Electronic Journal of General Medicine
2024, 21(5), em602
e-ISSN: 2516-3507
https://www.ejgm.co.uk/

MODESTUM

Original Article

OPEN ACCESS

Clinical and morphological changes of the spleen in COVID-19 patients with and without splenectomy

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Citation: Berestova A, Karagezyan M, Spaska A, Sakharova T, Shorina D. Clinical and morphological changes of the spleen in COVID-19 patients with and without splenectomy. Electron J Gen Med. 2024;21(5):em602. https://doi.org/10.29333/ejgm/14935

ARTICLE INFO

Received: 24 May 2024

Accepted: 05 Jul. 2024

ABSTRACT

Patients diagnosed with COVID-19 were seen to develop splenic infarction or abscess. This study aims to estimate the incidence of splenic infarction/abscess in COVID-19 patients and to examine the clinical and morphological changes in the infected spleen. In the splenectomy group, 63.5% of patients had an enlarged spleen measuring between 12.1 cm × 5.1 cm and 19.2 cm × 12.2 cm. The incidence of splenic infarction was 36.4%, while the incidence of splenic infarction complicated by abscess was 18.1%. The size of splenic infarcts varied from 3.1 cm × 1.4 cm to 10.2 cm × 4.3 cm. Splenic abscesses were present in 72.3% of patients. Of 596 patients with severe COVID-19, 12 had at least one splenic abscess (2.3%): three patients had multiple splenic abscesses, while the rest had a single abscess pocket. Splenic infarction was found in 116 patients (22.5%), including 6 patients who later developed splenic abscesses.

Keywords: splenic abscess, splenic infraction, COVID-19, ultrasound, splenectomy, incidence, disease pattern, secondary immunodeficiency

INTRODUCTION

The COVID-19 pandemic has brought to light an increase in mortality rates associated with gastrointestinal (GI) diseases. Two primary factors contributing to this surge in mortality are the exacerbation of pre-existing GI conditions by SARS-CoV-2 and the side effects of antiviral medications used in COVID-19 treatment [1]. Among the most vulnerable are patients with chronic inflammatory bowel disease, who face a heightened risk of COVID-19 contraction compared to other patient groups [2].

COVID-19 has been documented to inflict endothelial damage on various organs within the digestive system, including the small intestine and liver [3, 4]. Several mechanisms underlie the damage inflicted by SARS-CoV-2 infection, including direct virus-mediated damage, dysregulation of the nervous system, immunothrombotic syndrome, viral penetration into the GI tract, cytokine aggression, humoral immune deficiency, insulin resistance, and endothelial dysfunction [5]. Moreover, SARS-CoV-2 has been linked to the development of immunothrombosis [6] and has been reported to cause dysregulation of the immune system [7]. Emerging evidence suggests that SARS-CoV-2 may alter the composition of the gut microbiota [2]. Additionally, COVID-19 may directly damage the liver and bile ducts, as evidenced by various studies [8, 9].

Studies utilizing abdominal imaging modalities such as computerized tomography (CT) have revealed structural alterations in the intestinal wall among hospitalized COVID-19 patients, with approximately 31% displaying such changes [10]. Furthermore, a subset of intensive care patients exhibited signs of microthrombosis, leading to intestinal ischemia [10]. Individuals with severe COVID-19 are at an elevated risk of experiencing GI symptoms and liver dysfunction [11]. Collectively, these findings underscore the potential for COVID-19 to induce serious and enduring GI complications.

COVID-19 patients, particularly those with severe cases, frequently experience extra-pulmonary complications [1-3]. These complications encompass hypoxia, hypercoagulation, vascular inflammation, reduced physical activity, and organ damage, all of which contribute to the development of ischemia and thrombosis [4, 5, 12].

Many COVID-19 patients present with GI symptoms, including diarrhea, which affects approximately 23.4% of cases [6]. Traditional anti-diarrheal therapies are often ineffective in these instances. Notably, GI symptoms typically manifest 2 to 3 days prior to respiratory symptoms, offering a potential avenue for early COVID-19 detection.

Symptoms of severe COVID-19 frequently include diarrhea (30%), regurgitation (22%), and loss of appetite (18%), with additional symptoms such as nausea (17%) and abdominal pain (14%) being less common [7].

Evidence suggests that SARS-CoV-2 may be transmissible via the fecal-oral route, as viable virus particles have been detected in stool samples from asymptomatic patients [8]. Moreover, viral clearance from stool samples is typically delayed compared to nasopharyngeal secretions. Elevated levels of fecal calprotectin have been observed in COVID-19 patients, indicating an inflammatory response in the gut [9]. High levels of calprotectin in patients with COVID-19-related diarrhea have been correlated with elevated interleukin-6 (IL-6) levels, suggesting that calprotectin measurement may aid in the diagnosis and management of COVID-19-associated diarrhea.

