practice in Italy. All participating physicians worked in the GI units of hospitals managed by the Italian National Health System in different regions in North, Central, and South Italy and are members of the AIGO. Characterization as either a GG or GSIBD was based on self-identification and did not meet defined criteria. However, seven (7/10; 70%) GGs worked in centers with less than 200 IBD patients in follow-up, whereas GSIBDs worked only in centers with at least 200 patients and ten GSIBDs (10/16; 62%) in centers with more than 500 IBD patients in follow-up. These figures and the size of the professional activity dedicated to IBD as proved by the weekly clinical activity and a IBD outpatient clinic seem to confirm the veracity of the self-identification.

Our data show that the vast majority of UC patients managed by gastroenterologists in Italian hospitals receive long-term maintenance treatment, most often with oral aminosalicylates, alone or in combination with other treatments. The high rate of oral aminosalicylate prescriptions is confirmed in the treatment of active mild to moderate disease. The prescription of oral aminosalicylates, alone or in combination with steroids or anti-TNFα agents, is high regardless of the extent of disease. The daily dosage at enrollment was upgraded, as more than half of the patients were prescribed 3.6 g or more per day, with no difference between GGs and GSIBDs.

A significantly lower rate of proctitis was enrolled by the GSIBDs. Proctitis is generally a milder form more often managed by physicians with less experience in IBD.

The results indicate an underuse of rectal aminosalicylates. GGs underuse topical treatment more frequently than GSIBDs in proctitis and left-sided colitis, and as combination therapy with oral aminosalicylates in extensive and left-sided colitis. The low confidence in rectal treatment expressed by GGs may prove a difficulty for physicians with less specific experience to overcome patient resistance toward rectal formulations, especially during active disease. However, as a whole, Italian gastroenterologists prescribe more topical aminosalicylates (63% with daily dos ≥1 g) than gastroenterologists from the US (11–42%) [16,17] or other European countries (17–35%) [18,19], and oral aminosalicylates are prescribed in only approximately 50% of UC patients in other countries [16,18,20]. The high prescription rate of aminosalicylates in Italy was reported in a previous study addressing the cost determinants of a European IBD inception cohort with 10 years of follow-up [21]. There are several factors that can explain the wide use of aminosalicylates in Italy: the Italian root of research on topical aminosalicylates [22–24], the development of a national pharmaceutical production of aminosalicylates, and the lack of charge for medication for UC patients supported by the National Health System.

Rectal steroids are prescribed mainly in patients with proctitis and in combination with rectal aminosalicylates. The most commonly prescribed steroid for rectal treatment is BDP, a second-generation steroid with topical effects and minimal systemic activity, which is also prescribed as an oral formulation in a large number of patients with extensive and left-sided colitis who need oral steroids (67 out of 166, 40%). Oral beclomethasone is not inferior to prednisone (40 mg) [25] and is indicated in the treatment of UC refractory to aminosalicylates [26–28] as an alternative to systemic corticosteroids.

Endoscopic reassessment before therapeutic adjustment was performed in approximately 80% of patients, less frequently by GSIBDs, who may rely more on their clinical experience. Although the European guidelines consider endoscopic reevaluation at relapse to be appropriate, there is no agreement in the attitude of gastroenterologists from different countries [29]. A recent survey conducted among private gastroenterologists in France [19] reported a similar rate (88.3%) of endoscopy for monitoring disease activity, whereas only 14–20% of Spanish gastroenterologists questioned about adherence to ECCO guidelines on UC refer to the use of colonoscopy to document activity and extension at each flare-up [8].

Concerning severe UC, several discrepancies were observed. Severe UC is a potentially life-threatening condition that requires hospital admission, intensive treatment, and a multidisciplinary approach [7,30,31]. In our survey, less than half of the patients classified as having a severe attack were hospitalized and treated with i.v. steroids and anti-TNFα agents; the majority were managed with oral steroids and anti-TNFα agents on an outpatient basis. The greater ease of hospital admission due to the presence of an emergency department is the likely reason for the larger number of hospitalizations of patients with severe disease and managed by GSIBDs. Moreover, physicians with less experience may overestimate disease severity and define as severe a moderate-severe relapse that can be managed as outpatient using mainly oral steroids.

