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International register "Dynamics analysis of comorbidities in SARS-CoV-2 survivors" (AKTIV SARS-CoV-2): analysis of predictors of short-term adverse outcomes in COVID-19

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The international AKTIV register presents a detailed description of out- and inpatients with COVID-19 in the Eurasian region. It was found that hospitalized patients had more comorbidities. In addition, these patients were older and there were more men than among outpatients. Among the traditional risk factors, obesity and hypertension had a significant negative effect on prognosis, which was more significant for patients 60 years of age and older. Among comorbidities, CVDs had the maximum negative effect on prognosis, and this effect was more significant for patients 60 years of age and older. Among other comorbidities, type 2 and 1 diabetes, chronic kidney disease, chronic obstructive pulmonary disease, cancer and anemia had a negative impact on the prognosis. This effect was also more significant (with the exception of type 1 diabetes) for patients 60 years and older. The death risk in patients with COVID-19 depended on the severity and type of multimorbidity. Clusters of diseases typical for deceased patients were identified and their impact on prognosis was determined. The most unfavorable was a cluster of 4 diseases, including hypertension, coronary artery disease, heart failure, and diabetes mellitus. The data obtained should be taken into account when planning measures for prevention (vaccination priority groups), treatment and rehabilitation of COVID-19 survivors.

Keywords: AKTIV register, COVID-19, multimorbidity, mortality predictors.

Relationships and Activities: none.

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For more than a year, the coronavirus disease 2019 (COVID-19) pandemic continues, which has covered almost all countries of the world and claimed 2978935 lives (according to the World Health Organization as of April 16, 2021) [1]. To assess the specifics of COVID-19 in the Eurasian region, an international register "Dynamics analysis of comorbidities in SARS-CoV-2 survivors" (AKTIV) was created [2], which was attended by specialists from 7 countries: Russian Federation, Republic of Armenia, Republic of Belarus, Republic of Kazakhstan, Kyrgyz Republic, Republic of Moldova, Republic of Uzbekistan.

The central aim of the register is to assess the impact of multimorbidity, various combinations of comorbidities and risk factors (RF) (obesity, smoking, hypertension (HTN), age over 60 years) on the risk of a severe COVID-19 course and death, as well as to analyze the effect of SARS-CoV-2 infection on the course of main noncommunicable diseases and cancer.

The design and statistical analysis methods of the register, as well the first data (n=1000) were presented in detail in previous publications [3-5]. It should be noted that analysis of the complete cohort of patients (n=5808) confirmed the patterns that were found in the preliminary analysis [5], and new patterns were also found.

Results

The register included 5808 patients with COVID-19: 4751 (81,8%) inpatients and 1057 (18,2%) outpatients (Table 1). The diagnosis was confirmed by polymerase chain reaction (PCR) test in 67,6%, while in the rest of the patients the diagnosis was made based on clinical performance and lung computed tomography (CT). The mean age of patients was 58 [48, 68] years: women — 53,6% (mean age, 59 [49, 68] years), men — 46,4% (mean, 57 [46, 66] years). Women were significantly older than men (p<0,0001). The distribution of patients according to the degree of lung damage according

Table 1

Characteristics of in- and outpatients included in the AKTIV register

	Inpatients (1)	Outpatients (2)	P for difference between 1 and 2	Total cohort (% of condition/outcome across the entire sample)
N	4751	1057	-	5808
Age, years	59,00 [50, 69]	49,90 [38, 60]	<0,001	58 [48, 68]
Women, %	53,61	58,09	0,01	54,42
Deceased, %	7,56	0,30	<0,01	6,17
HTN, %	60,85	30,84	<0,01	55,41
Obesity, % BMI ⩾30 kg/m^2	38,11	24,84	<0,01	35,54
Smoking, %	4,61	7,76	<0,01	5,18
CAD, %	23,10	9,43	<0,01	20,62
Prior myocardial infarction,%	6,57	1,96	<0,01	5,73
Prior history, %	4,85	1,67	<0,01	4,27
T2D, %	19,20	9,92	<0,01	17,52
HF, %	19,10	3,80	<0,01	16,30
Class I-II HF, %	12,2	3,40	<0,01	10,60
Class III-IV HF, %	6,80	0,40	<0,01	5,60
AF, %	7,83	2,06	<0,01	6,78
CKD, %	8,11	4,91	<0,01	7,53
COPD, %	5,39	1,28	<0,01	4,65
Asthma, %	3,33	3,05	0,65	3,28
Active cancer, %	2,20	1,77	0,39	2,12

Abbreviations: HTN — hypertension, CAD — coronary artery disease, MI — myocardial infarction, BMI — body mass index, T2D — type 2 diabetes, AF — atrial fibrillation, CKD — chronic kidney disease, COPD — chronic obstructive pulmonary disease, HF — heart failure.

to CT data was presented as follows: CT 0 (normal and absence of CT signs of viral pneumonia) — 5,2%, CT 1 (pulmonary parenchymal involvement ⩽25%) — 29,6%, CT 2 (pulmonary parenchymal involvement of 25-50%) — 34,7%, CT 3 (pulmonary parenchymal involvement of 50-75%) — 18,8% and CT 4 — 11,6% (diffuse ground glass opacities, pulmonary parenchymal involvement more than 75%). The overall mortality rate was 6,2%, while the intrahospital mortality rate — 7,6%. Non-invasive and invasive mechanical ventilation (MV) was performed in 14,3% of cases. In the group of patients receiving mechanical ventilation, the mortality rate was 36,7%.

The most common complication of COVID-19 according to the AKTIV register was a cytokine storm (23,2%), followed by bacterial pneumonia (9,7%), acute kidney injury (AKI) (9,0%), acute respiratory distress syndrome (ARDS) (5,9%), pulmonary embolism (PE) (0,61%), stroke (0,47%), deep vein thrombosis (DVT) (0,44%), and myocarditis (0,25%).

The majority of patients had several comorbidities (Table 1). Among comorbid pathologies, the most common were HTN — 55,41%, obesity — 35,54%, coronary artery disease (CAD) — 20,62%, type 2 diabetes (T2D) — 17,52%, heart failure (HF) — 16,3%, class I-II HF — 10,6%, class III-IV HF — 5,7%, chronic kidney disease (CKD) — 7,53%, atrial fibrillation (AF) — 6,78%, prior myocardial infarction (MI) — 5,73% and stroke — 4,27%, chronic obstructive pulmonary disease (COPD) — 4,65%, asthma — 3,28%, active cancer — 2,12%.

