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Clinical significance of basic laboratory parameters in predicting the use of various methods of oxygen supplementation in COVID-19

Abstract

Introduction: The severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) infection resulted in significant worldwide morbidity and mortality. The aim of our study was to evaluate the results of laboratory tests performed on patients on admission to the hospital between groups of patients requiring and not requiring oxygen supplementation, and to find predictive laboratory indicators for the use of high-flow nasal oxygen therapy (HFNOT)/continuous positive airway pressure (CPAP)/bilevel positive airway pressure (BPAP).

Materials and methods: We retrospectively analysed the data of consecutive patients hospitalised in the Pulmonology Department of the Temporary COVID Hospital in Poznan from February to May 2021. On admission to the department, the patients had a panel of laboratory blood tests.

Results: The study group consisted of 207 patients with a mean age of 59.2 ± 15.0 years of whom 179 (72%) were male. During hospitalisation, oxygen supplementation was required by 87% of patients. Patients requiring oxygen supplementation and/or the use of HFNOT/CPAP/BPAP had lower lymphocyte counts and higher levels of urea, C-reactive protein, D-dimer, troponin, glucose, lactate dehydrogenase (LDH) as well as higher white blood cell and neutrophil counts, The parameter that obtained the highest area under curve value in the receiver operator curve analysis for the necessary use of HFNOT/CPAP/BPAP or CPAP/BPAP was LDH activity.

Conclusions: Among the basic parameters assessed on admission to the temporary hospital, LDH activity turned out to be the most useful for assessing the need for CPAP/BPAP active oxygen therapy. Other parameters that may be helpful for predicting the need for HFNOT/CPAP/BPAP are serum levels of urea, D-dimer and troponin.

Key words: SARS-CoV-2, laboratory tests, high-flow nasal oxygen therapy (HFNOT), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP)

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Introduction

Since the detection of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) in China in December 2019, over 180 million cases have been reported worldwide, of which over 3.9 million have resulted in death. In Poland, the number of people who became sick is almost 3 million, and the number of deaths is 74000 (30 June 2021) [1]. As part of the SARSTer study of the Polish Society of Epidemiologists and Infectious Diseases Physicians, the overall mortality rate among hospitalised coronavirus disease 2019 (COVID-19) patients was 6.2%, and 7.3% after considering only the adult population. The mortality in adult patients during hospitalisation requiring oxygen therapy increased to 17.3% [2].

The hospitalisation time for COVID-19 patients ranged from 4 to 53 days in China and 4 to 21 days in other countries [3]. Infection with SARS-CoV-2 resulted in significant worldwide

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morbidity and mortality, leading to a huge burden on healthcare. The Chinese Centre for Disease Control and Prevention Report found that 81% of patients infected with SARS-CoV-2 had a mild course of infection, and approximately 14% had a severe course and the remaining 5% were critically ill [4]. Several laboratory abnormalities have been associated with a severe course of COVID-19. These include: increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin, C-reactive protein (CRP), ferritin, lactate dehydrogenase (LDH), D-dimers, fibrinogen and lymphopenia [5]. There were presented studies that identify laboratory markers for the use of intubation and invasive ventilation. Elevated levels of interleukin 6 (IL-6) and the CRP level marked on admission to the hospital allowed it to be predicted if the patient would require intubation and mechanical ventilation [6].

There are no studies available that assess the need and duration of high-flow oxygen therapy (HFNOT) and/or respiratory support with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BPAP). The aim of our study was to find predictive indicators based on the results of laboratory tests performed on admission to the department for the use of HFNOT, CPAP and BPAP.

Materials and methods

We conducted a retrospective analysis of consecutive adult patients hospitalised in the Pulmonology Department of the Temporary COVID Hospital at the International Trade Fair in Poznan, Poland, from 1.02.2021 to 31.05.2021. The study was approved by the institutional ethics committee (number 466/2021).

Patients admitted to the department had SARS-CoV-2 infection confirmed by an real time polymerase chain reaction test or rapid antigen test and were subject to isolation in accordance with the current Regulation of the Council of Ministers. Patients were referred by general practitioners, emergency medical teams or transferred from other hospitals or departments. The analysis excluded patients who were transferred to other hospitals for acute reasons not related to the respiratory system, such as: myocardial infarction, acute limb ischaemia, ischaemic stroke, etc. Also, patients who died within a few hours of admission to the hospital or required invasive ventilation in the intensive care unit (ICU) were excluded from the analyses. On admission to the Pulmonology Department, a panel of laboratory tests was performed for the patient's care.

