Obesity Research & Clinical Practice 15 (2021) 275–280

Contents lists available at ScienceDirect

Obesity Research & Clinical Practice

journal homepage: www.elsevier.com/locate/orcp

Original Article

Does there exist an obesity paradox in COVID-19? Insights of the international HOPE-COVID-19-registry

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ARTICLE INFO

Article history:
Received 25 February 2021
Accepted 26 February 2021

Keywords:
COVID-19
SARS-CoV-2
Obesity paradox
BMI

ABSTRACT

Background: Obesity has been described as a protective factor in cardiovascular and other diseases being expressed as 'obesity paradox'. However, the impact of obesity on clinical outcomes including mortality in COVID-19 has been poorly systematically investigated until now. We aimed to compare clinical outcomes among COVID-19 patients divided into three groups according to the body mass index (BMI).
Methods: We retrospectively collected data up to May 31st, 2020. 3635 patients were divided into three groups of BMI (<25 kg/m^2; n = 1110, 25–30 kg/m^2; n = 1464, and >30 kg/m^2; n = 1061). Demographic, in-hospital complications, and predictors for mortality, respiratory insufficiency, and sepsis were analyzed.
Results: The rate of respiratory insufficiency was more recorded in BMI 25–30 kg/m^2 as compared to BMI < 25 kg/m^2 (22.8% vs. 41.8%; p < 0.001), and in BMI > 30 kg/m^2 than BMI < 25 kg/m^2, respectively (22.8% vs. 35.4%; p < 0.001). Sepsis was more observed in BMI 25–30 kg/m^2 and BMI > 30 kg/m^2 as compared to BMI < 25 kg/m^2, respectively (25.1% vs. 42.5%; p = 0.02) and (25.1% vs. 32.5%; p = 0.006). The mortality

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https://doi.org/10.1016/j.orcp.2021.02.008

rate was higher in BMI 25–30 kg/m^2 and BMI > 30 kg/m^2 as compared to BMI < 25 kg/m^2, respectively (27.2% vs. 39.2%; p = 0.31) (27.2% vs. 33.5%; p = 0.004). In the Cox multivariate analysis for mortality, BMI < 25 kg/m^2 and BMI > 30 kg/m^2 did not impact the mortality rate (HR 1.15, 95% CI: 0.889–1.508; p = 0.27) (HR 1.15, 95% CI: 0.893–1.479; p = 0.27). In multivariate logistic regression analyses for respiratory insufficiency and sepsis, BMI < 25 kg/m^2 is determined as an independent predictor for reduction of respiratory insufficiency (OR 0.73, 95% CI: 0.538–1.004; p = 0.05).

Conclusions: HOPE COVID-19-Registry revealed no evidence of obesity paradox in patients with COVID-19. However, Obesity was associated with a higher rate of respiratory insufficiency and sepsis but was not determined as an independent predictor for a high mortality.

Introduction

The prevalence of obesity increases worldwide over the last decade which represents more health care challenges. It is associated with a high prevalence of diabetes mellitus type 2, fatty liver disease, hypertension, myocardial infarction, and several other cardiovascular diseases [1,2].

Obesity is identified as a predictor for the development of infections such as influenza A (H1N1) infection and community-acquired pneumonia (CAP) [3,4]. Recently, a high prevalence of coronavirus disease 2019 (COVID-19) in obese patients was reported [5,6]. It has been reported that the risk for a severe course of COVID-19 with intensive care unit (ICU) and requiring invasive mechanical ventilation is higher in COVID-19 with concomitant obesity than without [7–11]. On the other hand, the mortality rate in obesity is not higher as compared to non-obese patients in CVOID-19 [12]. However, data were based on a small number of patients and limited participating centers.

