ABSTRACT Objective: Present the abdominal findings of patients who were admitted to the hospital due to COVID-19 infection and had abdominal pain to demonstrate the relationship between the severity and prognosis of the disease and inflammatory parameters and discuss this relationship in the light of the literature.

Study Design: Retrospective study.

Place and Duration of Study: General Surgery Clinic, Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Turkey. From April 2020 to December 2020.

Methods: We examined the relationships between demographic characteristics, thoracic and abdominal findings (bowel wall abnormalities, intra-abdominal fluid, and bile stasis), CRP, D-dimer, length of hospital stay, need for intensive care, and mortality.

Results: Of 60 patients positive for COVID-19, 35 were male (58%), 25% were female (42%). The mean length of hospital stay was 8.8 days (range 3 to 37 days). The relationship between advanced age and the need for intensive care was found to be significantly high (p<0.05). In 30 (90.9%) of 33 (55%) patients with abdominal wall abnormalities, D-dimer was >500 ng/ml, which was found to be statistically significant (p<0.05). The association between lung involvement and mortality was found to be significantly high (p<0.05).

Conclusion: We believe that multiorgan pathologies caused by thrombosis and risky surgery can be prevented by starting medical therapy with hydration, steroids, anticoagulants, and antiaggregants in patients with COVID-19 who develop abdominal symptoms and have high D-dimer and CRP levels without any clear contraindication in the early period due to the increased risk of thrombosis.

KEYWORDS COVID-19 infection, abdominal pain, D-dimer, C-reactive protein

Introduction

Around the world, patients with Coronavirus Disease 2019 (COVID-19) were first identified and diagnosed in December 2019 in Wuhan, Hubei Province, China. Since it was first detected in humans at the end of 2019, COVID-19 has spread very rapidly around the world and caused respiratory infections of varying severity. Diagnosis of COVID-19 patients is essentially based on the positivity of coronavirus nucleic acid detected by reverse transcription-polymerase chain reaction (RT-PCR) test performed on nasopharyngeal and oropharyngeal swab samples taken from suspected patients who have epidemiological history and related symptoms. The most common symptoms developing 2-14 days after exposure to the disease have been recorded as dry cough, fever, fatigue, widespread muscle aches, diarrhoea, and lost sense of smell. Abdominal and gastrointestinal symptoms such as abdominal pain, nausea, vomiting, and diarrhoea have also been reported in the literature. These symptoms and diarrhoea occur secondary to the interaction between ACE2, which is highly expressed in the human small intestine, vascular endothelium, various intra-abdominal organs, and the COVID-19.
19 cell entry receptor. Recent studies have demonstrated that COVID-19 ribonucleic acid (RNA) was detected in stool samples, confirming faecal-oral transmission.6 Thoracic Computed Tomography (CT) scores, serum C-reactive protein (CRP) level, and D-dimer have good consistency in the diagnosis and follow-up of the disease, and their combination can dynamically and effectively evaluate disease progression and therapeutic effects.7 CRP is an inflammatory response protein whose increase in serum may reflect the activation of the inflammatory response.8 CRP is a cell membrane glycoprotein that damages the vascular intima by activating the complement system and the coagulation system that causes thrombosis by inducing monocytes and causing tissue factors to be expressed.9 Elevated D-dimer value indicates increased activity of secondary fibrinolysis, and its sensitivity in the diagnosis of thrombosis is 95%, which is quite significant in the diagnosis of acute thrombosis.10 The increase in D-dimer level is an indicator of increased coagulation reaction in serum patients with thrombosis. In this case, the complement system is activated, resulting in the acceleration of thrombus formation through the initiation of the exogenous coagulation pathway.11 Autopsy examination of a dead COVID-19 case showed micro thrombosis in the pulmonary artery and other organs.12 The most important way to fight this viral infection is to detect COVID-19 early, isolate cases, monitor contacts and inform people correctly.13 In this study, we aim to present the abdominal findings of patients who were admitted to the hospital due to COVID-19 infection and had abdominal pain to demonstrate the relationship between the severity and prognosis of the disease and inflammatory parameters and discuss this relationship in the light of the literature.

