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Predicting models of inpatient death risk accompanied by coronavirus disease in healthcare establishments as an additional tool for decision-making

Antonyuk Olena[1], Stavyskyi Oleksii[2]

[1] Bogomolets National Medical University, KAPITAL Ltd.
(Medical Centre Universal Clinic «Oberig»),
National Military Medical Clinical Centre «Main Military Clinical Hospital», Kyiv, Ukraine.

[2] Lyceum of Information Technologies, Oleksandriia, Ukraine

Adress for correspondence:

Antonyuk Olena

e-mail: lena.nmu@gmail.com

Abstract: *we aimed to analyse risk prediction models and propose a new model for predicting in-hospital death risks. Materials and methods. We conducted a retrospective case-control study, analysing cases of hospitalisations of patients with severe and moderate COVID-19 from 2020 to 2021 (n=129). Results. We found that such factors significantly influence mortality risk: age (OR 0,866; 95% CI 0,8–0,9; p<0,001), lymphocyte absolute ratio (OR 0,000144; 95% CI 0.00000513-0.00407; p<0,001), C-reactive protein (OR 1,2; 95% CI 1,010-1,030; p<0,001), albumin baseline (OR 0,796; 95% CI 0,661-0,959; p<0,05), minimal albumin (OR 0,716; 95% CI 0,593-0,864; p<0,001), eGFR minimal (OR 0,951; 95% CI 0,93-0,972; p<0,001), INDEX PLRI score (OR 1,7; 95% CI 1,3–2,2; p<0,001), PADUA score (OR 4,49; 95% CI (2,25-8,94; p<0,001), respiratory insufficiency (OR 22,6; 95% CI (7,79-65,6; p<0,001), parenchymal involvement on multisectoral computer tomography (MSCT), % (OR 1,04; 95% CI 1,02-1,060; p<0,001), severity of lung damage on MSCT (pulmonary parenchymal involvement) over 50% (OR 4,96; 95% CI 2,08-11,8; p<0,001), hypertension in the medical history (OR 2,38; 95% CI 1,1–5,1; p = 0,026). Conclusion. We used models to predict the risk of in-hospital death. The area under the curve is 0.976, with a 95% confidence interval (CI) of 0.951-1. At the threshold point, 0.366, sensitivity is 95%, and specificity is 92,6%. We created a web version of the COVID-19 lethality calculator, which also works in Excel and could be helpful for viral or bacterial pneumonia. The calculator is available online. We propose to focus on clinical conditions and underlying comorbidities in decision-making despite the absence of data on the decompensation of diabetes mellitus, as we did not find any difference in the groups in the level of HbA1c (p=0.0662). Respiratory insufficiency could worsen progressively, so it is necessary to monitor clinical data. We analysed the presence of hypertension, diabetes mellitus and cardiovascular diseases (ischemic heart diseases, stroke, myocardial infarction, etc.) in medical history. We didn't focus on decompensation for diabetes or destabilisation of heart diseases as in the pandemic, the presence of SARS-CoV-2 could rapidly influence the severe course of COVID-19, which was proved in numerous studies and clinical recommendations. If there are enough resources, it is advisable to hospitalise patients with noncommunicable diseases after assessment of risk before SpO2 rapid decline. In the discussable*

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cases, a Calculator for evaluating underlying conditions could be used as an additional tool (the area under the curve is 0.766, 95% CI 0.548 – 0.984). At the threshold of 0.244, sensitivity is 87,5% and specificity – 68,8%. We suggest adding information on hospital admission criteria concerning underlying conditions rather than age factors. As in the elderly population, we received comparable results in risks in younger individuals with signs of metabolic syndrome or other non-communicable diseases. Further study is necessary to assess body mass index (BMI) as in our cohort, there was minor information on anthropological data. For a better understanding of the influence of adipose tissue on inflammatory laboratory results, we should use international study data, focus on outcomes assessment for the Ukrainian population, and assess risk individually.

Keywords: Health Policy; Public Health; Noncommunicable Diseases; Pneumonia; Linear Models; Delivery of Health Care; Metabolic Syndrome.

Introduction

Focusing on COVID-19 outcomes is still a relevant research direction; nevertheless, the pandemic has already stopped. Such considerations have led to numerous studies of previous disease results, which may help manage further healthcare emergencies.

Aim

The study aimed to analyse risk prediction models and propose a new model for predicting in-hospital death risks.

Materials and methods

We used the statistical method, modelling, and structural-logical analysis methods. We conducted a retrospective case-control study at KAPITAL Ltd. (Medical Centre «Universal Clinic «Oberig»), analysing cases of hospitalisations of patients with severe and moderate COVID-19 from 2020 to 2021 (n=129). We divided patients into two groups: discharged from the hospital (hospitalized (not deceased), group 1, n=88) and deceased (those who died, group 2, n=41). All patients had COVID-19 diagnosed due to PCR tests in the presence of RNA or a rapid test for SARS-CoV-2 antigens (table 1).

The data were processed using EZR [1]. Statistical analysis was conducted in R (R Core Team, 2023; R Foundation for Statistical Computing, Vienna, Austria). We used the medical data from the database of medical cards of inpatients of COVID-departments. Obtained data included demographical information (gender, age), where available – body mass index (BMI), complaints on the admission, presence of comorbidities, results of laboratory tests including absolute count (10*9/L) of lymphocytes (LYM), biochemical blood analysis results on admission (baseline): ALT, AST, their ratio, creatinine, maximal C-reactive protein (CRP); estimated GFR on admission (eGFR CKD-EPI), the maximum creatinine level (μmol/L), the minimum eGFR CKD-EPI, the severity of COVID-19 and degree of respiratory insufficiency. We used continuous Shapiro-Wilk normality test for quantitative indicators, after that, we calculated the mean value (M), standard error (±m) and 95% confidence interval (95% CI) (in the case of normal distribution) and the median value (Me) and interquartile range (IQR) for values with non-parametric distribution. We defined prevalence (%) and 95% confidence interval (95% CI) for qualitative values. We used the Mann-Whitney test for comparing mean values in the groups for quantitative values, and the chi-square test (with Yates' correction) for qualitative ones. After that we used logistic regression to estimate the association of factorial features with further risk assessment. We also assessed the odds ratio (OR) with 95% CI. We performed all calculations for a critical significance level of 0.05.