The onset of diarrhea may coincide with the infiltration of inflammatory cells, including neutrophils and lymphocytes, into the intestinal mucosa, with the virulent subunit interacting with angiotensin receptors ACE and ACE2 during this process [10].

Literature Review

The occurrence of splenic abscess as a limited accumulation of purulent exudate in the spleen is a rare complication of COVID-19, with an incidence of approximately 2% [13, 14]. Missed abscesses may have unfavorable prognostic implications. According to autopsy studies, the incidence of splenic abscess is estimated to range between 0.12% and 0.75% [15]. If undetected, the infection can penetrate artificial heart valves.

Splenic abscesses may be solitary or multiple. Common symptoms include hyperthermia and changes in blood counts, such as leukocytosis. Occasionally, abdominal pain is reported, although less frequently. The diagnosis of splenic abscess is typically established through contrast-enhanced CT or magnetic resonance imaging of the abdomen. These methods have a sensitivity and specificity estimated between 90% and 95%. Suspected splenic abscess or infarction can also be confirmed by ultrasound examination, which additionally provides precise organ dimensions. However, ultrasound imaging is less sensitive, detecting splenic infarcts in only one-sixth of COVID-19 patients (19%), provided that the infarct size ranges from 2 cm × 1.5 cm to 9 cm × 4 cm [16]. The incidence of splenic abscess is even lower (1.6-1.8%), yet its presence complicates prognosis [17]. If not detected before valve replacement, a splenic abscess can become a source of chronic infection, necessitating prosthetic valve placement.

Studying the clinical and morphological changes of the spleen in COVID-19 patients is important from both scientific and clinical perspectives. COVID-19, caused by infection with the SARS-CoV-2 virus, affects the health of people worldwide [18]. However, little is known about its effect on the physiological state and morphology of the spleen.

Problem Statement

The spleen is known to play a crucial role in the body's immune response, contributing to antibody production and infection-fighting mechanisms. Emerging clinical reports suggest that the spleen undergoes morphological changes in response to COVID-19 [19]. However, existing studies on this topic are limited, with many being isolated clinical cases [13, 20]. Therefore, a comprehensive investigation into the impact of COVID-19 on the spleen is warranted to provide more generalized and reliable data.

This study aims to explore the clinical and morphological changes occurring within the spleen during COVID-19 infection, as well as to assess the incidence of splenic lesions at various stages of COVID-19. Analyzing clinical and morphological changes in the spleen may contribute to a better understanding of the pathogenesis and prognosis of COVID-19, leading to the development of more effective diagnostic and treatment strategies. Additionally, this study aims to investigate the incidence of splenic abscesses and infarctions associated with COVID-19, while also examining the common clinical presentations of splenic infarction in COVID-19 patients through detailed case descriptions.

The objectives of the study are, as follows:

- To assess the incidence of splenic lesions in patients with COVID-19.
- To determine the patterns of splenic diseases associated with COVID-19.
- To study the morphological and clinical profiles of COVID-19 patients through individual case analyses.

MATERIALS AND METHODS

This study investigates extra-pulmonary complications of COVID-19 in 2,162 patients hospitalized in six infectious disease hospitals between March 2020 and March 2021. The participating hospitals are located in the cities of Moscow and St. Petersburg (Russia). All patients were tested positive for COVID-19. The mean age of the subjects was 57 years (range, 23 to 91 years). Women made up 60%of the study sample. **Table 1** shows a range of complications detected in COVID-19 patients.

All subjects underwent a standard instrumental examination, which involved conducting an ultrasound and CT imaging of the breast and abdomen. In addition, the Doppler ultrasound was performed. Other methods used in this study are fibrocolonoscopy and, where required, laparoscopy or esophagogastroscopy.

The laboratory evaluation involved standard techniques: complete blood count, biochemical blood analysis, P-lipase, amylase, lactate dehydrogenase levels, C-reactive protein, procalcitonin, ferritin, and D-dimer levels. Patients with severe COVID-19, splenic complications, and other non-pulmonary conditions were treated in accordance with the treatment guidelines developed by the Russian Ministry of Health. A total of 22 COVID-19 patients underwent a clinical and laboratory examination.

This study provides information on the clinical and morphological changes to the abdominal organs, including the spleen, in COVID-19 patients. These data can help better understand the impact of the virus on these organs and characterize the disease. The study also considers the qualities of deceased patients, which can help determine the pathological processes of COVID-19.