In summary, the data show overall good adherence to the European guidelines for the management of UC by the gastroenterologists working in Italian public hospitals. The number of GSIBDs and GGs involved in the study was different, however this may not influence the detected differences in behavior. There are a few areas, such as the high prescription rate of aminosalicylates and BDP, where the approach of Italian gastroenterologists differs from that of gastroenterologists in other European and North American countries. Different cultural values and specific features of the National Health System may underlie these differences. The variation between GGs and GSIBDs is related to the use of topical treatment in mild to moderate distal disease and the hospitalization and intensive management of severe colitis. GSIBDs demonstrate greater adherence to guidelines with a higher rate of rectal and combination therapy prescriptions [32] and a higher rate of hospitalization in severe disease. In Italy, the scientific gastroenterology societies could take on the task of improving the performance of GGs in this specialized field, organizing widespread educational interventions on the management of distal disease and the assignment of patients with severe disease to hospitals with GI wards and specific expertise in IBD [33]. In this respect, the scientific societies can support the actions of health authorities to reduce the expenses of inappropriate medical management.

Conflict of interest

Maria Lia Scribano: speaker and/or advisory board member for Abbvie, Janssen, Mundipharma, Pfizer, Takeda, outside the submitted work.

Claudio Papi: grants from Abbvie, Takeda, MSD, Chiesi, Sofar, outside the submitted work.

Francesco Costa: personal fees and non-financial support from Abbvie, MSD, Takeda, Otsuka outside the submitted work, personal fees from DIASORIN, Zambon, outside the submitted work.

Maria Cappello: lecture fees from Abbvie, MSD, Takeda, Shire, Vifor, Pharmanutra, outside the submitted work.

Silvia Mazzuoli: grants from Abbvie, MSD, Mundipharma, Takeda, outside the submitted work.

Anna Kohn: financial support for research not related to the present study from MSD and Abbvie.

Other authors: no conflicts of interest.

Appendix A.

AIGO IBD study group: Chrysanthi Balatsinu (Endoscopy Unit, ASUR Marche AV3, PO Civitanova Marche, MC), Linda Ceccarelli (Gastroenterology Unit, AOUP Cisanello Hospital, Pisa), Marco Cedola (Gastroenterology Unit, Spaziani Hospital, Frosinone), Roberto Faggiani (Gastroenterology Unit, PO Belcolle, Viterbo), Andrea Geccherle (IBD Unit, SacroCuore Don Calabria Hospital, Negrar, VR), Alessandro Gigliozzi (Gastroenterology Unit, San Camillo De Lellis Hospital, Rieti), Renzo Gullotta (Gastroenterology Unit, Clinica San Carlo, Paderno Dugnano, MI), Roberto Lorenzetti (Gastroenterology Unit, Nuovo Regina Margherita Hospital, Rome), Guido Lupinacci (Gastroenterology Unit, Maggiore Hospital, Crema), Mauro Mastronardi (Endoscopy Unit, IRCSS De Bellis, Castellana Grotte, BA), Giammarco Mocci (Gastroenterology Unit, AO G Brotzu, Cagliari), Giuseppe Scarpulla (Gastroenterology Unit, PO Maddalena Raimondi San Cataldo, Caltanissetta), Renzo Shalling (Endoscopy Unit, Vimercate Hospital, Vimercate, MB), Michele Sozzi (Gastroenterology Unit, Cattinara Hospital, Trieste), Ottaviano Tarantino (Gastroenterology Unit, ASL 11, Empoli, FI).

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.dld.2018.08.006.