We searched PubMed for the terms «model covid-19 death in-hospital prediction». We tried to summarise information on the presence of underlying clinical conditions which may interfere with the risk of death. In our previous study we proposed a methodology of assessment of a personalized lethality risk index (PLRI), which allowed us to integrate some clinical characteristics such as age, BMI over 30 kg/m^2), cerebrovascular events, heart diseases, presence

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of respiratory insufficiency with SpO2<92% and typical for COVID-19 computer tomographical pattern of parenchymal involvement (over 50%) [2]. In this paper we used results of previous calculations and named PLRI as INDEX. For the patients with severe hypoxemia hospitalisation to the intensive care unit ward was organised.

We presented clinical and demographic characteristics in the table 1.

As we can see that the group of patients were predominantly older than in general population (there were 914 cases of hospitalisation with COVID-19 since late September 2020 till July 2021 (males – 503 (55%), females 411 (45%), median age is 61 years). In 2020 19 patients (4,83%) died in COVID-departments among 393. It means that the rate of in-patient death was not high and could be comparable with good results of prominent European and USA centres, for example, the mortality rate in the patient cohort was 5.3% in USA [32].

Results

The results of laboratory tests and instrumental results in the groups are presented below in Table 2.

It should be noted that 29 patients with diabetes mellitus were in both groups, with mean (IQR) HbA1c 6.8% (5.9-6.9). Six of them (20.7% (95% CI 8-39.7%) had decompensated diabetes with HbA1c over 7.5%. There was no significant difference between the medium level of HbA1c in the groups (p=0.066).

Table 1. Demographic and clinical characteristics of the study population

Characteristic	Measures	Both groups N (%)	Hospitalized (not deceased) (n=88) N (%)	Deceased (n=41) N (%)	p
Sex	Females	73 (56.6%)	53 (60.2%)	20 (48.8%)	p=0.3
Age	Me (IQR)	79.1 (78-83)	81.18 (79-84)	74.59 (70-80)	*p<0.0001
Comorbidities	Hypertension	58 (45%)	34 (38.6%)	24 (58.5%)	*p=0.04
	CVD	15 (11.6%)	8 (9.1%)	7 (17.1%)	p=0.30
	Diabetes	29 (22,5%)	16 (18,2%)	13 (31,7%)	p=0.14
	Malignancy	16 (12.4%)	10 (11.4%)	6 (14.6%)	p=0.8
BMI, kg/m^2	M (sd)	28.8 (5.4)	27.6 (4.7)	31.2 (6.2)	p=0.12
eGFR on admission, ml/min	M (sd)	60.1 (20.8)	60.2 (19.1)	59.9 (4.2)	p=0.95
HbA1c on admission, %	Me (IQR)	5.6 (4.8-6.1)	5.4 (4.8-5.9)	5.95 (5.1-6.5)	p=0.07
Prevalence of cough	Absolute data, n/% (95% CI)	60/46.5 (37.7-55.5)	44/50 (39.1–60.9)	16/39 (24.2–55.5)	p=0.33
Prevalence of dyspnoea	Absolute data, n/% (95% CI)	59/45.7 (36.9-54.7)	26/29.5 (20.3–40.2)	23/56.1 (39.7–71.5)	*p=0.007
Reported fever	Absolute data, n/% (95% CI)	97/75.2 (66.8-82.4)	67/76.1 (65.9–84.6)	30/73.2 (57.1–85.8)	p=0.89
Prevalence of weakness	Absolute data, n/% (95% CI)	124/96.1 (91.2-98.7)	86/97.7 (92–99.7)	38/92.7 (80.1–98.5)	p=0.37
Diarrhoeal syndrome	Absolute data, n/% (95% CI)	11/8.5 (4.3-14.7)	8/9.1 (4–17.1)	3/7.3 (1.5–19.9)	p=1
COMORBIDY, scores	Me (QI–QIII)	2.1 (1-3)	2.04 (1-3)	2.27 (2-3)	p=0.12
INDEX PLRI, score	Me (QI–QIII)	4.4 (3-5)	3.98 (3-5)	5.3 (4-6)	*p<0.001
PADUA score	Me (IQR)	3.16 (3-4)	2.97 (3-3)	3.58 (3-4)	*p<0.0001

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Table 2. Laboratory and instrumental parameters in the study groups

Parameter	Hospitalized (not deceased) (n=88)	Deceased (n=41)	p
Severity of lung damage on MSCT (pulmonary parenchymal involvement), % (95% CI)	31.43 (15–42.5)	57.9 (40–75.8)	*p<0.001
Minimal absolute lymphocyte count, x109/L, Me (QI–QIII)	0.7 (0.4–0.9)	0.24 (0.11–0.28)	*p<0.001
Maximal C-reactive protein level, mg/L, Me (QI–QIII)	55.1 (16.9–78.4)	129.4 (73–178.9)	*p<0.001
Ferritin, µg/L, Me (QI–QIII)	479.5 (156–558)	1012 (446.5–1175)	*p<0.001
IL-6, pg/mL, Me (QI–QIII)	40.4 (9.3–43.5)	64.5 (17.7–74.9)	*p<0.01
HbA1c, Me, % (95% CI)	5.4 (4.8–5.9)	5.95 (5.08–6.52)	p=0.066
Alanine aminotransferase (ALT), U/L Me (QI–QIII)	30.7 (16.6–40)	44 (20.3–41.9)	p=0.442
Aspartate transaminase (AST), U/L Me (QI–QIII)	39.3 (25.7–47.3)	59.5 (28.5–53.5)	p=0.078
AST/ALT Me (QI–QIII)	1.4 (1.0–1.8)	1.8 (1.1–1.5)	p=0.803
Baseline albumin, g/L M (sd)	36.5 (4.2)	32.8 (4)	*p=0.009
Minimal albumin, g/L M (sd)	34.7 (5.1)	28.2 (3.5)	*p<0.001
Creatinine on admission, mcmol/L	94.9 (71.9-107.7)	112.19 (73.71-124.95)	p=0.253
Maximal creatinine, mcmol/L	96.7 (75.2-112.3)	206.72 (106.94-246.3)	*p<0.001
eGFR CKD-EPI on admission, M (sd) ml/min	60.2 (19)	59.9 (24.2)	p=0.949
Minimal eGFR CKD-EPI Me (QI–QIII), ml/min	59.8 (43.4-75.7)	36.9 (16.4-52.9)	*p<0.001

