Initial clinical, laboratory and radiological features of SARS-CoV-2-infected patients and their impact on the course of the disease

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Abstract

Background. On March 11, 2020, coronavirus disease (COVID-19) was declared a global threat by the World Health Organization (WHO). It quickly became apparent that reducing inpatient mortality rates and early phase prediction of possible deterioration or severe disease course relied on finding more specific biomarkers.

Objectives. This retrospective study assessed initial clinical, laboratory and radiological features of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected patients and explored their impact on mortality and the course of the disease. Such efforts aimed to facilitate the identification of high-risk patients and to improve the formulation of treatment plans for these individuals.

Materials and methods. The cohort comprised 111 consecutive adult inpatients diagnosed with COVID-19 and hospitalized in the Internal Medicine Ward of the University Clinical Center of prof. K. Gibiński of the Medical University of Silesia in Katowice, Poland, a COVID-19 Treatment Unit, between November 16, 2020 and February 15, 2021. All available clinical, laboratory and radiological findings were extracted from electronic records and assessed as possible risk factors for poor prognosis.

Results. Clinicasl and radiological features with higher frequency in COVID-19 non-survivors included older age, history of smoking, concomitant cardiovascular diseases, low oxygen saturation (SpO_2), and high infection risk assessed on admission as well as high opacity score, percentage of opacity and percentage of high opacity in computed tomography. Non-survivors had decreased serum lymphocytes, monocytes, calcium, magnesium, and hemoglobin oxygen saturation. They also had increased red cell distribution width (RDW), C-reactive protein (CRP), procalcitonin, alkaline phosphatase (ALP), creatinine, blood urea nitrogen (BUN), D-dimer, troponin, and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels, as well as a base deficit.

Conclusions. This retrospective study identified several markers associated with a fatal course of COVID-19. The early assessment of SARS-CoV-2-infected inpatients should consider these markers.

Key words: COVID-19, SARS-CoV-2, markers of poor prognosis

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Background

A novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in China and caused coronavirus disease (COVID-19), which became a health concern at the end of 2019. On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic.[1] Epidemiological reports from the WHO, as of July 6, 2021, confirmed over 180 million COVID-19 diagnoses worldwide, and more than 3.9 million infected patients died.[2] The constant spread of novel viral mutations, inadequate prophylactic methods and the lack of highly effective targeted treatment caused a growing number of hospitalizations and the breakdown of the healthcare systems in many countries.

The most common symptoms of COVID-19 are fever, cough, fatigue, anorexia, shortness of breath, and muscle pain.[3] According to the available data, typical changes in laboratory tests include leukopenia with decreased lymphocyte count and elevated serum levels of C-reactive protein (CRP), lactate dehydrogenase (LDH) and D-dimers.[4,5] Typical radiological manifestations presented in high-resolution computed tomography (HRCT) include ground-glass opacities (GGO), consolidations, crazy paving, and reticular patterns.[6,7]

Approximately 15% of patients suffer from severe COVID-19 symptoms that require oxygen support, and 5% develop critical complications such as acute respiratory distress syndrome (ARDS), sepsis, multiple organ failure, and thromboembolism.[8] There is a link between older age (over 60 years), smoking, obesity, pregnancy, and concomitant diseases such as diabetes, hypertension, chronic diseases of the heart, lungs, and kidneys, and severe disease and death.[8–10] Furthermore, high sequential organ failure assessment (SOFA) scores and D-dimer levels above 1 μg/mL are associated with poor prognosis.[11]

The treatment of COVID-19 patients depends on the phase of the disease. According to the recommendations of the Polish Association of Epidemiologists and Infectiologists, there are 4 clinical stages of COVID-19:

Stage 1. Asymptomatic or mildly symptomatic, oxygen saturation (SpO_2) ≥ 95%, and no hospitalization is necessary;

Stage 2. Fully symptomatic (viral multiplication), SpO_2 drops below 95%, usually during the 1st week after disease onset, and hospitalization is required;

Stage 3. Respiratory failure (cytokine storm), SpO_2 < 90%, usually occurs in the 2nd week after disease onset, and hospitalization is required;

Stage 4. ARDS, mechanical ventilation and intensive care unit treatment are required.[12]

According to the international guidelines of contagious disease associations, there is some evidence for the efficacy of anti-inflammatory drugs (glucocorticoids (GKs) and tocilizumab), antiviral drugs (remdesivir), anticoagulants (low-molecular-weight heparin), and oxygen (O_2) supplementation, especially in patients with a severe condition.[13]

The reduction of COVID-19 mortality was one of the main objectives during the pandemic and relied on finding specific markers capable of predicting possible worsening or severe disease course (including death) at an early stage. Therefore, this retrospective study compared the clinical, laboratory and imaging results of survivors and non-survivors hospitalized for COVID-19 in order to identify clinical features and early markers of poor prognosis. Clustering of the biomarkers should constitute a warning sign and may lead to the earlier introduction of a more aggressive therapy, which may improve patient outcomes.

