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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplementary material and methods

Supplementary methods

Study design and participants

For this cross-sectional study of patients with COVID-19, we included a population of patients admitted for severe form of COVID-19 at Lyon University Hospital (Lyon, France). We also included a retrospective comparison group of patients admitted in intensive care unit (ICU) without COVID-19 from the same hospital. In addition, we performed additional analysis in a previously published population of ICU patients from Lille University Hospital, CHU Lille, Roger Salengro (Lille, France).[1]

The population included all adult (≥18 years old) inpatients from Lyon University Hospital who were currently hospitalised on March 27, 2020, and had a confirmed diagnosis of COVID-19 according to WHO interim guidance.[2] Lyon University Hospital has set up specific COVID-19 departments to which all patients with a laboratory confirmed diagnosis by RT-PCR of COVID-19 or with as strong clinical and imaging suspicion of COVID-19 were transferred. All patients in this department were included except pregnant women.

For the ICU non-COVID-19 comparison group, we retrospectively included adult patients who had been admitted to ICU units for any indication in Lyon University Hospital on March 27th between 2007 and 2019. Patient data were obtained through a systematic extraction of a research institutional database registered according to the French reference methodology MR-004 number: 17-253. Because these patients were hospitalised before December, 2019, no COVID-19 cases could have been included in the comparison group.

We also performed additional analysis in a previously published population that comprised of adult patients diagnosed with COVID-19 pneumonia who were consecutively admitted to ICU at Roger Salengro Hospital, CHU Lille (Lille, France) between February 27 and April 5, 2020.[1] The independent comparison group comprised adult patients admitted to ICU at Lille University Hospital, CHU Lille, Roger Salengro for a non-SARS-CoV-2-related, severe acute respiratory disease from Jan 1, 2019, to Dec 31, 2019, extracted from electronic medical records in institutional database.[1]

Data collection and laboratory procedures

We reviewed the electronic medical records including demographic, anthropometric data, medical history, medication and medical unit from all the departments exclusively dedicated to the clinical care of adult inpatients with COVID-19 hospitalised on March 27, 2020, at Lyon University Hospital.

SARS-CoV-2 infection was detected by real-time RT-PCR from respiratory specimens, bronchoalveolar lavage or nasopharyngal samples. Briefly, 200 µl of respiratory samples were inactivated in 400 µl of cobas omni LYS buffer for 10 min before testing (Roche Diagnostics France). SARS-CoV-2 diagnosis was performed using the qualitative assay cobas SARS-CoV-2 kit on the cobas 6800 system as recommended by manufacturer's instructions (Roche diagnostics France). This technique targets the ORF1a nonstructural gene, specific for the SARS-CoV-2 detection and the structural envelope E-gene, detecting pan-Sarbecovirus including SARS-CoV-2. Amplification of RNA internal control is also included. The systematic extraction of positive RT-PCR for SARS-CoV-2 was matched with the identified patients in order to systematically exclude any patients admitted with a negative RT-PCR for SARS-CoV-2 despites a strong clinical suspicion of COVID-19.

All the clinical history was based upon extraction of the medical history from the electronic medical records. We have also collected medication information and have crossed the information between medical history and medication and the results were consistent.

As per standard procedure in Lyon University Hospital, all patients are weighted and measured in admission and data entered in the electronic medical record that we extracted for this study.

Definitions

Confirmed COVID-19 was defined as a positive real-time RT-PCR for SARS-CoV-2 infection from respiratory specimens obtained by nasopharyngeal samples or bronchoalveolar lavage.

Obesity was defined by BMI ≥ 30 kg/m^2.

The severe forms of COVID-19 were defined by all inpatient for COVID-19 including ICU and non-ICU inpatients. The criteria for hospitalization due to severe form of COVID-19 were the requirement of oxygen therapy; patients older than 70 years with diarrhea or cognitive impairment or dehydration; renal impairment, severe lymphopenia.