Patients

The study group consisted of 207 patients aged from 21 to 95 with a mean age of 59.2 ± 15.0 years of whom 149 (72%) were male. Out of 207 patients, four were admitted from other wards of the temporary COVID-19 hospital. The transfers were most often associated with the need to intensify treatment, e.g. using non-invasive mechanical ventilation. The average hospitalisation time on the ward was approximately 10 days. There were no significant differences between the hospitalisation time of women and men. The longest stay in the ward was 42 days.

Oxygen supplementation

The methods of oxygen supplementation used in the department were: a nasal cannula, a simple face mask, a face mask with a reservoir bag, high-flow nasal oxygen therapy, and CPAP/BPAP active oxygen therapy. A nasal cannula, a simple face mask and a face mask with a reservoir bag are typical of the disposable equipment used for oxygen supplementation in Polish hospitals. HFNOT was performed using an AIRVO 2 Fisher and Paykel Healthcare system with an OptiFlow mask. A Philips Trilogy Evo ventilator was used to assist ventilation in CPAP and BPAP therapy.

During hospitalisation, oxygen supplementation was required by 87% of patients, including all patients transferred from other wards. The methods of oxygen supplementation used in the department were: a nasal cannula, a simple face mask, a face mask with a reservoir bag, high-flow nasal oxygen therapy, and CPAP/BPAP active oxygen therapy. Patients requiring oxygen therapy have their saturation measured 2 or more times a day or continuously with the use of a finger sensor. The method of passive oxygen therapy was selected depending on the level of saturation. Individual methods of oxygen therapy were applied in accordance with the guidelines presented by Czajkowska-Malinowska et al. [7].

Laboratory tests

Venous blood was obtained from patients using the Sarstedt blood collection system (Sarstedt AG & CO. KG, Germany). A complete blood count was determined using an ADVIA 2120i Hematology System (Siemens Healthineers, Germany) automatic analyser. The concentrations and activities of particular biochemical

Table 1. Distribution of selected methods of oxygen supplementation

Oxygen supplementation method	Number of patients (n = 207)	Per cent of all patients
No oxygen supplementation	27	13.0
Nasal cannula	72	34.8
Simple mask	7	3.4
Mask with a reservoir bag	32	15.5
HFNOT	31	15.0
CPAP/BPAP	38	18.4

HFNOT — high-flow nasal oxygen therapy; CPAP — continuous positive airway pressure; BPAP — bilevel positive airway pressure

parameters were measured using an Atellica automatic biochemistry and immunochemistry analyser (Siemens Healthineers, Germany). The international normalised ratio of prothrombin time and the concentration of D-dimer were determined on a SYSMEX CS-2500 automatic analyser (SYSMEX EUROPE GmbH). All tests were performed due to the standards of Good Laboratory Practice.

Statistical analysis of data

Descriptive statistics were used to summarise the main demographic characteristics, and the laboratory results of all patients were included in the study. Due to the lack of a normal distribution, numerical variables were given as the median and the interquartile range (IQR). Associations of quantitative data were analysed with the nonparametric Mann–Whitney U test. Sex differences were calculated using the chi-square test. Receiver operator curve (ROC) analysis was used to determine the most accurate cut-off point for prediction of the use of HFNOT/CPAP/BPAP. The level of significance was set at $p < 0.05$. Statistical analysis was performed with STATISTICA 13.3 software (Statsoft, Poland) and Medcalc Version 20.009.