* – p<0.05 statistically significant difference between groups

Table 3. Univariate logistic regression model lethality (inpatient death) risk

Factorial characteristic	Model coefficient, b±m	Significance, p	Odds ratio, OR (95% CI)	Area under receiver operating-characteristic (ROC) curve AUC (95% CI)
Lymphocytes absolute ratio, 10^9/L	-8.8424±1,73	0.000000208	0.000144 (0.00000513-0.00407)	0.905 (95% CI 0.844 – 0.965)
max CRP, mg/L	0.0178±0,0037	0.00000203325	1,02 (1,010-1,030)	0.813 (95% CI 0.735 – 0.892)
Baseline albumin, g/L	-0.23±0,095	0.01615	0,796 (0,661-0,959)	0.741 (95% CI 0.572 – 0.91)
Min albumin, g/L	-0.33±0,096	0.000500	0,716 (0,593-0,864)	0.851 (95% CI 0.705 – 0.997)
min eGFR, ml/min	-0.05±0,011	0.00000688	0,951 (0,93-0,972)	0.773 (95% CI 0.67 – 0.876)
INDEX, scores	0.53±0,14	0.00011400	1,7 (1,3-2,2)	0.733 (95% CI 0.642 – 0.824)
PADUA score	1.5±0,35	0.00001948	4,49 (2,25-8,94)	0.717 (95% CI 0.629 – 0.804)
Respiratory insufficiency	3.12±0,54	0.00000000963	22,6 (7,79-65,6)	0.929 (95% CI 0.869 – 0.988)

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Table 3. (continued)

Factorial characteristic	Model coefficient, b±m	Significance, p	Odds ratio, OR (95% CI)	Area under receiver operating-characteristic (ROC) curve AUC (95% CI)
Severity of lung damage on MSCT (pulmonary parenchymal involvement), %	0.043±0,0099	0.000018222	1,04 (1,02-1,060)	0.785 (95% CI 0.687 – 0.882)
Computer tomographical pattern of parenchymal involvement (over 50%)	1.6±0,44	0.000295	4,96 (2,08-11,8)	0.651 (95% CI 0.566 – 0.736)
Age, years	-0.14±0,037	0.000132	0,866 (0,805-0,933)	0.731 (95% CI 0.63- 0.832)
BMI, kg/m^2	0.144±0.097	0.1390	1.15 0.95 1.40	0.656 (95% CI 0.4 – 0.913)
Diabetes mellitus	0.7368±0.43	0.09	2.09 0.891 4.9	0.568 (95% CI 0.485 – 0.65)
Hypertension	0.8681±0.39	0.026	2.380 (1.11-5.12)	0.607 (95% CI 0.514 – 0.699)
CVD	0.7221±0.56	0.194	2.060 (0.692-6.13)	0.54 (95% CI 0.474 – 0.606)

Note: * – p<0.05 statistically significant difference between groups

We found that such factors significantly influence mortality risk: age (OR 0,866; 95% CI 0,8–0,9; p<0,001), lymphocyte absolute ratio (OR 0,000144; 95% CI 0.00000513-0.00407; p<0,001), C-reactive protein (OR 1,2; 95% CI 1,010-1,030; p<0,001), albumin baseline (OR 0,796; 95% CI 0,661-0,959; p<0,05), minimal albumin (OR 0,716; 95% CI 0,593-0,864; p<0,001), eGFR minimal (OR 0,951; 95% CI 0,93-0,972; p<0,001), INDEX PLRI score (OR1,7; 95% CI 1,3–2,2; p<0,001), PADUA score (OR 4,49; 95% CI (2,25-8,94; p<0,001), respiratory insufficiency (OR 22,6; 95% CI (7,79-65,6; p<0,001), parenchymal involvement on

Table 4. Multivariate logistic regression model for lethality (inpatient death) risk as calculator for evaluating underlying conditions

Factorial characteristic	Units for numerical data/ or categorical data	Model coefficient, b±m	Significance, p	Odds ratio, OR (95% CI)
(Intercept)	n/a	1.98015±6.45694	0.759	2320.00 (1.56-3440000
Age	Continuous, years	-0.08674±0.06626	0.191	0.917 (0.805-1.04)
Body mass index (BMI)	Continuous, kg/m^2	0.11577±0.11549	0.316	1.12 (0.895-1.41)
Diabetes mellitus (DM)	Yes	0.79701±1.06622	0.455	2.22 (0.275-17.9)
	No	Referral		
Hypertension	Yes	0.54169±1.04757	0.605	1.72 (0.221-13.4)
	No	Referral		
Cardio-vascular disease (CVD)	Yes	0.91526±1.81259	0.614	2.5 (0.0715-87.2)
	No	Referral		

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CT, % (OR 1,04; 95% CI 1,02-1,060; p<0,001), severity of lung damage on MSCT (pulmonary parenchymal involvement) over 50% (OR 4,96; 95% CI 2,08-11,8; p<0,001), hypertension in the medical history (OR 2,38; 95% CI 1,1–5,1; p=0,026).

For calculating risk of in-patient death (IPD) we can use formula:

$$pVSevIPD=1/(1+e^{-(1.98015--0.08674*X1+0.11577*X2+0.79701*X3+0.54169*X4+0.91526*X5)}),$$

where X1 – age, years, X2 – body mass index (BMI), kg/m^2, X3 – diabetes mellitus (DM), yes – 1 score, X4 – hypertension, yes – 1 score, X5 – Cardio-vascular disease (CVD), yes – 1 score.

Figure 2 presents the receiver operating-characteristic (ROC) curve (AUC 0.766 95% CI 0.548 – 0.984).