The critical forms of COVID-19 were defined by the requiring ICU admission.

The criteria for ICU admission were based upon a standardised procedure implemented in the Lyon University Hospital since the beginning of COVID-19 pandemic. They included: oxygen therapy > 3L /min or saturation <90%, polypnea with respiratory rate > 25/min, signs of respiratory distress or vigilance disorders, hemodynamic instability, clammy skin, heart failure. These criteria were similar in Lille University Hospital.

Statistical analysis

We present continuous variables as median (IQR) and categorical variables as n (%). Comparisons between groups were done using the independent Wilcoxon two-sample test, χ^2 test, or Fisher exact test, as appropriate.

The prevalence of obesity in patients with COVID-19 in both Lyon and Lille populations was compared with the prevalence in the French general population (considered as a reference population) using the Eurostat survey 2014[3], standardised on age (≤65 years *vs* >65 years) and sex (standardised prevalence ratio), using the indirect standardisation approach.[4] We have assumed that during the pandemic period of COVID-19, all individuals had the same risk of infection by COVID-19.

We used logistic regression to compare the prevalence of obesity between different groups within Lyon University Hospital population, adjusted by age (≤65 years *vs* >65 years) and sex.[4] These analyses provided prevalence odds ratios (ORs) and 95% CIs. We compared the prevalence of obesity between ICU patients with and without COVID-19 in Lyon, adjusted for age (≤65 years *vs* >65 years) and sex.[4] We also performed additional analysis in a previously published ICU population from Lille University Hospital[1] following the same statistical analysis by comparing the prevalence of obesity between the COVID-19 and non-COVID-19 ICU population using prevalence odds ratio adjusted for age and sex obtained by logistic regression.

Finally, we used logistic regression to do an exploratory analysis of the association between obesity and hospitalisation with critical COVID-19 (*vs* non-critical COVID-19) in the Lyon population, adjusted for age and sex. We performed univariable analyses of the association between specific and previously reported risk factors

of severity of COVID-19 and hospitalisation in ICU for critical COVID-19 (vs hospitalisation for non-critical COVID-19)[5] including presence of medical history of chronic pulmonary disease, immunodepression, malignancy, cardiomyopathy, dyslipidaemia, hypertension, or type 2 diabetes. We also performed multivariable analysis of the association between obesity and hospitalisation with critical COVID-19 (*vs* non-critical COVID-19) adjusted for these specific risk factors.