It is noteworthy that hospitalized patients were older than outpatients: 59,00 [50-69] vs 49,90 [38-60] years (p<0,0001). Among hospitalized patients compared with outpatients, there were fewer women (53,61 vs 58,09%, p=0,01), more patients with HTN (60,85 vs 30,84%, p<0,001) and obesity (38,11 vs 24,84%, p<0,001), but fewer smokers (4,61 vs 7,76%, p<0,001). Hospitalized patients more often than outpatients had CAD (23,10 vs 9,43%, p<0,001), prior MI (6,57 vs 1,96%, p<0,001) and stroke (4,85 vs 1,67%, p<0,001), T2D (19,20 vs 9,92%, p<0,001) and HF (19,10 vs 3,80%, p<0,001), both class I-II and III-IV (Table 1). In addition, hospitalized patients were more likely to have AF (7,83 vs 2,06%, p<0,001), CKD (8,11 vs 4,91%, p<0,001), and COPD (5,39 vs 1,28%, p<0,001).

Thus, hospitalized patients were more severe, older and there were more men among them than among outpatients.

Comparative analysis of surviving and deceased patients

When comparing deceased and surviving patients, predictors of intrahospital mortality were determined (Table 2). This is, first of all, the age ⩾60 years; this factor was more important for men (odds ratio (OR), 3,055 (95% confidence interval (CI), 2,418-3,86) p<0,001) than for women (OR, 1,462 (95% CI, 1,154-1,852) p<0,001). The mean age of the deceased and surviving patients was 70,24 [62, 80] and 56,65 [47, 67] years (p<0,001), respectively. Male sex was also an unfavorable prognostic factor that increased the death risk by one and a half times (OR, 1,529 (95% CI, 1,22-1,92) p<0,001). It is noteworthy that an extremely unfavorable factor is a positive PCR test at visit 3, i.e. 10-20 days after the admission. Grade 3 and 4 CT lung involvement increased the risk of death almost 4 times compared to grade 1-2. HTN increased the death risk by more than 3 times (OR, 3,123 (95% CI, 2,324-4,198) p<0,001), and this pattern was more pronounced for patients ⩾60 years of age (Table 2). Obesity was an unfavorable factor only for patients aged ⩾60 years (OR, 2,067 (95% CI, 1,558-2,743)), but a reduced body mass index (BMI) <18,5 kg/m^2 was also more often observed in deceased patients in comparison with survivors (2,79% vs 0,82%, respectively, p=0,01). Thus, among traditional RFs, obesity and HTN had a significant negative effect on prognosis, which was more pronounced for patients aged ⩾60 years.

Among comorbidities, CAD had a pronounced negative effect on the prognosis of patients, which was associated with an increase in the death risk by almost 4 times (OR, 3,829 (95% CI, 3,032-4,836) p<0,001). With age adjustment, this pattern persisted only for patients aged ⩾60 years. Prior MI also negatively affected the prognosis of patients, being associated with an increased risk of death (OR, 3,005 (95% CI, 2,165-4,170) p<0,001). Prior stroke had an even stronger negative effect on prognosis, which increased the risk by 5 times (OR, 5,02 (95% CI, 3,592-7,015) p<0,001). Any type of AF increased the mortality risk by more than 4 times (OR, 4,239 (95% CI, 3,17-5,669) p<0,001). With age

Table 2

Characteristics of survivors and deceased inpatients from the AKTIV register

Parameter	Total cohort, N=4751	Survivors, N=4390	Deceased patients, N=361	P	OR (95% CI)
Men, %	46,39	45,63	56,21	<0,01	1,529 (1,22-1,92)
Age, years	59,00 [50, 69]	56,65 [47, 67]	70,24 [62, 80]	<0,01	
Age <40 years, %		9,96	1,87	<0,01	
Age of 40-59 years, %		40,84	17,13		
Age of 60-80 years, %		42,41	52,96		
Age >80 years, %		6,79	28,04		
Male age ⩾60, %		20,20	43,61	<0,01	3,055 (2,418-3,86)
Female age ⩾60, %		29,00	37,38	<0,01	1,462 (1,154-1,852)
Positive 1st PCR test, %	63,66	62,12	74,26	<0,01	
Positive 2nd PCR test, %	18,10	16,32	35,60		
Positive 3rd PCR test, %	3,62	3,57	66,67		
CT 3-4, %	30,40	16,18	44,65	<0,01	4,178 (3,143-5,552)
HTN, %	55,41	59,88	82,33	<0,01	3,123 (2,324-4,198)
HTN ⩾60 years, %		38,78	70,57	<0,01	3,785 (2,946-4,862)
HTN <60 years, %		21,06	11,71	<0,01	0,497 (0,35-0,706)
Obesity (BMI ⩾30 kg/m^2), %	38,11	37,64	39,44	0,57	1,079 (0,829-1,404)
Obesity ⩾60 years, %		17,91	31,08	<0,01	2,067 (1,558-2,743)
Obesity <60 years, %		19,74	8,37	<0,01	0,371 (0,235-0,586)
BMI <18,5 kg/m^2, %	1,03	0,82	2,79	0,01	
BMI ⩾40 kg/m^2, %	4,78	4,51	7,57		
AF, %	7,83	6,59	23,03	<0,01	4,239 (3,17-5,669)
AF ⩾60 years, %		5,72	21,84	<0,01	4,606 (3,414-6,214)