Objectives

To identify potential biomarkers of severe SARS-CoV-2 infection among clinical, laboratory and radiological features at the beginning of the treatment process.

Materials and methods

Study design

This retrospective study included 111 adult inpatients diagnosed as SARS-CoV-2 nucleic acid-positive using real-time polymerase chain reaction (PCR; 78 patients) or tested SARS-CoV-2 antigen-positive using antigen test (33 patients) between November 16, 2020 and February 15, 2021. Patients were admitted to the Internal Medicine Ward of the University Clinical Center of prof. K. Gibiński of the Medical University of Silesia in Katowice, Poland, which was converted into a COVID-19 Treatment Unit.

A screening tool devised by Grzesiowski (Table 1) and modified for the initial assessment of all patients admitted to our hospital was used to estimate the risk of infection.[14] The screening tool estimated the probability of infectious complications in the hospitalized subjects, though it was not specifically devised or validated for use in research concerning SARS-CoV-2-like infections. A score of at least 1 point designated a patient to the high-risk infection group. Analyses at the central laboratory utilized commercially available equipment: Sysmex XN-1000 (Sysmex Corporation, Kobe, Japan), ACL 500 (Werfen, Barcelona, Spain), Rapid Point 500 (Siemens Healthcare, Erlangen, Germany), and Cobas PRO (Roche Diagnostics GmbH, Mannheim, Germany).

A validated image processing plug-in package, Siemens Syngo.via® (Siemens Healthcare, Erlangen, Germany), was used for assessing HRCT scans with a VB50. Parenchymal lung changes caused by SARS-CoV-2 and observed as an abnormal increase in lung density were measured in Hounsfield units (HU) and defined as opacities.[15]

Table 1. Risk factors for infection on admission to hospital

Risk factors for infection on admission to hospital	Points
Age >75 years	0/1
Transfer from other ward or hospitalization in the last 6 months	0/1
Surgery/invasive test in the last 6 months	0/1
Alert pathogen colonization	0/1
Presence of catheters	0/1
Skin injury	0/1
Unconsciousness/aspiration/sudden cardiac arrest/ immobilization	0/1
Antimicrobial therapy in the last 3 months	0/1
Current immunosuppressive therapy/radiotherapy/ chemotherapy	0/1
Metabolic disease (i.e., diabetes, obesity, uremia)	0/1
Malnutrition	0/1
Current neoplastic disease	0/1
COPD/asthma/respiratory failure	0/1
Total	0–13

Low infection risk = 0; high infection risk ≥1; COPD – chronic obstructive pulmonary disease.

A semi-quantitative scoring system devised by Pan et al.[6] classified the opacity score by assessing the involvement of each lobe as 0 (no involvement), 1 (<5% involvement), 2 (6–25% involvement), 3 (26–49% involvement), 4 (50–75% involvement), or 5 (>75% involvement). The total opacity score was the sum of the score of each lobe, and ranged from 0 (no involvement) to 25 (maximum involvement). A HU threshold of –200 was applied by default for the high-density opacities. The approximate density determined for healthy lung parenchyma was between –700 and –600 HU.[16]

The 2 study groups included survivors (n = 76) and non-survivors (n = 35). The definition of survivors was patients discharged without symptoms of COVID-19 after isolation. Non-survivors were patients who died during isolation. According to the Chief Sanitary Inspectorate Guidelines, the minimum isolation for symptomatic patients was 13 days from symptom occurrence, with at least 3 symptom-free days. In cases of persistent clinical features of COVID-19, the isolation was prolonged.[17]

According to the Ethics Committee of the Medical University of Silesia (Katowice, Poland), this retrospective study did not require the approval of the Ethics Committee (statement No. PCN/0022/KB/62121).