The obesity paradox in cancer, heart failure, and acute respiratory distress syndrome (ARDS) has been studied recently [13–15]. Obesity was associated with a lower mortality rate in patients with ARDS [13]. A chronic pro-inflammatory status in obesity may limit the worse effects of second inflammation due to sepsis or ventilator-induced lung injury [16]. Of note, patients with COVID-19 are suffering from ARDS [17]. If there is an obesity paradox in COVID-19, has not been yet studied.

This present study investigated the impact of BMI on in-hospital complications and the outcome of COVID-19 e.g., respiratory insufficiency, sepsis, and mortality of the international HOPE-Registry.

Material and methods

Study design and participants

HOPE-COVID-19 (Health Outcome predictive Evaluation for COVID-19, NCT04334291) is an international project [18,19]. It is designed as a retrospective cohort registry without any financial support. Hospitalized COVID-19 patients were included. An online database was built and completed by each participating center (www.HopeProjectMD.com). We analyzed all included patients up to to May 31st, 2020. We excluded 4503 patients due to a lack of data about body mass index (BMI). Additionally, 30 patients were excluded due to age <18, Fig. 1. The study was approved by the central Ethics Committee and, when needed, in all involved centers.

BMI

We divided included patients into three categories of BMI: 1110 patients with BMI < 25 kg/m^2, 1464 patients with 25–30 kg/m^2, and 1061 patients with >30 kg/m^2, Fig. 1. Obesity is defined as a BMI ≥ 30 kg/m^2 according to the recommended classification by the World Health Organization (WHO) [20].

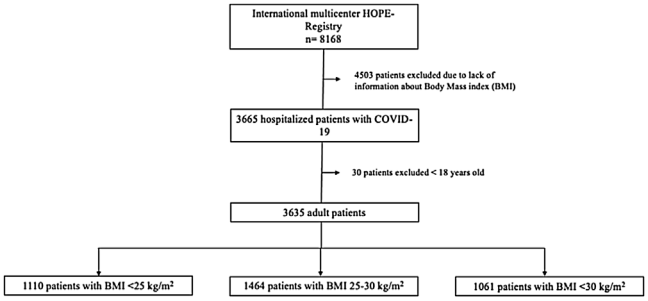

Fig. 1. Flow chart of study selection process.

Outcomes

We described as primary end-point all-cause mortality, respiratory insufficiency, and sepsis. Requiring Oxygen at admission including high nasal-canula, non-invasive ventilation, and invasive mechanical ventilation, heart failure, clinically relevant bleeding, and embolic events as secondary endpoints were also evaluated.

Statistical analysis

Descriptive and comparative analyses were presented. Categorical variables were performed as frequency rates and percentages, while continuous variables were presented as mean ± standard deviation if the distribution was normal, or median (interquartile range) if not. For group comparisons, the chi-square test was used for categorical variables. Comparative analysis of the quantitative variables was presented using the Mann–Whitney U test for non-parametric variables and the T-student test was used for parametric variables, as verified by the Kolmogorov–Smirnov test. Odds ratios (OR) with 95% confidence intervals (95% CI) were calculated in a multivariable logistic regression test for the determination of risk factors for endpoints. Hazard ratios (HR) and survival curves with 95% CI were calculated in the survival analysis by Cox regression and Kaplan–Meier method, respectively. P-value <0.05 was recognized as statistically significant. Statistical analysis was presented in two subgroups. The first subgroup consisted of patients with a BMI < 25 kg/m^2 and BMI 25–30 kg/m^2, while the second group consisted of patients with BMI < 25 kg/m^2 and BMI > 30 kg/m^2. We analyzed all variables that were described recently with a high impact on outcomes [19]. Predictors of mortality, respiratory insufficiency, and sepsis were identified by univariate analysis. Predictors with p < 0.05 were analyzed by the Cox or logistic multivariate regression. The multivariable Cox regression was used to investigate predictors of mortality, while multivariable logistic regression was used to investigate predictors of respiratory insufficiency and sepsis adjusting all significant variables: age, gender, ICU (intensive care unit) admission, BMI < 25 kg/m^2, BMI > 30 kg/m^2, previous

Table 1
Baseline characteristics of patients with COVID-19.