Table 2. Continuation

Parameter	Total cohort, N=4751	Survivors, N=4390	Deceased patients, N=361	P	OR (95% CI)
AF <60 years, %		0,85	0,95	0,86	1,113 (0,339-3,649)
CAD, %	23,10	21,02	50,47	<0,01	3,829 (3,032-4,836)
CAD ⩾60 years, %		17,70	47,50	<0,01	4,195 (3,314-5,310)
CAD <60 years, %		3,20	2,80	0,71	0,877 (0,442-1,742)
Prior MI, %	6,57	6,00	16,10	<0,01	3,005 (2,165-4,170)
High Tn, %	5,85	5,05	16,33	<0,01	3,665 (1,542-8,712)
HF, %	19,10	14,50	44,00	<0,01	4,614 (3,633-5,859)
Class I-II HF, %	12,20	9,90	21,20	<0,01	2,446 (1,831-3,267)
Class III-IV HF, %	6,80	4,50	22,50	<0,01	6,124 (4,538-8,266)
Prior stroke, %	4,85	3,93	17,03	<0,01	5,02 (3,592-7,015)
T2D, %	19,20	18,43	37,54	<0,01	2,659 (2,089-3,386)
T2D ⩾60 years, %		12,08	31,33	<0,01	3,32 (2,568-4,291)
T2D <60 years, %		6,34	6,33	0,99	0,998 (0,623-1,599)
T1D, %	0,39	0,34	1,26	0,01	3,79 (1,228-11,691)
T1D ⩾60 years, %		0,05	0,32	0,09	6,132 (0,554-67,808)
T1D <60 years, %		0,28	0,95	0,05	3,358 (0,932-12,1)
CKD, %	8,11	7,01	20,19	<0,01	3,358 (2,486-4,536)
CKD ⩾60 years, %		4,92	17,09	<0,01	3,987 (2,874-5,53)
CKD <60 years, %		2,07	3,16	0,20	1,546 (0,793-3,014)
COPD, %	5,39	5,09	9,78	<0,01	2,02 (1,358-3,005)
COPD ⩾60 years, %		3,80	8,54	<0,01	2,363 (1,541-3,623)
COPD <60 years, %		1,29	1,27	0,97	0,978 (0,351-2,726)
Active cancer, %	2,20	2,07	5,05	<0,01	2,517 (1,453-4,36)
Cancer ⩾60 years, %		1,35	4,11	<0,01	3,146 (1,694-5,842)
Cancer <60 years, %		0,72	0,95	0,65	1,313 (0,397-4,344)
Anemia, % Hb in men <130 г/л Hb in women <120 г/л	18,08	16,67	35,04	<0,01	2,697 (2,073-3,508)

Abbreviations: HTN — hypertension, CI — confidence interval, CAD — coronary artery disease, MI — myocardial infarction, BMI — body mass index, CT — computed tomography, OR — odds ratio, PCR — polymerase chain reaction, T1D — type 1 diabetes, T2D — type 2 diabetes, Tn — troponin, AF — atrial fibrillation, CKD — chronic kidney disease, COPD — chronic obstructive pulmonary disease, HF – heart failure, Hb — hemoglobin.

adjustment, this pattern persisted only for patients aged ⩾60 years. HF of any functional class was associated with a poor prognosis, increasing the death risk by more than 4 times (OR, 4,614 (95% CI, 3,633-5,859) p<0,001). With class I-II and III-IV HF, the risk increased almost 2,5 times (OR, 2,446 (1,831-3,267) p<0,001) and 6 times (OR, 6,14 (4,538-8,266) p<0,001), respectively.

T2D was associated with a death risk (OR, 2,659 (95% CI, 2,089-3,386) p<0,001) predominantly for patients aged ⩾60 years. Type 1 diabetes (T1D) as also associated with a risk of death (OR, 3,790 (95% CI, 1,228-11,691) p<0,001), but mainly for patients under 60 years of age (Table 2). CKD was a strong risk factor for lethal outcome (OR, 3,358 (95% CI, 2,486-4,536) p<0,001), which was most significant for patients aged ⩾60 years. Among the deceased patients with CKD, the proportion of patients with a glomerular filtration rate (GFR) <45 ml/min/1,73 m^2 was 40,6%, and among survivors with CKD, the proportion of patients with a GFR <45 ml/min/1,73 m^2 was only 11,5% (p<0,001). COPD significantly increased the death risk (OR, 2,02 (CI 95% 1,358-3,005) p<0,001). With age adjustment, this pattern persisted only for patients aged ⩾60 years. Active cancer was also associated with the death risk (OR, 2,517 (1,453-4,36) p<0,001), which was most significant for patients over 60 years of age. Anemia was associated with an increased death risk by more than 2,5 times (OR, 2,697 (2,073-3,508) p<0,001). The deceased patients had a lower hemoglobin level (127,05 vs 134,51 g/l, p<0,001). Thus, among

Table 3

Characteristics of survivors and deceased inpatients from the AKTIV register, depending on the degree and type of multimorbidity

	Survivors, N=4390	Deceased patients, N=361	P	OR (95% CI)
No comorbidities, %	21,44	4,88	<0,01	-
1 comorbidity, %	26,49	10,57		-
2-3 comorbidities, %	33,98	32,52		-
⩾4 comorbidities, %	18,09	52,03		-
⩾2 comorbidities, ⩾60 years, %	34,85	71,14	<0,01	4,608 (3,462-6,132)
⩾3 comorbidities, <60 years, %	17,17	13,41	0,13	0,747 (0,512-1,091)
⩾2 comorbidities and obesity, ⩾60 years, %	11,78	27,24	<0,01	2,802 (2,072-3,79)
⩾2 comorbidities and obesity, <60 years, %	6,60	5,69	0,58	0,855 (0,489-1,494)
Diabetes + obesity + CVD*, %	9,53	19,11	<0,01	2,242 (1,595-3,151)
Diabetes + obesity + CVD* in patients aged ⩾60 years, %	5,99	13,82	<0,01	2,516 (1,699-3,725)
Diabetes + obesity + CVD* patients in patients aged <60 years, %	3,55	5,28	0,16	1,516 (0,84-2,739)
Most common combination of 2 diseases (HTN + Obesity)	26,12	36,99	<0,01	1,661 (1,266-2,178)
Most common combination of 2 diseases, 2nd place (HTN + CAD)	18,86	43,50	<0,01	3,311 (2,532-4,33)
Most common combination of 2 diseases, 3rd place (HTN + HF)	15,82	42,68	<0,01	3,963 (3,022-5,197)
Most common combination of 3 diseases (HTN + CAD + HF)	10,74	32,93	<0,01	4,082 (3,054-5,455)
Most common combination of 3 diseases, 2nd place (HTN + Obesity + Diabetes)	9,10	17,89	<0,01	2,177 (1,535-3,086)
Most common combination of 3 diseases, 3rd place (HTN + Obesity + CAD)	7,42	16,26	<0,01	2,421 (1,68-3,488)
Most common combination of 4 diseases (HTN + CAD + HF + Obesity)	3,98	13,82	<0,01	3,869 (2,578-5,806)
Most common combination of 4 diseases, 2nd place (HTN + CAD + HF + Diabetes)	3,55	13,41	<0,01	4,215 (2,784-6,382)
Most common combination of 4 diseases, 3rd place (HTN + CAD + HF + OMI)	3,65	10,16	<0,01	2,990 (1,896-4,716)

Note: * — CVD = HTN, CAD, MI, stroke, DVT, HF.