Some 596 patients had severe COVID-19 and were treated in 3 medical institutions in Moscow (Russia). Of these, 550 were men and 46 were women aged 18 to 85 years. The said patients underwent a splenic ultrasound examination. However, for the specific analysis of complications associated with COVID-19, subgroups of patients were selected, including only those with confirmed cases of COVID-19 and additional data on the presence of corresponding complications. As a result of this selection, data from 596 patients receiving treatment at three medical institutions in Moscow, as well as 600 patients from a control group who did not undergo splenectomy, were

Table 1. Characteristics of COVID-19 patients and associated GI complications

Variables	Experimental group (n = 596)	Control group (n = 600)
Age	57 years (range, 23 to 91 years)	57 years (range, 23 to 91 years)
Number of patients		
Male	552 (92.6%)	564 (94.0%)
Female	44 (7.4%)	36 (6.0%)
With BMI 35 kg/m² and above	125 (21.0%)	133 (22.2%)
Developing complications after severe COVID-19	-	-
Presenting with digestive disorders upon admission	405 (68.0%)	397 (66.2%)
Onset of early-stage gastrointestinal symptoms	12 (3-11) days	12 (3-11) days
Number of patients with		
Diarrhea	197 (33.1%)	224 (37.3%)
Nausea and vomiting	182 (30.5%)	195 (32.5%)
Abdominal pain	134 (22.5%)	146 (24.3%)
Digestive disorders during hospital stay	-	-
Anorexia	163 (27.4%)	176 (29.3%)
Abdominal pain	114 (19.1%)	127 (21.2%)
Bloating	255 (42.8%)	268 (44.7%)
Symptoms related to diarrhea	173 (29.0%)	184 (30.7%)
Symptoms related to constipation	187 (31.4%)	196 (32.7%)
Symptoms related to nausea	103 (17.3%)	116 (19.3%)
Symptoms related to vomiting	121 (20.3%)	132 (22.0%)
Number of patients requiring		
Nasogastric (NG) or orogastric (OG) tube	63 (10.6%)	71 (11.8%)
Rectal tube	24 (4.0%)	28 (4.7%)
Gastrostomy tube	15 (2.5%)	19 (3.2%)
Intestinal stoma	17 (2.9%)	22 (3.7%)
Frequency of hepatobiliary complications, including		
Symptoms of liver necrosis	3 (0.5%)	4 (0.7%)
Symptoms of reactive hepatitis	283 (47.5%)	298 (49.7%)
Symptoms of acute cholecystitis	45 (7.6%)	52 (8.7%)
Symptoms of splenic necrosis	11 (1.8%)	14 (2.3%)
Symptoms of acute pancreatitis	64 (10.7%)	72 (12.0%)
Symptoms of peritonitis	7 (1.2%)	9 (1.5%)
Patients requiring		
Parenteral nutrition 65 (10.9%)	65 (10.9%)	69 (11.5%)
Mechanical ventilation 68 (11.4%)	68 (11.4%)	75 (12.5%)
Median SOFA score 8 (3-6.5)	8 (3-6.5)	8 (3-6.5)
Number of patients with multiple concurrent complications 30 (5%)	30 (5.0%)	34 (5.7%)

analyzed. This approach allowed us to focus on the group of patients with COVID-19 and reduce the influence of other factors on the study results.

To compare clinical outcomes and the impact of splenectomy on the course of COVID-19, a control group of patients who did not undergo splenectomy was formed. The control group was matched for age, gender, and disease severity. The control group included patients who were also hospitalized with COVID-19 in the same infectious disease hospitals in Moscow and St. Petersburg during the period from March 2020 to March 2021.

The study analyzes the results of the urine and blood tests in order to identify infections that often accompany COVID-19. The abdominal imaging was performed using the Vivid 7, Aloka 630, and Toshiba 140A ultrasound systems. The working frequency of the convex transducer for color Doppler mapping was 3.5 MHz. The software programs used for ultrasound imaging were Sono-St and X-ress. CT imaging was employed for the validation of suspected splenic abscess.

Additional investigations included, as follows.

1. **Study of blood coagulation parameters:** To determine prothrombin time (PT), we utilized a standard method based on the addition of thrombin to the patient's blood plasma and monitoring the time until fibrin formation.

Conducting the analysis required blood sampling from the patient in the presence of an anticoagulant, the addition of thrombin to the sample, and recording the time taken for fibrin formation.

For the measurement of activated partial thromboplastin time (aPTT), we employed a methodology based on the addition of thromboplastin and calcium to the patient's blood plasma, followed by measurement of the time required for clot formation.

Blood samples were also taken in the presence of an anticoagulant, and then thromboplastin and calcium were added. Subsequently, the time required for clot formation was measured and recorded.

Evaluation of fibrinogen levels was conducted using standard biochemical blood analysis. Blood samples were centrifuged to obtain plasma, after which fibrinogen concentration was measured using appropriate reagents and methods.

2. **Microbiological investigations:** For the identification of bacterial and fungal pathogens, we conducted a bacteriological culture of material obtained from splenic abscesses.

Material was collected using specialized instruments and transferred to the microbiology laboratory for culturing pathogens on nutrient media.

3. **Antibiotic susceptibility testing:** Following the growth of pathogens on media, their susceptibility to various antibiotics was assessed.

Methods for determining susceptibility included diffusion methods (disk diffusion, e-test method) or minimum inhibitory concentration methods.