		BMI (kg/m^2)				
	All patients N = 3635	<25 N = 1110	25–30 N = 1464	>30 N = 1061	P[1] value	P[2] value
Age –– years, median (min-max)	63 (18–99)	59 (18–99)	64 (21–99)	66 (19–98)	–	–
Age –– no. (%)						
<70	2206/3585 (61.5)	719 (32.6)	892 (40.4)	595 (27)	**<0.001**	**<0.001**
≥70	1379/3585 (38.5)	377 (34.4)	547 (39.7)	454 (32.9)	**<0.001**	**<0.001**
Male –– no. (%)	2117/3635 (58.2)	527 (24.9)	976 (46.1)	614 (29)	**<0.001**	**<0.001**
ICU at admission*	537/3635 (14.8)	118 (22)	239 (44.5)	180 (33.5)	**<0.001**	**<0.001**
Chronic conditions — no. (%)						
Arterial hypertension	1808/3593 (50.3)	415 (23)	724 (40)	669 (37)	**<0.001**	**<0.001**
Dyslipidemia	1076/3579 (30.1)	208 (19.3)	454 (42.2)	414 (38.5)	**<0.001**	**<0.001**
Diabetes mellitus	678/3539 (19.2)	134 (19.8)	252 (37.2)	292 (43.1)	**<0.001**	**<0.001**
Current smoking	266/3394 (7.8)	77 (28.9)	114 (42.9)	75 (28.2)	0.55	0.89
Renal insufficiency ¥	191/3526 (5.4)	53 (27.7)	67 (35.1)	71 (37.2)	0.79	0.06
Lung disease	624/2772 (22.5)	128 (20.5)	239 (38.3)	257 (41.2)	**<0.001**	**<0.001**
Heart disease	824/3552 (23.2)	228 (27.7)	341 (41.4)	255 (30.9)	0.08	**0.04**
Cerebrovascular disease	269/3515 (7.7)	84 (31.2)	113 (42)	72 (26.8)	0.84	0.55
Connective tissue disease	89/3538 (2.5)	30 (33.7)	33 (37.1)	26 (29.2)	0.47	0.73
Liver disease	133/3527 (3.8)	39 (29.3)	41 (30.8)	53 (39.8)	0.30	0.08
Cancer disease	401/3554 (11.3)	112 (27.9)	178 (44.4)	110 (27.4)	0.09	0.77
Hypothyroidism	134/3635 (3.7)	29 (21.6)	47 (35.1)	58 (43.3)	0.37	**0.001**
Immunosuppression «	239/3426 (7)	76 (31.8)	95 (39.7)	68 (28.5)	0.68	0.68
Home oxygen therapy	100/3583 (2.8)	22 (22)	29 (29)	49 (49)	0.98	**<0.001**
Anemia	481/3521 (13.7)	162 (33.7)	176 (36.6)	143 (29.7)	0.06	0.46
Hemoglobin g/dl –– median (min–max)	13 (4–21)	13 (4–19)	14 (6–21)	14 (4–19)	–	–
Premedication –– no. (%)						
Oral anticoagulation	374/3575 (10.5)	96 (25.7)	147 (39.3)	131 (35)	0.23	**0.005**
Beta blockers	609/3579 (17)	144 (23.6)	265 (43.5)	200 (32.8)	**<0.001**	**<0.001**
ACEi/ARBμ	1304/3570 (36.5)	280 (21.5)	528 (40.5)	496 (38)	**<0.001**	**<0.001**
Clinical presentation –– no. (%)						
Dyspnea	2184/3556 (61.4)	618 (28.3)	864 (39.6)	700 (32.1)	**<0.001**	**<0.001**
Tachypnoea >22 breaths per minute	908/3502 (25.9)	212 (23.3)	374 (41.2)	322 (35.5)	**<0.001**	**<0.001**
Anosmia/hyposmia	262/3465 (7.6)	88 (33.6)	106 (40.5)	68 (26)	0.52	0.17
Dysgeusia	302/3462 (8.7)	96 (31.8)	126 (41.7)	80 (26.5)	0.98	0.36
Fever	2720/3572 (76.1)	784 (28.8)	1118 (41.1)	817 (30)	**<0.001**	**<0.001**
Cough	2328/3569 (65.2)	632 (27.1)	945 (40.6)	750 (32.2)	**<0.001**	**<0.001**
Diarrhea	589/3514 (16.8)	140 (23.8)	243 (41.3)	206 (35)	**0.006**	**<0.001**
Clinical parameters — no. (%)						
Peripheral oxygen saturation <92%	1224/3512 (34.9)	277 (22.6)	510 (41.7)	437 (35.7)	**<0.001**	**<0.001**
Reduced blood pressure §	231/3387 (6.8)	68 (29.4)	90 (39)	73 (31.6)	0.90	0.36
GCS ø <15 –– no. (%)	305/3185 (9.6)	97 (31.8)	122 (40)	86 (28.2)	0.80	0.75
Laboratory parameters –– no. (%)						
Elevated D-dimer	1976/3250 (60.8)	503 (25.5)	818 (41.4)	655 (33.1)	**<0.001**	**<0.001**
Elevated procalcitonin	725/2829 (25.6)	157 (21.7)	310 (42.8)	258 (35.6)	**<0.001**	**<0.001**
Elevated CRP ∂	2945/3538 (83.2)	810 (27.5)	1203 (40.8)	931 (31.6)	**<0.001**	**<0.001**
Elevated TnI ∞	400/2227 (18)	113 (28.2)	174 (43.5)	113 (28.2)	**0.01**	0.17
Elevated Transaminases •	1258/3389 (37.1)	311 (24.7)	543 (43.2)	403 (32)	**<0.001**	**<0.001**
Elevated creatinine	547/3539 (15.5)	167 (30.5)	221 (40.4)	159 (29.1)	0.95	0.99
Leukocytopenia	442/3532 (12.5)	204 (46.2)	154 (34.8)	84 (19)	**<0.001**	**<0.001**
Lymphocytopenia	2418/3455 (70)	687 (28.4)	998 (41.3)	732 (30.3)	**<0.001**	**<0.001**
Radiological findings –– no. (%)					**0.02**	**<0.001**
Unilateral infiltrates	557/3548 (15.7)	200 (32.1)	252 (40.4)	172 (27.6)	–	–
Bilateral infiltrates	2438/3548 (68.7)	600 (28.1)	851 (39.8)	685 (32.1)	–	–
Absent	553/3548 (15.6)	245 (39)	260 (41.4)	123 (19.6)	–	–