In Germany, guidelines suggest hospitalisation if the person has cardiovascular diseases (for example, hypertension), diabetes mellitus, chronic lung diseases, and obesity [3]. In Saudi Arabic Republic it is also recommended in such cases: «Clinical or radiological evidence of pneumonia; age >65 years, low oxygen saturation SpO2 < 94% on room air, acute respiratory distress syndrome (ARDS), chronic pulmonary disease, chronic kidney disease, history of comorbidities diabetes Mellitus or/and hypertension, history of cardiovascular disease, obesity (BMI ≥40), use of biological (immunosuppressants) medications (e.g., TNF inhibitors, interleukin inhibitors, anti-B cell agents), history of organ transplant or another immunosuppression disease, history of active malignancy, other Co-illness that requires admission» [4]. According to Table 4, we received that an adequate model was proposed for predicting the risk of inpatient death. The area under the curve is 0.766, 95% CI 0.548 – 0.984. At the point of the threshold 0.244, sensitivity is 87,5% and specificity 68,8% (figure 2). Even though p-values for factorial characteristics had low significance, the model had a high sensitivity and satisfactory specificity. We wrote a risk assessment calculator in Excel and a web version using JavaScript. The Calculator for evaluating underlying conditions https://covidcalculator.great-site.net/?i=1 (Figure 3) is proposed as an additional tool for decision-making. We analysed the presence of hypertension, diabetes mellitus and cardiovascular diseases (ischemic heart diseases, stroke, myocardial infarction, etc.) in medical history. We didn't focus on decompensation for diabetes or destabilisation of heart diseases as in the pandemic, the presence of SARS-CoV-2 could rapidly influence the

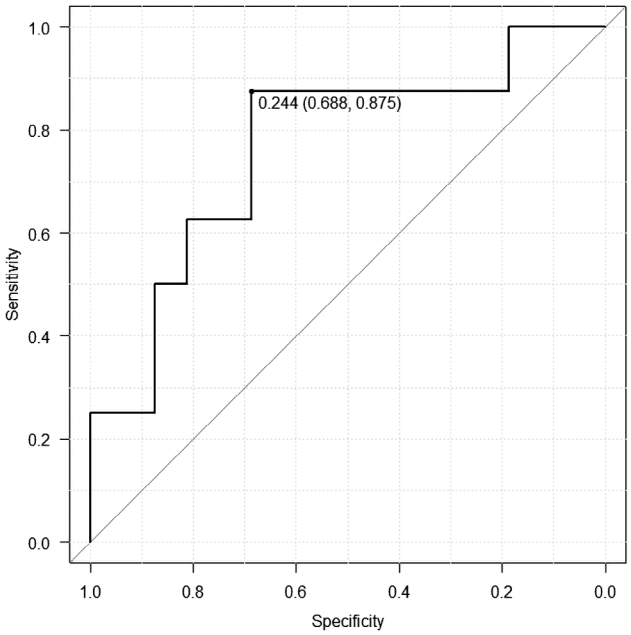

Figure 2. Area under receiver operating-characteristic (ROC) curve AUC (95% CI) AUC 0.766 95% CI 0.548 – 0.984

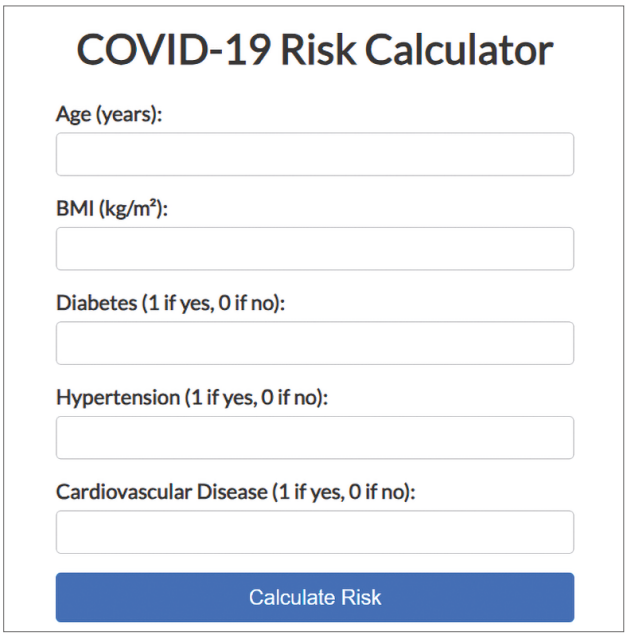

Figure 3. Web version of COVID-19 death risk calculator (Calculator for evaluating underlying conditions)

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severe course of COVID-19 which was proved in numerous studies and clinical recommendations.

As an additional tool, we propose to assess age, body mass index, and underlying health conditions such as diabetes, hypertension, and CVD in medical history. Hospitalisation could be suggested if the person receives a positive answer with a high score. We also found that adding information on the severity of respiratory insufficiency (1, 2, or 3) and absolute lymphocyte rate and CRP could be useful for predicting the risk of death (Table 5).

We wrote a web-version of COVID-19 Lethality Risk Calculator covidcalc1.freesite.online. The calculator also works in Excel. The area under the curve is 0.976, with a 95% confidence interval (CI) of 0.951 – 1. At the threshold point, 0.366, sensitivity is 95% and specificity is 92,6% (Figure 4). There was a high opportunity for death, but the patient could be treated, and the clinical situation could change as a laboratory parameter of inflammation. That is why the calculator could be used with dynamically changed characteristics as an additional tool for clinicians in decision-making. We found the positive influence of respiratory insufficiency and CRP, while lymphocytes were influenced in the opposite direction. The lower rate of lymphocytes the higher the risk, which could be explained as a condition of immunodeficiency.

For calculating risk of in-patient death (IPD) we can use formula:

$$pVSevIPD=1/(1+e^{(-6.237647+2.792388*X1-4.670305*X2+0.015773*X3)}),$$

where X1 – respiratory insufficiency (1, 2 or 3), X2 – absolute lymphocyte rate, 10^9/L, X3 – C-reactive protein, mg/L.