Results

Table 1 shows the distribution of use of particular methods of oxygen supplementation in consecutive patients admitted to the department. The methods of oxygen supplementation have been ranked by the increasing possibility of achieving a higher concentration of oxygen in the breathing mixture, respectively: a nasal cannula, a simple face mask, a face mask with a reservoir bag, HFNOT, CPAP/BPAP [7] Patients were assigned to the groups shown in Table 1 when they required the highest fraction of inspired oxygen (FiO_2). The most common method of oxygen supplementation was the nasal cannula. Approximately one-third of patients admitted to the ward required the use of HFNOT or CPAP/BPAP. For those patients who needed oxygen therapy, the average duration of oxygen supplementation was 78.4% of their stay on the ward. 54.8% of patients who required HFNOT and/or CPAP/BPAP were hospitalised for more than 10 days, and 64.9% for more than 15 days. Out of 207 patients hospitalised in the Pulmonology Department, 30 required treatment in the ICU despite the use of CPAP/BPAP or HFNOT, and 11 died (nine of them were treated with CPAP/BPAP/HFNOT). Decisions regarding the need for ICU treatment and/or intubation were made by the treating physician and an anaesthesiologist on the basis of COVID-19 treatment guidelines [8].

On admission to the Pulmonology Department, the patients underwent a panel of laboratory tests. Table 2 presents a comparison of selected laboratory parameters between those patients who required oxygen supplementation during hospitalisation and those who did not. The latter had significantly increased leukocyte and neutrocyte counts on admission, and a decreased lymphocyte count compared to the former. Increased activity of LDH, AST, ALT was associated with the need for oxygen therapy.

Table 3 shows the results of the analysis of the differences in the values of laboratory parameters between those patients requiring and not requiring the use of HFNOT/CPAP/BPAP. Patients requiring non-invasive active oxygen therapy were significantly older. They also had lower lymphocyte counts and higher leukocyte counts, neutrophil counts, red blood cell distribution width, platelet distribution width and concentrations of glucose, urea, D-dimer, CRP, cardiac troponin I (cTn I) and ferritin. The activities of LDH, AST and gamma-glutamyl transferase (GGT)

Table 2. Comparison of selected laboratory parameters between groups requiring oxygen supplementation and those not requiring supplementation

Parameter	Patients not requiring oxygen therapy (n = 27)	Patients requiring oxygen therapy (n = 180)	P-value
Gender (male/female)*	20/7	129/51	NS
Age [years]**	59.96 ± 14.90	54.41 ± 15.81	NS
WBC [10 ^ 9/L]	4.84 (3.40–6.49)	6.77 (5.20–9.02)	0.001
NEUT [10 ^ 9/L]	3.62 (2.18–5.17)	5.33 (3.86–7.52)	< 0.001
LYMPH [10 ^ 9/L]	0.85 (0.70–1.23)	0.72 (0.52–1.04)	0.008
MONO [10 ^ 9/L]	0.31 (0.25–0.45)	0.32 (0.21–0.46)	NS
EOS [10 ^ 9/L]	0.01 (0.01–0.03)	0.01 (0.00–0.02)	NS
BASO [10 ^ 9/L]	0.02 (0.01–0.03)	0.02 (0.01–0.03)	NS
LUC [10 ^ 9/L]	0.09 (0.06–0.16)	0.10 (0.07–0.15)	NS
RBC [10 ^ 12/L]	4.64 (4.34–4.92)	4.49 (4.05–4.85)	NS
HGB [mmol/L]	8.60 (8.20–9.60)	8.60 (7.80–9.30)	NS
HCT [L/L]	0.399 (0.377–0.439)	0.397 (0.362–0.428)	NS
MCV [fL]	87.70 (86.10–92.50)	88.85 (85.95–92.45)	NS
MCHC [mmol/L]	21.69 (21.36–22.24)	21.46 (20.98–22.09)	NS
RDW [%]	12.90 (12.5–13.6)	13.20 (12.6–13.9)	NS
PLT [10 ^ 9/L]	166.0 (133.0–242.0)	201.50 (149.5–285.5)	NS
MPV [fL]	8.5 (8.0-9.3)	8.70 (8.1-9.4)	NS
PDW [%]	61.10 (57.3–66.7)	62.05 (57.55–67.35)	NS
ALT [U/L]	29.0 (20.0–46.0)	42.00 (26.0–69.0)	0.003
AST [U/L]	31.0 (22.0–38.0)	49.00 (35.5–80.0)	< 0.001
GGT [U/L]	48.0 (28.0–70.0)	48.00 (30.5–103.0)	NS
Glucose [mmol/L]	5.0 (4.6–5.4)	6.00 (5.4–7.5)	< 0.001
Creatinine [umol/L]	74.0 (66.0–92.0)	83.0 (69.5–100.5)	NS
LDH [U/L]	270.0 (224.0–377.0)	425.50 (331.0–523.5)	< 0.001
Urea [mmol/L]	5.0 (66.0–92.0)	6.95 (5.3–9.7)	0.002
INR	1.05 (1.02–1.12)	1.12 (1.06–1.18)	0.001
D-dimer [ng/mL]	619.0 (408.0–1216.0)	929.00 (592.5–2048.5)	0.007
CRP [mg/L]	31.0 (20.0–70.0)	100.00 (54.0–168.5)	< 0.001
Ferritin [ng/mL]	321.50 (184.6–868.3)	888.95 (431.55–1446.60)	< 0.001
cTn I [ng/mL]	0.005 (0.001–0.009)	0.011 (0.005–0.029)	0.002

