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Abdominal gastrointestinal imaging findings on computed tomography in patients with COVID-19 and correlation with clinical outcomes

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ABSTRACT

Purpose: Pulmonary imaging finding of Coronavirus disease 2019 (COVID-19) has been widely described, but until now few studies have been published about abdominal radiological presentation. The aim of this study was to provide an overview of abdominal imaging findings in patients with COVID-19 in a multicenter study and correlate them with worse clinical outcomes.

Materials and methods: This retrospective study included adult COVID-positive patients with abdominal CT performed from 4/1/2020 to 5/1/2020 from two institutions. Demographic, laboratory and clinical data were recorded, including clinical outcomes.

Results: Of 81 COVID-positive patients, the average age was 61 years, 42 (52%) women and 45 (55%) had positive abdominopelvic findings. The most common abdominal imaging features were intestinal imaging findings (20/81, 24%), including colorectal (4/81, 5%) and small bowel thickening (10/81, 12%), intestinal distension (15/81, 18%), pneumatosis (1/81, 1%) and intestinal perforation (1/81, 1%). On multivariate analysis, intestinal imaging findings were associated with higher risk of worse outcome (death or invasive mechanical ventilation) (RR = 2.6, p = 0.04) and higher risk of invasive mechanical ventilation alone (RR = 6.2, p = 0.05).

Conclusion: Intestinal abnormalities were common findings in COVID-19 patients who underwent abdominal CT and were significantly correlated to worse outcomes in the clinical follow-up.

1. Introduction

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first discovered in Wuhan, China, in December 2019. Symptoms of infection are variable and nonspecific, but it is well established that most patients with COVID-19 have fever and flu-like symptoms, such as cough and dyspnea [1,2]. Gastrointestinal symptoms have also been recognized, including diarrhea, nausea, vomiting, abdominal pain, and loss of appetite [2–6]. Patients with these symptoms cannot be ignored, and lack of respiratory manifestation should not rule out the SARS-CoV-2 infection [2–7].

The infection mechanisms and pathogenesis of SARS-CoV-2 remain to be fully understood. Angiotensin-converting enzyme 2 (ACE2) has been identified as a functional receptor for the SARS-CoV-2 [8,9]. This receptor was found to be expressed not only in pulmonary epithelial

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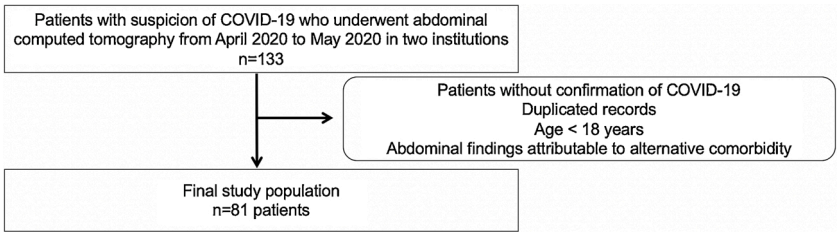

Fig. 1. Flowchart of patients' accrual.

cells, but also in gastrointestinal and hepatobiliary cells [6,10–12]. Consequently, SARS-CoV-2 can actively infect and replicate in these tracts.

Despite the wide recognition of pulmonary imaging finding, until now few studies and case reports have been published about abdominal radiological presentation of patients with COVID-19 [13–17]. Most of these studies approach the changes related to disease-related thrombotic events [13,15,16], including portal and upper mesenteric vein thrombosis, but bowel wall involvement, pancreatitis, hepatitis and gallbladder sludge and distention were also described [13,14,17]. The main limitations of these studies are their small sample size, single center and retrospective study, which limits its generalizability and introduces selection bias.

The aim of this study is to provide an overview of various abdominal imaging findings in patients presenting with COVID-19 in a multicenter retrospective study and correlate them with worse clinical outcomes.