Statistical analyses

All available data were collated in a Microsoft Excel 365 spreadsheet (Microsoft Corp., Redmond, USA) and transferred to the Statistica software package v. 13.0 (StatSoft Inc., Tulsa, USA) and Plus Set v. 5.0 (TIBCO Software Inc., Palo Alto, USA). Data are presented in tables as mean with 95% confidence interval (95% CI) for normal distribution or median with interquartile range (IQR) for non-normal distribution. The Shapiro–Wilk test and visual inspection of histograms assessed the distribution of continuous variables. Normally distributed data had the Shapiro–Wilk test $p \geq 0.05$ and a dome-shaped histogram distribution, while data with a non-normal distribution had a value of $p < 0.05$. The Student's t-test was used to compare means of continuous data between survivors and non-survivors, and the Mann–Whitney U test was used to evaluate medians of non-normal distributions. At the same time, the Fisher's exact test was employed to compare categorical variables. A value of $p < 0.05$ indicated statistical significance.

Results

Clinical features

This retrospective study included a total of 111 inpatients with a mean age of 68.3 (65.9–71.3) years, with 51 females and 60 males classified as survivors (n = 76) or non-survivors (n = 35). The mean age of non-survivors (73.2 (69.1–77.4) years) was significantly higher (p = 0.019) than that of survivors (66.1 (65.5–69.7) years). The medical history of non-survivors indicated a significantly greater incidence of cardiovascular and metabolic diseases such as hypertension, ischemic heart disease, heart failure, and type 2 diabetes (88.6% compared to 68.4%; p = 0.033). Meanwhile, non-survivors used nicotine more often (60% compared to 35.6%; p = 0.023) and had an increased risk of infection (62.9% compared to 38.2%; p = 0.033) on admission to the hospital (Table 2). However, treatment before the infection with angiotensin-converting-enzyme inhibitors (ACEIs), angiotensin-II-receptor antagonists (sartans), β-blockers, direct oral anticoagulants (DOACs), vitamin K antagonists (VKAs), mineralocorticoid receptor antagonists (MRAs), or antiplatelet drugs, did not significantly differ between survivors and non-survivors.

One of the most vital elements for selecting high-risk patients was infection risk assessment on admission, based on data gathered during anamnesis (Table 1). It revealed a higher probability of COVID-19-related death in patients at an increased risk of infection due to clinical predispositions. Moreover, physical examination revealed significantly lower peripheral capillary hemoglobin SpO_2 values in survivors (94% (87%–97%) compared to 96% (93%–97%); p = 0.046).

Laboratory findings

Initial laboratory findings in non-survivors revealed significantly lower lymphocyte (0.76×10^9/L (0.48–1.33) compared to 1.15×10^9/L (0.69–1.57); p = 0.031) and monocyte (0.39×10^9/L (0.28–0.75) compared to 0.6×10^9/L (0.45–0.835); p = 0.021) counts, significantly higher red cell distribution width (RDW) (47.05 (43–50) fL compared to 43.7

Table 2. Clinical features of coronavirus disease (COVID-19) patients

Clinical feature	Survivors (n = 76)	Non-survivors (n = 35)	test value	df	p-value	Statistical test
Age [years] (mean and 95% CI)	66.1 (62.5–69.7)	73.2 (69.1–77.4)	−2.382 (t value)	109	0.019	Student's t-test
Cardiovascular and metabolic diseases (hypertension or coronary artery disease or heart failure or type 2 diabetes)	52/76 (68.4%)	31/35 (88.6%)	–	1	0.033	Fisher's test
Nicotine use	27/76 (35.6%)	21/35 (60.0%)	–	1	0.023	
High risk for infection	29/76 (38.2%)	22/35 (62.9%)	–	1	0.033	
SpO_2 [%] (median and 25%–75% Q)	96 (93–97)	94 (87–97)	1.999 (U value)	N/A	0.046	Mann–Whitney U test

SpO_2 – oxygen saturation; 95% CI – 95% confidence interval; df – degrees of freedom; N/A – not applicable.

(39.8–50.4) fL; p = 0.021), and significantly higher serum levels of CRP (80.3 (40.5–128) ng/mL compared to 45.7 (9.6–88.8) mg/L; p = 0.003), procalcitonin (0.39 (0.199–1.04) ng/mL compared to 0.17 (0.068–0.347) ng/mL; p = 0.001) and D-dimers (2409 (1170–11,412) ng/mL compared to 1410.5 (867–2849) ng/mL; p = 0.026) than those in survivors.

