

Online supplemental material 1. Control group description.

Control group (COVID-19 negative patients) was composed by 296 hospitalized patients prospectively enrolled in Internal Medicine units within participating centers, without other infection, acute admitted and thereafter discharged for the following diseases/disorders other than trauma and surgery, by specialty pertinence: neurological (n. 20), cardiovascular (n. 63), respiratory (n. 36), liver (n. 13), kidney (n. 14), diabetes (n. 14), metabolic (n. 3), psychiatric and psychological (n. 3), gynaecological (n. 9), urological (n. 12), rheumatological (n. 6), autoimmune (n. 5), haematological (n. 4), other (n. 58).

Online supplemental Table 1. Presence of gastrointestinal symptoms according to GSRS at enrolment in the population included in primary aim analysis.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe	p
Upper digestive symptoms								
Acid regurgitation								0.086
Controls	257 (96.3)	5 (1.9)	1 (0.4)	4 (1.5)	0	0	0	
COVID-19 positive	562 (92.1)	7 (1.2)	16 (2.6)	15 (2.5)	4 (0.7)	4 (0.7)	2 (0.3)	
Eructation								0.843
COVID-19 negative	246 (92.5)	7 (2.6)	5 (1.9)	4 (1.5)	1 (0.4)	3 (1.1)	0	
COVID-19 positive	555 (90.7)	19 (3.1)	15 (2.5)	8 (1.3)	6 (1)	6 (1)	3 (0.5)	
Heartburn								0.201
COVID-19 negative	251 (94)	4 (1.5)	5 (1.9)	5 (1.9)	0	2 (0.8)	0	
COVID-19 positive	544 (88.7)	13 (2.1)	28 (4.6)	12 (2)	6 (1)	8 (1.3)	2 (0.3)	
Hunger pain								0.102
COVID-19 negative	253 (95.1)	6 (2.3)	5 (1.9)	1 (0.4)	1 (0.4)	0	0	
COVID-19 positive	560 (91.5)	9 (1.5)	13 (2.1)	17 (2.8)	3 (0.5)	6 (1)	4 (0.7)	
Nausea								<0.001
COVID-19 negative	233 (87.3)	10 (3.8)	8 (3)	6 (2.3)	5 (1.9)	4 (1.5)	1 (0.4)	
COVID-19 positive	433 (71.2)	33 (5.4)	55 (9.1)	49 (8.1)	19 (3.1)	13 (2.1)	6 (1)	
Lower digestive symptoms								
Diarrhea								<0.001
COVID-19 negative	242 (90.6)	10 (3.8)	9 (3.4)	4 (1.5)	0	2 (0.8)	0	
COVID-19 positive	383 (62.7)	15 (2.5)	70 (11.5)	74 (12.1)	35 (5.7)	16 (2.6)	18 (3)	
Loose stool								<0.001
COVID-19 negative	246 (92.1)	4 (1.5)	9 (3.4)	5 (1.9)	1 (0.4)	2 (0.8)	0	
COVID-19 positive	445 (72.8)	23 (3.8)	49 (8)	49 (8)	19 (3.1)	14 (2.3)	12 (2)	
Urgency								0.001
COVID-19 negative	254 (95.1)	2 (0.8)	4 (1.5)	6 (2.3)	1 (0.4)	0	0	
COVID-19 positive	513 (84.1)	18 (3)	23 (3.8)	32 (5.3)	5 (0.8)	11 (1.8)	8 (1.3)	
Constipation								0.089
COVID-19 negative	231 (86.5)	5 (1.9)	10 (3.8)	10 (3.8)	6 (2.3)	3 (1.1)	2 (0.8)	
COVID-19 positive	558 (91.2)	14 (2.3)	17 (2.8)	15 (2.5)	5 (0.8)	3 (0.5)	0	
Hard stools								0.038
COVID-19 negative	233 (87.3)	5 (1.9)	10 (3.8)	9 (3.4)	7 (2.6)	2 (0.8)	1 (0.4)	
COVID-19 positive	562 (92.3)	13 (2.1)	17 (2.8)	10 (1.6)	3 (0.5)	4 (0.7)	0	
Incomplete evacuation								0.794
COVID-19 negative	244 (91.7)	6 (2.3)	5 (1.9)	6 (2.3)	4 (1.5)	0	1 (0.4)	
COVID-19 positive	552 (90.6)	11 (1.8)	19 (3.1)	16 (2.6)	6 (1)	3 (0.5)	2 (0.3)	

Abdominal symptoms								
Abdominal distension								0.290
COVID-19 negative	237 (88.8)	4 (1.5)	12 (4.5)	8 (3)	5 (1.9)	0	0	
COVID-19 positive	529 (86.6)	19 (3.1)	22 (3.6)	21 (3.4)	7 (1.2)	9 (1.5)	4 (0.7)	
Abdominal pain								0.088
COVID-19 negative	231 (86.5)	6 (2.3)	14 (5.2)	9 (3.4)	2 (0.8)	4 (1.5)	1 (0.4)	
COVID-19 positive	473 (77.8)	25 (4.1)	39 (6.4)	35 (5.8)	18 (3)	13 (2.1)	5 (0.8)	
Borborygmi								0.072
COVID-19 negative	236 (88.4)	13 (4.9)	10 (3.8)	5 (1.9)	3 (1.1)	0	0	
COVID-19 positive	519 (84.9)	18 (3)	26 (4.3)	23 (3.8)	9 (1.5)	8 (1.3)	8 (1.3)	
Increased flatus								0.063
COVID-19 negative	236 (88.4)	11 (4.1)	11 (4.1)	6 (2.3)	3 (1.1)	0	0	
COVID-19 positive	542 (88.4)	16 (2.6)	11 (1.8)	19 (3.1)	14 (2.3)	9 (1.5)	2 (0.3)	