Methodology

Sixty patients whose nasopharyngeal and oropharyngeal swab samples were positive for RT-PCR coronavirus nucleic acid, who were treated as inpatients at our hospital’s pandemic wards between during the highest period of the pandemic, namely April 2020 and December 2020, and who underwent thoracic and abdominal CT due to concurrent abdominal pain were included in the study. Patients who underwent abdominal surgery for other reasons before COVID-19 disease and who used chronic anticoagulants and antiaggregants due to a history of hypercoagulability, pulmonary embolism, and deep vein thrombus (DVT) were excluded from the study. The patients’ thoracic and Abdominal CT images were re-interpreted by two radiologists with 5 years of work experience. D-dimer and CRP values obtained simultaneously with CT imaging and patients’ information in the medical files were analysed retrospectively. We examined the relationships between demographic characteristics, thoracic (bilateral and unilateral involvement) and abdominal findings (bowel wall abnormalities, intra-abdominal fluid, and bile stasis), CRP, D-dimer, length of hospital stay, need for intensive care, and mortality.

This study was designed as a single-centre cohort study. Prior to initiation, the study was approved by our hospital’s ethics committee (2021/514/201/5) and the Scientific Research Platform of the Ministry of Health. Furthermore, the study was planned per the principles of the revised Declaration of Helsinki.

Analysis was carried out using the SPSS (Statistical Package for Social Sciences) for Windows 20.0. Data were summarized as average ± standard deviation, numbers(n), and percentage(%). Categorical variables were compared using the Chi-square test or Fisher’s exact test. All statistical calculations were two-way, and p <0.05 was considered statistically significant at the 95% confidence interval.

Results

Of the 60 patients included in the study whose reverse transcription-polymerase chain reaction (RT-PCR) tests performed on nasopharyngeal and oropharyngeal swab samples were positive for COVID-19, 35 were male (58%), 25 were female (42%). The average age of the patients was 62 years (range 24 to 87 years). The mean length of hospital stay was 8.8 days (range 3 to 37 days). The mean age of 9 (15%) patients who needed intensive care was 75.9±5.3 years, and the relationship between advanced age and need for intensive care was found to be significantly high (p<0.05). In 30 (90.9%) of 33 (55%) patients with abdominal wall abnormalities, D-dimer was >500 ng/ml, which was found to be statistically significant (p<0.05) (Table I). Bilateral lung involvement was present in 7 (11.6%) patients who died, and 4 (57%) of them had abdominal intestinal wall abnormalities and intra-abdominal fluid besides lung involvement. The relation between lung involvement and mortality was significantly high (p<0.05). Although there was an increase in the impact of lung involvement, elevated D-dimer and CRP levels, and presence of intra-abdominal fluid and bile stasis on the length of stay, need for intensive care. Mortality, no statistically significant difference was found (Tables II-III). In 53 (88%) patients discharged, clinical improvement was achieved in terms of abdominal findings through hydration, steroids, antibiotherapy, and conservative medical therapy with antiaggregants and anticoagulants during their follow-up. In the patients, no progressive pathology was detected in abdominal findings due to COVID-19 infection that required surgery.

Discussion

COVID-19, which had led to a pandemic all around the world, was first introduced in Wuhan, Hubei Province, China.1 Since it was first detected in humans at the end of 2019, COVID-19 has spread very rapidly around the world and caused respiratory infections of varying severity (1). COVID-19 is a novel type of coronavirus of the enveloped β genus.2 The virus is transmitted mainly by respiratory tract and contact. It invades the inside of the cell and impairs its functions by completing the receptor binding of the mucosal cells with angiotensin-converting enzyme 2 (ACE2).4

In a study of patients with COVID-19 pneumonia, the most common initial symptoms were fever (98.6%), fatigue (69.6%), dry cough (59.4%), anorexia (40%), myalgia (34.8%), dyspnoea (31.2%) and expectation (26.8%).14 At the beginning of the pandemic, our screening criteria for COVID-19 did not include abdominal pain symptoms.2 As the pandemic progressed, abdominal symptoms, including gastrointestinal symptoms and liver enzyme elevation, were frequently reported in patients with COVID-19.4,15