Disturbances in plasma electrolytes manifested in non-survivors as lower levels of total serum calcium (8.32 (8.02–8.62) mmol/L compared to 8.66 (8.47–8.83) mmol/L; p = 0.043) and magnesium (1.69 (1.61–1.92) mmol/L compared to 1.94 (1.73–2.09) mmol/L; p = 0.037). Other laboratory findings reflecting internal organ function in non-survivors included significant elevations in serum alkaline phosphatase (ALP) activity (97 (78–145) U/L compared to 68 (55–102) U/L; p = 0.027), creatinine concentration (1.19 (0.85–1.83) mg/dL compared to 0.99 (0.75–1.21) mg/dL; p = 0.012), blood urea nitrogen (BUN) (28.4 (17.4–59.4) mg/dL compared to 15.84 (12.2–24.7) mg/dL; p = 0.012), troponin (43.25 (27.6–78.6) ng/L compared to 22.7 (10.2–36.3) ng/L; p = 0.001), and N-terminal pro-B-type natriuretic peptide (NT-proBNP) (3734.5 (740–12,080) pg/mL compared to 792 (154–1952) pg/mL; p = 0.003). Furthermore, acid-base balance assessment of arterial blood samples revealed significantly lower hemoglobin SpO_2 (88.85% (77.8–93.5%) compared to 94.2% (89.4–95.7%); p = 0.039) and higher base excess in non-survivors (5 (2.45–9.25) mmol/L compared to 2.6 (0.8–3.1) mmol/L; p = 0.022), as compared with survivors (Table 3).

Computed tomography findings

Initial inpatient computer tomography (CT) records (n = 83) (61 from survivors and 22 from non-survivors) provided opacity scores and their derivatives. The group of non-survivors had a significantly higher opacity score (7 (4–11) compared to 4 (2–7); p = 0.004), percentage of opacity (16.0% (6.4–41.4%) compared to 7.9% (1.3–19.1%); p = 0.001) and volume of opacity (609.9 (259.1–1209.2) mL compared to 279.6 (41.3–685.9) mL; p = 0.011), as well as a higher percentage of high opacity (5.3% (1.5–17.2%) compared to 1.6% (0.1–5.2%); p = 0.003) and volume of high opacity (200.8 (61.1–548.8) mL compared to 43.3 (3.2–163.5) mL; p = 0.002) than survivors (Table 4).

Therapeutic interventions

Intravenous drug use (GKs, including 4 mg of dexamethasone daily and 200 mg remdesivir on day 1, followed by a maintenance dose of 100 mg for 4 days) and O_2 therapy in the study group followed the recommendations of the Polish Association of Epidemiologists and Infectiologists. In detail, GKs are indicated for SARS-CoV-2-infected patients at stages 2, 3 and 4, whereas remdesivir is indicated for stage 2.[12] Remdesivir was used to a similar extent in both groups (28.8% compared to 34.4%; p = 0.647), while dexamethasone was used much more often in non-survivors (90.6% compared to 49.3%; p < 0.001). The passive O_2 supply used a facial mask with O_2 flow up to 15 L/min and was more frequent in non-survivors (88.6% compared to 53.3%; p < 0.001), as was mechanical ventilation (31.4% compared to 2.7%; p < 0.001). Breathing support methods were not evaluated due to the limited access to high-flow O_2 therapy and noninvasive ventilation devices during the first stages of the pandemic.

Discussion

This retrospective analysis described the clinical, laboratory and radiological parameters of COVID-19 patients and aimed to identify differences that may affect the course of the disease in survivors and non-survivors. Our observations appear to confirm prior reports on the COVID-19 risk factors for severe disease or death, including older age, history of smoking and concomitant cardiovascular diseases.[8,9,18] On the other hand, obesity was not a risk factor for a poor prognosis. However, this may be due to insufficient number of participants with a body mass index (BMI) >30 (15%).

Taking into consideration the ability of SARS-CoV-2 to induce silent hypoxemia, measuring SpO_2 using a pulse oximeter is indispensable to physical examination.[19] In the current study, pulse oximetry demonstrated