Online supplemental Table 2. Presence of gastrointestinal symptoms according to GSRS at 1 month follow-up in the population included in primary aim analysis.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe	p
Upper digestive symptoms								
Acid regurgitation								0.006
COVID-19 negative	234 (97.9)	1 (0.4)	3 (1.3)	0	1 (0.4)	0	0	
COVID-19 positive	504 (91.6)	19 (3.5)	13 (2.4)	9 (1.6)	0	5 (0.9)	0	
Eructation								0.819
COVID-19 negative	221 (92.5)	12 (5)	2 (0.8)	3 (1.3)	1 (0.4)	0	0	
COVID-19 positive	513 (92.9)	23 (4.2)	8 (1.5)	5 (0.9)	1 (0.2)	2 (0.4)	0	
Heartburn								0.166
COVID-19 negative	230 (96.6)	4 (1.7)	3 (1.3)	1 (0.4)	0	0	0	
COVID-19 positive	509 (91.9)	17 (3.1)	9 (1.6)	13 (2.4)	2 (0.4)	4 (0.7)	0	
Hunger pain								0.085
COVID-19 negative	238 (99.6)	2 (0.4)	0	0	0	0	0	
COVID-19 positive	526 (95.3)	8 (1.5)	9 (1.6)	6 (1.1)	1 (0.2)	2 (0.4)	0	
Nausea								0.015
COVID-19 negative	235 (98.3)	2 (0.8)	2 (0.8)	0	0	0	0	
COVID-19 positive	504 (91.3)	29 (5.3)	10 (1.8)	5 (0.9)	2 (0.4)	2 (0.4)	0	
Lower digestive symptoms								
Diarrhea								0.893
COVID-19 negative	224 (93.7)	5 (2.1)	7 (2.9)	2 (0.8)	0	1 (0.4)	0	
COVID-19 positive	510 (92.2)	16 (2.9)	15 (2.7)	9 (1.6)	1 (0.2)	2 (0.4)	0	
Loose stool								0.723
COVID-19 negative	223 (93.7)	3 (1.3)	8 (1.3)	3 (1.3)	1 (0.4)	0	0	
COVID-19 positive	503 (91.3)	16 (2.9)	22 (4)	5 (0.9)	2 (0.4)	2 (0.4)	1 (0.2)	
Urgency								0.756
COVID-19 negative	229 (95.8)	6 (2.5)	2 (0.8)	0	1 (0.4)	1 (0.4)	0	
COVID-19 positive	523 (94.8)	12 (2.2)	9 (1.6)	4 (0.7)	1 (0.2)	2 (0.4)	1 (0.2)	
Constipation								0.074
COVID-19 negative	211 (88.3)	14 (5.9)	5 (2.1)	4 (1.7)	3 (1.3)	2 (0.8)	0	
COVID-19 positive	488 (88.4)	17 (3.1)	31 (5.6)	8 (1.5)	2 (0.4)	3 (0.5)	3 (0.5)	
Hard stools								0.178
COVID-19 negative	215 (90.3)	9 (3.8)	6 (2.5)	3 (1.3)	2 (0.8)	3 (1.3)	0	
COVID-19 positive	492 (89.1)	15 (2.7)	26 (4.7)	13 (2.4)	1 (0.2)	2 (0.4)	3 (0.5)	
Incomplete evacuation								0.098
COVID-19 negative	227 (95)	8 (3.4)	2 (0.8)	1 (0.4)	1 (0.4)	0	0	
COVID-19 positive	506 (92)	10 (1.8)	18 (3.3)	9 (1.6)	1 (0.2)	5 (0.9)	1 (0.2)	

Abdominal symptoms								
Abdominal distension								0.210
COVID-19 negative	221 (92.5)	6 (2.5)	5 (2.1)	4 (1.7)	2 (0.8)	0	1 (0.4)	
COVID-19 positive	483 (87.3)	23 (4.2)	25 (4.5)	13 (2.4)	6 (1.1)	3 (0.5)	0	
Abdominal pain								0.065
COVID-19 negative	227 (95)	9 (3.8)	3 (1.3)	0	0	0	0	
COVID-19 positive	498 (90.1)	17 (3.1)	18 (3.3)	10 (1.8)	2 (0.4)	7 (1.3)	1 (0.2)	
Borborygmi								0.774
COVID-19 negative	221 (92.5)	8 (3.4)	5 (2.1)	4 (1.7)	1 (0.4)	0	0	
COVID-19 positive	502 (90.9)	18 (3.3)	18 (3.3)	10 (1.8)	1 (0.2)	3 (0.5)	0	
Increased flatus								0.326
COVID-19 negative	225 (94.1)	6 (2.5)	3 (1.3)	4 (1.7)	1 (0.4)	0	0	
COVID-19 positive	490 (88.9)	17 (3.1)	20 (3.6)	15 (2.7)	5 (0.9)	3 (0.5)	1 (0.2)	