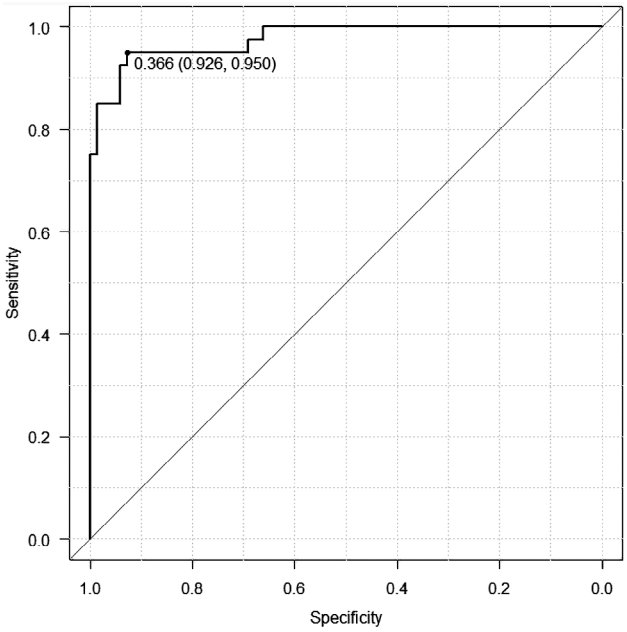

Figure 4. Area under receiver operating-characteristic (ROC) curve AUC (95% CI) 0.976 95% CI 0.951 – 1

The formula could be implemented in R and Python as well. For example, in R, it looks like a script, while respiratory insufficiency is 2, CRP 130 mg/L and LYM 0.89: «RI <- c(2); CRP << c(130); LYM<< c(0.89); df=data.frame (RI, CRP, LYM); print(1/1+exp(-predict(GLM.1, df))))». The estimated risk is low (figure 5). The same calculation is presented in Excel (figure 6).

The tool's diagnostic accuracy is high at 93,5% (95% CI 87,1-97,4%), with sensitivity of 95% (95% CI 83,1-99,4%), specificity of 92,6% (95% CI 83,7-97,6%), positive predictive value of 88,4% (95% CI 74,9-96,1%), and negative predictive value of 96,9% (95% CI 89,3-99,6).

Table 5. Multivariate logistic regression model for inpatient death risk assessment

Factorial characteristic	Units for numerical data/ or categorical data	Model coefficient, b±m	Significance, p	Odds ratio, OR (95% CI)
(Intercept)	n/a	-6.237647±2.100308	0.00298	0.002 (0.000032-0.12)
Respiratory insufficiency	1, 2 or 3	2.792388±0.644297	0.0000146	16.3 (4.6-57.7)
LYM	Continuous, 10^9/L	-4.670305±1.906489	0.01430	0.00937 (0.0002-0.39)
CRP	Continuous, mg/L	0.015773±0.006587	0.01665	1.02 (1.0-1.03)

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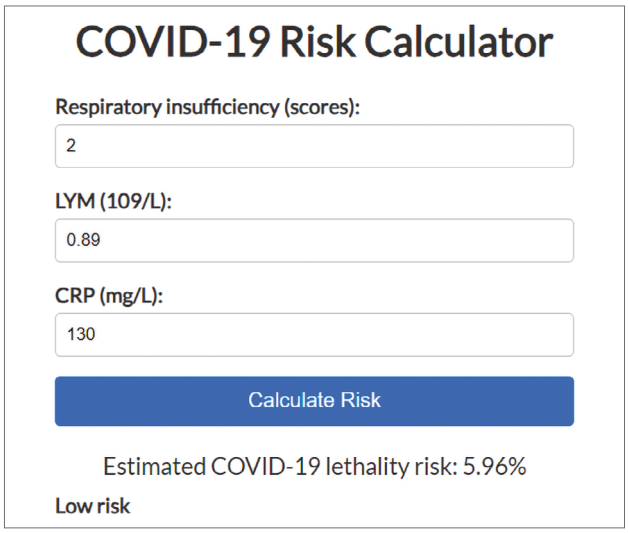

Figure 5. Calculator in web-version (COVID-19 Lethality Risk Calculator https://covidcalc1.great-site.net/?i=1).

Discussions

We studied the elderly population mainly, and there was no significant difference in the symptoms on admission between the groups except dyspnoea (p=0.00697). We focused on the relationship between COVID-19 and patients with diabetes and/or obesity, exploring the associated risks, outcomes, and management strategies in depth.

Our study contributes to the growing body of research on risk prediction models for in-hospital death among COVID-19 patients. The developed COVID-19 Lethality Risk Calculator demonstrates high predictive accuracy, with an AUC of 0.976, sensitivity of 95%, and specificity of 92.6%. Given these performance metrics, our tool has the potential to assist clinicians in stratifying patient risk and optimizing resource allocation.

The calculator can be integrated into daily clinical practice for early risk assessment of COVID-19 patients upon hospital admission. By providing an individualized mortality risk score, it enables healthcare professionals to make more informed decisions regarding hospitalization, intensive care unit (ICU) admission, and early interventions. Our findings support the use of dynamic monitoring, particularly in cases of respiratory insufficiency, to guide patient management. Additionally, we propose that the tool be adapted for other infectious diseases, including bacterial and viral pneumonia, where similar risk factors contribute to adverse outcomes.

In cases of sepsis or pneumonia, where rapid clinical deterioration is common, our model may provide an advantage over standard scoring systems by incorporating key laboratory and clinical parameters such as respiratory insufficiency, lymphocyte count, and C-reactive protein levels. This allows for real-time updates in prognosis based on patient condition changes. Future studies should focus on implementing the calculator in hospital settings and evaluating its impact on clinical outcomes.

Strålin et al. reported results of COVID-19 hospitalization with one of the lowest mortality rates, showing a trend in the decline of mortality from the nationwide observational cohort study; they used the Charlson Comorbidity Index (CCI) for the assessment of comorbidities during the last 5 years [9]. According to Israel et al., modelling is a valuable tool for predicting the risks of death [5]. Krzanowska et al. studied acute kidney injury and proposed a calculator for its prediction in a Polish study [7]. Popescu et al. developed prediction models for COVID-19 outcomes in a Romanian study [8]. Machine learning approaches have also been explored, with studies such as the CRACoV-AKI model in Poland and the COVID-19 outcome prediction models in Romania, both of which utilized electronic health records and artificial intelligence [7, 8]. While these models offer robust predictive power, their clinical applicability in resource-limited settings remains a challenge. Our calculator, in contrast, is designed to be accessible and interpretable, making it practical for frontline healthcare professionals

A	B	C	D	E	F	G	H	I	J	K	L
respiratory insufficience (1, 2, 3 or absent)	Lymphocytes, abs. 109/L	CRP, mg/L		Ci	Result	Critical Value=	0,366			Sensitivity, %	95
2	0,89	130								Specificity, %	92,6
2,792388	-4,670305	0,015773		#	**low risk of death**						

Figure 6. Calculator COVID-19 death risk prognosis in Excel

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in Ukraine and other similar settings. We also calculated an upgraded predicting model adding IL-6 to the lymphocytes, CRP, and respiratory insufficiency (area under the curve 0.974 95% CI 0.948 – 1), but it has limitations caused by its price and checking in dynamic is not available in smaller regional hospitals.