2. Methods

2.1. Study population

The institutional review board from the two institutions approved our retrospective study and the requirement of informed consent was waived. Both are tertiary hospitals and COVID-19 reference. The institutional databases of patients with suspicion of COVID-19 from both hospitals were prospectively maintained. The inclusion criteria were consecutive patients with suspicion of COVID-19 who underwent abdominal CT from April 1st 2020 to May 1st 2020. The exclusion criteria were patients without confirmation of COVID-19 on PCR-RT or on serology, age less than 18 years, duplicated records and abdominal findings unequivocally attributable to an alternative comorbidity. The final study population was 81 patients. Patient accrual is summarized in the Fig. 1.

2.2. Demographic, clinical and laboratorial data

The clinical and laboratorial data were obtained from a medical record review led by 3 radiologists using a standardized form. The following clinical data were assessed: age, gender, presence of comorbidities (including tobacco smoke, systemic hypertension, diabetes mellitus, dyslipidemia, cancer, chronic obstructive pulmonary disease, and heart disease), symptoms on admission (including upper respiratory symptoms, lower respiratory symptoms, fever, chill, abdominal pain, diarrhea, nausea and vomiting). Regarding physical examination at admission, the following data were collected: systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, temperature, oxygen saturation, and weight. With regards to laboratorial data, the white blood count, lymphocytes, C-reactive protein, D-dimer, lactate, and lactate dehydrogenase (LDH) were collected.

2.3. Patient outcome

The following clinical outcome were collected: death confirmation, need of invasive mechanical ventilation, intensive care unit (ICU) admission, and days of hospitalization. The patients were divided into two groups: good clinical outcome and worse clinical outcome. Patients who needed invasive mechanical ventilation or died were classified as worse clinical outcome.

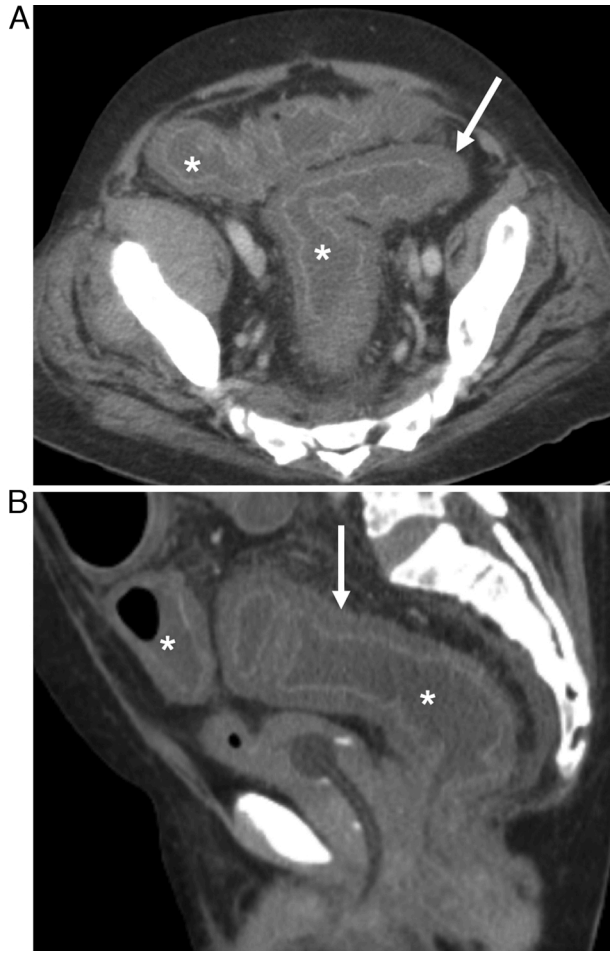

Fig. 2. 73-year-old man with COVID-19. Axial (A) and sagittal (B) IV contrast-enhanced CT images show colorectal thickening (arrows), intestinal distention of the colon (asterisks). The patients were admitted in the intensive care unit and underwent mechanical ventilation 2 days after the CT.