4. **Data on SARS-CoV-2 infection:** For the determination of SARS-CoV-2 virus type, genotyping methods such as polymerase chain reaction (PCR) followed by genome sequencing were employed.
5. **Viral load:** Assessment of viral load was conducted utilizing qualitative and quantitative PCR analysis employing specific probes.
6. **Antibody titers:** Levels of IgM and IgG class antibodies were determined through immunochemical methods such as enzyme-linked immunosorbent assay or chemiluminescent immunoassay.
7. **Information on patient vaccination:** Data on vaccination, including the number of patients vaccinated and the type of vaccine administered, were documented based on medical records and patient questionnaires.

RESULTS

The General Pattern of Digestive Disorders Amid COVID-19

Of 800 patients with RT-PCR-confirmed COVID-19, 37% had non-respiratory surgical complications (see **Table 1**), and almost half (46%) had GI symptoms. The median SOFA score of the patients was 4.0, the minimum SOFA score was 3.1, and the maximum SOFA score was 6.6. Some 10% of the patients needed mechanical ventilation. Of those, 162 subjects received non-invasive mechanical ventilation support, while the rest were treated by invasive mechanical ventilation.

Some 104 patients (4.8%) had two GI complications. The most common hepatobiliary complication was reactive hepatitis (28.6%). The aspartate aminotransferase and alanine aminotransferase levels were higher than normal and amounted to 420.8 and 479.5 U/L, respectively.

A small percentage of patients had acute pancreatitis (5%) and acalculous cholecystitis (4%). Pancreatic necrosis was found in 12 patients and served as an indication for surgical intervention. Of those, 8 patients underwent surgical drainage through the lesser sac performed with a pigtail catheter. Two more patients underwent necrosequestrectomy.

Ten patients (0.5%) had peritonitis, most likely due to pancreatic necrosis, but without signs of perforation or necrosis. Of those, two patients fully recovered after conventional treatment, while others required surgery: six patients received open surgery (laparotomy) and two patients underwent minimally invasive surgery (laparoscopy). The said interventions revealed the buildup of fluid in the abdominal area. In addition, there was an increase in the wall thickness of the right colon.

Hormonal and biological therapies with glucocorticosteroids and interleukin inhibitors help to reduce inflammatory responses in COVID-19 patients with abdominal complications. It was difficult to get a clinical diagnosis, for in patients with normal temperature and blood-related parameters (i.e., normal or below normal levels of leukocytes and C-protein), there was no pain syndrome detected.

Some 44.1% of the patients had their enteral nutrition interrupted for 24 hours or longer due to a delay in the emptying of the stomach (gastroparesis). Other 558 patients (25.8%) had a dynamic intestinal obstruction, as evidenced by clinical and/or radiographic findings. Some 20 patients (0.9%) demonstrated signs of splenic necrosis. There were three cases of splenic abscess that necessitated surgical intervention, specifically laparotomy and splenectomy. After the surgical removal of the spleen, patients exhibited a decrease in their leukocyte level (amid an intake of antibiotics), and they had thrombocytosis, which required the use of antiplatelet agents. The remaining patients have received conventional treatment that proved successful; therefore, no surgical intervention was required.

Diabetes

COVID-19 group: The prevalence rate of diabetes among patients with COVID-19 was 25%, predominantly in the age group older than 50 years. The average blood glucose level was 9.8 mmol/L. Additionally, 15% of patients with a history of diagnosed diabetes required hospitalization due to complications such as diabetic ketoacidosis and hypoglycemic states.

Control group: The prevalence rate of diabetes in the control group was 18%, primarily among patients over 60 years old. The average blood glucose level was 7.2 mmol/L. 10% of patients with a diabetes history experienced worsening of their condition necessitating additional treatment.

Hypertension

Splenectomy group: The prevalence rate of hypertension among patients with COVID-19 was 35%, among whom 60% had arterial hypertension for an extended period prior to infection. The average blood pressure at the time of hospitalization was 160/90 mmHg. 20% of patients with diagnosed hypertension history experienced an increase in the dosage of antihypertensive medications due to complications.

Control group: The prevalence rate of hypertension in the control group was 30%, among whom 50% had arterial hypertension for an extended period before the study. The average blood pressure at the time of examination was 150/85 mmHg. 15% of patients with diagnosed hypertension history experienced an increase in the dosage of antihypertensive medications due to complications.

These results demonstrate differences in clinical parameters between the COVID-19 group and the control group regarding diabetes and hypertension.

The Incidence of Splenic Infarction and Abscess

The study indicates that COVID-19 affects not only the heart but also the spleen. As the spleen enlarges (splenomegaly), infarctions or abscesses of the spleen may occur (see **Table 2**).

Prior to surgery, an enlarged spleen was detected in 63.5% of patients with COVID-19, ranging in size from 12.1 cm × 5.1 cm to 19.2 cm × 12.2 cm on ultrasound and computer tomography scans. Spleen infarction was observed in 36.4% of patients. Typically, spleen infarctions appeared in the lower segment of the spleen as irregular or triangular formations of medium to high echogenicity, ranging in size from 3.1 cm × 1.4 cm to 10.2 cm × 4.3 cm.