Abbreviations: HTN — hypertension, CI — confidence interval, CAD — coronary artery disease, MI — myocardial infarction, OR — odds ratio, OMI — old myocardial infarction, CVD — cardiovascular disease, DVT — deep vein thrombosis, HF — heart failure.

comorbidities, cardiovascular diseases (CVDs) had the maximum negative effect on prognosis, and this effect was more significant for patients aged ⩾60 years. Among other comorbidities, T2D, T1D, CKD, COPD, cancer and anemia had a negative impact on the prognosis. This effect was also more significant (with the exception of T1D) for patients aged ⩾60 years.

One of the most significant risk factors for lethal outcomes was the multimorbidity. So, among the deceased patients, there were only 4,88% without comorbidities, while among the surviving ones — 21,44% (p<0,001) (Table 3). Four or more comorbidities were present in 52,03% and 18,09% of deceased and surviving patients, respectively (p<0,001). With age adjustment, multimorbidity as RF was most significant for patients aged 60 years and older. For such patients, the presence of 2 or more comorbidities was associated with an increased death risk by more than 4,5 times (OR, 4,608 (95% CI, 3,462-6,132) p<0,001). We analyzed the influence of the most common combinations of comorbidities on the death risk. Among the most common combinations of two diseases, the most significant negative effect on the prognosis had a combination of HTN and HF (OR, 3,963 (95% CI, 3,022-5,197) p<0,001). This combination of two diseases occurred in 43,5% of deceased patients and only in 18,9% of survivors. Among the common combinations of three diseases, the combination of HTN, CAD and HF had a great adverse effect on the prognosis (OR, 4,082 (95% CI, 3,054-5,455) p<0,001). This cluster of diseases was observed in 32,93% and 10,74% of deceased and surviving patients, respectively. Among the common combinations of four diseases, the combination of

Table 4

Characteristics of survivors and deceased patients included in the AKTIV register

	Survivors, N=4944	Deceased patients, N=325	p
Age, years	56,65 [47, 67]	70,24 [62, 80]	<0,01
SBP, mm Hg	127,79 [120, 136]	127,96 [110, 140]	0,94
RR	19,84 [18, 21]	23,49 [20, 26]	<0,01
Heart rate	85,98 [77, 94]	92,47 [80, 100]	<0,01
SaO_2, %	94,41 [93, 97]	85,78 [82, 92]	<0,01
Hb, g/L	134,51 [125, 146]	127,05 [111, 144]	<0,01
WBC, ×10*9/L	6,64 [4,5, 7,87]	9,19 [5,8, 11,7]	<0,01
Lymphocytes, %	22,39 [12,55, 31,55]	13,31 [6, 18]	<0,01
Platelets ×10*9/L	225,36 [166, 267]	202,89 [150, 256]	<0,01
CRP, mg/L	54,24 [10, 77]	102,52 [20,5, 160]	<0,01
D-dimer, μg FEU/ml	1,62 [0,3, 1,5]	2,4 [0,6, 2,8]	<0,01
GFR, ml/min/1,73 m^2	73,08 [57,79, 89,78]	53,65 [35,32, 72,92]	<0,01
AST, U/Ll	38,38 [22, 43]	64,81 [27,6, 62,3]	<0,01
Glucose, mmol/L	6,41 [5, 6,97]	8,37 [5,5, 9,6]	<0,01
Glucose in patients with T2D, mmol/L	9,19 [6,1, 11]	10,38 [6,7, 12,85]	0,02
Glucose in patients with T1D, mmol/L	11,05 [6,9, 14,2]	12,12 [3,86, 20,38]	0,778
Fibrinogen, g/L	4,64 [3,5, 5,5]	4,50 [3,39, 5,5]	0,13
Procalcitonin, ng/ml	0,62 [0,05, 0,3]	2,09 [0,2, 1,06]	<0,01
Troponin T, ng/ml	0,01 [0, 0,02]	0,21 [0,03, 0,36]	<0,01
Troponin I, ng/ml	0,26 [0, 0,1]	0,25 [0,01, 0,14]	0,12
Total cholesterol, mmol/L	4,57 [3,63, 5,3]	3,6 [2,96, 4,08]	<0,01
LDL-C, mmol/L	2,63 [1,9, 3,2]	1,94 [1,43, 2,3]	0,02
Triglycerides, mmol/L	1,46 [1, 1,88]	1,4 [0,99, 1,69]	0,91
Potassium, mmol/L	4,11 [3,8, 4,5]	4,17 [3,6, 4,6]	0,97

Abbreviations: AST — aspartate aminotransferase, TC — total cholesterol, SBP — systolic blood pressure, T1D — type 1 diabetes, T2D — type 2 diabetes, GFR — glomerular filtration rate, CRP — C-reactive protein, RR — respiratory rate, HR — heart rate, LDL-C — low density lipoprotein cholesterol, Hb — hemoglobin, SaO_2 — blood oxygen saturation.

HTN, CAD, HF and diabetes was most associated with a negative prognosis (OR, 4,215 (2,784-6,382) p<0,001). This cluster of diseases occurred in 13,41% and 3,55% of deceased and surviving patients, respectively. Thus, the death risk in patients with COVID-19 depended on the degree and type of multimorbidity; the most unfavorable factor was the presence of 4 or more comorbidities, among which the most unfavorable cluster was a combination of HTN, CAD, HF and diabetes.

Analysis of clinical and laboratory data (Table 4) revealed that subsequently deceased patients had a higher respiratory rate (23,49 vs 19,84, p<0,001), a higher heart rate (92,47 vs 85,98, p<0,001), and lower blood oxygen level (SaO_2) (85,78 vs 94,41%, p<0,001). The deceased patients had a high level of white blood cells (9,19 vs 6,64 × 10*9/L, p<0,001), a reduced proportion of lymphocytes (13,31 vs 22,39%, p<0,001) and platelet count (202,89 vs 225,36 × 10*9/L, p<0,001).