2.4. Abdominal CT protocol

All CT scans were performed on a 64-,128- or 256-row CT scanner. Fifty-one patients underwent contrast-enhanced CT. In those patients, images were acquired in the portal venous phase, 70–80 seconds after intravenous injection of 1.5 mL/Kg of iodinated contrast agent (Iopromide; Bayer, Berlin, Germany), at a rate of 3−5 ml/sec using a power injector, followed by 30 mL of saline flush. Axial images were reconstructed using a thickness and interval of 5 mm. Sagittal and coronal

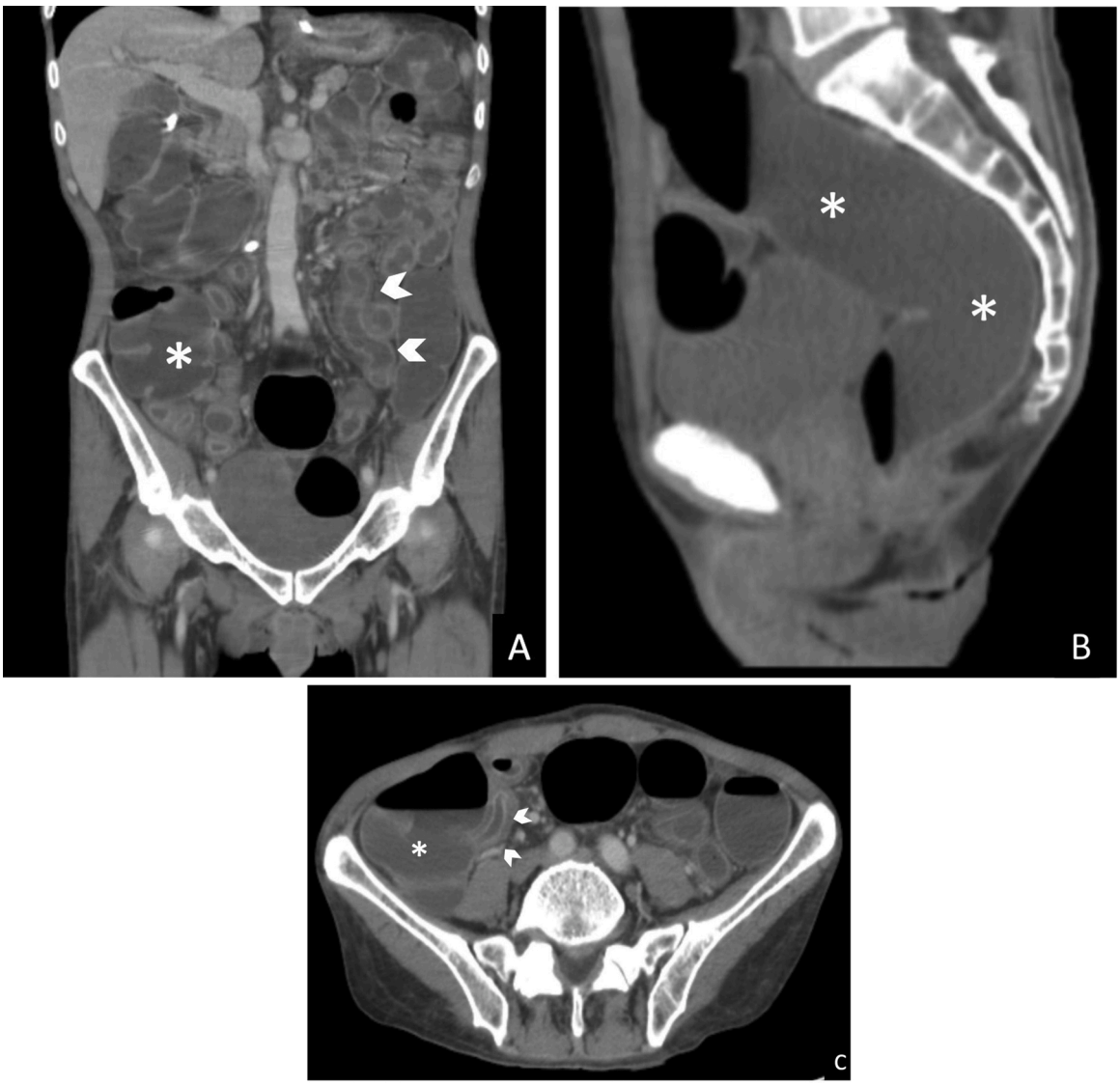

Fig. 3. 46-year old male with COVID-19. Portal phase contrast enhanced CT on coronal (A), sagittal (B) and axial (C) planes showing diffuse colonic and sigmoid distention (white asterisk) without mechanical or obstructive causes, associated with small bowel wall thickening and mucosal hyperenhancement (white arrowheads), suggestive of adynamic ileus possibly due to direct viral inflammatory effect.

reconstructions were done using 3 mm thickness.

2.5. Image review

Two board-certificated abdominal radiologists independently reviewed the abdominal CT and reached a consensus. In cases of disagreements, a senior abdominal radiologist with 10 years of experience reviewed the findings. The radiologists were aware that the patients had the diagnosis of COVID-19 and were blinded for clinical, laboratorial and outcome data.

The following intestinal findings were assessed: bowel-wall thickening (small bowel, colonic or rectal, defined as single-wall thickness greater than 3 mm in distended loops and greater than 5 mm in collapsed loops), pneumatosis (presence of intramural bowel gas), suspected intestinal