A two-sided α of less than $0·05$ was considered statistically significant. Statistical analyses were done using R (version 3.6.1).
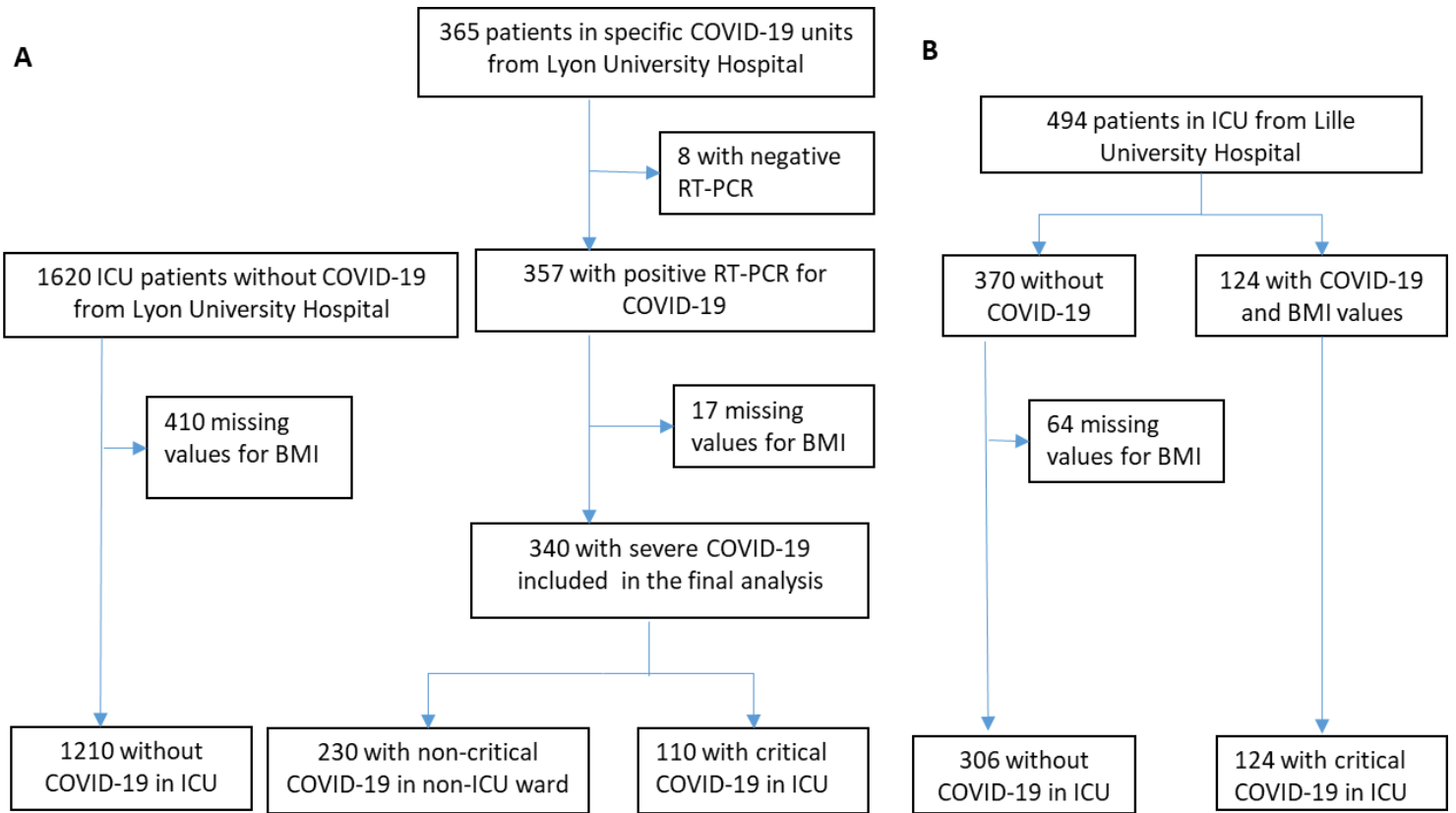
Ethic committee approval

The Hospices Civils de Lyon is the sponsor of this study. All the data collected from the identified patients were pseudonymized. In light of the situation of the health public emergency of the COVID-19 pandemic, a special dispensation regarding the principle of information and non-opposition of the patients related to their data processing have been granted. Thus, in accordance with the French regulation, this study has been considered to be consistent with the MR004 (Methodology of reference) and registered to the registry of the Hospices Civils de Lyon, handled by the Data Protection Officer.

The study was approved by the Research Ethics Commission of Lyon University Hospital (IRB number 20-44) and the requirement for written informed consent was waived by the Ethics Commission of the designated Hospital.

The observational study at Lille University Hospital was in strict compliance with the French reference methodology MR-004, established by French National Commission on Informatics and Liberties, and approved by the institutional data protection authority of CHU Lille.