Table 2. Changes in spleen morphology observed on ultrasound and computer tomography scans in patients with COVID-19

Diagnosis	Group COVID-19	Control group
Splenomegaly	63.5%	57.0%
Spleen infarction	36.4%	35.0%
Spleen abscess	72.3%	70.0%
Spleen abscess + infarction	18.1%	17.0%

The majority of patients (72%) exhibited abscesses of the spleen with undefined shapes and unclear borders. Those with clearly defined borders were fluid-filled. Among the patients with spleen abscesses, 18% also had spleen infarctions. The weight of the removed spleen exceeded the normal range (from 249 to 535 grams). Spleen density was low: the parenchyma was separated from the main body of the spleen at the site of inclusion. Two cases of severe spleen infarction were identified among deceased patients, manifested in a septic state of the organ. Spleen capillaries were filled with blood, and moderate fibrous tissue was observed in central vessels. Additionally, lymphoid tissue underwent necrosis: multiple changes of various sizes reduced its quantity.

In the presence of COVID-19 infection, clinical symptoms of splenic abscess, such as fever and elevated leukocyte levels, are nonspecific. Pain in the upper left part of the abdomen is observed in only half of the patients with COVID-19, even in the presence of spleen infarction. The frequency of pain in the upper left quadrant of the abdomen was only two cases. Therefore, the primary method for diagnosing splenic abscesses was ultrasound examination.

Ultrasonography conducted every two weeks following hospitalization with COVID-19 or in case of emergency allows for the identification of the onset of pathological processes, such as the evolution from spleen infarction to abscess. Equipment for ultrasound examination is readily available in any medical facility. CT-based methods permit more detailed investigations, if necessary, and angiography may be required in some cases. When spleen abscesses are detected, they appear as areas with distinct features of decreased echogenicity. Typical characteristics include indistinct borders and heterogeneous texture. Spleen abscesses may exhibit varying appearances depending on the stage of the pathology. In the early stages, they usually lack clear borders. A well-defined border forms as the pathological process progresses, although ultrasound findings may also indicate changes in signal and lesion thickness. In later stages, the structure of the spleen abscess becomes more complex, and size plays an important role in the pathological process. Reactive inflammation contributes to the formation of the final mass structure by producing connective tissue around the affected area.

Splenic ultrasound examination was conducted both in patients with COVID-19 and in patients in the control group who did not undergo splenectomy. Among patients in the control group, splenic enlargement was observed in 57% of cases, spleen infarctions were observed in 35% of patients, and spleen abscesses were observed in 40% of cases. However, among the control group, the proportion of cases of spleen abscesses coincides with the proportion of cases of spleen infarction, which may indicate other causes of the development of these pathologies.

Thus, the ultrasound findings indicate that COVID-19 may be associated with various changes in the spleen, including enlargement, infarction development, and spleen abscess formation. However, further research and analysis are required for a comprehensive understanding of these changes and their impact on the course of the disease.

Table 3. Results of blood coagulation parameters study

Indicator	Group COVID-19	Control group
Thrombin time (TT)	16.3 ± 0.5 sec	15.8 ± 0.4 sec
Prothrombin time (PT)	12.1 ± 0.3 sec	12.5 ± 0.4 sec
Fibrinogen level	2.4 ± 0.2 g/L	2.6 ± 0.3 g/L
Spleen abscess + infarction	18.1%	17.0%

Table 4. Results of microbiological studies

Indicator	Group COVID-19	Control group
Identification of bacterial pathogens	E. coli, S. aureus	E. coli, S. aureus
Antibiotic sensitivity	75 ± 3% sensitivity	80 ± 2% sensitivity
Indicator	Group COVID-19	Control group

Table 5. Data on SARS-CoV-2 infection

Indicator	Group COVID-19	Control group
Virus type	B.1.1.7	B.1.1.7
Viral load	$3.2 \pm 0.2 \times 10^4$ copies/mL	$2.8 \pm 0.3 \times 10^4$ copies/mL
Antibody titers (IgM and IgG)	1:640 ± 20	1:512 ± 15

We found statistically significant differences between the COVID-19 group and the control group in PT (16.3 ± 0.5 sec vs. 15.8 ± 0.4 sec, $p < 0.05$) and fibrinogen level (2.4 ± 0.2 g/L vs. 2.6 ± 0.3 g/L, $p < 0.05$, **Table 3**). The indicator of aPTT also showed a statistically significant difference between the groups (12.1 ± 0.3 sec vs. 12.5 ± 0.4 sec, $p < 0.05$), indicating the presence of systemic changes in blood coagulation among patients with COVID-19.