1, BMI < 25 vs. BMI 25–30. **2,** BMI < 25 vs. MBI > 30; *, intensive care unit; ¥, CrCL <30; «, Immunosuppressive therapy for psoriasis arthritis, lung transplantation, kidney transplantation or systemic lupus erythematosus; oncological disease such as mamma-ca, prostate-ca, myelodysplastic syndrome or gammopathy, glucocorticoid therapy caused by COPD, dialysis, HIV or hepatitis; Ω, acetylsalicylic acid; μ, angiotensin-converting enzyme/angiotensin receptor blocker; § Systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg. **Ø** Glasgow coma scale. ∂ C-reactive Protein. ∞ High sensitive Troponin I (cardiac injury; troponin >99th percentile upper reference limit). • ALAT and ASAT; elevated Creatinine, >1.5 mg/dl; Leukocytopenia, <4000 10E9/l; Lymphocytopenia, <1500 10E9/l.

medical history, and comorbidities such as arterial hypertension, dyslipidemia, diabetes mellitus (DM), renal insufficiency, heart-, cerebrovascular-, liver-, cancer disease, immunosuppression, home oxygen therapy, peripheral oxygen saturation (SpO_2) <92%, Glasgow Coma scale (GCS), reduced blood pressure (Systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg), laboratory parameters, and radiological findings (unilateral and bilateral infiltrates). Statistical analysis was showed with SPSS statistics version 27.