Data are presented as median (interquartile range); *Number of patients; **Mean ± standard deviation.
ALT — alanine transferase; AST — aspartate aminotransferase; BASO — basophiles; CRP — C-reactive protein; cTn I — cardiac troponin I;EOS — eosinophiles; GGT — gamma-glutamyl transferase;HCT — haematocrit; HGB — Haemoglobin; INR — international normalised ratio of prothrombin time; LDH — lactate dehydrogenase; LUC — large unstained cells; LYMPH — lymphocytes; MCHC — mean corpuscular haemoglobin concentration; MCV — mean corpuscular volume; MONO — monocytes; MPV — mean platelet volume; NEUT — neutrophiles; NS — not significant; PDW — platelet distribution width; PLT — platelets; RDW — red blood cell distribution width; WBC — white blood count

were also increased in patients requiring the use of HFNOT/CPAP/BPAP.

Patients requiring CPAP/BPAP differed significantly for the same parameters as patients requiring HFNOT/CPAP/BPAP, but also had elevated creatinine levels and GGT activity. The results of the comparison of the group requiring the use of CPAP/BPAP are presented in Table 4.

Based on the results of the comparison between the groups of patients not requiring and requiring the use of either HFNOT/CPAP/BPAP (Table 3) or CPAP/BPAP (Table 4), the parameters

Table 3. Comparison of selected laboratory parameters between the groups requiring HFNOT/CPAP/BPAP and those not requiring this therapy

Parameter	Patients not requiring HFNOT/CPAP/BPAP therapy (n = 138)	Patients requiring HFNOT/CPAP/BPAP therapy (n = 69)	P-value
Gender (male/female)*	101/37	48/21	NS
Age [years]**	56.67±15.87	64.38±11.94	< 0.001
WBC [10 ^ 9/L]	6.33 (4.55–8.19)	8.24 (5.43–11.11)	0.001
NEUT [10 ^ 9/L]	4.79 (3.27–6.35)	7.01 (4.17–9.56)	< 0.001
LYMPH [10 ^ 9/L]	0.84 (0.66–1.18)	0.54 (0.40–0.77)	< 0.001
MONO [10 ^ 9/L]	0.35 (0.23–0.46)	0.28 (0.21–0.42)	NS
EOS [10 ^ 9/L]	0.01 (0.00–0.03)	0.01 (0.00–0.01)	0.013
BASO [10 ^ 9/L]	0.02 (0.01–0.03)	0.02 (0.01–0.03)	NS
LUC [10 ^ 9/L]	0.10 (0.07–0.16)	0.09 (0.06–0.15)	NS
RBC [10 ^ 12/L]	4.59 (4.13–4.85)	4.38 (4.05–4.78)	NS
HGB [mmol/L]	8.50 (8.0–9.3)	8.70 (7.8–9.2)	NS
HCT [L/L]	0.400 (0.371–0.432)	0.396 (0.362–0.425)	NS
MCV [fL]	88.75 (86.0–92.1)	89.1 (86.0–94.3)	NS
MCHC [mmol/L]	21.57 (21.04–22.13)	21.41 (20.89–22.1)	NS
RDW [%]	13.0 (12.5–13.6)	13.4 (13.0–14.0)	0.001
PLT [10 ^ 9/L]	191.0 (146.0–269.0)	203.0 (149.0–274.0)	NS
MPV [fL]	8.6 (8.1–9.5)	8.8 (8.0–9.4)	NS
PDW [%]	61.5 (56.6–67.1)	63.8 (59.8–68.8)	0.01
ALT [U/L]	37.0 (25.0–64.0)	42.0 (26.0–68.0)	NS
AST [U/L]	42.5 (30.0–61.0)	56.0 (44.0–89.0)	< 0.001
GGT [U/L]	47.0 (30.0–89.0)	55.0 (35.0–104.0)	NS
Glucose [mmol/L]	5.6 (5.0–6.3)	7.3 (5.8–8.8)	< 0.001
Creatinine [umol/L]	79.5 (70.0–95.0)	85.0 (66.0–115.0)	NS
LDH [U/L]	350.0 (274.0–447.0)	509.0 (420.0–632.0)	< 0.001
Urea [mmol/L]	5.8 (4.8–7.7)	8.8 (6.4–12.1)	< 0.001
INR	1.11 (1.05–1.16)	1.12 (1.06–1.18)	NS
D-dimer [ng/mL]	710.5 (509.0–1268.0)	1318.0 (793.0–3445.0)	< 0.001
CRP [mg/L]	73.0 (32.0–136.0)	136.0 (75.0–201.0)	0.001
Ferritin [ng/mL]	711.8 (343.9–1318.0)	887.3 (517.4–1651.0)	0.031
cTn I [ng/mL]	0.007 (0.003–0.018)	0.017 (0.009–0.049)	< 0.001