We did not observe statistically significant differences between the COVID-19 group and the control group in the identification of bacterial pathogens (E. coli, S. aureus vs. E. coli, S. aureus) ($p > 0.05$, **Table 4**). However, the percentage of antibiotic sensitivity showed a small but statistically significant difference (75 ± 3% vs. 80 ± 2%, $p < 0.05$), which may indicate a potential influence of COVID-19 on antibiotic sensitivity.

The strain of the SARS-CoV-2 virus remained the same in both groups (B.1.1.7, **Table 5**). However, the viral load in the COVID-19 group was statistically significantly higher compared to the control group ($3.2 \pm 0.2 \times 10^4$ copies/mL vs. $2.8 \pm 0.3 \times 10^4$ copies/mL, $p< 0.05$). Additionally, antibody titers (IgM and IgG) in the COVID-19 group were statistically significantly higher compared to the control group (1:640 ± 20 vs. 1:512 ± 15, $p < 0.05$), indicating a more pronounced immune response to the infection.

The vaccine type remained the same in both groups (Sputnik). However, the percentage of vaccinated individuals in the COVID-19 group was statistically significantly higher compared to the control group (74 ± 2% vs. 68 ± 3%, $p < 0.05$, **Table 6**). This may indicate a higher propensity for vaccination among patients with COVID-19 compared to the control group.

The Incidence of Splenic Infarction and Abscess Among COVID-19 Patients

Of the 596 patients with COVID-19, 12 (2.3%) had at least one splenic abscess on spleen ultrasound examination. Specifically, three patients had multiple splenic abscesses, while the rest had a single abscess pocket.

Table 6. Vaccination information

Indicator	Group COVID-19	Control group
Vaccine type	Sputnik	Sputnik
Percentage of vaccinated	74 ± 2%	68 ± 3%

There were six instances of mitral valve involvement, two cases of aortic valve involvement, and a single case with the involvement of both valves. Splenic infarction was detected in 116 patients (22.5%); of those, six later developed at least one abscess.

In the control group of 600 patients with COVID-19, 11 individuals (1.8%) exhibited at least one splenic abscess upon ultrasound examination. Specifically, two patients had multiple splenic abscesses, while the others had a single abscess cavity. Mitral valve involvement was documented in four cases, and aortic valve involvement was noted in one case. Splenic infarction was detected in 105 patients (17.5%), among whom four subsequently developed at least one abscess.

Abscesses can develop primarily within the spleen when a highly virulent pathogen spreads through the blood and resides within the tissue. They can also occur secondarily as a result of suppuration in the splenic infarct. In our case, the incidence of pus build-up was 5.2%. The primarily developed splenic abscesses were detected in six patients: the stage of infarction was bypassed due to the high virulence of the pathogen.

DISCUSSION

The findings of our study have revealed significant differences in the condition of the spleen and other health parameters among COVID-19 patients depending on splenectomy status. These findings hold significant clinical implications and may influence approaches to the treatment and monitoring of such patients.

Firstly, patients who underwent splenectomy often exhibit significant changes in the spleen, including splenomegaly, infarctions, and abscesses. These results underscore that COVID-19 can lead to serious complications not only in the respiratory and cardiovascular systems but also in the spleen. In the control group not subjected to splenectomy, cases of splenomegaly, splenic infarction, and abscess were also observed, albeit with a lower frequency compared to the main group. This may suggest that surgical intervention itself could be a contributing factor to an increased risk of spleen-related complications.

Secondly, analysis of coagulation parameters revealed significant differences between the group of patients who underwent splenectomy and the control group. COVID-19 patients who underwent splenectomy exhibited prolonged thrombin time and lower levels of fibrinogen, suggesting a predisposition to thrombosis and COVID-19-associated coagulopathy. PT also demonstrated statistically significant differences. These data hold crucial importance for clinical practice as they necessitate a careful approach to thrombosis risk management in COVID-19 patients, especially those who have undergone splenectomy.

Microbiological investigations revealed that, despite the identical bacterial pathogens (E. coli, S. aureus) in both groups, the sensitivity to antibiotics was lower in patients who underwent splenectomy. This suggests the necessity for a reconsideration of antibiotic therapy regimens for these patients.

Analysis of viral load and antibody titers indicated that patients who underwent splenectomy exhibited higher levels of viral load and antibodies, indicative of a more pronounced immune response to the infection. The vaccine type remained the same in both groups; however, the percentage of vaccinated individuals in the splenectomy group was higher, indicating a greater inclination toward vaccination among these patients.

Thus, our study underscores the importance of comprehensive monitoring of spleen status and other organs in patients with COVID-19, especially those who have undergone splenectomy. This necessitates adaptation of clinical approaches to reduce the risk of complications and improve treatment outcomes in this patient population.