The deceased patients had a higher level of C-reactive protein (CRP) (102,52 vs 54,24 mg/L, p<0,001), D-dimer (2,40 vs 1,62 μg FEU/ml, p<0,001), troponin (Tn) T (0,21 vs 0,01 ng/ml), and procalcitonin (2,09 vs 0,62 ng/ml, p<0,001). An increase in the Tn level was observed in 16,33% of deceased patients and was a RF for lethal outcome (OR, 3,665 (95% CI, 1,542-8,712) p<0,001).

It was noteworthy that the deceased patients had a lower GFR (53,65 vs 73,08 ml/min/1,73 m^2, p<0,001) and a high level of aspartate aminotransferase (AST) (64,81 vs 38,38 U/L, p<0,001). The deceased patients were characterized by hyperglycemia both in the general cohort of patients (8,37 vs 6,41 mmol/L, p<0,001) and in those with T2D (10,38 vs 9,19 mmol/L, p<0,02). In addition, the deceased patients had lower levels of total cholesterol (3,60 vs 4,57 mmol/L, p<0,001) and low-density lipoprotein cholesterol (1,94 vs 2,63 mmol/L, p<0,001).

Table 5

Characteristics of survivors and deceased inpatients from the AKTIV register, depending on the complications developed

	Survivors, N=4390	Deceased patients, N=361	P	OR (95% CI)
DVT, %	0,41	0,93	0,17	2,305 (0,668-7,953)
PE, %	0,33	5,59	<0,01	17,877 (8,677-36,832)
Stroke, %	0,30	3,73	<0,01	12,665 (5,643-28,425)
Bacterial pneumonia, %	11,40	14,91	0,06	1,361 (0,986-1,878)
ARDS, %	3,30	55,59	<0,01	36,667 (27,688-48,556)
Cytokine storm, %	22,45	35,97	<0,01	1,94 (1,355-2,777)
AKI, %	6,52	43,50	<0,01	11,04 (7,846-15,535)
Myocarditis, %	0,30	0,31	0,99	1,019 (0,132-7,863)
Sepsis, %	0,13	4,04	<0,01	33,093 (11,722-93,43)

Abbreviations: CI — confidence interval, AKI — acute renal injury, ARDS — acute respiratory distress syndrome, OR — odds ratio, DVT — deep vein thrombosis, PE — pulmonary embolism.

In the group of deceased patients, severe COVID-19 complications, such as PE (5,59 vs 0,33%, p<0,001), were more often observed, which was associated with an almost 18-fold increased risk of death (OR, 17,877 (95% CI, 8,677- 36,832) p<0,001) (Table 5). Strong risk factors for lethal outcome were ARDS (OR, 36,667 (95% CI, 27,688-48,556) p<0,001) and sepsis (OR, 33,093 (95% CI, 11,722-93,43)). The development of stroke (OR, 33,093 (95% CI, 11,722-93,43) p<0,001) and AKI (OR, 11,04 (95% CI, 7,846-15,535) p<0,001) significantly increased the risk of death. Cytokine storm (OR, 1,94 (95% CI, 1,355-2,777) p<0,001) and bacterial pneumonia (OR, 1,361 (95% CI, 0,986-1,878)) also increased the death risk in COVID-19 patients. Thus, the most common complications in deceased patients were ARDS (55,59%), AKI (43,50%), cytokine storm (35,97%). Bacterial pneumonia (14,91%), PE (5,59%), sepsis (4,04%) and stroke (3,73%) were somewhat less common. The rare complications were deep vein thrombosis (0,93%) and myocarditis (0,31%).

Conclusion

In terms of sex-related parameters, the AKTIV register patients did not differ significantly from those included in the foreign registries: for comparison, the mean age in the AKTIV register was 63,4 years, which is similar to the registries of China — 64 years [6], USA — 63 years [7], Italy — 63 years [8] and slightly less than in the registers of Spain — 69 years [9] and Great Britain — 73 years [10]. The proportion of women in the AKTIV register was higher (54%) than in the following foreign registers: Italy (18%) [8], Great Britain (40%) [10], USA (40%) [7], Spain (43%) [9] and China (51%) [6]. Mortality in the total cohort was 6,2%, which is higher than in the registries from China (2,3% and 3,2%) [11, 12], in the registry that included patients from the United States and China (4,8%) [13], but slightly lower than in the Italian register (7,2%) [14]. Intrahospital mortality rate in the AKTIV register (7,6%) is lower than in other studies. Thus, according to observational study from the United States, among 2634 inpatients, 21% died [7]. According to the meta-analysis by Abate SM, et al., which included 32 studies and 23082 patients, intrahospital mortality was 15%, while a range of this parameter was 1-52% in different countries [15]. The low intrahospital mortality rate according to the AKTIV register may be due to the fact that patients with a mild COVID-19 were often hospitalized in the Eurasian region, especially in the spring and summer of 2020.

According to the AKTIV register, the most common complication of COVID-19 was a cytokine storm (23,2%), followed by bacterial pneumonia (9,7%), AKI (9,0%), and ARDS (5,9%). According to various studies, cytokine storm was observed in 10-20% of patients with COVID-19 [16, 17], which is consistent with our data. The incidence of AKI according to the AKTIV register corresponds to the meta-analysis by Hansrivijit P, et al. with 26 included studies (n=5497), according to which the average incidence of AKI in COVID-19 patients was 8,4% (95% CI, 6,0-11,7%) with an average renal replacement therapy prevalence of 3,6% (95% CI, 1,8-7,1%) [18].

ARDS in patients from the AKTIV register was observed less frequently than in other studies. For example, one of the first Chinese reports indicated that ARDS occurred in 31% of cases [17]. According

to the meta-analysis by Abate SM, et al., ARDS was diagnosed in 32% of patients [15], which indicates a more severe contingent of hospitalized patients in these studies.

The incidence of in-life diagnosed thrombotic events according to the AKTIV register was less than in other studies: PE — 0,61%, stroke — 0,47%, DVT — 0,44%. According to the Bilaloglu S, et al., the incidence of DVT, PE, and stroke was 3,9%, 3,2%, and 1,6% [19]. According to the study by Mestre-Gómez B, et al., in-life PE was diagnosed in 6,4% of patients [20]. During lower limb deep vein ultrasound, DVT was detected in 46,1% of cases [21]. The low incidence of in-life diagnosed thrombotic events in the AKTIV register is probably due to the fact that in actual clinical practice a targeted search for these conditions was rarely carried out, and lower limb vein ultrasound and multislice computed tomography-angiopulmonography were not performed.