Results

Baseline characteristics of three groups

In HOPE-COVID-19-Registry, the data of 3635 consecutive hospitalized patients with COVID-19 were gathered. These patients were divided into three categories of BMI with a median age of 59 (18–99) years, 64 (21–99) years, and 66 (19–98) years, respectively. A slight predominance of men and ICU admission were

Table 2
Complications and supporting procedures during the admission.

	All patients N = 3635	BMI (kg/m²) <25 N = 1110	25–30 N = 1464	>30 N = 1061	P[1] value	P[2] value
Complication –– no. (%)						
Respiratory insufficiency	1690/3579 (46.8)	385 (22.8)	706 (41.8)	598 (35.4)	**<0.001**	**<0.001**
Heart failure	247/3565 (6.9)	62 (25.1)	92 (37.2)	93 (37.7)	0.43	**0.003**
Acute kidney injury	550/3572 (15.4)	117 (21.3)	224 (40.7)	209 (38)	**<0.001**	**<0.001**
Pneumonia	2995/3548 (84.4)	847 (28.3)	1198 (40)	949 (31.7)	**<0.001**	**<0.001**
Sepsis	459/3526 (13)	115 (25.1)	195 (42.5)	149 (32.5)	**0.02**	**0.009**
Any relevant bleeding ç	112/3517 (3.2)	34 (30.4)	53 (47.3)	25 (22.3)	0.42	0.32
Embolic event	115/3525 (3.3)	28 (24.3)	58 (50.4)	29 (25.2)	**0.04**	0.77
Oxygen therapy –– no. (%)						
O_2 support at the admission	2552/3562 (71.6)	717 (28.1)	1015 (39.8)	819 (32.1)	**0.003**	**<0.001**
High flow nasal cannula	785/3513 (22.3)	192 (24.5)	333 (42.4)	260 (33.1)	**<0.001**	**<0.001**
Non-invasive mechanical ventilation	606/3538 (17.1)	162 (26.7)	279 (46)	165 (27.2)	**0.002**	0.49
Invasive mechanical ventilation	445/3513 (12.7)	92 (20.7)	191 (42.9)	162 (36.4)	**<0.001**	**<0.001**
Proning –– no. (%)	459/3513 (13.1)	90 (19.6)	202 (44)	167 (36.4)	**<0.001**	**<0.001**
ECMO* –– no. (%)	302/3509 (8.6)	67 (22.2)	136 (45)	99 (32.8)	**0.002**	**0.004**
Death † –– no. (%)	674/3634 (18.5)	183 (27.2)	264 (39.2)	226 (33.5)	0.31	**0.004**

[1], BMI < 25 vs. BMI 25–30; [2], BMI < 25 vs. MBI > 30; **Ç** Rectorrhagia, hematuria, epistaxis, and popliteal aneurysm bleeding with relevant decreased hemoglobin >2 mg/l; *, extracorporeal membrane oxygenation, other extracorporeal life support devices, and vasoactive therapy.

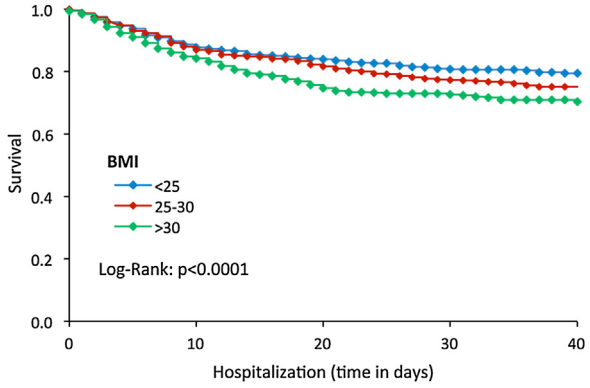

Fig. 2. Survival analysis in normal weight, overweight, and obese patients with COVID-19.

observed in BMI 25–30 kg/m² and >30 kg/m² as compared to BMI < 25 kg/m², respectively (men: 24.9% vs. 46.1% vs. 29%) (ICU: 22% vs. 44.5% vs. 33.5%). Baseline characteristics are listed in Table 1.