Online supplemental Table 3. Presence of gastrointestinal symptoms according to GSRS at 6 months follow-up in the population included in primary aim analysis.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe	p
Upper digestive symptoms								
Acid regurgitation								
COVID-19 negative	189 (90)	7 (3.3)	7 (3.3)	3 (1.4)	4 (1.9)	0	0	
COVID-19 positive	454 (87.6)	26 (5)	20 (3.9)	11 (2.1)	6 (1.2)	1 (0.2)	9	
Eructation								0.605
COVID-19 negative	178 (84.8)	16 (7.6)	7 (3.3)	7 (3.3)	0	2 (1)	0	
COVID-19 positive	458 (88.3)	24 (4.6)	18 (3.5)	12 (2.3)	2 (0.4)	4 (0.8)	1 (0.2)	
Heartburn								0.363
COVID-19 negative	187 (89.5)	8 (3.8)	7 (3.4)	2 (1)	4 (1.9)	1 (0.5)	0	
COVID-19 positive	456 (88)	23 (4.4)	22 (4.3)	12 (2.3)	5 (1)	0	0	
Hunger pain								0.463
COVID-19 negative	201 (96.2)	4 (1.9)	1 (0.5)	3 (1.4)	0	0	0	
COVID-19 positive	484 (93.4)	12 (2.3)	10 (1.9)	9 (1.7)	0	3 (0.6)	0	
Nausea								0.727
COVID-19 negative	191 (91.4)	7 (3.4)	4 (1.9)	4 (1.9)	1 (0.5)	2 (1)	0	
COVID-19 positive	476 (91.9)	17 (3.3)	14 (2.7)	7 (1.4)	3 (0.6)	1 (0.2)	0	
Lower digestive symptoms								
Diarrhea								0.775
COVID-19 negative	188 (89.5)	10 (4.8)	4 (1.9)	7 (3.3)	1 (0.5)	0	0	
COVID-19 positive	461 (88.8)	26 (5)	16 (3.1)	11 (2.1)	3 (0.6)	2 (0.4)	0	
Loose stool								0.882
COVID-19 negative	188 (89.5)	8 (3.8)	7 (3.3)	6 (2.9)	1 (0.5)	0	0	
COVID-19 positive	467 (90)	17 (3.3)	14 (2.7)	14 (2.7)	4 (0.8)	3 (0.6)	0	
Urgency								0.731
COVID-19 negative	201 (96.2)	3 (1.4)	3 (1.4)	2 (1)	0	0	0	
COVID-19 positive	492 (94.8)	9 (1.7)	5 (1)	8 (1.5)	4 (0.8)	0	1 (0.2)	
Constipation								<0.001
COVID-19 negative	174 (82.9)	17 (8.1)	5 (2.4)	9 (4.3)	0	2 (1)	3 (1.4)	
COVID-19 positive	471 (91.1)	12 (2.3)	19 (3.7)	13 (2.5)	1 (0.2)	1 (0.2)	0	
Hard stools								0.030
COVID-19 negative	173 (82.8)	12 (5.7)	8 (3.8)	10 (4.8)	1 (0.5)	2 (1)	3 (1.4)	
COVID-19 positive	467 (90.5)	19 (3.7)	11 (2.1)	15 (2.9)	2 (0.4)	2 (0.4)	0	
Incomplete evacuation								0.495
COVID-19 negative	187 (90.3)	6 (2.9)	6 (2.9)	3 (1.5)	2 (1)	1 (0.5)	2 (1)	
COVID-19 positive	472 (91.8)	17 (3.3)	10 (2)	9 (1.8)	5 (1)	0	1 (0.2)	

Abdominal symptoms								
Abdominal distension								0.967
COVID-19 negative	176 (83.8)	16 (7.6)	7 (3.3)	7 (3.3)	2 (1)	2 (1)	0	
COVID-19 positive	424 (81.9)	37 (7.1)	22 (4.3)	20 (3.9)	8 (1.5)	6 (1.2)	1 (0.2)	
Abdominal pain								0.857
COVID-19 negative	188 (89.5)	8 (3.8)	8 (3.8)	5 (2.4)	1 (0.5)	0	0	
COVID-19 positive	451 (86.9)	23 (4.4)	24 (4.6)	14 (2.7)	14 (2.7)	4 (0.8)	3 (0.6)	
Borborygmi								0.428
COVID-19 negative	170 (81.3)	20 (9.6)	9 (4.3)	7 (3.4)	1 (0.5)	1 (0.5)	1 (0.5)	
COVID-19 positive	431 (83)	34 (6.6)	23 (4.4)	19 (3.7)	8 (1.5)	4 (0.8)	0	
Increased flatus								0.024
COVID-19 negative	169 (80.9)	13 (6.2)	16 (7.7)	6 (2.9)	1 (0.5)	4 (1.9)	0	
COVID-19 positive	427 (82.4)	34 (6.6)	14 (2.7)	25 (4.8)	11 (2.1)	5(1)	2 (0.4)	