Myocarditis according to the AKTIV register was found in 0,25% of cases, which is much less common than according to Wang D, et al. (7,2%) [22] and according to autopsy studies — 4,5% and 7,2% [23, 24].

Patients in the AKTIV register and a high level of multimorbidity with a predominance of CVD, which coincides with the other studies. The incidence of HTN in hospitalized patients in the AKTIV registry (60,8%) was slightly higher than in the US (45,6%) [7], Italian (48,8%) [8], Chinese registries (30,5%) [6]. According to the large meta-analysis, which included 45 meta-analyzes, the incidence of HTN in all categories of COVID-19 patients was 27% (95% CI, 27-28) [25]. Obesity was observed in a third of the AKTIV register patients (35,5%), which was slightly less than in the register from the USA (41,7%) [7], and more than in the Spanish register (21,2%) [9].

The incidence of coronary artery disease in hospitalized patients in the AKTIV register (23,1%) was close to the data of the Italian register (21,4%) [8], was slightly less than in the US register (27,8%) [7], and significantly more than in the register from China (14,7%) [6]. Attention was drawn to the incidence of HF in patients of the AKTIV register — 16,3%, which was significantly higher than in the registers of the United States (6,9%) [7] and Spain (9,2%) [9].

The incidence of diabetes in the AKTIV register patients (17,5%) was close to that in the register from Italy (17%) [8], Spain (19,4%) [9] and China (14,4%) [6], but was significantly lower than in the US (33,8%) [7] and UK (29,8%) registries [10]. The prevalence of CKD in the AKTIV register patients (7,5%) was close to the register from Spain (6,1%) [9] and significantly more common than in the registers from Italy (3,0%) [8], China (3,4%) [6] and USA (5,0%) [7], and less common more than 2 times than in the UK register (16,0%) [10].

According to the AKTIV register, the death predictors was the age ⩾60 years, which increased the risk for men 3 times, and for women almost 1,5 times, which coincides with the other studies [17, 26-28]. Male sex also had a death risk, increasing the risk by one and a half times, which was noted in many observational studies. Thus, according to the study by Abate SM, et al., men had a 37% higher risk of death compared to women [15].

According to the AKTIV register, among the comorbidities, CVDs had the most unfavorable effect on the prognosis. Thus, HTN and CAD increased the death risk by 3 and almost 4 times, respectively. This is slightly more than in the meta-analysis by Noor FM, et al. with 58 studies (n=122191), which showed that HTN and CAD increases the risk by 2,1 and 3,6 times, respectively [29]. According to the meta-analysis by Parohan M, et al. (14 studies, n=29909), HTN and CAD increases the risk by 2,7 and 3,7 times, respectively [30]. According to the AKTIV register, HF of any functional class is associated with a poor prognosis, increasing the death risk by more than 4 times; severe class III-IV HF increased the death risk by 6 times. Similar findings were reported in the study by Tomasoni D, et al. involving 13 centers and 692 patients: HF was a strong independent predictor of increased intrahospital mortality (OR, 2,25, 95% CI 1,26-4,02, p=0,006) [31]. According to the study by Rey JR, et al., patients with HF were more likely to develop acute heart failure (11,2% vs 2,1%, p<0,001) and had a higher level of NT-proBNP. In addition, in the HF group, the mortality rate was higher (48,7% vs 19,0%, p<0,001) [32].

According to the AKTIV register, prior stroke was of great importance for the outcome, which increased the death risk by 5 times. According to the review by Trejo-Gabriel-Galán JM, prior stroke increases the death risk from COVID-19 by 3 times [33].

According to the AKTIV register, type 1 and 2 diabetes was associated with an increased risk of death by 3,8 and 2,7 times, respectively. Other researchers have also reported adverse effects of diabetes on prognosis. For example, according to the meta-analysis by Noor FM, et al. [29], diabetes increased the death risk by 1,9 times, and according to the meta-analysis by Parohan M, et al. [30] — 2,4 times. According to the AKTIV register, CKD was also associated with a poor prognosis, increasing the risk by more than 3 times, and the risk was maximally increased at a GFR <45 ml/min/1,73 m^2.

The meta-analysis by Noor FM, et al. [29] also indicated a 2,1-fold increase in the death risk in patients with CKD.

According to the AKTIV register, obesity in patients aged ⩾60 years was an unfavorable factor that increased the death risk by 2 times, but a significantly reduced body weight (BMI <18,5 kg/m^2) was also associated with a poor prognosis. Thus, U-shaped dependence of risk on the patient's body weight. The negative impact of obesity on prognosis has been reported by many researchers [29, 34]. Previously, it was also indicated that there is a U-shaped relationship between BMI and influenza pneumonia risk [35]. According to Zheng KI, et al., the association between obesity and the COVID-19 severity remained significant even after statistical adjustments for age, sex, smoking, diabetes, HTN, and dyslipidemia [36]. According to the AKTIV register, obesity posed the greatest danger for patients aged ⩾60 years. In contrast, Lighter J, et al. showed that obesity was more dangerous for patients younger than 60 years old [37].

According to the AKTIV register, any type of AF increased the death risk by more than 4 times. This factor represented the greatest risk for patients over 60 years of age. The incidence of AF in this registry was less (6,78%) than on other studies, according to which, among patients with COVID-19, AF was detected from 19% to 21% of all cases and was more common in patients with a severe COVID-19 course, and in the death cohort was observed in 44% of cases [38].

According to the current register, COPD had a negative impact on the prognosis, increasing the death risk by 2 times. According to the meta-analysis by Lippi G, et al., which included 7 studies involving 1592 COVID-19 patients, COPD was found to be significantly associated with severe COVID-19 (hazard ratio (HR), 5,69 (95% CI, 2,49-13,00) [39].

As for the effect of cancer on the COVID-19 severity, the literature data are contradictory. According to the AKTIV register, active cancer is a predictor of an unfavorable outcome and increases the death risk by 2,5 times, which was most significant for patients aged ⩾60 years. These data are consistent with the South Korean registry (n=7590), which showed that cancer is a predictor of a poor prognosis: among deceased patients, it was found significantly more often compared with survivors (11,9 vs 3,2%, p<0,001) [40].