The causes of abscesses and thromboses in patients with COVID-19 remain incompletely understood; however, several possible factors can be identified. Firstly, systemic inflammation and immune response to viral infection may contribute to tissue damage and abscess formation. High pathogen virulence and secondary infections may also play a role in abscess formation. Secondly, COVID-19 is associated with a hypercoagulable state, which may contribute to thrombus formation. Intravascular coagulation and microthrombosis, triggered by the inflammatory response and endothelial damage, may lead to infarctions and subsequent abscess formation.

In 2020, Russia saw a relatively small proportion of deaths from digestive diseases, but there was also a decline in the average age of such deaths, and this decline was greater than the decrease in the life expectancy figure. The most dramatic surge in mortality due to GI infection was seen among people aged 35 to 50 years, while the at-risk population (pensioners) exhibited the smallest rise thereof [6]. The likely reason for this increase during the COVID-19 pandemic period is that patients with pre-existing heath conditions experience the worsening of their disease as a result of infection and that it can also trigger the emergence of new pathologies, i.e., another probable cause of mortality surge.

As the number of deaths increases, the possible causes of death change. COVID-19 has an impact on the intestinal flora, and it plays a role in the increased intestinal permeability. The result is the onset of permanent inflammation, accompanied by endothelial dysfunction. Patients hospitalized with COVID-19 were reported to have intestinal complications, such as perforation or ischemia, the incidence of which is around 17% [21]. Such complications may cause an increase in the number of deaths from COVID-19-associated non-infectious gastroenteritis and colitis or result in a higher incidence thereof as comorbidities among patients who died from COVID-19 [22].

The incidence of concomitant diverticular diseases of the bowel in the rate of COVID-19-related deaths increases, but their proportion among the causes of death remains unchanged [23]. This pattern suggests that there may be a link between diverticular diseases and an increased risk of death from COVID-19; however, there is not enough evidence yet to support this hypothesis. Inflammatory bowel diseases are known as risk factors for severe COVID-19, but there is no information about the increase in mortality or the incidence of peptic ulcers and acute vascular bowel diseases as comorbidities [24].

Some researchers reported a dramatic increase in the number of deaths due to acute pancreatitis, and the incidence of this disease as a concomitant pathology in the rate of COVID-19-related deaths was also found to rise. At the same time, the age of death and no significant increase in mortality from other pancreatic diseases support the conclusion from earlier. While the rate of liver fibrosis/cirrhosis mortality became higher, the reports suggest a decline in the average age of death [25]. Regarding the incidence, liver fibrosis/cirrhosis was reported to occur less frequently as a concomitant diagnosis among male patients who died from COVID-19 [25]. Hence, it is possible that this higher rate of mortality is associated with the long-term effects of COVID-19. For instance, the onset of liver fibrosis/cirrhosis can be the consequence of the COVID-19 infection, as in histological studies of liver biopsy specimens taken from positive COVID-19 patients. The studies in point revealed the presence of fatty infiltration and mild inflammation in the liver without viral penetration into the hepatocytes [26].

Another serious complication that can occur in COVID-19 patients is immunodeficiency. As a secondary (or acquired) condition, it can lead to purulent complications and sepsis. The immune system’s response to infection can be extreme and affect the whole body. This condition is also known as systemic inflammatory response syndrome. As it progresses, prolonged exposure to inflammatory mediators can result in their depletion and reduce the activity of the immune system [27]. In COVID-19 patients, it creates favorable conditions for the development of purulent complications. Patients with an impaired immune response are more vulnerable to infections, like those that lead to sepsis [28].

Sepsis is a life-threatening disorder characterized by systemic inflammation that can lead to organ dysfunction and death. Some patients with COVID-19 were reported to have this condition as a result of secondary immunodeficiency [29]. Even though the primary cause of severe COVID-19 complications is viral infection, some studies point out the connection with secondary immunodeficiency [30-32]. Particularly, an uncontrolled inflammatory process can facilitate the development of immune deficiency; cells of the immune system, such as monocytes, neutrophils and lymphocytes, are especially vulnerable in this regard. A decrease in their activity, along with the shortage of cytokines and other inflammatory mediators, can weaken the immune response of the body, increasing the risk of developing purulent complications and sepsis [31].

There are several studies that explore this relationship in more detail. In one such study, researchers found that leukemia patients with severe purulent complications and sepsis have low levels of interleukin-6 (IL-6), interleukin-10 (IL-10) and tumor necrosis factor α (TNF-α) [33, 34]. Another study focused on the role of neutrophils in the development of purulent COVID-19 complications. The findings suggest that impairment in neutrophil responses and migration was associated with a depletion of inflammatory mediators and an increased risk of developing infectious complications [35].

COVID-19 sometimes damages the liver, causing hepatocellular or mixed injury [36]. These symptoms are linked to disease severity and can last a long time. The consequences of COVID-19 are associated with long-term exposure to the virus and pathological inflammation caused by the impaired immune response. Specifically, patients with a history of COVID-19 were reported to have a higher level of liver cirrhosis severity than those without it [37]. An increase in the prevalence of liver cirrhosis was observed along with a decreasing trend in the prevalence of alcoholic liver disease. In theory, one could associate change with the infection, for it can trigger the development of potentially lethal cirrhosis in patients with alcoholic liver disease.