The difference in hypoxemia in patients was standardised by appropriate oxygen supply. According to the research data from the Switzerland, «in the absence of dyspnea and/or confusion, a SpO_2 cutoff up to 85% for ICU admission was not burdened by negative outcomes», but for «the SpO2 cutoff of 92%, as a threshold for ICU admission, needs critical re-evaluation» [10].

The hospitalization criteria used in different countries also provide a useful comparison. Germany and Saudi Arabia recommend hospital admission for patients with cardiovascular diseases, diabetes, and chronic pulmonary conditions [3, 4]. Our model aligns with these guidelines but further emphasizes the importance of individualized risk assessment rather than age-based cutoffs, as younger patients with metabolic syndrome and comorbidities exhibited comparable mortality risks to elderly individuals [6].

We proposed our tool for Ukrainian clinicians, which could be easily interpreted in a web version or Excel. Future research should focus on these areas to develop more effective prevention and treatment strategies for COVID-19 in patients with diabetes and obesity. Public health initiatives should also prioritize metabolic health improvement as a key component of pandemic preparedness and response.

Despite the strengths of our model, some limitations must be acknowledged. First, further validation on a larger multi-center cohort is required. Second, the lack of comprehensive anthropometric data limited our ability to fully assess the role of BMI and adipose tissue in COVID-19 severity. Third, while the calculator demonstrates high sensitivity and specificity, it should be used as an adjunct to clinical judgment rather than a sole decision-making tool.

Future studies should explore the integration of machine learning techniques to refine predictive accuracy and assess long-term outcomes in post-COVID-19 patients. Additionally, expanding the model to include markers of metabolic instability (e.g., HbA1c trends, inflammatory cytokines) may enhance its utility in predicting deterioration in patients with diabetes and obesity.

The calculator can be integrated into daily clinical practice for early risk assessment of COVID-19 patients upon hospital admission. By providing an individualized mortality risk score, it enables healthcare professionals to make more informed decisions regarding hospitalization, ICU admission, and early interventions. Dynamic monitoring is particularly important, especially for patients with progressing respiratory insufficiency (RI). Previous studies have shown that persistent hypoxemia and elevated inflammatory markers are associated with worsening outcomes in hospitalized COVID-19 patients [12].

Several international models have been developed to predict COVID-19 outcomes, including the Charlson Comorbidity Index (CCI), qSOFA (quick Sequential Organ Failure Assessment), and COVID-GRAM [9, 12, 13].

Our model differs by emphasizing dynamic laboratory markers and respiratory status rather than a purely comorbidity-based approach.

In cases of sepsis and pneumonia, where rapid clinical deterioration is common, our model provides an advantage over standard scoring systems by integrating real-time updates in prognosis based on respiratory and laboratory data. Traditional scores like SOFA (Sepsis-related Organ Failure Assessment) and CURB-65 (for pneumonia) have been widely used [11, 12], but they often do not include markers such as C-reactive protein (CRP) or lymphocyte count. The addition of these parameters improves the ability to detect progressive deterioration in patients. In another study, we proposed several additional tools for acute kidney injury risk assessment (based on lymphocytes, CRP, respiratory insufficiency and Padua score), but it is worth discussing in a separate article.

Ukrainian researchers Matskevych V et al. reported the results of death risk assessment based on durations of mechanical ventilation and face-mask support (the sensitivity 68.3%, specificity 87.5%, 78.0% and 71.9%, respectively) [11].

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Table 6. Predicting models in COVID-19 outcomes

Author	Country	Type of Study	Study Cohort	Outcomes	Variables	AUC of Model
Israel A, et al. (2022) [4]	Israel	Retrospective Cohort Study	N = 101,039	Development of a COVID-19 severity calculator	Patient risk factors, vaccination status	AUC = 0.889
Krzanowska et al. (2024) [7]	Poland	Retrospective Cohort Study	N = 4630	AKI in hospitalized patients with COVID 19	History of kidney disease (prior acute or prevalent CKD, status post kidney transplantation), hypertension, circulatory failure and / or need for respiratory support, selected, raised PCT, altered neutrophil count, and / or elevated myoglobin levels)	AUC = 0.798
Popescu IM, et al. (2023) [8]	Romania	Retrospective Cohort Study	N = 483 patients; Mean age: Not specified	Prediction models for COVID-19 outcomes in resource-limited hospitals	Clinical parameters, laboratory findings (age, absolute neutrophil count, and CRP)	AUC = 0.845
Matskevych V, et al. (2023) [13]	Ukraine	Retrospective Cohort Study	N = 41; Patients on respiratory support	Morphological prediction of lethal outcomes	Lung tissue structural changes, histopathology	Not specified
Knight M, et al. (2020) [14]	UK	National Cohort Study	N = 427; Pregnant women with COVID-19	Outcomes in pregnant women with COVID-19	Demographics, clinical features, pregnancy outcomes	Not specified
Liang W, et al. (2020) [15]	China	Retrospective Cohort Study	N = 1590; Mean age: 48.9 years	Risk score for predicting critical illness	Age, comorbidities, clinical symptoms, lab tests	AUC = 0.88
Stoeckle K, et al. (2022) [16]	USA	Retrospective Cohort Study	N = Not specified; COVID-19 patients on remdesivir	Association of inflammatory markers with outcomes	CRP, ferritin, D-dimer levels	Not specified
Garrafa E, et al. (2021) [17]	Italy	Retrospective Cohort Study	N = 1000; Mean age: Not specified	Early prediction of in-hospital death	Age, blood analyses, chest X-ray score; Machine learning model	AUC = 0.91
Hippisley-Cox J, et al. (2021) [18]	UK	Prospective Cohort Study	N = 6.9 million; Vaccinated adults	Risk prediction after COVID-19 vaccination	Demographics, clinical risk factors, vaccination status	Not specified