According to the AKTIV register, anemia was a death predictor, increasing its risk by more than 2,5 times. The deceased patients had a lower hemoglobin level in comparison with the survivors: 127,05 (111-144) vs 134,51 (125-146) g/L (p<0,001). Similar data were found in the meta-analysis by Taneri PE, et al., which showed that, compared with moderate course, patients with severe COVID-19 had lower hemoglobin (weighted mean difference (WMD), -4,08 g/L (95% CI, -5, 12; -3,05) and red blood cell levels (WMD, -0,16×10^{12}/L (95% CI, -0,31; -0,014), as well as higher ferritin (WMD, -473,25 ng/ml (95% CI, 382,52; 563,98)); but unlike our study, this meta-analysis found a significant difference only in mean ferritin levels of 606,37 ng/ml (95% CI, 461,86; 750,88) between surviving and deceased patients but not in hemoglobin ones [41].

According to the AKTIV register, the most important risk factor of lethal outcome is multimorbidity, while a pattern is observed: the more comorbidities, the more unfavorable the prognosis in COVID-19. For patients aged ⩾60 years, the presence of 2 or more comorbidities was associated with an increased death risk by more than 4,5 times. According to other studies, multimorbidity was also a predictor of an unfavorable disease course. According to the meta-analysis by Abate SM, et al., mortality among COVID-19 inpatients was 2 times higher in those with any comorbidities compared with those without comorbidities (HR, 2,20 (95% CI, 1,75-2,77) [15]. According to the Cho SI registry, et al., age-adjusted Charlson comorbidity index (CCI) correlated with patient mortality, and an ICI threshold >3,5 provided the best cut-off point for predicting mortality [40]. Analysis of the AKTIV register revealed the most common clusters of comorbidities and their influence on the patient prognosis. The clusters were dominated by CVDs in various combinations and diabetes. Four-disease cluster (HTN, CAD, HF, diabetes) had the most unfavorable effect on the prognosis. No similar data were found in the available literature.

According to the AKTIV register, patients with a poor prognosis were characterized by a complete blood count abnormalities: a decrease in hemoglobin and lymphocyte (%) levels, platelet count, as well as an increase in white blood cell count. In addition, the deceased patients had higher levels of CRP, D-dimer, AST and troponin, which is consistent with the other studies [17]. According to the AKTIV register, a troponin increase was observed in 16,33% of deceased patients, which increased the death risk by more than 3,5 times. According to the meta-analysis by Bavishi C, et al. an increase in Tn level occurs in 20% of inpatients with COVID-19 [42]. Qin JJ, et al showed that increased Tn level is a strong predictor of 28-day mortality (HR, 7,12 (95% CI, 4,60-11,03, p<0,001) [43].

Conclusion

The international AKTIV register presents a detailed description of out- and inpatients with COVID-19

in the Eurasian region. Hospitalized patients had more comorbidities and were older, as well as there were more men than among outpatients. Among the traditional risk factors, obesity and HTN had a significant negative effect on prognosis, which was more significant for patients 60 years of age and older. Among comorbidities, CVDs had the maximum negative effect on prognosis, and this effect was more significant for patients 60 years of age and older. Among other comorbidities, type 2 and 1 diabetes, CKD, COPD, cancer and anemia had a negative impact on the prognosis. This effect was also more significant (with the exception of T1D) for patients 60 years and older. The death risk in patients with COVID-19 depended on the severity and type of multimorbidity. Clusters of diseases typical for deceased patients and their impact on prognosis were identified. The most unfavorable was a cluster of 4 diseases, including hypertension, coronary artery disease, heart failure, and diabetes mellitus. The data obtained should be taken into account when planning measures for prevention (vaccination priority groups), treatment and rehabilitation of COVID-19 survivors.

Relationships and Activities: none.