Table 3. Laboratory findings of coronavirus disease (COVID-19) patients

Laboratory markers	Reference range	Survivors (n = 76)	Non-survivors (n = 35)	test value	df	p-value	Statistical test
Lymphocyte count [×10^9/L]	1.5–3.5	1.15 (0.69–1.57)	0.76 (0.48–1.33)	786.0	N/A	0.031	Mann–Whitney U test
Monocyte count [×10^9/L]	0.2–0.8	0.6 (0.45–0.835)	0.39 (0.28–0.75)	765.0	N/A	0.021	
RDW-SD [fL]	36.3–47.3	43.7 (39.8–50.4)	47.05 (43–50)	921.5	N/A	0.021	
C-reactive protein [mg/L]	<5	45.7 (9.6–88.8)	80.3 (40.5–128)	856.0	N/A	0.003	
Procalcitonin [ng/mL]	<0.5	0.17 (0.068–0.347)	0.39 (0.199–1.04)	468.0	N/A	0.001	
ALP [U/L]	40–129	68 (55–102)	97 (78–145)	488.0	N/A	0.027	
Creatinine [mg/dL]	0.67–1.17	0.99 (0.75–1.21)	1.19 (0.85–1.83)	854.0	N/A	0.012	
BUN [mg/dL]	44081.00	15.84 (12.2–24.67)	28.365 (17.41–59.35)	238.5	N/A	0.012	
D-dimer [ng/mL]	<500	1410.5 (867–2849)	2409 (1170–11,412)	735.0	N/A	0.026	
Magnesium [mg/dL]	1.6–2.4	1.94 (1.73–2.09)	1.69 (1.61–1.92)	292.0	N/A	0.037	
Calcium [mg/dL]	8.8–10.2	8.66 (8.47–8.83)	8.32 (8.02–8.62)	2.064	109	0.043	t-test
Troponin [ng/L]	<14.5	22.7 (10.2–36.3)	43.25 (27.6–78.6)	429.5	N/A	0.001	Mann–Whitney U test
NT-proBNP [pg/mL]	<125	792 (154–1952)	3734.5 (740–12,080)	282.0	N/A	0.003	
Hemoglobin oxygen saturation, %	>96	94.2 (89.4–95.7)	88.85 (77.8–93.5)	87.5	N/A	0.039	
Base excess [mmol/L]	(–2.0)–3.0	2.6 (0.8–3.1)	5 (2.45–9.25)	81.0	N/A	0.022	

ALP – alkaline phosphatase; BUN – blood urea nitrogen; NT-proBNP – N-terminal pro B-type natriuretic peptide; RDW-SD – red blood cell distribution width standard deviation; df – degrees of freedom; N/A – not applicable.

Table 4. Computed tomography findings of coronavirus disease (COVID-19) patients

CT findings	Survivors (n = 61)	Non-survivors (n = 22)	U value	p-value	Statistical test
Opacity score	4 (2–7)	7 (4–11)	–2.88	0.004	Mann–Whitney U test
Volume of opacity [mL]	279.6 (41.3–685.9)	609.9 (259.1–1209.2)	–2.53	0.011	
Opacity [%]	7.9 (1.3–19.1)	16.0 (6.4–41.4)	–2.62	0.001	
Volume of high opacity [mL]	43.3 (3.2–163.5)	200.8 (61.1–548.8)	–3.14	0.002	
High opacity [%]	1.6 (0.1–5.2)	5.3 (1.5–17.2)	–2.97	0.003	
Mean HU total	–742.8 (–803.2––683.9)	–675.1 (–753.1––556.7)	–2.52	0.012	
Mean HU of opacity	–486.6 (–551.4––375.1)	–396.4 (–493.4––310.8)	–2.15	0.031	

CT – computed tomography; HU – Hounsfield units.

significantly lower hypoxemia in non-survivors, and arterial blood gas analysis confirmed this finding. These observations highlight the necessity of early evaluation of arterial blood gases in severely ill patients and support using pulse oximeters as a readily available patient screening tool. Despite the limitations of this method among patients with peripheral circulation disturbances or varnished nails, it appears to be the simplest and fastest way to predict a severe course of COVID-19.[20–22] However, identifying the exact SpO_2 cutoff point for determining the severity of the prognosis requires further investigations.

In earlier studies, typical changes in peripheral blood cell counts associated with the severity of COVID-19 included increased leukocyte and neutrophil counts with concomitant lymphopenia.[23,24] Leukocytosis and neutrophilia indicate an increased inflammatory status in patients with severe disease. Both groups had similar white blood count (WBC), though non-survivors had significantly lower lymphocyte levels.[18] Lymphopenia is the most characteristic blood cell change associated with COVID-19 severity. It is caused by multiple factors, including direct attachment of the virus to lymphocytes with subsequent impairment of their immune functioning or inflammatory mediator-induced injury.[24]

Non-survivors had significantly lower peripheral blood monocyte counts than survivors. Monocytes and macrophages are attracted to the alveolar spaces of the lungs, are the first cells to respond to viruses, and are responsible for the local antiviral response. The SARS-CoV-2 infects monocytes and macrophages in an angiotensin-converting enzyme 2 (ACE2)-dependent or -independent manner and inactivates them, allowing viruses to spread through different tissues.[25] A detailed explanation of antiviral immune responses could simplify the development of an effective COVID-19 treatment method.