Online supplemental Table 4. Presence of gastrointestinal symptoms according to GSRS at 12 months follow-up in the population included in primary aim analysis.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe	p
Upper digestive symptoms								
Acid regurgitation								0.627
COVID-19 negative	152 (89.9)	7 (4.1)	4 (2.4)	3 (1.8)	3 (1.8)	0	0	
COVID-19 positive	344 (87.1)	19 (4.8)	15 (3.8)	13 (3.3)	3 (0.7)	1 (0.3)	0	
Eructation								0.764
COVID-19 negative	150 (88.8)	12 (7.1)	4 (2.4)	1 (0.6)	2 (1.2)	0	0	
COVID-19 positive	353 (89.4)	19 (4.8)	12 (3)	5 (1.3)	3 (0.8)	1 (0.3)	2 (0.5)	
Heartburn								0.591
COVID-19 negative	151 (89.9)	6 (3.6)	8 (4.8)	1 (0.6)	1 (0.6)	1 (0.6)	0	
COVID-19 positive	342 (87)	21 (5.3)	16 (4.1)	10 (2.5)	3 (0.8)	1 (0.3)	0	
Hunger pain								0.622
COVID-19 negative	160 (95.2)	1 (0.6)	4 (2.4)	2 (1.2)	0	1 (0.6)	0	
COVID-19 positive	361 (92.1)	9 (2.3)	12 (3.1)	8 (2)	1 (0.3)	1 (0.3)	0	
Nausea								0.490
COVID-19 negative	154 (91.7)	7 (4.2)	3 (1.8)	4 (2.4)	0	0	0	
COVID-19 positive	366 (92.9)	11 (2.8)	8 (2)	4 (1)	2 (0.5)	3 (0.8)	0	
Lower digestive symptoms								
Diarrhea								0.411
COVID-19 negative	153 (90.5)	4 (2.4)	6 (3.6)	5 (3)	0	1 (0.6)	0	
COVID-19 positive	354 (89.9)	18 (4.6)	11 (2.8)	6 (1.5)	4 (1)	1 (0.3)	0	
Loose stool								0.510
COVID-19 negative	151 (89.4)	7 (4.1)	8 (4.7)	3 (1.8)	0	0	0	
COVID-19 positive	361 (91.4)	13 (3.3)	10 (2.5)	6 (1.5)	2 (0.5)	3 (0.8)	0	
Urgency								0.577
COVID-19 negative	158 (93.5)	5 (3)	3 (1.8)	3 (1.8)	0	0	0	
COVID-19 positive	370 (93.7)	10 (2.5)	2 (0.5)	10 (2.5)	2 (0.5)	1 (0.3)	0	
Constipation								0.019
COVID-19 negative	142 (84)	4 (2.4)	15 (8.9)	5 (3)	1 (0.6)	1 (0.6)	1 (0.6)	
COVID-19 positive	357 (90.4)	16 (4.1)	11 (2.8)	6 (1.5)	4 (1)	1 (0.3)	0	
Hard stools								0.011
COVID-19 negative	139 (82.3)	7 (4.1)	14 (8.3)	4 (2.4)	1 (0.6)	2 (1.2)	2 (1.2)	
COVID-19 positive	350 (89.1)	19 (4.8)	9 (2.3)	10 (2.5)	3 (0.8)	2 (0.5)	0	
Incomplete evacuation								0.769
COVID-19 negative	151 (90.4)	8 (4.8)	3 (1.8)	3 (1.8)	1 (0.6)	0	1 (0.6)	
COVID-19 positive	359 (91.8)	16 (4.1)	7 (1.8)	7 (1.8)	1 (0.3)	1 (0.3)	0	

Abdominal symptoms								
Abdominal distension								0.302
COVID-19 negative	145 (85.8)	11 (6.5)	8 (4.7)	4 (2.4)	1 (0.6)	0	0	
COVID-19 positive	316 (80)	26 (6.6)	17 (4.3)	24 (6.1)	6 (1.5)	4 (1)	2 (0.5)	
Abdominal pain								0.945
COVID-19 negative	150 (89.3)	6 (3.6)	5 (3)	6 (3.6)	0	1 (0.6)	0	
COVID-19 positive	341 (86.8)	15 (3.8)	17 (4.3)	16 (4.1)	1 (0.3)	3 (0.8)	0	
Borborygmi								0.101
COVID-19 negative	140 (83.3)	19 (11.3)	6 (3.6)	2 (1.2)	1 (0.6)	0	0	
COVID-19 positive	329 (83.3)	24 (6.1)	14 (3.5)	16 (4.1)	6 (1.5)	4 (1)	2 (0.5)	
Increased flatus								0.388
COVID-19 negative	137 (81.1)	15 (8.9)	11 (6.5)	5 (3)	1 (0.6)	0	0	
COVID-19 positive	317 (80.5)	27 (6.9)	18 (4.6)	18 (4.6)	9 (2.3)	4 (1)	1 (0.3)	