References

1. World Health Organization (WHO). https://www.who.int.
2. ClinicalTrials.gov: NCT04492384. https://clinicaltrials.gov.
3. Arutyunov GP, Tarlovskaya EI, Arutyunov AG, et al. International register "Analysis of Chronic Non-infectious Diseases Dynamics After COVID-19 Infection in Adult Patients (ACTIV SARS-CoV-2)". Kardiologiia. 2020;60(11):31-4. (In Russ.)
4. Arutyunov GP, Tarlovskaya EI, Arutyunov AG, et al. International register "Dynamics analysis of comorbidities in SARS-CoV-2 survivors" (AKTIV) and the register "Analysis of hospitalizations of comorbid patients infected during the second wave of SARS-CoV-2 outbreak" (AKTIV 2). Russian Journal of Cardiology. 2021;26(3):4358. (In Russ.) doi:10.15829/1560-4071-2021-4358.
5. Arutyunov GP, Tarlovskaya EI, Arutyunov AG, et al. International register "Dynamics analysis of comorbidities in SARS-CoV-2 survivors" (AKTIV SARS-CoV-2): analysis of 1,000 patients. Russian Journal of Cardiology. 2020;25(11):4165. (In Russ.) doi:10.15829/1560-4071-2020-4165.
6. Shi S, Qin M, Shen B, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol. 2020;5(7):802-10. doi:10.1001/jamacardio.2020.0950.
7. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area [published correction appears in doi:10.1001/jama.2020.7681]. JAMA. 2020;323(20):2052-9. doi:10.1001/jama.2020.6775.
8. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020;323(16):1574-81. doi:10.1001/jama.2020.5394.
9. Casas-Rojo JM, Antón-Santos JM, Millán-Núñez-Cortés J, et al. Clinical characteristics of patients hospitalized with COVID-19 in Spain: results from the SEMI-COVID-19 Registry [Características clínicas de los pacientes hospitalizados con COVID-19 en España: resultados del Registro SEMI-COVID-19] [published online ahead of print, 2020 Sep 9]. Rev Clin Esp (Barc). 2020;22(8):480-94. doi:10.1016/j.rceng.2020.07.003.
10. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ. 2020;369:m1985. doi:10.1136/bmj.m1985.
11. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-42. doi:10.1001/jama.2020.2648.
12. Hu Y, Sun J, Dai Z, et al. Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Virol. 2020;127:104371. doi:10.1016/j.jcv.2020.104371.
13. Sun P, Qie S, Liu Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis. J Med Virol. 2020;92(6):612-7. doi:10.1002/jmv.25735.
14. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. 2020;323(18):1775-6. doi:10.1001/jama.2020.4683.
15. Abate SM, Checkol YA, Mantefardo B. Global prevalence and determinants of mortality among patients with COVID-19: A systematic review and meta-analysis. Ann Med Surg (Lond). 2021;64:102204. doi:10.1016/j.amsu.2021.102204.
16. Moore JB, June CH. Cytokine release syndrome in severe COVID-19. Science. 2020;368:473-4. doi:10.1126/science.abb8925.
17. 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;395:1054-62. doi:10.1016/S0140-6736(20)30566-3.
18. Hansrivijit P, Qian C, Boonpheng B, et al. Incidence of acute kidney injury and its association with mortality in patients with COVID-19: a meta-analysis. J Investig Med. 2020;68(7):1261-70. doi:10.1136/jim-2020-001407.
19. Bilaloglu S, Aphinyanaphongs Y, Jones S, et al. Thrombosis in Hospitalized Patients With COVID-19 in a New York City Health System. JAMA. 2020;324(8):799-801. doi:10.1001/jama.2020.13372.
20. Mestre-Gómez B, Lorente-Ramos RM, Rogado J, et al. Incidence of pulmonary embolism in non-critically ill COVID-19 patients. Predicting factors for a challenging diagnosis. J Thromb Thrombolysis. 2021;51:40-6. doi:10.1007/s11239-020-02190-9.
21. Zhang L, Feng X, Zhang D, et al. Deep Vein Thrombosis in Hospitalized Patients With COVID-19 in Wuhan, China: Prevalence, Risk Factors, and Outcome. Circulation. 2020;142:114-28.
22. 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):1061-9. doi:10.1001/jama.2020.1585.
23. Kawakami R, Sakamoto A, Kawai K, et al. Pathological Evidence for SARS-CoV-2 as a Cause of Myocarditis: JACC Review Topic of the Week. J Am Coll Cardiol. 2021;77(3):314-25. doi:10.1016/j.jacc.2020.11.031.
24. Halushka MK, Vander Heide RS. Myocarditis is rare in COVID-19 autopsies: cardiovascular findings across 277 postmortem examinations. Cardiovascular Pathology. 2021;50:107300. doi:10.1016/j.carpath.2020.107300.
25. Naeini MB, Sahebi M, Nikbakht F, et al. A meta-meta-analysis: Evaluation of meta-analyses published in the effectiveness of cardiovascular comorbidities on the severity of COVID-19. Obes Med. 2021;22:100323. doi:10.1016/j.obmed.2021.100323.
26. Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ. 2020;371:m3731. doi:10.1136/bmj.m3731.

27. Karagiannidis C, Mostert C, Hentschker C, et al. Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study. Lancet Respir Med. 2020;8(9):853-62. doi:10.1016/S2213-2600(20)30316-7.
28. Ioannou GN, Locke E, Green P, et al. Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10 131 US Veterans With SARS-CoV-2 Infection. JAMA Netw Open. 2020;3(9):e2022310. doi:10.1001/jamanetworkopen.2020.22310.
29. Noor FM, Islam MM. Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis. J Community Health. 2020;45:1270-82. doi:10.1007/s10900-020-00920-x.
30. Parohan M, Yaghoubi S, Seraji A, et al. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. Aging Male. 2020;23(5):1416-24. doi:10.1080/13685538.2020.1774748.
31. Tomasoni D, Inciardi RM, Lombardi CM, et al. Impact of heart failure on the clinical course and outcomes of patients hospitalized for COVID-19. Results of the Cardio-COVID-Italy multicentre study. Eur J Heart Fail. 2020;22:2238-47.
32. Rey JR, Caro-Codón J, Rosillo SO, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. Eur J Heart Fail. 2020;22(12):2205-15. doi:10.1002/ejhf.1990.
33. Trejo-Gabriel-Galán JM. Stroke as a complication and prognostic factor of COVID-19. Neurologia. 2020;35(5):318-22. English, Spanish. doi:10.1016/j.nrl.2020.04.015.
34. Sattar N, McInnes IB, McMurray JJV. Obesity Is a Risk Factor for Severe COVID-19 Infection: Multiple Potential Mechanisms. Circulation. 2020;142:4-6. doi:10.1161/CIRCULATIONAHA.120.047659.
35. Phung DT, Wang Z, Rutherford S, et al. Body mass index and risk of pneumonia: a systematic review and meta-analysis. Obes Rev. 2013;14(10):839-57. doi:10.1111/obr.12055.
36. Zheng KI, Gao F, Wang XB, et al. Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease. Metabolism. 2020:154244. doi:10.1016/j.metabol.2020.154244.
37. Lighter J, Phillips M, Hochman S, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. Clin Infect Dis. 2020;71(15):896-7. doi:10.1093/cid/ciaa415.
38. Inciardi RM, Adamo M, Lupi L, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy [published correction appears in Eur Heart J. 2020 Dec 21;41(48):4591]. Eur Heart J. 2020;41(19):1821-9. doi:10.1093/eurheartj/ehaa388.
39. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). Respir Med. 2020;167:105941. doi:10.1016/j.rmed.2020.105941.
40. Cho SI, Yoon S, Lee HJ. Impact of comorbidity burden on mortality in patients with COVID-19 using the Korean health insurance database. Sci Rep. 2021;11(1):6375. doi:10.1038/s41598-021-85813-2.
41. Taneri PE, Gómez-Ochoa SA, Llanaj E, et al. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. Eur J Epidemiol. 2020;35(8):763-73. doi:10.1007/s10654-020-00678-5.
42. Bavishi C, Bonow RO, Trivedi V, et al. Acute myocardial injury in patients hospitalized with COVID-19 infection: A review [published online ahead of print, 2020 Jun 5]. Prog Cardiovasc Dis. 2020;S0033-0620(20)30123-7. doi:10.1016/j.pcad.2020.05.013.
43. Qin JJ, Cheng X, Zhou F, et al. Redefining cardiac biomarkers in predicting mortality of inpatients with COVID-19 [published online ahead of print, 2020 Jul 14]. Hypertension. 2020;76:1104-12. doi:10.1161/HYPERTENSIONAHA.120.15528.