The widespread distribution of red blood cells in non-survivors was the only significant disturbance in erythroid lineage, which is consistent with previous observations

associated with impaired synthesis of mature red blood cells due to hypoxia.[26]

The COVID-19-infected inpatients, both survivors and non-survivors, had elevated serum levels of CRP and procalcitonin, which is consistent with previous studies.[23] These simple parameters are examples of cytokine storm indicators that are useful for monitoring the course of the disease.[27]

The SARS-CoV-2-induced coagulopathy, revealed in laboratory tests as increased serum levels of D-dimers, results in an increased thromboembolic risk and complications, such as pulmonary embolism.[18] The significantly higher serum D-dimer levels in non-survivors on admission, their potential use as markers of poor prognosis, and the correlation between their level and disease severity are consistent with previous studies.[11,28]

Hyponatremia, hypokalemia and hypocalcemia are the most common electrolyte disturbances in COVID-19 patients.[29] The current study revealed lower serum levels of calcium and magnesium in non-survivors. Possible explanations for these electrolyte imbalances include gastrointestinal and renal loss due to SARS-CoV-2 invasion, hypoxic damage to the central nervous system, and the actions of pro-inflammatory cytokines.[29]

Liver injury in the course of SARS-CoV-2 infection, manifested by elevated serum levels of alanine transaminase (ALT), aspartate aminotransferase (AST), ALP, gamma-glutamyl transpeptidase (GGTP), LDH, and total bilirubin, is frequently observed and its risk and severity are related to the condition of infected patients.[30–32] Moreover, serum levels of LDH are one of the most valuable factors for predicting mortality.[33] In the current study, non-survivors had higher serum levels of LDH, though the difference was non-significant ($p < 0.08$), and significantly higher ALP ($p < 0.03$). The causes of liver damage are still unclear but are mainly related to general hypoxia, direct viral cytotoxicity through ACE2 receptors on the surface of hepatic cells, and a hepatocyte cell membrane dysfunction-induced cytokine storm.[34,35]

Concomitant kidney disease is another risk factor for death during SARS-CoV-2 infection,[36] with acute kidney injury (AKI) observed in up to 46% of patients hospitalized for COVID-19.[37] This study demonstrated significantly higher serum creatinine levels and BUN in non-survivors. Other studies observed pathological changes in tubular kidney regions and urine samples.[38,39]

Despite the fact that the heart contains ACE2 receptors, direct myocardial SARS-CoV-2 infection data are limited.[40] Elevated levels of heart damage and overload enzymes, including troponin and NT-proBNP, may be secondary to the general condition, circulating cytokines and endotoxin levels of patients with severe disease.[41] Moreover, significantly higher levels of troponin and NT-proBNP in non-survivors suggest their association with COVID-19 severity and mortality.[42]

In our study, the results of CT examinations of hospitalized patients are consistent with previous reports. A higher opacity score and percentage of opacity correlate with disease severity and poor prognosis.[43] Therefore, we recommend HRCT as a simple imaging test for infected patients.

Data from the current study suggest that no single abnormality demonstrates a strong relationship with the course of the disease and that numerous factors are responsible for multiple organ damage. Future studies should seek to develop a prospective prediction model for fatal COVID-19.

The delay between symptom onset and hospital admission in the group of non-survivors might explain no difference in remdesivir use between survivors and non-survivors. The early stage of the disease was consistent with the signs and symptoms of pneumonia, which justified the use of remdesivir. Most patients received GK treatment, which may reflect the more severe clinical condition and the development of a systemic inflammatory response (tocilizumab was unavailable). The increased frequency of O_2 support and mechanical ventilation use in non-survivors confirmed the severity of the disease.

Limitations

Limitations to consider when interpreting the results include the retrospective design of the study, which meant that the groups were not homogenous in terms of clinical features. Furthermore, not all laboratory and imaging tests were available for every patient. There were also slight differences between the onset of symptoms and the day of admission to the hospital.

Conclusions

This retrospective study aimed to find the most useful biomarkers for predicting the severity and poor prognosis of COVID-19 inpatients using medical parameters assessed on admission to the hospital. In this regard, the most valuable parameters appear to be advanced age, a history of cardiovascular disease, nicotine addiction, low peripheral SpO_2, low lymphocyte count, low monocyte count, and high CRP, PCT, D-dimer, ALP, creatinine, magnesium, calcium, troponin, NT-proBNP, and oxyhemoglobin levels, as well as a high opacity score in CT. The deterioration of organ functions observed during clinical examination, laboratory tests and radiological scans at the beginning of infection do not predict a severe course of the disease with certainty. Nevertheless, combining biomarkers and symptoms increases the risk of a fatal COVID-19 outcome. However, a full explanation of COVID-19 pathogenesis should facilitate the search for novel early biomarkers of severe disease. Further prospective studies are required to develop a predictive outcome model based on data collected on admission. Such an attempt would require cumulative analysis of numerous reports, similar to this study.