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Table 6. (continued)

Author	Country	Type of Study	Study Cohort	Outcomes	Variables	AUC of Model
Zhu Y, et al. (2023) [19]	China	Retrospective Cohort Study	N = Not specified Hospitalized COVID-19 patients	Prediction model based on comorbidities	Comorbidity index, demographics	Not specified
Ma X, et al. (2020) [20]	China	Retrospective Cohort Study	N = 523; Mean age: Not specified	Death prediction model	Clinical symptoms, lab findings, comorbidities	AUC = 0.92
Abdol-lahpour I, et al. (2021) [21]	Iran	Case-Control Study	N = 630; Cases: 210; Controls: 420	In-hospital mortality prediction	Demographics, clinical features, lab data	Not specified
Tang CY, et al. [22]	USA/ China	Review Article	N=4471	Overview of COVID-19 prediction models	Various models and variables	Not applicable
Tanboğa IH, et al. (2021) [23]	Turkey	Retrospective Cohort Study	N = 1500; Mean age: 56 years	Probability of death estimation	Clinical parameters, lab findings	AUC = 0.79
Deschepper M, et al. (2021) [24]	Belgium	Retrospective Observational	N = 222	Hospital bed capacity prediction	Patient flow data, admission/discharge rates	Not applicable
Hiraga K, et al. (2023) [25]	Japan	Retrospective Cohort Study	N = 8288; Patients with COVID-19	Prediction of in-hospital deaths	Electronic healthcare data, clinical and lab parameters	AUC 0.88
Estiri H, et al. (2021) [26]	USA	Retrospective Cohort Study	N = Not specified; COVID-19 patients	Individualized adverse outcomes prediction	Machine learning model, healthcare data	AUC 0.91
Natanov D, et al. (2023) [27]	USA/ Israel	Retrospective Cohort Study	N = 969; Hospitalized COVID-19 patients	Prognosis prediction based on early status (intensive care unit admission, intubation, or death)	Platelet count, lactate, age, blood urea nitrogen, aspartate aminotransferase, and C-reactive protein (PLABAC) and platelet count, red blood cell distribution width, age, blood urea nitrogen, lactate, and eosinophil count (PRABLE)	AUC 0.808
Schiaffino S, et al. (2021) [28]	Italy	Retrospective Cohort Study	N = 552	Outcome prediction using chest muscle metrics	CT-derived muscle metrics, clinical parameters	Not specified

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Table 6. (continued)

Author	Country	Type of Study	Study Cohort	Outcomes	Variables	AUC of Model
Gavelli F, et al. (2021) [29]	Italy	Retrospective Cohort Study	N = 480; COVID-19 patients	Clinical stability and in-hospital mortality prediction (Novara COVID score)	Demographics, clinical features, lab data	Not specified
Vaid A, et al. (2021) [30]	USA	Retrospective Cohort Study	N = 6093 patients; Mean age: Not specified	Acute dialysis requirement and death prediction predicting treatment with dialysis or death at various time horizons (1, 3, 5, and 7 days) after hospital admission	Clinical parameters, lab findings, comorbidities	Not specified
Shen Q, et al. (2023) [31]	China	Retrospective Cohort Study	N = 4711; COVID-19 patients	Mortality risk prediction	Hospital admission data (mean arterial pressures, ages, C-reactive protein tests' values, values of blood urea nitrogen and their clinical troponin values)	Not specified
Booth AL, et al. (2021) [32]	USA	Retrospective Cohort Study	N = 398; COVID-19 patients (43 expired and 355 non-expired)	Prognostic model for mortality	Machine learning, laboratory data (CRP, blood urea nitrogen, serum calcium, serum albumin, and lactic acid)	AUC 0.93
Antonyuk O, Stavyskyi O.	Ukraine	Retrospective Cohort Study	N =129, mean age 79.1 (78-83)	In-hospital death in COVID-19	CRP, lymphocytes, respiratory insufficiency	AUC 0.976

We should think about the risk of bacterial superinfection and sepsis in such patient cohorts, which was based on autopsy data as well. In our study, we did not focus on the terms of respiratory support, but studying its influence on AKI risk did not find a significant difference.

Furthermore, our risk calculator can be adapted for other infectious diseases, including bacterial pneumonia, influenza, and emerging respiratory infections, by modifying predictor variables based on evolving evidence. Prospective studies should assess its role in other viral pneumonia, such as H1N1 or RSV, to determine its broader applicability.

Conclusions

We used models to predict the risk of death. The area under the curve is 0.976, with a 95% confidence interval (CI) of 0.951 – 1. At the threshold point, 0.366, sensitivity is 95%, and specificity is 92.6%. We created a web version of the COVID-19 lethality calculator, which also works in Excel and could be useful for viral or bacterial pneumonia. We propose to focus on clinical conditions and underlying comorbidities

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in decision-making despite the absence of data on the decompensation of diabetes mellitus, as there was no significant difference in the level of HbA1c in the studied groups (p=0.0662). Respiratory insufficiency could worsen progressively, so it is necessary to monitor clinical data. We analyzed the presence of hypertension, diabetes mellitus, and cardiovascular diseases (ischemic heart diseases, stroke, myocardial infarction, etc.) in medical history. We didn't focus on decompensation for diabetes or destabilization of heart diseases as in the pandemic, the presence of SARS-CoV-2 could rapidly influence the severe course of COVID-19, which was proved in numerous studies and clinical recommendations. If there are enough resources, it is advisable to hospitalize patients with noncommunicable diseases after assessment of risk before SpO2 rapid decline. In the discussable cases, a calculator for evaluating underlying conditions could be used as an additional tool (the area under the curve is 0.766, 95% CI 0.548 – 0.984). At the threshold of 0.244, sensitivity is 87.5%, and specificity 68.8%. We suggest adding information on hospital admission criteria concerning underlying conditions rather than age factors. As in the elderly population, we received comparable results in risks in younger individuals with signs of metabolic syndrome or other non-communicable diseases. Further study is necessary to assess BMI as in our cohort, there was minor information on anthropological data. For a better understanding of the influence of adipose tissue on inflammatory laboratory results, we should use international study data, focus on outcomes assessment for the Ukrainian population, and assess risk individually.