perforation (defined as presence of free peritoneal or retroperitoneal air), and intestinal distension (defined as >3 cm for small bowel and >6 cm for large bowel) Figs. 2 and 3. Other imaging findings assessed visually were: heterogeneous liver enhancement, portal venous gas, gallbladder thickening, gallbladder distention, periportal edema, signs of pancreatitis, and infarction of solid organ.

2.6. Statistical analysis

Clinical, demographic and imaging data were presented for all the patients and then compared according to their outcome status using logistic regression and student's *t*-test. We also analyzed the association between lower gastrointestinal imaging findings (intestinal thickening, perforation and distension) and clinical outcomes using *Poisson* regression for survival analyses and multilinear regression for quantitative analysis. Selection of variables composing the final models was done based on predetermined variables associated COVID-19 prognosis. Significance was regarded as a P value lower than 0.05. The statistical analyses were performed using Stata (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP)

3. Results

A total of 81 patients were included in this study, 42/81 (52%) were female and the mean age was 61 years (range, 25–92). At the time of CT, 37/81 (46%) were inpatients, 35/81 (43%) were imaged in the emergency department, and 9 (11%) were imaged as outpatients. The most frequent comorbidities were current or previous cancer (49/81, 60%),

Table 1
Patients's characteristics on admission and comparison of them between patients with good and worse clinical outcome (death or invasive mechanical ventilation).