Supplementary material

The Supplementary files are available at https://doi.org/10.5281/zenodo.7693350. The package contains the following files:

Supplementary Table 1. Data concerning laboratory findings in COVID-19 patients with and without statistical significance.

Supplementary Table 2. Data concerning statistical assesment of the equality of variances in clinical and laboratory parameters of COVID-19 patients.

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References

1. Jin Y, Yang H, Ji W, et al. Virology, epidemiology, pathogenesis, and control of COVID-19. *Viruses*. 2020;12(4):372. doi:10.3390/v12040372
2. World Health Organization. Weekly epidemiological update on COVID-19: July 6, 2021. Geneva, Switzerland: World Health Organization; 2021. https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---6-july-2021. Accessed July 10, 2021.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506. doi:10.1016/S0140-6736(20)30183-5
4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet*. 2020;395(10223):507–513. doi:10.1016/S0140-6736(20)30211-7
5. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585
6. Pan F, Zheng C, Ye T, et al. Different computed tomography patterns of coronavirus disease 2019 (COVID-19) between survivors and non-survivors. *Sci Rep*. 2020;10(1):11336. doi:10.1038/s41598-020-68057-4
7. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): A pictorial review. *Eur Radiol*. 2020;30(8):4381–4389. doi:10.1007/s00330-020-06801-0
8. World Health Organization. COVID-19 clinical management living guidance. Geneva, Switzerland: World Health Organization; 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1. Accessed May 10, 2021.
9. World Health Organization. WHO statement: Tobacco use and COVID-19. Geneva, Switzerland: World Health Organization; 2021. https://www.who.int/news/item/11-05-2020-who-statement-tobacco-use-and-covid-19. Accessed May 12, 2021.
10. Allotey J, Fernandez S, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. *BMJ*. 2020;370:m3320. doi:10.1136/bmj.m3320
11. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet*. 2020;395(10229):1054–1062. doi:10.1016/S0140-6736(20)30566-3
12. Flisiak R, Parczewski M, Horban A, et al. Management of SARS-CoV-2 infection: Recommendations of the Polish Association of Epidemiologists and Infectiologists. Annex no. 2 as of October 13, 2020. *Pol Arch Intern Med*. 2020;130(10):915–918. doi:10.20452/pamw.15658
13. Flisiak R, Horban A, Jaroszewicz J, et al. Management of SARS-CoV-2 infection: Recommendations of the Polish Association of Epidemiologists and Infectiologists as of April 26, 2021. *Pol Arch Intern Med*. 2021;131(5):487–496. doi:10.20452/pamw.15979
14. Grzesiowski P. Ocena ryzyka zakażenia przy przyjęciu do szpitala – propozycja formularza. *Biuletyn Stowarzyszenia Higieny Lecznictwa Kwartalnik*. 2009;4:27–28.
15. Klein JS, Brant WE, Helms CA, Vinson EN, eds. *Brant and Helms Fundamentals of Diagnostic Radiology*. 5th ed. Philadelphia, USA: Wolters Kluwer; 2019. ISBN:978-1-4963-6739-6.
16. Kazerooni EA, Gross BH. *Cardiopulmonary Imaging*. Philadelphia, USA: Lippincott Williams & Wilkins; 2004. ISBN:978-0-7817-3655-8.
17. Chief Sanitary Inspectorate. Polish guidelines for quarantine and isolation of COVID-19 as of September 2, 2020 [in Polish]. Warszawa, Poland: Chief Sanitary Inspectorate; 2020. https://www.gov.pl/web/gis/zasady-odbywania-kwarantanny-i-izolacji-obowiazujace-od-2-wrzesnia-2020-r. Accessed January 21, 2021.
18. Gao Y, Ding M, Dong X, et al. Risk factors for severe and critically ill COVID-19 patients: A review. *Allergy*. 2021;76(2):428–455. doi:10.1111/all.14657
19. Dhont S, Derom E, Van Braeckel E, Depuydt P, Lambrecht BN. The pathophysiology of 'happy' hypoxemia in COVID-19. *Respir Res*. 2020;21(1):198. doi:10.1186/s12931-020-01462-5
20. Liu S, Luo H, Wang Y, et al. Clinical characteristics and risk factors of patients with severe COVID-19 in Jiangsu province, China: A retrospective multicentre cohort study. *BMC Infect Dis*. 2020;20(1):584. doi:10.1186/s12879-020-05314-x
21. Duan J, Wang X, Chi J, et al. Correlation between the variables collected at admission and progression to severe cases during hospitalization among patients with COVID-19 in Chongqing. *J Med Virol*. 2020;92(11):2616–2622. doi:10.1002/jmv.26082
22. Xie J, Covassin N, Fan Z, et al. Association between hypoxemia and mortality in patients with COVID-19. *Mayo Clin Proc*. 2020;95(6):1138–1147. doi:10.1016/j.mayocp.2020.04.006
23. Zhang J, Cao Y, Tan G, et al. Clinical, radiological, and laboratory characteristics and risk factors for severity and mortality of 289 hospitalized COVID-19 patients. *Allergy*. 2021;76(2):533–550. doi:10.1111/all.14496
24. Ou M, Zhu J, Ji P, et al. Risk factors of severe cases with COVID-19: A meta-analysis. *Epidemiol Infect*. 2020;148:e175. doi:10.1017/S0950268820001790X
25. Jafarzadeh A, Chauhan P, Saha B, Jafarzadeh S, Nemati M. Contribution of monocytes and macrophages to the local tissue inflammation and cytokine storm in COVID-19: Lessons from SARS and MERS, and potential therapeutic interventions. *Life Sci*. 2020;257:118102. doi:10.1016/j.lfs.2020.118102
26. Wang C, Zhang H, Cao X, et al. Red cell distribution width (RDW): A prognostic indicator of severe COVID-19. *Ann Transl Med*. 2020;8(19):1230–1230. doi:10.21037/atm-20-6090
27. Azkur AK, Akdis M, Azkur D, et al. Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. *Allergy*. 2020;75(7):1564–1581. doi:10.1111/all.14364
28. Yao Y, Cao J, Wang Q, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: A case control study. *J Intensive Care*. 2020;8:49. doi:10.1186/s40560-020-00466-z
29. Lim JH, Jung HY, Choi JY, et al. Hypertension and electrolyte disorders in patients with COVID-19. *Electrolyte Blood Press*. 2020;18(2):23–30. doi:10.5049/EBP.2020.18.2.23
30. Zhao X, Lei Z, Gao F, Xie Q, Jang K, Gong J. The impact of coronavirus disease 2019 (COVID-19) on liver injury in China: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2021;100(4):e24369. doi:10.1097/MD.0000000000024369
31. An YW, Song S, Li WX, et al. Liver function recovery of COVID-19 patients after discharge, a follow-up study. *Int J Med Sci*. 2021;18(1):176–186. doi:10.7150/ijms.50691
32. Benedé-Ubieto R, Estévez-Vázquez O, Flores-Perojo V, et al. Abnormal liver function test in patients infected with coronavirus (SARS-CoV-2): A retrospective single-center study from Spain. *J Clin Med*. 2021;10(5):1039. doi:10.3390/jcm10051039