Online supplemental Table 5. Presence of gastrointestinal symptoms according to GSRS at 12 months follow-up in the population included in the entire study cohort for exploratory endpoints.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe	p
Upper digestive symptoms								
Acid regurgitation								0.204
COVID-19 negative	377 (84.2)	23 (5.1)	19 (4.2)	14 (3.1)	9 (2)	4 (0.9)	2 (0.5)	
COVID-19 positive	646 (78.9)	60 (7.3)	52 (6.4)	38 (4.6)	14 (1.7)	8 (1)	1 (0.1)	
Eructation								0.330
COVID-19 negative	376 (83.7)	27 (6)	17 (3.8)	13 (2.9)	10 (2.2)	5 (1.1)	1 (0.2)	
COVID-19 positive	675 (82.5)	54 (6.6)	46 (5.6)	19 (2.3)	9 (1.1)	8 (1)	7 (0.9)	
Heartburn								0.883
COVID-19 negative	371 (82.8)	26 (5.8)	27 (6)	12 (2.7)	8 (1.8)	3 (0.7)	1 (0.2)	
COVID-19 positive	654 (80.3)	56 (6.9)	51 (6.3)	29 (3.6)	13 (1.6)	8 (1)	4 (0.5)	
Hunger pain								0.041
COVID-19 negative	397 (88.6)	9 (2)	21 (4.7)	15 (3.4)	3 (0.7)	3 (0.7)	0	
COVID-19 positive	699 (85.8)	48 (5.9)	36 (4.4)	21 (2.6)	7 (0.9)	2 (0.3)	2 (0.3)	
Nausea								0.130
COVID-19 negative	384 (85.7)	20 (4.5)	24 (5.4)	13 (2.9)	2 (0.5)	3 (0.7)	2 (0.5)	
COVID-19 positive	716 (87.6)	48 (5.9)	21 (2.6)	19 (2.3)	7 (0.9)	5 (0.6)	1 (0.1)	
Lower digestive symptoms								
Diarrhea								0.073
COVID-19 negative	382 (85.1)	19 (4.2)	25 (5.6)	20 (4.5)	1 (0.2)	1 (0.2)	1 (0.2)	
COVID-19 positive	688 (84.2)	58 (7.1)	35 (4.3)	24 (2.9)	8 (1)	4 (0.5)	0	
Loose stool								0.012
COVID-19 negative	383 (85.5)	21 (4.7)	26 (5.8)	17 (3.8)	0	0	1 (0.2)	
COVID-19 positive	700 (85.5)	55 (6.7)	26 (3.2)	25 (3.1)	8 (1)	5 (0.6)	0	
Urgency								0.059
COVID-19 negative	412 (91.8)	10 (2.2)	11 (2.5)	15 (3.3)	0	1 (0.2)	0	
COVID-19 positive	743 (90.8)	26 (3.2)	10 (1.2)	21 (2.6)	7 (0.9)	6 (0.7)	5 (0.6)	
Constipation								0.013
COVID-19 negative	318 (70.8)	20 (4.5)	59 (13.1)	28 (6.2)	11 (2.5)	8 (1.8)	5 (1.1)	
COVID-19 positive	626 (76.7)	54 (6.6)	60 (7.4)	36 (4.4)	19 (2.3)	14 (1.7)	7 (0.9)	
Hard stools								0.196
COVID-19 negative	324 (72.2)	29 (6.5)	43 (9.6)	26 (5.8)	12 (2.7)	11 (2.5)	4 (0.9)	
COVID-19 positive	625 (76.5)	62 (7.6)	48 (5.9)	41 (5)	17 (2.1)	14 (1.7)	10 (1.2)	
Incomplete evacuation								0.886
COVID-19 negative	374 (83.9)	20 (4.5)	18 (4)	17 (3.8)	9 (2)	5 (1.1)	3 (0.7)	
COVID-19 positive	701 (86)	32 (3.9)	26 (3.2)	31 (3.8)	10 (1.2)	8 (1)	7 (0.9)	

Abdominal symptoms								
Abdominal distension								0.413
COVID-19 negative	314 (70.1)	38 (8.5)	32 (7.1)	31 (6.9)	19 (4.2)	7 (1.6)	7 (1.6)	
COVID-19 positive	581 (71.1)	71 (8.7)	65 (8)	52 (6.4)	20 (2.5)	21 (2.6)	7 (0.9)	
Abdominal pain								0.213
COVID-19 negative	346 (77.4)	23 (5.2)	35 (7.8)	29 (6.5)	5 (1.1)	6 (1.3)	3 (0.7)	
COVID-19 positive	633 (77.5)	63 (7.7)	60 (7.3)	36 (4.4)	12 (1.5)	12 (1.5)	1 (0.1)	
Borborygmi								0.048
COVID-19 negative	350 (78.1)	45 (10)	25 (5.6)	18 (4)	9 (2)	1 (0.2)	0	
COVID-19 positive	650 (79.5)	64 (7.8)	30 (3.7)	39 (4.8)	16 (2)	12 (1.5)	7 (0.9)	
Increased flatus								0.687
COVID-19 negative	328 (73.2)	33 (7.4)	32 (7.1)	25 (5.6)	19 (4.2)	6 (1.3)	5 (1.1)	
COVID-19 positive	621 (76)	56 (6.9)	53 (6.5)	32 (3.9)	29 (3.6)	18 (2.2)	8 (1)	

Online supplemental Table 6. DGBI, anxiety and depression occurrence at 6 and 12 months follow-up in the population included in the entire study cohort for exploratory endpoints.