References

[1] Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology 2012;142:46–54.

[2] Rubin DT, Dubinsky MC, Panaccione R, Siegel CA, Binion DG, Kane SV, et al. The impact of ulcerative colitis on patients' lives compared to other chronic diseases: a patient survey. Dig Dis Sci 2010;55:1044–52.

[3] Høivik ML, Moum B, Solberg IC, Henriksen M, Cvancarova M, Bernklev T, et al. Work disability in inflammatory bowel disease patients 10 years after disease onset: results from the IBSEN Study. Gut 2013;62:368–75.

[4] De Boer AG, Bennebroek Evertsz' F, Stokkers PC, Bockting CL, Sanderman R, Hommes DW, et al. Employment status, difficulties at work and quality of life in inflammatory bowel disease patients. Eur J Gastroenterol Hepatol 2016;28:1130–6.

[5] Burisch J, Vardi H, Pedersen N, Brinar M, Cukovic-Cavka S, Kaimakliotis I, et al. Costs and resource utilization for diagnosis and treatment during the initial year in a European inflammatory bowel disease inception cohort: an ECCO-EpiCom Study. Inflamm Bowel Dis 2015;21:121–31.

[6] Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A, Barreiro-de Acosta M, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. J Crohns Colitis 2017;11:649–70.

[7] Harbord M, Eliakim R, Bettenworth D, Karmiris K, Katsanos K, Kopylov U, et al. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 2: current management. J Crohns Colitis 2017;11:769–84.

[8] Gisbert JP, Gomollón F, Hinojosa J, López San Román A. Adherence of gastroenterologists to European Crohnós and Colitis Organisation consensus on ulcerative colitis: a real-life survey in Spain. J Crohns Colitis 2010;4:567–74.

[9] Spiegel BMR, Ho W, Esrailian E, Targan S, Higgins PDR, Siegel CA, et al. Controversies in ulcerative colitis: a survey comparing decision making of expert versus community gastroenterologists. Clin Gastroenterol Hepatol 2009;7:168–74.

[10] Pittet V, Maillard MH, Lauvergeon S, Timmer M, Michetti P, Froehlich F, et al. Acceptance of inflammatory bowel disease treatement recommendations based on appropriateness ratings: do practicing gastroenterologists agree with experts? J Crohns Colitis 2015;9:132–9.

[11] Orlando A, Armuzzi A, Papi C, Annese V, Ardizzone S, Biancone L, et al. The Italian Society of Gastroenterology (SIGE) and the Italian Group for the study of Inflammatory Bowel Disease (IG-IBD). Clinical practice guidelines: the use of tumor necrosis factor-alpha antagonist therapy in inflammatory bowel disease. Dig Liver Dis 2011;43:1–20.

[12] Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, et al. Guidelines for the management of inflammatory bowel disease in adults. Gut 2011;60:571–607.

[13] Stein J, Bager P, Befrits R, Gasche C, Gudehus M, Lerebours E, et al. Anaemia management in patients with inflammatory bowel disease: routine practice across nine European countries. Eur J Gastroenterol Hepatol 2013;25:1456–63.

[14] Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J 1955;2:1041–8.

[15] Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a working party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol 2005;19:5–36.

[16] Reddy SI, Friedman S, Telford JJ, Strate L, Ookubo R, Banks PA. Are patients with inflammatory bowel disease receiving optimal care? Am J Gastroenterol 2005;100:1357–61.

[17] Richter JM, Kushkuley S, Barrett JA, Oster G. Treatment of new-onset ulcerative colitis and ulcerative proctitis: a retrospective study. Aliment Pharmacol Ther 2012;36:248–56.

[18] Seibold F, Fournier N, Beglinger C, Mottet C, Pittet V, Rogler G, et al. Topical therapy is underused in patients with ulcerative colitis. J Crohns Colitis 2014;8:56–63.