	All patients (N%)	Good clinical outcome (N%)	Worse clinical outcome (N %)	P-value
Number of patients	81	53 (65%)	28 (35%)	–
Age years (range)	61 (25–92)	60 (27–92)	64 (25–92)	0.2
Female Male	42 (52%) 39 (48%)	29 (54%)24 (45%)	13 (46%)15 (54%)	0.4
Comorbidities				
Hypertension	40 (49%)	21 (39%)	19 (67%)	**0.02**
Diabetes	17 (21%)	6 (11%)	11 (40%)	**0.05**
Dyslipidemia	14 (19%)	8 (17%)	6 (23%)	0.5
Cancer	49 (60%)	27 (51%)	22 (78%)	**0.02**
Smoking (ever)	20 (24%)	12 (22%)	8 (29%)	**0.05**
Chronic Obstructive Pulmonary Disease / asthma	9 (11%)	6 (11%)	3 (11%)	0.9
Heart disease	7 (8%)	5 (10%)	2 (7%)	0.6
Respiratory symptoms				
Upper respiratory	40 (49%)	31 (59%)	9 (32%)	0.1
Lower respiratory	35 (43%)	18 (34%)	17 (60%)	**0.02**
Fever / Chill	56 (69%)	38 (71%)	18 (64%)	0.4
GI symptoms	45 (55%)	25 (47%)	20 (71%)	**0.04**
Abdominal pain	34 (44%)	18 (36%)	16 (59%)	**0.05**
Diarrhea	19 (23%)	13 (24%)	6 (22%)	0.7
Nausea / Vomiting	22 (30%)	13 (27%)	9 (37%)	0.3
Physical exam				
Systolic blood preassure (SD)	120 (21)	119 (20)	122 (22)	0.5
Diastolic blood preassure (SD)	74 (14)	74 (14)	74 (15)	0.8
Heart rate (SD)	88 (12)	88 (12)	87 (17)	0.7
Respiratory rate (SD)	18 (4)	18 (4)	19 (5)	0.5
Temperature (SD)	36.6 (0.8)	36.7 (0.8)	36.5 (1.0)	0.2
Saturation (SD)	94 (4.5)	95 (2.3)	92 (6.0)	**0.001**
Weight (SD)	76 (18)	79 (19)	68 (12)	0.1
Laboratory				
White Blood Count (SD)	8.9 (5.3)	7.0 (3.7)	12.5 (6.1)	**0.0001**
Lymphocytes (SD)	1.9 (2.3)	2.1 (2.2)	1.6 (2.4)	0.3
C-reactive protein (SD)	72 (111)	41 (85)	135 (132)	**0.0004**
D-dimer (SD)	3135 (4800)	2549 (4877)	4536 (4500)	0.14
Lactate (SD)	17 (11)	15 (10)	19 (11)	0.22
Lactate dehydrogenase (SD)	442 (339)	394 (158)	550 (558)	0.08
Outcome				
Mortality	23 (28%)	0 (0%)	23 (100%)	–
Invasive mechanical ventilation	14 (17%)	0 (0%)	14 (100%)	–
ICU admission	31 (38%)	11 (20%)	20 (71%)	**<0.0001**
Days of hospitalizations (mean)	16.4 (14)	11.9 (8.5)	24.8 (18.6)	**<0.0001**
Days on ICU (mean)	9.6 (8.3)	6.1 (3.7)	11.8 (9.8)	0.08

ICU: intensity care unit.

Table 2
Abdominal findings on computed tomography among all patients, patients with good clinical outcome and worse clinical outcome.

	All patients (N%)	Good clinical outcome (N%)	Worse clinical outcome (N%)	P-Value
Intestinal imaging findings	20 (24%)	9 (17%)	11 (39%)	**0.03**
Colorrectal thickening	4 (5%)	1 (1%)	3 (10%)	0.1
Small bowel thickening	10 (12%)	5 (9%)	5 (17%)	0.2
Pneumatosis	1 (1%)	0 (0%)	1 (3.5%)	–
Intestinal perforation	1 (1%)	1 (1%)	0 (0%)	–
Intestinal distension	15 (18%)	6 (11%)	9 (32%)	**0.02**
Solid organ infarction	2 (2%)	1 (1.7%)	1 (3.5%)	0.8
Pancreatitis	1 (1%)	0 (0%)	1 (3.5%)	–
GB thickening	1 (1%)	1 (1.7%)	0(0%)	–
Heterogenous liver	2 (2%)	2 (3.7%)	0 (0%)	0
Steatosis	29 (35%)	21 (39%)	8 (28%)	0.3