In addition to the initial symptoms of COVID-19, gastrointestinal symptoms such as diarrhea (3.8-10.1%), nausea (5-10.1%), vomiting (3.6-5%), and abdominal pain (2.2%) have also been reported as presenting complaints about the time.16

Causes for abdominal complaints in patients with COVID-19 include viral infection, small vessel thrombosis, or non-occlusive mesenteric ischemia.12 The fact that ACE2 surface expression is most abundant in lung alveolar epithelial cells and ACE2 is abundantly present in various abdominal organs, small intestinal enterocytes, and vascular endothelium indicates that various
### Table 1 Abdominal wall abnormalities

| n = 60 | None       | Present      | p  |
|--------|------------|--------------|----|
| Age    | 63.7±15.0  | 61.5±17.4    | 0.385 |
| Gender | Male 13    | 22           | 0.418 |
|        | Female 14  | 11           |      |
| Bilateral Involvement | No 8 | 7 | 0.454 |
|        | Yes 19     | 26           |      |
| Unilateral Involvement | No 24 | 29 | 0.903 |
|        | Yes 3      | 4            |      |
| D-dimer (ng/ml) | ≤500 8 | 3 | 0.041 |
|        | >500 19    | 30           |      |
| CRP (mg/L) | ≤5 4 | 1 | 0.100 |
|        | >5 23      | 32           |      |

*Fisher’s Exact Test

### Table 2 Intra-abdominal Fluid

| n = 60 | None       | Present      | p  |
|--------|------------|--------------|----|
| Age    | 62.1±16.2  | 63.6±16.9    | 0.760 |
| Gender | Male 26    | 9            | 0.606 |
|        | Female 20  | 5            |      |
| Bilateral Involvement | No 12 | 3 | 0.724 |
|        | Yes 34     | 11           |      |
| Unilateral Involvement | No 41 | 12 | 0.727 |
|        | Yes 5      | 2            |      |
| D-dimer (ng/ml) | ≤500 10 | 1 | 0.217 |
|        | >500 36    | 13           |      |
| CRP (mg/L) | ≤5 4 | 1 | 0.854 |
|        | >5 42      | 13           |      |

*Fisher’s Exact Test

### Table 3 Bile Stasis

| n = 60 | None       | Present      | p  |
|--------|------------|--------------|----|
| Age    | 61.0±16.1  | 69.8±16.0    | 0.137 |
| Gender | Male 28    | 7            | 0.412 |
|        | Female 22  | 3            |      |
| Bilateral Involvement | No 13 | 2 | 0.689 |
|        | Yes 37     | 8            |      |
| Unilateral Involvement | No 45 | 8 | 0.369 |
|        | Yes 5      | 2            |      |
| D-dimer (ng/ml) | ≤500 10 | 1 | 0.456 |
|        | >500 40    | 9            |      |
| CRP (mg/L) | ≤5 5 | 0 | 0.388 |
|        | >5 45      | 10           |      |

*Fisher’s Exact Test
abdominal organs, small intestine, and vessels may be susceptible to COVID-19 infection. Many publications have reported results showing that COVID-19 has a direct inflammatory effect on the vascular endothelium.

Although coronaviruses are generally considered respiratory viruses that are transmitted through the respiratory tract, primary or secondary oral contamination may be the reason for abdominal symptoms.

The reports of COVID-19 RNA detected in stool samples published by recent studies confirm faecal-oral transmission. Moreover, coagulopathy, which adversely affects the entire system, is common in severe COVID-19 cases.

Systemic coagulopathy has been supported by autopsy results showing complement-mediated microvascular injury and explanations for vascular imaging abnormalities.

D-dimer is a specific fibrin degradation product from cross-linked fibrin and a hallmark of secondary fibrinolysis (2). Elevated D-dimer shows the increased activity of secondary fibrinolysis, and it has a sensitivity of 95% in the diagnosis of thrombosis. Therefore, it is a very valuable indicator for the diagnosis of acute thrombosis.