	<i>6 Months follow-up</i>			<i>12 Months follow-up</i>		
	Controls n (%) <i>n=633</i>	COVID-19 n (%) <i>n=1167</i>	P	Controls n (%) <i>n=532</i>	COVID-19 n (%) <i>n=918</i>	P
DGBI						
Epigastric pain syndrome	18 (2.8)	41 (3.5)	0.446	20 (3.8)	36 (3.9)	0.872
Post-prandial distress syndrome	23 (3.6)	32 (2.7)	0.294	30 (5.6)	50 (5.5)	0.877
Functional dyspepsia	34 (5.4)	64 (5.5)	0.920	31 (5.9)	55 (6)	0.892
Chronic nausea and vomiting syndrome	12 (1.9)	15 (1.3)	0.309	11 (2.1)	15 (1.6)	0.552
Cyclic vomiting syndrome	4 (0.6)	4 (0.3)	0.379	4 (0.8)	1 (0.1)	0.044
Functional diarrhea	2 (0.3)	4 (0.3)	0.925	0	5 (0.6)	0.088
Irritable bowel syndrome	30 (4.7)	43 (3.7)	0.279	28 (5.3)	48 (5.3)	0.983
HADS						
<i>Depression</i>			0.083			0.111
Normal	555 (87.7)	981 (84.1)		467 (88.1)	768 (84.1)	
Borderline abnormal	45 (7.1)	118 (10.1)		41 (7.7)	97 (10.6)	
Abnormal	33 (5.2)	68 (5.8)		22 (4.2)	48 (5.3)	
<i>Anxiety</i>			0.409			0.091
Normal	531 (87.8)	938 (85.6)		465 (87.7)	783 (85.8)	
Borderline abnormal	52 (8.5)	89 (8.1)		45 (8.5)	71 (7.8)	
Abnormal	29 (4.7)	69 (6.3)		20 (3.8)	59 (6.5)	

Abbreviations: COVID-19: coronavirus 19 associated disease; n: number; DGBI: Disorders of Gut-Brain Interaction; HADS: Hospital Anxiety and Depression Scale.

Online supplemental Table 7. Baseline laboratory and clinical characteristics of hospitalized COVID-19 patients selected for primary aim analysis.

	No IBS n (%) or Mean \pm SD <i>n=421</i>	IBS n (%) or Mean \pm SD <i>n= 14</i>	p
Demographics and anamnestics			
Age	49.1 \pm 15.4	53.7 \pm 14.2	0.322
Sex (male)	250 (60.2)	8 (57.1)	0.816
BMI	28 \pm 5.5	25.5 \pm 3.6	0.119
Smoke			0.450
No	295 (70.9)	12 (85.7)	
Current	39 (9.4)	1 (7.1)	
Former	82 (19.7)	1 (7.1)	
Alcohol consumption	66 (15.9)	3 (21.4)	0.580
Physical activity (at least 30 minutes 3 times/week)	134 (34)	4 (33.3)	0.961
Comorbidities			
Neurological	13 (3.1)	0	0.505
Cardiovascular	111 (26.2)	5 (35.7)	0.430
Respiratory	28 (6.6)	0	0.320
Liver	14 (3.3)	2 (14.3)	0.031
Kidney	16 (3.8)	1 (7.1)	0.522
Diabetes	62 (14.7)	4 (28.6)	0.153
Metabolic other than diabetes	39 (9.2)	1 (7.1)	0.791
Musculoskeletal	8 (1.9)	1 (7.1)	0.173
Psychiatric	6 (1.4)	0	0.654
Gynecological	1 (0.2)	0	0.855
Urological	13 (3.1)	1 (7.1)	0.395
Rheumatological	8 (1.9)	1 (7.1)	0.173
Allergies	11 (2.6)	2 (14.3)	0.011
Autoimmune	11 (2.6)	1 (7.1)	0.306
Neoplastic	7 (1.7)	0	0.628
Psychological	7 (1.7)	0	0.628
Hematological	5 (1.2)	1 (7.1)	0.059
Chronic medication intake with GI effect			
Proton pump inhibitors	51 (12.1)	5 (35.7)	0.009
Non-steroidal anti-inflammatory drugs	20 (4.7)	0	0.405
Steroids	7 (1.7)	0	0.628
Metformin	23 (5.4)	0	0.370
Serotonin selective re-uptake inhibitors	10 (2.4)	0	0.561
Antipsychotic	3 (0.7)	0	0.752
Iron	4 (1)	0	0.715
Fibrates	4 (1)	0	0.715
ACE-I	38 (9)	1 (7.1)	0.812
Beta-blockers	49 (11.6)	2 (14.3)	0.757
Angiotensin-2 antagonist	35 (8.3)	2 (14.3)	0.427
Lithium	-	-	-
Carbamazepine	1 (0.2)	0	0.855

Furosemide	6 (1.4)	0	0.654
5-ASA	5 (1.2)	0	0.682
Rifaximin	-	-	-
Opiates	2 (0.5)	0	0.797
Anticholinergics	-	-	-
Verapamil	2 (0.5)	0	0.797
Levothyroxine	13 (3.1)	0	0.505
Cholestyramine	-	-	-
Monoclonal antibodies	-	-	-
Digoxin	2 (0.5)	0	0.797
Dopaminergic agents	1 (0.2)	0	0.855
H2 blockers	0	1 (7.1)	<0.001
Benzodiazepines	8 (1.9)	1 (7.1)	0.173
Tricyclic antidepressant	2 (0.5)	0	0.797
Antibiotics in the last 3 months	101 (24.1)	7 (50)	0.027
Probiotics in the last 3 months	33 (7.9)	4 (28.6)	0.006
Blood tests			
WBC (*10 ³ /mm ³)	6.4 ±3	5.2 ±2.2	0.088
Hb (g/dL)	13.4 ±1.9	13.2 ±2	0.709
Platelet (*10 ³ /mm ³)	220 ±89.6	204 ±111	0.141
INR	1.1 ±0.3	1.1 ±0.1	0.469
Creatinine (mg/dL)	1.18 ±0.27	0.87 ±0.22	0.983
AST (U/L)	38 ±33	30 ±12	0.664
ALT (U/L)	42 ±50	36 ±31	0.541
Total bilirubin (mg/dL)	0.89 ±1.84	0.61 ±0.30	0.637
GGT (U/L)	72 ±153	32 ±18	0.434
Ferritin (ng/mL)	418 ±520	411 ±275	0.438
C reactive protein (mg/dL)	12.3 ±25.4	12.8 ±35.9	0.119
Common symptoms			
Fever	295 (70.1)	13 (92.9)	0.065
Fatigue	234 (55.6)	6 (42.9)	0.346
Cough	231 (54.9)	12 (85.7)	0.022
Myalgia	151 (35.9)	4 (28.6)	0.575
Dyspnea	127 (30.2)	9 (64.3)	0.007
Runny nose	32 (7.6)	1 (7.1)	0.949
Headache	129 (30.6)	1 (7.1)	0.059
Anosmia	112 (26.6)	4 (28.6)	0.870
Dysgeusia	99 (23.5)	3 (21.4)	0.856
HRCT			
HRCT with pattern COVID-19 like	195 (83.7)	11 (100)	0.145
In-hospital treatments			
Antibiotics	254 (60.3)	12 (85.7)	0.055
Antimycotic	10 (2.4)	1 (7.1)	0.268
COVID-19 targeted therapies	321 (77)	13 (92.9)	0.162
Outcomes			
Need for ICU	42 (10.3)	1 (7.1)	0.698
Need for mechanical ventilation	26 (6.4)	0	0.328