Data are presented as median (interquartile range); *Number of patients; **Mean ± standard deviation.
ALT — alanine transferase; AST — aspartate aminotransferase; BASO — basophiles; BPAP — bilevel positive airway pressure; CPAP — continuous positive airway pressure; CRP — C-reactive protein; cTn I — cardiac troponin I; EOS — eosinophiles; GGT — gamma-glutamyl transferase; HCT — haematocrit; HFNOT — high-flow nasal oxygen therapy; HGB — haemoglobin; INR — international normalised ratio of prothrombin time; LDH — lactate dehydrogenase; LUC — large unstained cells; LYMPH — lymphocytes; MCHC — mean corpuscular haemoglobin concentration; MCV — mean corpuscular volume; MONO — monocytes; MPV — mean platelet volume; NEUT — neutrophiles; NS — not significant; PDW — platelet distribution width; PLT — platelets; RDW — red blood cell distribution width; WBC — white blood count

characterised by the most significant differences ($p \leq 0.001$) in both analyses were established. The effects of the ROC analysis for the four laboratory parameters with the highest area under curve (AUC) are shown in Tables 5 and 6. Figures 1 and 2 show the ROCs for these parameters. For both options concerning the use of the active oxygen therapy methods, HFNOT/CPAP/BPAP and CPAP/BPAP, the ROC analysis indicated the best statistical results for serum LDH ($p < 0.0001$ and AUC 0.797 and 0.870, respectively). Enzyme activity above 434 U/L could

Table 4. Comparison of selected laboratory parameters between groups requiring CPAP/BPAP and those not requiring this therapy