33. Yan L, Zhang HT, Goncalves J, et al. An interpretable mortality prediction model for COVID-19 patients. *Nat Mach Intell*. 2020;2(5):283–288. doi:10.1038/s42256-020-0180-7
34. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M. COVID-19 and the liver. *J Hepatol*. 2020;73(5):1231–1240. doi:10.1016/j.jhep.2020.06.006
35. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: Little cause for concern. *Lancet Gastroenterol Hepatol*. 2020;5(6):529–530. doi:10.1016/S2468-1253(20)30084-4
36. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int*. 2020;97(5):829–838. doi:10.1016/j.kint.2020.03.005
37. Chan L, Chaudhary K, Saha A, et al. AKI in hospitalized patients with COVID-19. *J Am Soc Nephrol*. 2021;32(1):151–160. doi:10.1681/ASN.2020050615
38. Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int*. 2020;98(1):219–227. doi:10.1016/j.kint.2020.04.003
39. Nogueira SÁR, de Oliveira SCS, de Carvalho AFM, et al. Renal changes and acute kidney injury in COVID-19: A systematic review. *Rev Assoc Med Bras*. 2020;66(Suppl 2):112–117. doi:10.1590/1806-9282.66.s2.112
40. Imazio M, Klingel K, Kindermann I, et al. COVID-19 pandemic and troponin: Indirect myocardial injury, myocardial inflammation or myocarditis? *Heart*. 2020;106(15):1127–1131. doi:10.1136/heartjnl-2020-317186
41. Shi S, Qin M, Cai Y, et al. Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019. *Eur Heart J*. 2020;41(22):2070–2079. doi:10.1093/eurheartj/ehaa408
42. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):811–818. doi:10.1001/jamacardio.2020.1017
43. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: Correlation with disease severity and short-term prognosis. *Eur Radiol*. 2020;30(12):6808–6817. doi:10.1007/s00330-020-07033-y