C-Reactive Protein (CRP) is a cell membrane glycoprotein that damages the vascular intima by activating the complement system and activates the coagulation system that causes thrombosis by inducing monocytes and causing tissue factor to be expressed.

Deng et al. examined the relation of thoracic CT scores with serum CRP levels and mortality at different stages of the clinical progression of COVID-19 disease and showed a significant correlation between CT scores and elevated serum CRP and mortality. Additionally, and Jin Zhu et al. indicated that D-dimer and CRP levels increased significantly in clinically severe patients, and this increase was consistent with the severity of thoracic CT lesions. The authors also reported that increased D-dimer and CRP levels caused systemic multi-organ failure in some patients. An autopsy examination of a dead COVID-19 case showed the presence of micro thrombosis in the pulmonary artery and some abdominal organs.

In our study, bilateral lung involvement was present in 7 (11.6%) patients who died, and 4 of them had abdominal intestinal wall abnormalities and intra-abdominal fluid besides lung involvement. Furthermore, in 30 (90.9%) of 33 (55%) patients with abdominal wall abnormalities, D-dimer was >500 ng/ml, which was found to be statistically significant (p<0.05). The relation between lung involvement and mortality was significantly high (p<0.05).

For these reasons, D-dimer and CRP levels should be closely monitored for COVID-19 patients, and routine anticoagulant treatment should be performed provided that there are no contraindications.

A study showed ischemic mucosal necrosis and fibrin thrombus in the submucosal arterioles of the necrotic segments in the pathological findings obtained after a surgical procedure in patients with COVID-19 infection. The development of the need for intensive care was significant in patients who have common abdominal wall findings on abdominal CT images. Among the findings, intestinal wall thickening, intra-abdominal fluid, oedema and inflammation, and mesenteric ischemia findings were frequently observed.

Previous studies have reported that advanced age is a risk factor for intensive care needs. In this study, the average age of 9 (15%) patients who needed intensive care was 75.9±5.3 years. Moreover, we found that the relationship between advanced age and the need for intensive care was significantly high, in line with the literature (p<0.05).

Although high liver enzyme levels are frequently reported in patients with COVID-19, the exact cause is still unclear. In a study, bile stasis was observed in the gallbladder in 54% of the right upper quadrant ultrasound images, and there was a significant relationship between imaging and laboratory results referring to cholestasis and the need for intensive care. Although COVID-19 patients in the intensive care unit are often prone to hypercoagulability, no patients with portal vein thrombosis were identified.

In our study, although there was an increase in the impact of lung involvement, high D-dimer and CRP levels, and presence of intra-abdominal fluid and bile stasis on the length of hospital stay, need for intensive care, and mortality, no statistically significant difference was found. In 53 patients who were discharged, clinical improvement was achieved in terms of abdominal findings through hydration, steroids, antibiotherapy, antiaggregant, and anticoagulant conservative medical treatment during their follow-up. Abdominal pain may develop due to life-threatening causes of surgery that require an acute solution and, for many reasons that can be treated with conservative solutions, which can be seen in COVID-19 infection. Therefore, abdominal pain is a finding that requires great attention in surgical patient management, and surgeons should consider all these difficult processes in the approach to abdominal pain during the pandemic period. In the patients included in the study, no progressive pathology was detected in terms of abdominal findings due to COVID-19 infection that required surgery.

Conclusion
We believe that multiorgan pathologies caused by thrombosis and risky surgery can be prevented by starting medical treatment with hydration, steroids, anticoagulants, and antiaggregants in patients with COVID-19 who develop abdominal symptoms and have high D-dimer and CRP levels without any clear contraindication in the early period due to the increased risk of thrombosis. However, this theory needs to be supported with results from multicenter publications conducted with high patient numbers.

Ethical approval
This retrospective study was carried out in Kartal Dr Lutfi Kirdar City Hospital, Istanbul, Turkey, General Surgery Clinic. Local ethics committee approval (2021/514/201/5).

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Conflict of interest
There are no conflicts of interest to declare by any of the authors of this study.

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