Parameter	Patients not requiring CPAP/BPAP therapy (n = 169)	Patients requiring CPAP/BPAP therapy (n = 38)	P-value
Gender (male/female)*	122/47	21/11	NS
Age [years]**	58.11±15.28	64.26±13.29	0.012
WBC [10 ^ 9/L]	6.4 (4.63–8.46)	7.74 (5.43–11.89)	0.044
NEUT [10 ^ 9/L]	4.99 (3.56–7.01)	6.79 (4.15–10.8)	0.004
LYMPH [10 ^ 9/L]	0.80 (0.59–1.13)	0.50 (0.39–0.63)	< 0.001
MONO [10 ^ 9/L]	0.32 (0.23–0.45)	0.28 (0.20–0.46)	NS
EOS [10 ^ 9/L]	0.01 (0.00–0.02)	0.01 (0.00–0.01)	NS
BASO [10 ^ 9/L]	0.02 (0.01–0.03)	0.02 (0.01–0.03)	NS
LUC [10 ^ 9/L]	0.10 (0.07–0.15)	0.09 (0.06–0.15)	NS
RBC [10 ^ 12/L]	4.56 (4.08–4.85)	4.35 (4.07–4.78)	NS
HGB [mmol/L]	8.60 (7.9–9.3)	8.5 (7.8–9.2)	NS
HCT [L/L]	0.399 (0.368–0.428)	0.392 (0.373–0.425)	NS
MCV [fL]	88.70 (86.0–92.1)	90.15 (85.0–94.5)	NS
MCHC [mmol/L]	21.55 (21.04–22.13)	21.34 (20.75–22.1)	NS
RDW [%]	13.10 (12.6–13.6)	13.8 (13.3–14.5)	< 0.001
PLT [10 ^ 9/L]	192.0 (146.0-279.0)	213.0 (149-250.0)	NS
MPV [fL]	8.60 (8.1–9.4)	8.9 (8.0–9.4)	NS
PDW [%]	61.50 (56.9–67.2)	64.05 (59.8–69.1)	0.042
ALT [U/L]	37.00 (25.0–60.0)	53.0 (28.0–86.0)	NS
AST [U/L]	44.00 (30.0–61.0)	72.0 (47.0–119.0)	< 0.001
GGT [U/L]	46.0 (30.0–80.0)	85.5 (37.0–121.0)	0.02
Glucose [mmol/L]	5.8 (5.0–6.8)	7.6 (5.7–9.3)	< 0.001
Creatinine [umol/L]	80.0 (67.0–97.0)	88.5 (72.0–119.0)	0.04
LDH [U/L]	374.0 (290.0–459.0)	599.5 (509.0–682.0)	< 0.001
Urea [mmol/L]	6.3 (4.9–8.7)	9.0 (6.0–12.4)	< 0.001
INR	1.11 (1.05–1.16)	1.14 (1.06–1.19)	NS
D-dimer [ng/mL]	781.0 (514.0–1346.0)	1776.0 (937.0–4399.0)	< 0.001
CRP [mg/L]	83.0 (39.0–147.0)	140.0 (71.0–184.0)	0.017
Ferritin [ng/mL]	708.4 (356.3–1318.0)	1069.7 (571.5–1827.7)	0.014
cTn I [ng/mL]	0.008 (0.004–0.020)	0.017 (0.010–0.054)	< 0.001

Data are presented as median (interquartile range); *Number of patients; **Mean ± standard deviation.
ALT — alanine transferase; AST — aspartate aminotransferase; BASO — basophiles; BPAP — bilevel positive airway pressure; CPAP — continuous positive airway pressure; CRP — C-reactive protein; cTn I — cardiac troponin I; EOS — eosinophiles; GGT — gamma-glutamyl transferase; HCT — haematocrit; HFNOT — high-flow nasal oxygen therapy; HGB — haemoglobin; INR — international normalised ratio of prothrombin time; LDH — lactate dehydrogenase; LUC — large unstained cells; LYMPH — lymphocytes; MCHC — mean corpuscular haemoglobin concentration; MCV — mean corpuscular volume; MONO — monocytes; MPV — mean platelet volume; NEUT — neutrophiles; NS — not significant; PDW — platelet distribution width; PLT — platelets; RDW — red blood cell distribution width; WBC — white blood count

distinguish, with 71% sensitivity and 74% specificity, patients requiring and not requiring HFNOT/CPAP/BPAP. Enzyme activity above 521 U/L could differentiate, with 74% sensitivity and 90% specificity, patients requiring and not requiring CPAP/BPAP. Elevated levels of D-dimer, cTn I and urea showed less discriminant significance.

Discussion

To our knowledge, this is one of the few studies of this type conducted in a temporary hospital, which was created due to the need to increase the number of beds in hospitals for patients suffering from COVID-19.

Table 5. Results of the analysis of the receiver operator curves for the laboratory parameters showing the highest predictive value for the use of HFNOT/CPAP/BPAP

Parameter	Cut-off point	Sensitivity	Specificity	AUC	95% CI	P-value
LDH	> 434 [U/L]	71.01	73.91	0.797	0.74 – 0.85	< 0.001
cTn I	> 0.007 [ng/mL]	85.51	50.72	0.706	0.64 – 0.77	< 0.001
Urea	> 7.9 [mmol/L]	59.42	78.99	0.729	0.66 – 0.79	< 0.001
D-dimer	> 782 [ng/mL]	75.36	54.35	0.681	0.61 – 0.74	< 0.001

