Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Digestive and Liver Disease 52 (2020) 1238–1240

Contents lists available at ScienceDirect

Digestive and Liver Disease

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

Correspondence

The management of inflammatory bowel diseases in the era of COVID-19 pandemic: When "non-urgent" does not mean "deferrable"

Dear Editor,

The widespread diffusion of the Severe Acute Respiratory Syndrome-CoronaVirus-2 (SARS-CoV-2) infection has significantly reshaped all healthcare systems. The high contagiousness and the unpredictable request of admission for symptomatic patients has led hospitals to reconvert several units into Coronavirus Disease-19 (COVID-19) facilities, requiring the recruitment of medical and nursing staff, taken from both medical and surgical departments for the treatment of pulmonary or infectious diseases. Moreover, to reduce the risk of transmission, outpatients' visits are currently limited to those considered urgent according to the priorities code of the Italian health system (i.e. requiring medical assistance within maximum 72 h or 10 days). Accordingly, Inflammatory Bowel Disease (IBD) Units throughout the country had to re-organize their own agenda, limiting the accesses to 3 categories of outpatients: (1) patients undergoing biological therapies, for whom the risk of disease relapse is considered more worrying than the risk of COVID-19 infection; (2) patients enroled in clinical trials in order to guarantee the prosecution of therapies and (3) patients complaining of acute symptoms, not manageable with telemedicine.[1-2] Examples of "non deferrable" visits are for patients complaining of moderate-to-severe IBD symptoms, new onset/relapse of extra-intestinal manifestations, active perianal disease or sub-acute obstruction symptoms requiring surgery.

All other schedules, including endoscopic, radiological and elective surgery procedures had to be indefinitely deferred.

However, whether these defined "urgency criteria" would perfectly fit all IBD patients could be a matter of debate. Treatment outcomes of Crohn's disease (CD) and ulcerative colitis (UC) have progressively evolved beyond symptomatic remission to more challenging "deep remission" and eventually "complete disease control", that is prevention of bowel-damage and long-term disability [3]. Medical strategies have been enhanced by the introduction of early intervention, treat-to target and tight monitoring approaches. In this context, deferring all scheduled procedures could reduce the level of care below acceptable standards for many IBD patients.

We consider 5 different scenarios of "non urgent" patients, who, anyway, should not be indefinitely postponed even in a pandemic situation:

(1) **Recent onset of symptoms suggestive of CD: when the suspicion is high**

Diagnostic delay is still a challenging issue for CD patients, especially in case of nonspecific abdominal complaints (usually ascribed to irritable bowel syndrome) and is associated with higher risk of complications at diagnosis and of early need for surgery. Moreover, in patients already diagnosed with CD, it is common experience to observe a poor correlation between clinical disease activity and mucosal lesions [4]. Accordingly, highly suspect CD patients should be promptly investigated in order to start early and effective treatment strategies, aimed to impact the long-term clinical course and to reduce the risk of complications.

(2) **Patients in clinical remission requiring prompt evaluation, tight follow-up and long-term strategies:**

(a) UC patient discharged after a severe acute flare on oral steroids: Up to 67% of patients, admitted for an acute severe flare of colitis, respond to intravenous steroids and, at discharge, according to the physicians' judgement, are placed on maintenance therapy with 5-amynosalicilates, thiopurines or biologics. However, up to 20% of these patients may experience a short-term clinical relapse during steroids tapering, requiring prompt escalation of therapy or change in the maintenance treatment [5]. A short term outpatient evaluation after discharge should not be deferred in these patients.

(b) CD patients having recently undergone bowel resection: Prophylactic therapy after bowel resection in CD is strictly recommended for patients with at least one risk factor for recurrence, including tobacco use, history of previous surgery and/or penetrating behaviour of the disease. Thiopurines or anti TNF-α agents seem to be the best options for preventing post-operative recurrence in high risk patients, and the treatment should be started early (usually within 1 to 3 months) after surgery, provided that there are no specific contraindications [6]. Moreover, endoscopic assessment should be performed within 6 to 12 months after surgery in order to promptly recognise endoscopic recurrence and consequently adapt the medical strategy. Therefore, early introduction of prophylactic treatment and endoscopic evaluation within 6–12 months should not be deferred, even in asymptomatic patients.