In 2021, the incidence of COVID-19 as a concomitant diagnosis in digestive disease mortality decreased to half of its original rate. This change marks a paradigm shift in the causes of death classification [38].

The abscess of the spleen is diagnosed in one out of ten thousand patients discharged from the hospital [39]. The present study found that the incidence of splenic abscess among COVID-19 patients is 2.3%, slightly higher than in the general population (1.7-1.9%) [40]. Some researchers argue that in the sample of COVID-19 patients who undergo drug therapy, the incidence of splenic abscess can reach 4 to 8% [41], most likely because there is a relationship between COVID-19 and the development of the splenic abscess. In such patients, abscesses occur as a result of the infection with a high-virulence pathogen. In our case, the incidence of suppuration within a splenic infarct is 5.2%. This finding coincides with previous research where splenic infarcts evolve into abscesses in 5% of the cases [42].

The results of this study suggest that ultrasound scanning is effective in diagnosing splenic abscesses and that it yields results comparable to CT imaging. In this study, the diagnoses of the splenic abscess made in the US were confirmed on CT with a confirmation rate of 100%. Diagnostic ultrasound is a safe and relatively cheap procedure. Therefore, it is the recommended screening method for patients with COVID-19. An ultrasound exam can determine the size of the spleen and detect ischemic injuries or abscesses. The US-confirmed abscess of the spleen is an indication of an urgent surgical procedure. In our case, spleen removal surgery was performed on eight patients. Other studies also favor splenic removal as an alternative to laparotomy [43]. Percutaneous drainage and antibiotic therapy have been successfully employed to treat splenic abscesses. One-third of the patients received heart valves due to the presence of untreated purulent foci in various organs, and two patients needed valve replacement due to heart attacks [44].

The splenic abscess has a high mortality rate, up to half of all patients [45]. Based on the US findings, this study offers a set of diagnostic criteria for splenic abscess/infarction:

(1) The subsequent ultrasound shows an increasing trend in heterogeneous mass dimensions.

(2) In the later stage of a splenic abscess, patients develop a fluid pocket.

(3) Then, the boundary of the capsule becomes well-defined.

(4) Fluid inside the capsule appears heterogeneous on ultrasound and moves when the patient changes their position.

CONCLUSIONS

The alterations induced by COVID-19 in the mortality pattern of digestive organ diseases affect not only the number of cases but also the age groups of patients. Compared to the control group, patients with COVID-19 who underwent splenectomy exhibited a higher number of cases of diabetes and hypertension. In the splenectomy group, the proportion of patients with diabetes was 25%, while in the control group, this indicator was significantly lower at 15%. It was also found that 30% of patients in the splenectomy group had arterial hypertension, whereas in the control group, this figure was 20%.

These results suggest a potential association between splenectomy and the development of diabetes and hypertension in patients with COVID-19. However, further research is needed to confirm these associations, including a deeper analysis of risk factors and pathogenesis mechanisms.

Additionally, patients with COVID-19 often experience extrapulmonary surgical complications, some of which are characteristic of this condition and require immediate surgical intervention. This underscores the importance of comprehensive training for frontline medical staff to timely identify and manage these complications.

The application of various investigative methods allows for a more accurate assessment of spleen pathology progression. The noted increase in linear dimensions serves as a significant clinical indicator. Identifying diagnostic features in imaging not only contributes to the development of individualized treatment strategies but also plays a key role in determining the necessity and timing of surgical intervention. Furthermore, these findings contribute to evaluating treatment effectiveness and predicting outcomes in patients with COVID-19 and spleen complications.

The practical significance of the obtained results lies in the development of more effective diagnostic, treatment, and management methods for spleen complications in patients with COVID-19. However, certain limitations and directions for future research need to be considered. Limitations include the small sample size and insufficient information on risk factors and prognostic indicators. Future research should focus on expanding the sample size, conducting multicenter studies, and conducting in-depth analyses of factors influencing treatment outcomes and prognosis.

Author contributions: AB: conceptualization, investigation, methodology, project administration, & writing–review & editing; **MK:** data curation, investigation, resources, software, & writing–original draft; **AS:** conceptualization, data curation, methodology, visualization, & writing–original draft; **TS:** conceptualization, formal analysis, project administration, supervision, & writing–review & editing; & **DS:** formal analysis, methodology, resources, validation, & writing–review & editing. All authors have agreed with the results and conclusions.

Funding: No funding source is reported for this study.

Ethical statement: The authors stated that the study protocol was approved by the Ethics Committee of I. M. Sechenov First Moscow State Medical University (Sechenov University) (protocol No. 745 of 11 Feb 2020). The study was conducted in accordance with the rules of the Declaration of Helsinki. All subjects gave written informed consent prior to participation.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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