We suggest hospitalisation in patients with pneumonia with any signs of respiratory insufficiency in a group of risks, including social indications (military servicemen, patients with severe underlying conditions or from the social settings (homes for elderlies, passionate or other social facilities) as early as possible. This principle has already been implemented in the Donetsk region in the Armed Forces since February 2023, when the author participated in evacuating combatants from Role 1-2 hospitals to Role 3. According to the analysis of pneumonia cases to improve health care quality, the Medical Command decided to implement obligatory urgent hospitalisation in the Military Medical Centres without postponement. Severe risks of rapid worsening of respiratory insufficiency could explain this decision.

Ethical issues. On the first day of hospitalisation, all patients agreed to use personal data, and the Bogomolets National Medical University's Ethical Committee proved the study.

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This study hadn't obtained external funding.

Conflicts of interest

Authors have no conflict of interest to declare.

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ORCID ID and authors contribution

0000-0002-3411-196X (A, B, C, D, E, F) Antonyuk Olena

(B, C) Stavyskyi Oleksii

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article.

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Прогностичні моделі ризику внутрішньолікарняної смертності від COVID-19 у закладах охорони здоров'я як додатковий інструмент для прийняття рішень

Антонюк Олена[1], Стависький Олексій[2]

[1] асистент кафедри громадського здоров'я Національного медичного університету імені О.О.Богомольця, лікар-терапевт, ендокринолог, нефролог Медичного центру «Універсальна клініка «Оберіг», ординатор клініки гематології (з палатами для інтенсивної та хіміотерапії) Національного військового медичного клінічного центру «Головний військовий клінічний госпіталь», Київ, Україна.

[2] учень Ліцею інформаційних технологій, Олександрія, Кіровоградська область, Україна

Adress for correspondence:

Antonyuk Olena

e-mail: lena.nmu@gmail.com

Анотація: *мимали на меті проаналізувати моделі прогнозування ризиків та запропонувати нову модель для прогнозування ризиків госпітальної смерті. Матеріали та методи. Ми провели ретроспективне дослідження випадок-контроль у ТОВ «КАПІТАЛ» (Медичний центр «Універсальна клініка «Оберіг»), що аналізує випадки госпіталізацій пацієнтів з важким та помірним перебігом COVID-19 з 2020 по 2021 рік (n=129). Результати. Встановлено, що на ризик смертності суттєво впливають такі фактори: вік (ВШ 0,866; 95% ДІ 0,8–0,9; p<0,001), абсолютне співвідношення лімфоцитів (ВШ 0,000144; 95% ДІ 0,00000513-0,00407; p<0,001), С-реактивний білок (ВШ 1,2; 95% ДІ 1,010-1,030; p<0,001), альбумін вихідний (ВШ 0,796; 95% ДІ 0,661-0,959; p<0,05), мінімальний альбумін (ВШ 0,716; 95% ДІ 0,593-0,864; p<0,001), мінімальний рівень eGFR (ВШ 0,951; 95% ДІ 0,972; p<0,001), оцінка INDEX PLRI (ВШ 1,7; 95% ДІ 1,3–2,2; p<0,001), оцінка за шкалою PADUA (ВШ 4,49; 95% ДІ (,25-8,94; p<0,001), дихальна недостатність (ВШ 22,6; 95% ДІ (7,79-65,6; p<0,001), ураження паренхіми на МСКТ, % (ВШ 1,04; 95% ДІ 1,02-1,060; p<0,001), тяжкість ураження легень на МСКТ (ураження легеневої паренхіми) понад 50% (ВШ 4,96; 95% ДІ 2,08-11,8; p<0,001), гіпертонія в анамнезі (ВШ 2,38; 95% ДІ 1,1–5,1; p = 0,026).*

Висновок. Ми використовували моделі для прогнозування ризику смерті. Площа під кривою дорівнює 0,976, при 95% довірчому інтервалі (ДІ) 0,951 – 1. У пороговій точці 0,366, чутливість становить 95%, а специфічність – 92,6%. Ми створили веб-версію калькулятора летальності COVID-19, який також працює в Excel і може бути корисним при вірусній або бактеріальній пневмонії. Калькулятор доступний в Інтернеті. Ми пропонуємо зосередитися на клінічних станах та супутніх захворюваннях при прийнятті рішень щодо доцільності госпіталізації, незважаючи на відсутність даних щодо декомпенсації цукрового діабету, оскільки ми не виявили різниці в групах за рівнем HbA1c (p=0,0662). Дихальна недостатність може погіршуватися прогресуюче, тому необхідно контролювати клінічні дані. В анамнезі ми проаналізували наявність гіпертонічної хвороби, цукрового діабету та серцево-судинних захворювань (ішемічна хвороба серця, інсульт, інфаркт міокарда та ін.). Ми не акцентували увагу на декомпенсації діабету чи дестабілізації серцевих захворювань, оскільки в умовах пандемії наявність SARS-CoV-2 могла швидко вплинути на важкий перебіг COVID-19, що було доведено численними дослідженнями та клінічними рекомендаціями. За наявності достатніх ресурсів доцільно госпіталізувати пацієнтів з неінфекційними захворюваннями

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після оцінки ризику до швидкого зниження SpO2. У обговорюваних випадках Калькулятор для оцінки супутніх захворювань може бути використаний як додатковий інструмент (площа під ROC кривою 0.766, 95% ДІ 0.548 – 0.984. В точці відсікання 0.244, чутливість становить 87,5% і специфічність 68,8%. Ми пропонуємо додати інформацію про критерії госпіталізації щодо основних захворювань, а не вікових факторів. Як і у людей похилого віку, ми отримали порівнянні результати щодо ризиків у молодших осіб з ознаками метаболічного синдрому або інших неінфекційних захворювань. Для оцінки ІМТ необхідні подальші дослідження, оскільки в нашій когорті була незначна інформація про антропологічні дані. Для кращого розуміння впливу жирової тканини на результати запальних лабораторій слід використовувати дані міжнародних досліджень, зосередитися на оцінці результатів для населення України та оцінювати ризик індивідуально.

Ключові слова: політика в охороні здоров'я, громадське здоров'я, неінфекційні хронічні захворювання, пневмонія, лінійні моделі, надання медичної допомоги, метаболічний синдром.