Abbreviations: COVID-19: coronavirus 19 associated disease; n: number; SD: standard deviation; BMI: body mass index; WBC: white blood cells; Hb: hemoglobin; INR: international normalized

ratio; AST: aspartate amino-transferase; ALT: alanine amino-transferase; GGT: gamma-glutamyl transferase; HRCT: High resolution computed tomography; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; ICU: intensive care unit.

Online supplemental Table 8. Post-hoc analysis reporting symptoms presence and severity of post-COVID-19 IBS patients according to GSRS.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe
Diarrhea	5 (35.7)	3 (21.4)	3 (21.4)	2 (14.3)	1 (7.1)	0	0
Loose stool	7 (50)	2 (14.3)	2 (14.3)	1 (7.1)	0	2 (14.3)	0
Urgency	8 (57.1)	3 (21.4)	0	2 (14.3)	1 (7.1)	0	0
Constipation	9 (64.3)	0	2 (18.2)	1 (7.1)	2 (14.3)	0	0
Hard stools	9 (64.3)	0	2 (18.2)	1 (7.1)	2 (14.3)	0	0
Incomplete evacuation	9 (64.3)	2 (14.3)	0	1 (7.1)	1 (7.1)	1 (7.1)	0
Abdominal pain	0	2 (14.3)	4 (28.6)	6 (37.5)	1 (7.1)	1 (7.1)	0

Online supplemental Table 9. Post-hoc analysis with Uni- and Multivariate Logistic Regression for Identifying Factors Associated with Irritable Bowel Syndrome Occurrence at 12 Months Follow-up in the study cohort (COVID-19 and controls) Selected for Primary Aim Analysis.

	<i>Univariate</i>		<i>Multivariate</i>	
	OR (95% CI)	P	OR (95% CI)	P
BMI	0.907 (0.810-1.016)	0.093		
Comorbidities				
Allergies	4.112 (0.874-19.341)	0.073	7.642 (1.476-39.563)	0.015
Chronic medication intake				
Proton pump inhibitors	3.483 (1.212-10.007)	0.020	5.439 (1.783-16.591)	0.003
Clinical course				
COVID-19 diagnosis	6.218 (0.812-47.636)	0.079	10.686 (1.291-88.479)	0.028
Fever	6.008 (1.344-26.849)	0.019		
Cough	5.879 (1.642-21.047)	0.006		
Dyspnea	4.682 (1.639-13.373)	0.004		
Diarrhea (GSRS at enrollment)	1.265 (0.985-1.626)	0.066		
Abdominal distension (GSRS at enrollment)	1.318 (0.971-1.789)	0.077		
Incomplete evacuation (GSRS at enrollment)	1.465 (1.058-2.029)	0.022		
In-hospital antibiotic administration	4.861 (1.088-21.727)	0.038		
Laboratory exams at baseline				
WBC (*10 ³ /mm ³)	0.823 (0.667-1.015)	0.069		
Depression according to HADS at 6 months	1.981 (0.955-4.109)	0.066		
Anxiety according to HADS at 6 months	2.014 (0.980-4.137)	0.057		

COVID-19 denotes coronavirus 19-associated disease, OR odds ratio, CI confidence interval, BMI body mass index, SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, GSRS Gastrointestinal Symptoms Rating Scale, WBC white blood cells and HADS hospital anxiety and depression scale.

Online supplemental Table 10. Post-hoc analysis reporting enrollment rate by country of Patients Selected for Primary Aim Analysis of the GI-COVID19 Study.

Country	Patient (n=883), n. (%)
Bangladesh	0
Cyprus	8 (0.9)
Egypt	33 (3.7)
Israel	9 (1)
Italy	183 (20.7)
India	34 (3.9)
Macedonia	47 (5.4)
Malaysia	28 (3.2)
Romania	56 (6.3)
Russian Federation	28 (3.2)
Serbia	9 (1)
Spain	75 (8.5)
Sweden	17 (1.9)
Turkey	356 (40.3)

Online supplemental Table 10. Post-hoc analysis reporting the presence of gastrointestinal symptoms according to GSRS at baseline in the population included in the primary aim analysis with a complete follow-up at 12 months compared to drop-out at 12 months.