In-hospital complications and supporting procedures

Respiratory insufficiency was significantly more recorded with an increase of BMI (22.8% vs. 41.8% vs. 35.4%; p < 0.001). The rate of sepsis was significantly more observed in BMI 25–30 kg/m² and BMI > 30 kg/m² as compared to BMI < 25 kg/m², respectively (25.1% vs. 42.5%; p = 0.02) (25.1% vs. 32.5%; p = 0.009). The mortality rate was higher in BMI 25–30 kg/m² than BMI < 25 kg/m² without statistically significance (27.2% vs. 39.2%; p = 0.31), and higher in BMI > 30 kg/m² as compared to BMI < 25 kg/m² with significance (27.2% vs. 33.5%; p = 0.004). Proning and the use of extracorporeal membrane oxygenation (ECMO) was significantly more required in BMI 25–30 kg/m² and BMI > 30 kg/m² as compared to BMI < 25 kg/m², respectively (proning: 19.6% vs. 44% vs. 36.4%) (ECMO: 22.2% vs. 45% vs. 32.8%). All in-hospital complications and supporting procedures are presented in Table 2.

Predictors of mortality

Kaplan–Meier analysis is presented in Fig. 2. Cox multivariate analysis for mortality determined age ≥70 (HR 2.76, 95% CI: 2.142–3.570; p < 0.001), ICU at admission (HR 2.17, 95% CI: 1.694–2.797; p < 0.001), SpO2 < 92% (HR 2.10, 95% CI: 1.635–2.698; p < 0.001), GCS < 15 (HR 2.03, 95% CI: 1.559–2.653; p < 0.001), connective tissue disease (HR 1.86, 95% CI: 1.132–3.087; p = 0.01), and elevated creatinine (HR 1.57, 95% CI: 1.185–2.089; p = 0.002) as independent predictors for mortality, while BMI < 25 kg/m² and BMI > 30 kg/m² did not impact the mortality (HR 1.15, 95% CI: 0.889–1.508; p = 0.27) (HR 1.15, 95% CI: 0.893–1.479; p = 0.27), Fig. 3. However, in multivariate logistic analyses for respiratory insufficiency and sepsis, BMI < 25 kg/m² is determined as independent predictor for reduction of respiratory insufficiency (OR 0.73, 95% CI: 0.538–1.004; p = 0.05), Table 3, Fig. 3.

Discussion

The present study shows patient characteristics at baseline, in-hospital complications, and mortality rate in patients with COVID-19 according to BMI. The main findings of the study are (1) The increase of BMI was associated with a higher incidence of respiratory insufficiency and sepsis; (2) BMI < 25 kg/m² is determined as an independent predictor for reduction of respiratory insufficiency; (3) The increase of BMI did not impact the mortality rate in patients with COVID-19.

The HOPE-COVID-19-Registry shows more comorbidities in patients with BMI > 30 kg/m² such as arterial hypertension, dyslipidemia, diabetes mellitus, lung-, and heart disease. Because of these comorbidities, obese patients may develop more in-hospitals complications for example respiratory insufficiency, heart failure, acute kidney injury, pneumonia, and sepsis. Of note, BMI < 25 kg/m² is determined as an independent predictor for reduction of respiratory insufficiency in COVID-19. In this context, respiratory insufficiency with acute respiratory distress syndrome (ARDS) was recently more observed in patients with severe obesity BMI > 35 kg/m² [21]. In addition, the rate of viral pneumonia was higher in obesity as compared to non-obesity [22,23]. Obesity seems to decrease chest-wall elastance, which leads to lower total respiratory compliance with a reduction of expiratory reserve volume and a higher susceptibility for infection [24]. Even more, obesity is associated with impaired total lung capacity and increased airway resistance as well as ventilation-perfusion mismatch [25]. In addition, adipose tissue may be vulnerable to more infection due to more expression of angiotensin-converting enzyme 2 with directly binding with SARS-CoV-2 [26]. These difficulties are a challenge for