Supplementary results

A

365 patients in specific COVID-19 units from Lyon University Hospital

8 with negative RT-PCR

1620 ICU patients without COVID-19 from Lyon University Hospital

357 with positive RT-PCR for COVID-19

410 missing values for BMI

17 missing values for BMI

340 with severe COVID-19 included in the final analysis

1210 without COVID-19 in ICU

230 with non-critical COVID-19 in non-ICU ward

110 with critical COVID-19 in ICU

B

494 patients in ICU from Lille University Hospital

370 without COVID-19

124 with COVID-19 and BMI values

64 missing values for BMI

306 without COVID-19 in ICU

124 with critical COVID-19 in ICU

Supplemental Figure 1: Study profiles

(A) Population from Lyon University Hospital. (B) Population from Lille University Hospital[1]
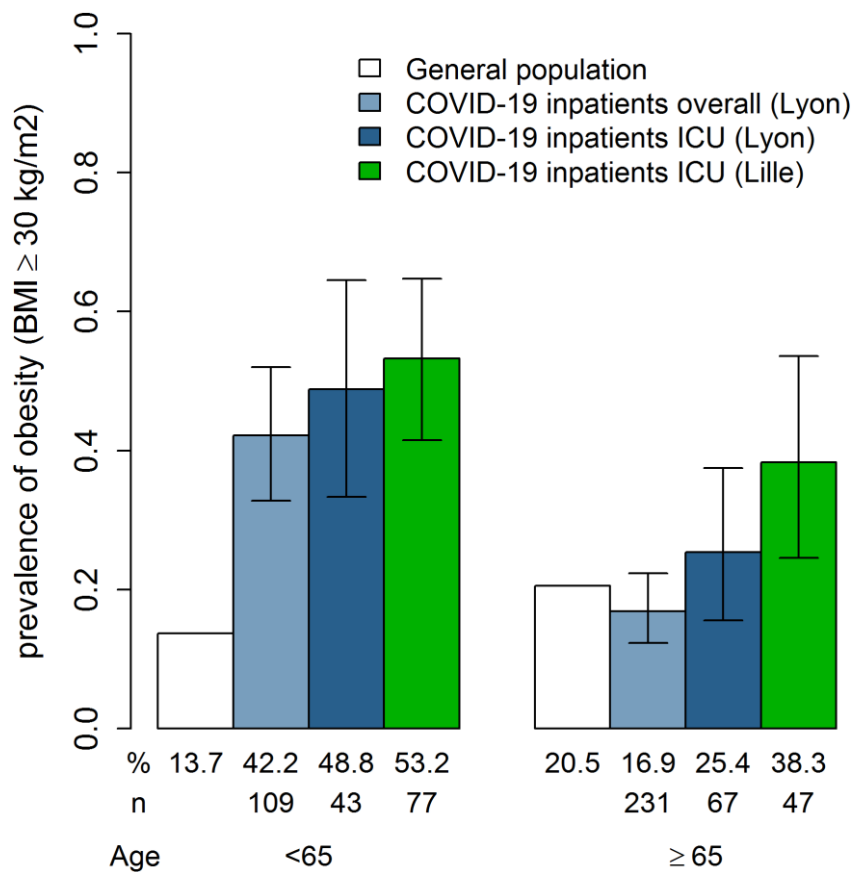
Supplemental Figure 2: Prevalence of obesity in COVID-19 inpatients aged <65 years compared with the French general population.

The prevalence of obesity is presented stratified by age < 65 years and ≥ 65 years in the COVID-19 overall inpatient group from Lyon (light blue bar), patients in ICU from Lyon (dark blue bar), COVID-19 ICU inpatients from Lille (green bar) and in the French general population (white bar) according to Eurostat 2014 data[3]
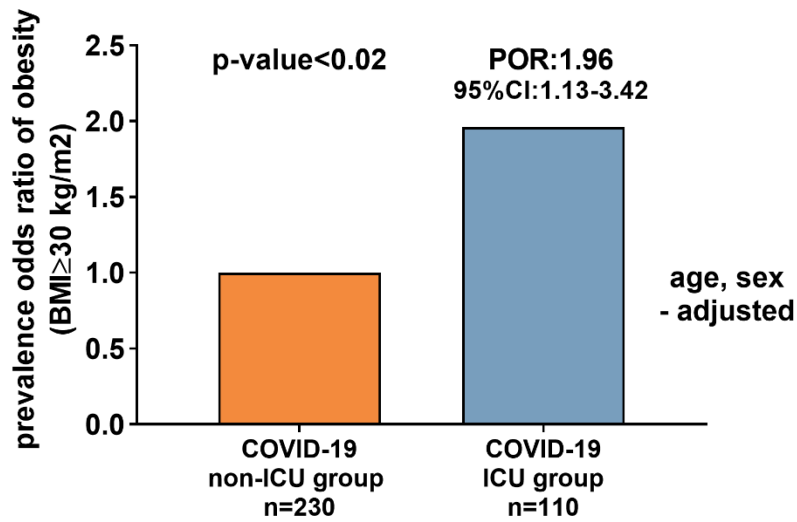
Supplemental Figure 3: Prevalence of obesity in COVID-19 inpatients in ICU compared to non-ICU in Lyon University Hospital.