(c) Patients with recent introduction of thiopurines: Thiopurines are still used as maintenance therapy in steroid-dependant IBD patients, as prophylactic therapy after bowel resection and in combination with anti TNF-α drugs. Despite several limitations of these drugs (i.e. effectiveness and safety), responders are offered a low cost, simple, oral maintenance therapy. Patients started on thiopurines require strict safety follow-up in order to promptly recognise intolerance or allergic toxicities (e.g. nausea, myalgia, pancreatitis) and to manage dose-dependant side-effects (e.g.

https://doi.org/10.1016/j.dld.2020.05.053
1590-8658/© 2020 Editrice Gastroenterologica Italiana S.r.l. Published by Elsevier Ltd. All rights reserved.

leukopenia). Checking metabolite levels, when available, can be helpful to assess therapeutic effect and compliance.

(3) **Patients with recent transition from a paediatric or low-volume adult centre to a tertiary referral centre**

Transition from paediatric to adult health care setting is a crucial phase for IBD patients, requiring structured programs, joint paediatric-adult clinic and an approach tailored to the patients. The acquisition of decision-making and self-efficacy skills seems to be the key of a successful transition [7]. For adults in transition to a tertiary centre, it is important to face potential barriers to efficacious transition, such as fear to receive lower attention because of high-volume or reluctance for the loss of the relationship with previous doctors. In both situations, assuring continuity of care with an established transition program can improve the engagement of patients and reduce the risk of non-adherence and loss to follow-up.

(4) **Special situations requiring tight and multidisciplinary approach and follow-up**

(a) IBD pregnant women: Women with IBD often have insufficient knowledge about pregnancy-related issues. Fears about potential side-effects can lead to inopportune medications withdrawal causing relapse. IBD flares-up during pregnancy are a great concern, because they are associated with an increased risk of pre-term birth. Therefore, a period of at least 3 months of steroid-free clinical remission prior to conception is strongly recommended, as well as a close monitoring (up to every 2 weeks on flare) during pregnancy by gastroenterologists in order to promptly adapt the medical therapy. A counselling on mode of delivery is advocated for patients with CD and perianal involvement [8].

(b) IBD patients with cancer: The management of IBD patients with cancer requires a strong multidisciplinary collaboration between gastroenterologists and oncologists. Risks and benefits of introducing/maintaining IBD medical therapies should be balanced for each patient, according to IBD clinical activity and cancer diagnosis. In case of withdrawal of IBD drugs, patients should not feel abandoned, but closely followed-up and engaged in an oncological treatment plan. A prompt intervention should be assured in case of IBD flare during anti-neoplastic therapies, to guarantee the prosecution of standard treatments.

(c) CD patients who require nutritional support: Enteral or parenteral nutritional support is mandatory for CD patients unable to obtain adequate calories intake, such as those ones with history of multiple bowel resections or with jejunostomy or proximal ileostomy or short bowel syndrome. Patients should be given dietary counselling and strictly followed-up in order to prevent de-hydration and nutrition-related disorders [9].

(5) **Patients pre-screened for clinical trial**

Participating in a clinical trial can be a challenging step for refractory IBD patients, who are torn between safety concerns, placebo risk and hopes for efficacy. Physicians should adequately discuss the informed consent form, in order to avoid therapeutic misconception, to ascertain that patients understand the purpose and procedures of the study and to reassure the patients that refusal to participate will not compromise the doctor–patient relationship [10].

In conclusion, SARS-CoV-2 pandemic has dramatically changed the level of assistance for patients affected by chronic conditions, with an almost complete preclusion to routine follow-up visits and procedures. Ragrding IBD, several concerns are emerging about how to maintain "optimal" standard of care also for patients considered "deferrable". Diagnostic delay, non-adherence and loss to follow-up, lack of optimal and timely treatment can represent concrete risks for such patients. In the era of ambitious therapeutic goals, treatment strategies and decisions cannot rely on symptoms only, but they require tight monitoring of disease including also objective inflammation markers. Therefore, close follow-up is mandatory for many IBD patients, even if in clinical remission and not considered "urgent" according to symptoms alone. The level of care for IBD and other chronic conditions should not be reduced below optimal quality standard even during a pandemic with reduced dedicated staff and facilities.

Authors' contribution

All the authors contributed to the conception and the design of this letter.

Daniela Pugliese and Claudio Papi wrote the manuscript. Giuseppe Privitera, Annalisa Aratari, Stefano Festa and Alessandro Armuzzi revised the manuscript critically.