95% CI — confidence interval; AUC — area under curve; BPAP — bilevel positive airway pressure; CPAP — continuous positive airway pressure; cTn I — cardiac troponin I; HFNOT — high-flow nasal oxygen therapy; LDH — lactate dehydrogenase

Table 6. Results of the analysis of the receiver operator curves for the laboratory parameters showing the highest predictive value for the use of CPAP/BPAP

Parameter	Cut-off point	Sensitivity	Specificity	AUC	95% CI	P-value
LDH	> 521 [U/L]	73.68	89.94	0.87	0.81–0.91	< 0.001
D-dimer	> 1161 [ng/mL]	68.42	70.41	0.74	0.67–0.80	< 0.001
cTn I	> 0.007 [ng/mL]	92.11	45.56	0.72	0.66–0.78	< 0.001
Urea	> 8.1 [mmol/L]	60.53	73.96	0.69	0.62–0.75	< 0.001

95% CI — confidence interval; AUC — area under curve; BPAP — bilevel positive airway pressure; CPAP — continuous positive airway pressure; cTn I — cardiac troponin I; LDH — lactate dehydrogenase

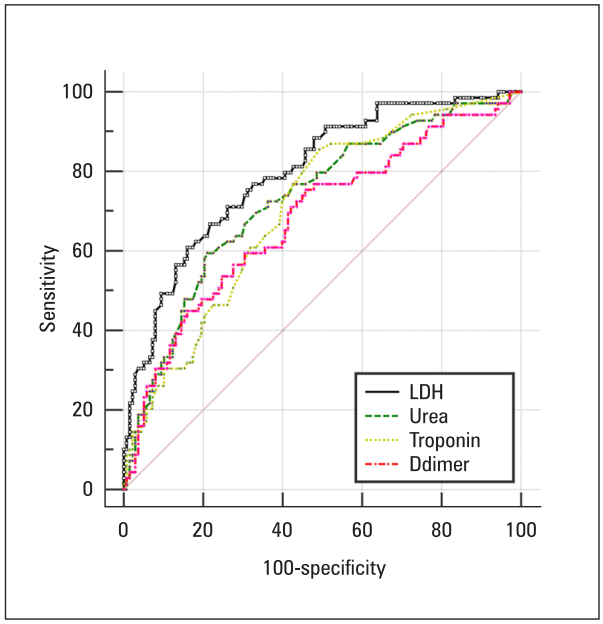

Figure 1. Receiver operator curves for predicting the use of high-flow oxygen therapy/continuous positive airway pressure/bilevel positive airway pressure; LDH — lactate dehydrogenase

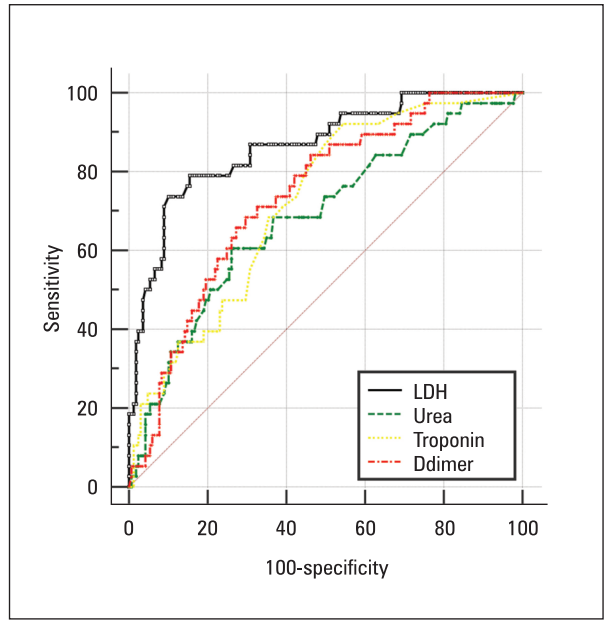

Figure 2. Receiver operator curves for predicting the use of continuous positive airway pressure/bilevel positive airway pressure; LDH — lactate dehydrogenase

