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Correspondence

Management of patients with inflammatory bowel disease and outcomes during the first wave of the Covid-19 pandemic


Dear Editor,

We read with great interest the recently published paper by Rizzello et al. [1] reporting on disease outcome and infections with SARS-COV-2 in patients with Inflammatory Bowel disease (IBD) during phase I of the Covid-19 pandemic in a high risk region in Northern Italy. In the present letter we focused on the outcome of IBD patients in a low-risk region of Italy, i.e. Sicily [2].

Six-hundred eighty-nine patients (Crohn's disease, CD: 369, ulcerative colitis, UC 320) with at least one appointment in the two months before March 8th, 2020 and within 2 months after the end of lockdown (28th May, 2020) were included in the study and divided into 3 groups: 1. patients on intravenous (i.v.) biologics ($n=247$) [vedolizumab (41%), infliximab (59%), and first infusion of ustekinumab (0.2%)] (IV Group); 2. patients on subcutaneously (s.c.) administered biologics ($n=217$) [adalimumab (63%), golimumab (3%), and ustekinumab (34%) in maintenance therapy] (SC Group), and 3. patients on oral conventional treatments ($n=225$) [mesalazine (64%), steroids (16%), or immunomodulators (20%)] (CT Group). The number of face-to-face appointments and that of patients managed with telemedicine in the three patient groups was assessed. Adherence to therapy, interruption, or delay were determined as follows: in SC and CT groups by checking the date of prescriptions and number of prescribed doses (for s.c. therapy) and specific interview. Delay was defined as an interval of more than 10 days for i.v. and s.c. medications; treatment interruption was defined as a therapy-free interval of more than 1 month.

Data on hospitalizations and endoscopies in our hospital during lockdown in Italy (March 8th, 2020–May 18th, 2020) were collected and compared with the corresponding period in 2019 (March 8th, 2019–May 18th, 2019). We also considered how many patients started a new therapy (first prescription or switch) with biological drugs (s.c. or i.v.) during lockdown compared with the corresponding period in 2019. The study was approved by the Ethics Committee of Messina, protocol n.119-20.

At baseline most patients were in remission or with mild disease according to clinical scores for CD (Harvey-Bradshaw, HBI) and UC (partial Mayo score) in all treatment groups and no significant differences were found at the end of lockdown period (data not shown).

As shown in Table 1, there was a significant difference ($p < 0.001$) between the number of scheduled face-to-face appointments and, consequently, of telemedicine management. In the IV, 15% of patients delayed scheduled visits or stopped therapy because of fear of exposure to the virus or concerns with biologic therapies. During the lockdown period, patients of the SC

group received steroids more frequently ($p=0.008$) and needed treatment changes more frequently ($p=0.038$) compared to the IV group. However, the need for unscheduled appointments due to disease flare was low never exceeding 5% in all groups. Considering the risk factors for disease flare, multivariate analysis identified only one risk factor during or after lockdown, i.e. belonging to the groups followed by remote visits (SC and CT groups) (OR 2.74; 95%CI:1.56–4.84, $p < 0.001$). Concerning hospitalizations for acute flare, no differences were observed between the study groups (IV group: 1 hospitalization; SC group: 4, and CT group: 1).

Compared with the corresponding reference period in 2019, there was no difference concerning new treatment starts, either switch from a previous biologic drug or a new treatment in a naïve patient, but a major difference ($p < 0.001$) was found for follow-up endoscopies with a reduction by 75% of scheduled colonoscopies.

Overall, none of our patients was infected by SARS-CoV2 virus during the period of the study.

In the present report we focused on the outcome of IBD patients managed with different approaches. Most former reports related to the Covid-19 pandemic investigated organizational adaption to the changing situation or on disease outcome in case of SARS-CoV-2 infection in IBD patients [3,4].

The possibility to provide healthcare by remote control was the only way to guarantee social distancing and reduce the transmission of SARS-CoV-2 infection but there was no time for an adequate preparation of staff members or patients, thus the “telemedicine” adopted by the remaining medical staff members in the limited sense of using phone calls or e-mail messages focused on simple questions including general wellbeing, abdominal pain, number of bowel movements and presence of visible blood in stools in combination with blood chemistry whenever available.