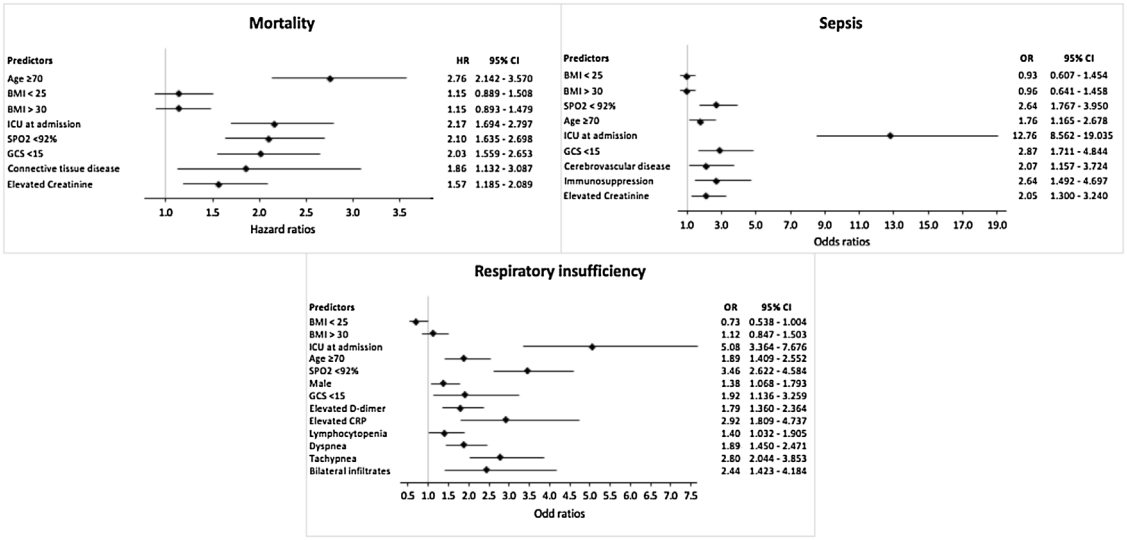

Fig. 3. Predictors for mortality, sepsis, and respiratory insufficiency. Abbreviations: BMI, body mass index; SPO_2, peripheral oxygen saturation; ECMO, extracorporeal membrane oxygenation.

Table 3
Predictors of respiratory insufficiency, sepsis, and mortality, multivariate analysis.

Variable	Multivariate analysis for respiratory insufficiency			Variable	Multivariate analysis for sepsis		
	OR	95% CI	P-value		OR	95% CI	P-value
Age ≥70	1.89	1.409–2.552	**<0.001**	Age ≥70	1.76	1.165–2.678	**0.007**
Male	1.38	1.068–1.793	**0.01**	BMI < 25	0.93	0.607–1.454	0.77
BMI < 25	0.73	0.538–1.004	**0.05**	BMI > 30	0.96	0.641–1.458	0.87
BMI > 30	1.12	0.847–1.503	0.41	ICU at admission	12.76	8.562–19.035	**<0.001**
ICU* at admission	5.08	3.364–7.676	**<0.001**	SpO_2 < 92% π	2.64	1.767–3.950	**<0.001**
SpO_2 < 92% π	3.46	2.622–4.584	**<0.001**	GCS < 15 Ω	2.87	1.711–4.844	**<0.001**
GCS < 15 Ω	1.92	1.136–3.259	**0.01**	**Chronic conditions**			
Clinical presentation				Cerebrovascular disease	2.07	1.157–3.724	**0.01**
Dyspnea	1.89	1.450–2.471	**<0.001**	Immunosuppression	2.64	1.492–4.697	**0.001**
Tachypnea	2.80	2.044–3.853	**<0.001**	**Laboratory parameters**			
Laboratory parameters				Elevated creatinine	2.05	1.300–3.240	**0.002**
Elevated D-dimer	1.79	1.360–2.364	**<0.001**				
Elevated CRP	2.92	1.809–4.737	**<0.001**				
Lymphocytopenia	1.40	1.032–1.905	**0.03**				
Radiological findings							
Bilateral infiltrates	2.44	1.423–4.184	**0.001**				