hypertension (40/81, 49%) and diabetes (17/81, 21%). The majority of the patients had fever or chill (56/81, 69%), upper and lower respiratory symptoms were observed in 40/81 (49%) and 35/81 (43%) patients. Forty-five patients (45/81, 55%) had gastrointestinal symptoms, including abdominal pain (34/81, 44%), diarrhea (19/81, 23%), and nausea or vomiting (22/81, 30%). With regards to the laboratory tests, of note the mean values of C-reactive protein, D-dimer, and lactate dehydrogenase were 72 (±111), 3135 (±4800), and 442 (±339), respectively. Regarding patient outcome, 31/81 (38%) patients were admitted in the intensive care unit, 14/81 (17%) underwent invasive mechanical ventilation, and 23/81 (28%) died. Table 1 summarizes the clinical findings of the included patients.

Considering the groups of clinical outcomes, 28/81 (35%) patients had worse outcome, including death or invasive mechanical ventilation. Patients with worse clinical outcomes had more hypertension ($p = 0.02$), diabetes ($p = 0.05$), and cancer history ($p = 0.02$). Higher proportion of patients who smoked or had previous history of smoking were observed in the group of patients with worse clinical outcome [8/28 (29%) *vs* 12/53 (20%), $p = 0.05$). Additionally, lower respiratory symptoms [17/28 (60%) *vs* 18/53 (34%), $p = 0.02$] and gastrointestinal symptoms [20/28 (71%) *vs* 25/53 (47%), $p = 0.04$], particularly abdominal pain [16/28 (59%) *vs* 18/53 (36%), $p = 0.05$] at admission, were more frequently observed in patients with worse clinical outcome. The O2 saturation at admission was significantly lower among patients with worse clinical outcome [92 (±6) *vs* 95 (± 2.3), $p = 0.001$]. Leucocytes and C-reactive protein at admission were significantly higher in patients with worse outcome [12.5 (±6.1) *vs* 7.0 (± 3.7), $p = 0.0001$] and [135 (±132) *vs* 41 (±85), $p = 0.0004$], respectively. Overall ICU admission rate was higher for patients with worse outcomes [20/28 (71%) *vs* 11/55 (11.9%), $p < 0.0001$), as well as the days of hospitalization [24.8 (±18.6) *vs* 11.9 (±8.5), $p < 0.0001$).

The most relevant abdominal imaging features on CT were intestinal imaging findings (20/81, 24%), including colorectal (4/81, 5%) and small bowel thickening (10/81, 12%), intestinal distension (15/81, 18%), pneumatosis (1/81, 1%) and intestinal perforation (1/81, 1%). Patients with worse outcome had more intestinal findings [11/28 (39%) *vs* 9/53 (17%), $p = 0.03$], especially intestinal distention [9/28 (32%) *vs* 6/53 (11%), $p = 0.02$]. Imaging findings of solid organs and hepatobiliary tract were rare. A vascular cause was not identified on any of the cases with nonspecific intestinal findings. Table 2 summarizes the abdominal imaging features.

On the multivariate analysis (Table 3), intestinal imaging findings were associated with higher risk of worse outcome (death or invasive mechanical ventilation) Fig. 4 (RR $= 2.6$, $p = 0.04$) and higher risk of

Table 3
Association between presence of intestinal finding on computed tomography and patients' outcome.

	No intestinal imaging findings (N %)	Intestinal imaging findings (N %)	Crude Rate Ratio (95% CI)	Minimally adjusted* Rate Ratio (95% CI)	Fully ajusted Rate Ratio* (95% CI)
Worse clinical outcome	17 (27%)	11 (55%)	RR = 2.7(1.3–5.9) P = 0.008	RR = 3.0 (1.2–7.2) P = 0.01	RR = 2.6 (1.1–6.7) P = 0.04
Death	14 (22%)	9 (45%)	RR = 1.4 (0.63–3.4) P = 0.3	RR = 1.4 (0.6–3.3) P = 0.02	RR = 1.4 (0.5–3.5) P = 0.6
Invasive mechanical ventilation	7 (11%)	7 (35%)	RR = 4.3 (1.5–12.2) P = 0.006	RR = 6.6 (1.9–23.4) P = 0.003	RR = 6.2 (1.7–22.6) P = 0.005
ICU admission	21 (34%)	10 (50%)	RR = 1.1(0.5–2.4) P = 0.7	RR = 1.1 (0.5–2.3) P = 0.7	RR = 1.1 (0.5–2.5) P = 0.7