The main finding of our study was that patients managed with remote monitoring were more likely to receive steroids or to change therapy compared with the IV group. These results were confirmed by multivariate analysis. No significant differences between the 3 groups related to the request of urgent appointments for disease flare or the number of patients with elevated CRP were noted. Treatment decisions made at a distance without endoscopy support may have led the physician to a more aggressive approach with steroids to treat a potential disease flare. These results suggest a possible overtreatment of patients probably as a consequence of hastily adopted treatment decisions by staff members not sufficiently trained for telemedicine or provoked by patients not sufficiently confident in interpreting and reporting their symptoms.

As expected, routine endoscopies dramatically decreased since only 1% of IBD patients followed at our center had a colonoscopy compared to 9% of the reference period. Identical figures were reported from the UK with a reduction of endoscopic procedures by 85% compared with a pre-pandemic cohort [5]. A strong reduction

Table 1

Comparison of visits (face-to-face or telemedicine); treatment interruption or delay of scheduled treatments, unscheduled appointments because of flare, steroid need or need to change therapy, hospitalisations, and surgery between the three study groups; s.c. subcutaneous administration; i.v. endovenous administration; chi-square-test.

	Biologics i.v. n = 247	Biologics s.c. n = 217	Conventional therapy n = 225	p value
Programmed visits in presence; n (%)	202 (82)	42 (19)	47 (21)	< 0.001
Stop or delay of therapy; n (%)	38 (15)	5 (2)	2 (0.8)	< 0.001
Unscheduled visits because of flare; n (%)	7 (3)	11 (5)	10 (4)	0.471
Steroid need; n (%)	11 (4)	28 (13)	26 (12)	0.008
Need to change therapy; n (%)	10 (4)	23 (11)	19 (8)	0.038
Hospitalization; n (%)	1 (0.4)	4 (2)	1 (0.4)	0.302

in endoscopic procedures occurred in all GI Divisions in Italy and procedures were limited to endoscopic emergencies [6]. In an international survey the majority of IBD centers reported a decrease of 75–100% in endoscopic activities [7]. This represents probably the major restriction with the most important impact on gastroenterology practice and IBD management.

In the present study, only patients on i.v. biological treatments were more likely to stop or to delay treatment. In a recent Chinese report, interruption of treatment with biologics or immunosuppressants was associated with disease worsening and increased need for hospitalizations [8]. In that study, about 51% of patients on biological agents discontinued therapy mostly because of restriction on going to hospitals, whereas 13% spontaneously stopped treatments because of concerns. Compared to our cohort, the aforementioned report by Rizzello et al. [1] observed a higher rate of treatment discontinuation or delay (16%) leading in approximately 95% of patients to worsening of disease. In the present analysis, discontinuation rate for every kind of biologic drug was lower (9%) and may be explained by the fact that Sicily was a low-risk region at the time of the first wave of the pandemic. This fact, with a consequent lower perception of infection risk compared to other Italian regions, may have contributed to a better adherence to therapy.

When assessing the different prescribing practices compared to the reference period in 2019, during lockdown the number of new prescriptions of biologics decreased numerically but without significant differences. Conversely, a study by Sharma et al. from the UK reported an increase of the use of biologic drugs during phase I of the pandemic favoring vedolizumab and ustekinumab, because of their better safety profile [5]. Among our patients similarly to the study by Rizzello et al. [1], no shift from i.v. anti-TNF agents to s.c. agents was performed, a practice followed in some other centers [3].

In conclusion, our study demonstrated that remote monitoring of IBD patients is feasible but burdened by a higher rate of steroid prescription, maybe due to an inadequate education of both patients and physicians. The main problem remained the strong reduction of endoscopic procedures leading to reduced surveillance and lower accuracy of activity assessments with the latter being eminently symptom-based during phase I of the Covid-19 pandemic.

Conflict of interest

None declared.

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