Variable	Multivariate analysis for mortality		
	HR	95% CI	P-value
Age ≥70	2.76	2.142–3.570	**<0.001**
BMI < 25	1.15	0.889–1.508	0.27
BMI > 30	1.15	0.893–1.479	0.27
ICU at admission	2.17	1.694–2.797	**<0.001**
SpO_2 < 92% π	2.10	1.635–2.698	**<0.001**
GCS < 15 Ω	2.03	1.559–2.653	**<0.001**
Chronic condition			
Connective tissue disease	1.86	1.132–3.087	**0.01**
Laboratory parameters			
Elevated creatinine	1.57	1.185–2.089	**0.002**

HR, hazard ratio; CI, confidence interval; SpO_2, peripheral oxygen saturation; *, intensive care unit; π, SpO_2 < 92% at admission; Ω, glasgow coma scale.

physicians regarding the management of COVID-19 with concomitant obesity.

Our data presented more need for proning in patients with BMI 25–30 kg/m^2 and BMI > 30 kg/m^2 due to more respiratory insufficiency in these groups. In addition, ECMO was more used in patients with a BMI > 30 kg/m^2. Concerning the management of ARDS patients, proning reduced the in-hospital-mortality and showed better effects on outcomes [27]. In this context, the alveolar volume distributions improved more in patients with BMI > 30 kg/m^2 as compared to BMI < 25 due to a greater reduction of alveolar volume variance when turning from supine to prone [28]. In 362 patients with BMI > 30 kg/m^2 who received ECMO, BMI > 30 kg/m^2 was not determined as an independent predictor for the high in-hospital mortality [29].

In the Cox multivariate analysis, BMI > 30 kg/m^2 is not determined as an independent predictor for a high mortality rate. In the first report of the international HOPE-registry in 1021 patients, obesity was an independent predictor for mortality particularly in patients <70 years [18]. However, in the present analysis, we investigated predictors of mortality in 3335 patients across all age categories. Another study showed that obesity was associated with a high rate of in-hospital mortality in patients with COVID-19 [21].

This cohort consisted of 162 patients with BMI > 25 kg/m^2, also the statement is not based on enough evidence in patients with COVID-19. However, the risk of death was high in severe obesity with BMI > 40 kg/m^2 [30]. In another analysis in 331 patients with COVID-19, ICU admission was more revealed in patients with BMI > 30 kg/m^2, but the obesity was not associated with a high mortality rate [12]. Additionally, the obesity paradox in COVID-19 was also reported [31].

Summarizing, normal BMI < 25 kg/m^2 is determined as an independent predictor for reduction of respiratory insufficiency, but not for mortality or sepsis. BMI 25−30 kg/m^2 and BMI > 30 kg/m^2 were not associated with a high mortality, respiratory insufficiency, or sepsis rate in patients with COVID-19.

Ethical statement

The study was approved by the central Ethics Committee and, when needed, in all involved centers.

Conflict of interest

Authors declare any competing financial interest

Acknowledgments

Cardiovascular Excellence SL, for their essential support in the database and HOPE webpage.

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