All the authors approved the final version of the manuscript.

Alessandro Armuzzi oversaw the project and guarantees for the integrity of the work.

Fundings

None

Declaration of Competing Interest

Daniela Pugliese received speaker fees from AbbVie, MSD, Takeda and Janssen, Pfeizer. Claudio Papi received consultancy and educational projects from Takeda, MSD, AbbVie, Sofar, Chiesi, and Alfa-Wasserman. Giuseppe Privitera received consultancies fee from Alphasigma. Stefano Festa received lecture fees and consulting from Takeda, Ferring, Sofar, and Alfa-Wasserman. Alessandro Armuzzi: consulting and/or advisory board fees from AbbVie, Allergan, Amgen, Biogen, Bristol-Myers Squibb, Celgene, Celltrion, Ferring, Janssen, Lilly, MSD, Mylan, Pfizer, Samsung Bioepis, Sandoz, Takeda; lecture and/or speaker bureau fees from AbbVie, Amgen, Biogen, Ferring, Janssen, MSD, Mitsubishi-Tanabe, Nikkiso, Pfizer, Sandoz, Samsung Bioepis, Takeda; and research grants from MSD, Pfizer, Takeda. All the remaining authors have no conflict of interest to delclare.

References

[1] Scaldaferri F, Pugliese D, Privitera G, et al. Impact of COVID-19 pandemic on the daily management of biotechnological therapy in Inflammatory Bowel Disease patients: the re-organizational response in a high-volume Italian inflammatory bowel disease center. United Eur Gastroent J 2020 Epub ahead of print. doi:10.1177/2050640620929133.

[2] Maida M, Sferrazza S, Savarino E, et al. Impact of COVID-19 pandemic on Gastroenterology Divisions in Italy: a national survey. Dig Liver Dis. May 2020 Epub ahead of print 16. doi:10.1016/j.dld.2020.05.017.

[3] Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. Lancet. 2017;389(10080):1741–55.

[4] Schoepfer A, Santos J, Fournier N, et al. Systematic analysis of the impact of diagnostic delay on bowel damage in paediatric versus adult onset crohn's disease. J Crohns Colitis 2019;13(10):1334–42.

[5] Salameh R, Kirchgesner J, Allez M, et al. Long-term outcome of patients with acute severe ulcerative colitis responding to intravenous steroids. Aliment Pharmacol Ther 2020.

[6] Burr NE, Hall B, Hamlin PJ, Selinger CP, Ford AC, O'Connor A. Systematic Review and Network Meta-Analysis of Medical Therapies to Prevent Recurrence of Post-Operative Crohn's Disease. J Crohns Colitis 2019;13(6):693–701.

[7] van Rheenen PF, Aloi M, Biron IA, et al. European Crohn's and Colitis Organisation Topical Review on Transitional Care in Inflammatory Bowel Disease. J Crohns Colitis 2017;11(9):1032–8.
[8] Mahadevan U, Robinson C, Bernasko N, et al. Inflammatory Bowel Disease in Pregnancy Clinical Care Pathway: a Report From the American Gastroenterological Association IBD Parenthood Project Working Group. Gastroenterology 2019;156(5):1508–24.
[9] Bischoff SC, Escher J, Hébuterne X, et al. ESPEN practical guideline: clinical Nutrition in inflammatory bowel disease. Clin Nutr 2020;39(3):632–53.
[10] Kurin M, Katz J, Kodish E, Lashner B. Informed Consent in IBD Trials: where We Are and Where We Need to Go. Inflamm Bowel Dis 2019;25(7):1115–19.

Daniela Pugliese
CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy

Claudio Papi
IBD UNIT, Ospedale San Filippo Neri, Largo Gemelli, 8, Rome, Italy

Giuseppe Privitera
Dipartimento Universitario di Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Rome, Italy

Annalisa Aratari, Stefano Festa
IBD UNIT, Ospedale San Filippo Neri, Largo Gemelli, 8, Rome, Italy

Alessandro Armuzzi*
CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy
Dipartimento Universitario di Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Rome, Italy

*Corresponding author at: CEMAD – IBD UNIT - Unità Operativa Complessa di Medicina Interna e Gastroenterologia, Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy.
E-mail addresses: alearmuzzi@yahoo.it, alessandro.armuzzi@unicatt.it (A. Armuzzi)