	No intestinal imaging findings (N %)	Intestinal imaging findings (N %)	Crude Difference	Minimally adjusted difference	Fully adjusted difference
Hospital lenght (days)	15.2	20.1	+4.9 (-2.5; + 12.4) P = 0.2	+5.5 (-2.1; +13.2) P = 0.2	+ 6.2 (-1.7; +14.4) P = 0.1
ICU lenght (days)	7.6	13.7	+6.6 (-12.8; +0.5) P = 0.06	+7.3 (-0.2; + 14.9) P = 0.05	+7.1 (-0.9; + 15.2) P = 0.07

*Minimally adjusted: age and gender **Fully adjusted: age, gender, hypertension, diabetes, chronic obstructive pulmonary disease, cancer.

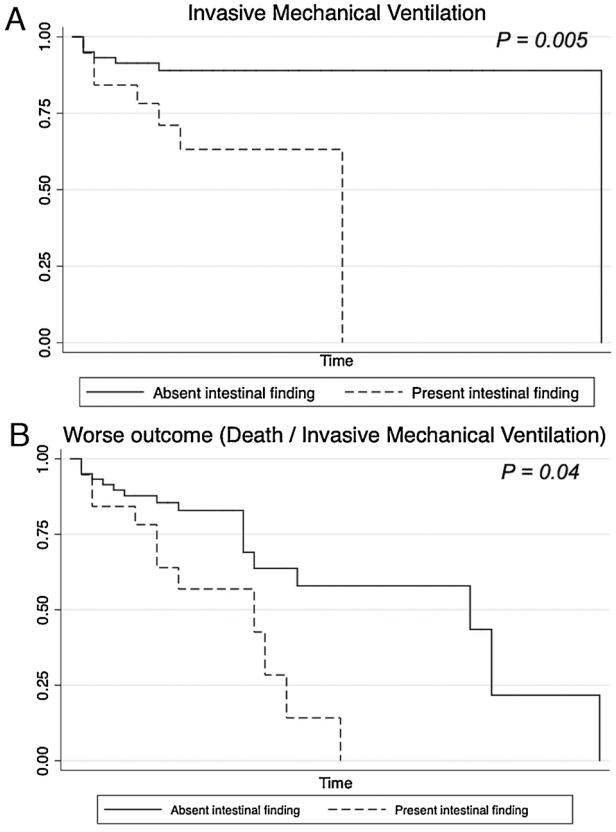

Fig. 4. Kaplan-Meier curves of invasive mechanical ventilation events (A) and combined worse outcomes (B), including death and invasive mechanical ventilation, comparing patients with and without intestinal imaging findings on computed tomography.

invasive mechanical ventilation alone (RR = 6.2, p = 0.05), but not mortality alone (RR = 1.4, p = 0.6). A trend was also seen for higher days of hospitalization (adjusted difference: +6.2 days, p = 0.1) and days on intensive care unit length (adjusted difference: +7.1, p = 0.07), although insufficient sample size impaired a significant result.

4. Discussion

Coronaviruses are a group of viruses that exhibit several tissue tropisms, which can cause acute or chronic damage to the respiratory system, digestive system, and nervous system. This broad tropism has been attributed to the high affinity of SARS-CoV-2 for ACE2 receptor, since it's find in the majority human tissues [6,10–12], being more abundant in lung alveolar epithelium, enterocytes of small intestine, and vascular endothelium [18,19].