[19] Duchesne C, Faure P, Kohler F, Pingannaud M-P, Bonnaud G, Devulder F, et al. Management of inflammatory bowel disease in France: a nationwide survey among private gastroenterologists. Dig Liver Dis 2014;46:675–81.

[20] Rungoe C, Langholz E, Andersson M, Basit S, Nielsen NM, Wohlfahrt J, et al. Changes in medical treatment and surgery rates in inflammatory bowel disease: a nationwide cohort study 1979-2011. Gut 2014;63:1607–16.

[21] Odes S, Vardi H, Friger M, Wolters F, Russel MG, Riis L, et al. Cost analysis and cost determinants in a European inflammatory bowel disease inception cohort with 10 years of follow-up evaluation. Gastroenterology 2006;131:719–28.

[22] Campieri M, Lanfranchi GA, Bazzocchi G, Brignola C, Sarti F, Franzin G, et al. Treatment of ulcerative colitis with high-dose 5-aminosalicylic acid enemas. Lancet 1981;2:270–1.

[23] Vecchi M, Meucci G, Gionchetti P, Beltrami M, Di Maurizio P, Beretta L, et al. Oral versus combination mesalazine therapy in active ulcerative colitis: a double-blind, double-dummy, randomized multicentre study. Aliment Pharmacol Ther 2001;15:251–6.

[24] Campieri M, Gionchetti P, Belluzzi A, Brignola C, Tampieri M, Iannone P, et al. Optimum dosage of 5-aminosalicylic acid as rectal enemas in patients with active ulcerative colitis. Gut 1991;32:929–31.

[25] Van Assche G, Manguso F, Zibellini M, Nuño JL, Goldis A, Tkachenko E, et al. Oral prolonged release beclomethasone dipropionate and prednisone in the treatment of active ulcerative colitis: results from a double-blind, randomized, parallel group study. Am J Gastroenterol 2015;110:708–15.

[26] Rizzello F, Gionchetti P, D'Arienzo A, Manguso F, Di Matteo G, Annese V, et al. Oral beclometasone dipropionate in the treatment of active ulcerative colitis: a double-blind placebo-controlled study. Aliment Pharmacol Ther 2002;16:1109–16.

[27] Campieri M, Adamo S, Valpiani D, D'Arienzo A, D'Albasio G, Pitzalis M, et al. Oral beclometasone dipropionate in the treatment of extensive and left-sided active ulcerative colitis: a multicentre randomised study. Aliment Pharmacol Ther 2003;17:1471–80.

[28] Papi C, Aratari A, Moretti A, Mangone M, Margagnoni G, Koch M, et al. Oral beclomethasone dipropionate as an alternative to systemic steroids in mild to moderate ulcerative colitis not responding to aminosalicylates. Dig Dis Sci 2010;55:2002–7.

[29] Schoepfer AM, Vavricka S, Zahnd-Straumann N, Straumann A, Beglinger C. Monitoring inflammatory bowel disease activity: clinical activity is judged to be more relevant than endoscopic severity or biomarkers. J Crohns Colitis 2012;6:412–8.

[30] Ordás I, Eckmann L, Talamini M, Baumgart DC, Sandborn WJ. Ulcerative colitis. Lancet 2012;380:1606–19.

[31] Chen JH, Andrews JM, Kariyawasam V, Moran N, Gounder P, Collins G, et al. Review article: acute severe ulcerative colitis — evidence-based consensus statements. Aliment Pharmacol Ther 2016;44:127–44.

[32] Ford AC, Khan KJ, Achkar JP, Moayyedi P. Efficacy of oral vs. topical, or combined oral and topical 5-aminosalicylates, in ulcerative colitis: systematic review and meta-analysis. Am J Gastroenterol 2012;107:167–76.

[33] Gagliardi AR, Brouwers MC, Palda VA, Lemieux-Charles L, Grimshaw JM. How can we improve guideline use? A conceptual framework of implementability. Implement Sci 2011;6:1–11.