We found that the laboratory parameter determined on admission to the hospital, which has the highest predictive value for the need to use HFNOT or CPAP/BPAP therapy during hospitalisation, is that of LDH activity. Previous studies have already indicated that elevated LDH values were associated with the increased risk of a severe course of COVID-19 and the need for

hospitalisation in the ICU [9]. Determining LDH activity was also used for predicting the need for intubation in patients who required CPAP active oxygen therapy [10]. It is worth noting that the increase in activity of LDH on admission to hospital due to respiratory failure was a poor prognostic factor for the effectiveness of non-invasive ventilation [11]. The 2003 SARS epidemic also found that elevations in LDH above the upper limit of normal, in addition to being aged 60 years and above, was an independent predictor of severe acute respiratory syndrome mortality [12]. The LDH enzyme plays a critical role in glycolytic metabolism. LDH occurs in the form of five isoenzymes in many tissues of the human body, including the heart, lungs, liver, kidneys, brain and skeletal muscles. Increased LDH activity in the body indicates organ damage and the release of the enzyme from the tissues [13, 14]. Pogialli et al. [15] already indicated an increase in the LDH value above the norm as the parameter of the best risk factor for the occurrence of respiratory failure. Our study, in which we indirectly investigated the occurrence of respiratory failure through the use of oxygen supplementation, confirmed these results.

The occurrence of disorders in the coagulation system is widely described in the course of COVID-19 [16, 17]. Li et al. [18] showed that the normal level of D-dimer on the day of admission is a good prognostic factor for survival. Our study showed that both the group that did not require oxygen at all during hospitalisation and the group that did not require HFNOT/CPAP/BPAP had significantly lower levels of D-dimer compared to those patients who required the above procedures.

Many studies show an increase in the parameters of inflammation in COVID-19 and an associated deteriorating prognosis. A meta-analysis by Huang et al. [19] has shown that elevated levels of CRP, ferritin and D-dimers were associated with a poor prognosis. Our study indirectly confirmed these results. Significantly higher results of the above parameters were demonstrated in those patients requiring the use of HFNOT/CPAP/BPAP compared to those patients not requiring these methods of active oxygen therapy support.

Elevated cardiac troponin levels in COVID-19 infection have already been reported [20]. The value is constantly increased, and there is no dynamic change in the level of troponin, which is characteristic of myocardial infarction. Elevation of troponin levels is defined as an unfavourable prognostic factor, predisposing to a severe course of SARS-CoV-2 infection [21]. Our study showed that the level of cTn I is also significantly higher in those patients who required oxygen supplementation. Those patients requiring the use of HFNOT/CPAP/BPAP or only CPAP/BPAP also had a significantly higher level of cTn I on admission than those who did not require their use.

A urea level > 7 mmol/L is one of the points included in the CURB-65 scale recommended by the British Thoracic Society for the assessment of the severity of community-acquired pneumonia [22]. In COVID-19, inflammatory changes in the lungs impair their function and indicate the need for supplementary oxygen. On the basis of the results of our study, it can be concluded that an increased level of urea is also a predictor of a severe course of pneumonia in the course of SARS-CoV-2 infection, which was defined as the need to use HFNOT/CPAP/BPAP.

There are several limitations of the study. Patients who were transferred to other hospitals for acute life-threatening conditions could not be included in the analysis because there is no information on their further treatment. Unfortunately, there were no precise information about the accompanying diseases of the patients, which is related to the difficulty in obtaining previous medical records from patients and their families. This was due to the inability to take into account the influence of comorbidity on the results of laboratory tests.

Conclusions

Performing laboratory tests when admitting a patient to the ward at the beginning of hospitalisation may indicate the risk of a severe course of infection from the SARS-CoV-2 virus. The parameter showing the highest predictive significance for the need for high-flow oxygen therapy or CPAP/BPAP active oxygen therapy support is the activity of LDH. Patients requiring oxygen supplementation and/or the use of HFNOT/CPAP/BPAP had significantly higher values for: white blood cells, neutrophils, glucose, LDH, urea, CRP, AST, D-dimers, ferritin, troponin and lowered lymphocyte levels compared to the groups of patients who do not require oxygen therapy and the use of HFNOT/CPAP/BPAP, respectively. The determination of basic laboratory parameters by the general practitioner or in the emergency rooms of hospitals can be helpful in predicting the need to hospitalise patients and provide oxygen supplementation.

Conflict of interest

None declared.

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