The presentation of patients with COVID-19 can vary, from asymptomatic to mild respiratory symptoms to acute respiratory distress syndrome [20]. Non-respiratory complaints has been also described in COVID-19 patients and digestive symptoms, such as abdominal pain and diarrhea, are related to an atypical presentation of the disease. Similar to previous published studies, abdominal pain was the most common clinical indication for abdominal CT scanning in our cohort [13,21], and other gastrointestinal symptoms, such as diarrhea (23%) and nausea or vomiting (30%) were also commonly registered. Given that only patients who underwent abdominal CT were selected, the percentage of patients who had gastrointestinal symptoms at presentation (55%) in our sample is greater than reported in previous studies with different selection criteria [3]. Although it's not clear if these symptoms are or not directly related to SARS-CoV-2 infection, they are not rare in COVID-19 patients, requiring further investigation in selected cases.

In our study, gastrointestinal tract CT findings were detected in 24% of COVID-19 patients who underwent abdominal CT scans, being intestinal distention and small bowel thickening the most prevalent findings. Intestinal findings were significantly related to worse outcomes in the clinical follow-up results, what is in line with a similar study published by Goldberg-Stein et al. [21]. We also reported a significant statistical correlation between intestinal imaging findings and death or invasive mechanical ventilation, similar to the results of another study that correlated bowel wall abnormalities with ICU admission (OR 15.5, p = 0.01) in COVID-19 patients [13]. Possible explanations for the spectrum of bowel findings and its relation with worse outcomes in these patients include direct viral inflammatory effect (supported by the ACE2 receptor theory) and indirect viral infection consequences, such as small

vessel thrombosis, nonocclusive mesenteric ischemia and immune-mediated response [13]. Moreover, these findings may also be related to the stress response related to hospitalization or may be due to pre-existing condition unrelated to COVID-19 [21] and new studies are warranted to clarify these and other open questions.

Our laboratorial data is also in line with previous reports [22,23] that correlated blood inflammatory markers (such as white blood count and C-reactive protein) with worse clinical outcomes. In parallel with the extensively discussed pulmonary involvement of COVID-19, our CT-based results reinforce the value of a comprehensive assessment – including clinical parameters, laboratorial and radiological data – for the risk stratification of COVID-19 patients, and for monitoring and evaluating the severity and prognosis of the disease.

Limitations of this study included its small sample size and retrospective study design. Our imaging features were determined by consensus and therefore, inter-reader agreement was not evaluated. Considering that radiologic-pathologic correlations were not performed and that the study design have not included a control group with COVID-negative patients, our results are not conclusive about which of the reported findings are directly related to COVID-19 and should be interpreted as an exploratory analysis. Future prospective studies with greater samples are need.

In conclusion, intestinal abnormalities were common findings in COVID-19 patients who underwent abdominal CT and were significantly correlated to worse outcomes in the clinical follow-up. More than just avoid misdiagnosing COVID-19 presented as an acute abdomen to reduce the further viral transmission, clinicians and surgeons should be familiar with the gastrointestinal and abdominal symptoms of the disease, since they're implicated with the development of poor clinical outcomes. Finally, radiologists should be aware of abdominal imaging findings in these patients and intestinal findings should be highlighted in the reports when present.

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Ethical approval

The Institutional Review Board of both institutions approved the study

and waived the requirement for patients' informed consent.

CRediT authorship contribution statement

Conceptualization NH, PVAP, ANA, CHN, PCCV; Data curation PVAP, JABAF, JMMMS, ABD, JAM, CVO, CSB, TCM; Formal analysis PVAP; Investigation NH, PVAP, ANA; Methodology NH, PVAP, JABAF; Project administration NH; Resources CHN; Supervision NH, CHN, PCCV; Validation NH, PVAP, CHN, PCCV; Roles/Writing - original draft NH, PVAP, JABAF, JMMMS, CVO ; Writing - review & editing all authors.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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