	No	Very Mild	Mild	Moderate	Moderate Severe	Severe	Very Severe	p
Upper digestive symptoms								
Acid regurgitation								0.066
Follow-up completed	526 (93.8)	11 (2)	9 (1.6)	7 (1.3)	4 (0.7)	3 (0.5)	1 (0.2)	
Drop-out	300 (92.6)	2 (0.6)	8 (2.5)	12 (3.7)	0	1 (0.3)	1 (0.3)	
Eructation								0.049
Follow-up completed	506 (89.9)	18 (3.2)	11 (2)	12 (2.1)	5 (0.9)	8 (1.4)	3 (0.5)	
Drop-out	304 (93.8)	8 (2.5)	9 (2.8)	0	2 (0.6)	1 (0.3)	0	
Heartburn								0.355
Follow-up completed	502 (89.2)	16 (2.8)	21 (3.7)	11 (1.9)	5 (0.9)	7 (1.24)	1 (0.2)	
Drop-out	300 (92.3)	2 (0.6)	12 (3.7)	6 (1.9)	1 (0.3)	3 (0.9)	1 (0.3)	
Hunger pain								0.822
Follow-up completed	516 (91.8)	11 (2)	14 (2.5)	12 (2.1)	2 (0.4)	4 (0.7)	3 (0.5)	
Drop-out	304 (93.8)	4 (1.2)	4 (1.2)	7 (2.2)	2 (0.6)	2 (0.6)	1 (0.3)	
Nausea								0.135
Follow-up completed	422 (75.2)	35 (6.2)	40 (7.1)	34 (6.1)	12 (2.1)	14 (2.5)	4 (0.7)	
Drop-out	251 (78)	9 (2.8)	23 (7.1)	21 (6.5)	12 (3.7)	3 (0.9)	3 (0.9)	
Lower digestive symptoms								
Diarrhea								0.162
Follow-up completed	391 (69.5)	19 (3.4)	51 (9.1)	49 (8.7)	23 (4.1)	14 (2.5)	16 (2.8)	
Drop-out	240 (74.3)	6 (1.9)	28 (8.7)	31 (9.6)	12 (3.7)	4 (1.2)	2 (0.6)	
Loose stool								0.001
Follow-up completed	427 (75.8)	24 (4.3)	41 (7.3)	30 (5.3)	17 (3)	13 (2.3)	11 (2)	
Drop-out	273 (84.3)	3 (0.9)	17 (5.3)	24 (7.4)	3 (0.9)	3 (0.9)	1 (0.3)	
Urgency								0.153
Follow-up completed	494 (87.9)	12 (2.1)	15 (2.7)	20 (3.6)	4 (0.7)	10 (1.8)	7 (1.3)	
Drop-out	280 (86.4)	8 (2.5)	14 (4.3)	18 (5.6)	2 (0.6)	1 (0.3)	1 (0.3)	
Constipation								0.183
Follow-up completed	496 (87.9)	15 (2.7)	19 (3.4)	21 (3.7)	7 (1.2)	4 (0.7)	2 (0.4)	
Drop-out	302 (93.2)	4 (1.2)	8 (2.5)	4 (1.2)	4 (1.2)	2 (0.6)	0	
Hard stools								0.310
Follow-up completed	503 (89.5)	12 (2.1)	19 (3.4)	17 (3)	6 (1.1)	4 (0.7)	1 (0.2)	
Drop-out	301 (93.2)	6 (1.9)	8 (2.5)	2 (0.6)	4 (1.2)	2 (0.6)	0	
Incomplete evacuation								0.456
Follow-up completed	506 (89.9)	15 (2.7)	15 (2.7)	16 (2.8)	7 (1.2)	2 (0.4)	2 (0.4)	
Drop-out	297 (92.8)	2 (0.6)	10 (3.1)	6 (1.9)	3 (0.9)	1 (0.3)	1 (0.3)	

Abdominal symptoms								
Abdominal distension								0.593
Follow-up completed	485 (86.2)	14 (2.5)	23 (4.1)	20 (3.6)	10 (1.8)	7 (1.2)	4 (0.7)	
Drop-out	287 (88.6)	11 (3.4)	12 (3.7)	9 (2.8)	2 (0.6)	2 (0.6)	1 (0.3)	
Abdominal pain								0.261
Follow-up completed	454 (81.2)	13 (2.3)	34 (6.1)	30 (5.4)	12 (2.2)	12 (2.2)	4 (0.7)	
Drop-out	255 (78.7)	19 (5.9)	19 (5.9)	15 (4.6)	8 (2.5)	6 (1.9)	2 (0.6)	
Borborygmi								0.042
Follow-up completed	470 (83.5)	23 (4.1)	28 (5)	18 (3.2)	10 (1.8)	8 (1.4)	6 (1.1)	
Drop-out	294 (90.7)	8 (2.5)	8 (2.5)	10 (3.1)	2 (0.6)	0	2 (0.6)	
Increased flatus								0.298
Follow-up completed	489 (86.7)	21 (3.7)	15 (2.7)	16 (2.8)	13 (2.3)	8 (1.4)	2 (0.4)	
Drop-out	297 (91.4)	7 (2.2)	7 (2.2)	9 (2.8)	4 (1.2)	1 (0.3)	0	