COVID-19 patients in intensive care unit (ICU) (blue bar, n=110), COVID-19 non-ICU group (orange bar, n=230). POR: Prevalence Odds Ratio.

Supplemental Table 1: Baseline characteristics of patients with COVID-19 at Lyon University Hospital

	Overall (n=340)	BMI <30 kg/m² (n=255)	BMI ≥30 kg/m² (n=85)	p value*
Demographics				
Age ≥65 years	231 (68%)	192 (75%)	39 (46%)	<0·0001
Sex	..	..	..	0·568
Female	143 (42%)	110 (43%)	33 (39%)	..
Male	197 (58%)	145 (57%)	52 (61%)	..
Clinical				
Type 2 diabetes	72 (21%)	45 (18%)	27 (32%)	0·010
Hypertension	194 (57%)	144 (57%)	50 (59%)	0·857
Dyslipidaemia	88 (26%)	60 (24%)	28 (33%)	0·125
Cardiomyopathy	88 (26%)	73 (29%)	15 (18%)	0·058
Stroke	32 (9%)	24 (9%)	8 (9%)	1·000
Chronic pulmonary disease	65 (19%)	47 (19%)	18 (21%)	0·714
Malignancy	29 (9%)	25 (10%)	4 (5%)	0·218
Immunodepression	42 (12%)	38 (15%)	4 (5%)	0·021
Haemodialysis	3 (1%)	3 (1%)	0	0·576
Hospitalisation units				
Non-ICU ward (non-critical COVID-19)	230 (68%)	183 (72%)	47 (55%)	0·0074
ICU (critical COVID-19)	110 (32%)	72 (28%)	38 (45%)	0·0074

Data are n (%) or median (IQR), unless specified otherwise. ICU=intensive care unit. *p value for the comparison between patients with BMI <30 kg/m² versus BMI ≥30 kg/m², using independent Wilcoxon two-sample test, χ^2, or Fisher exact test as appropriate.

Supplemental Table 2: Baseline characteristics of study groups in Lyon and Lille patient populations

	Lyon population					Lille population		
	Non-critical COVID-19 (n=230)	Critical COVID-19 (n=110)	ICU patients without COVID-19 (n=1210)	Non-critical *vs* critical COVID-19; p value	Critical COVID-19 *vs* ICU patients without COVID-19; p value	Critical COVID-19 (n=124)	ICU patients without COVID-19 (n=306)	Critical COVID-19 *vs* ICU patients without COVID-19; p value
Age ≥65 years	164 (71%)	67 (61%)	777 (64%)	0·072	0·014	47 (38%)	131 (43%)	0·408
Male sex	110 (48%)	87 (79%)	760 (63%)	<0·0001	0·00095	90 (73%)	107 (35%)	<0·0001
Obesity	47 (20%)	38 (35%)	314 (26%)	0·0074	0·066	59 (48%)	79 (26%)	<0·0001

Data are n (%). ICU=intensive care unit. p values determined using independent Wilcoxon two-sample test, χ^2 test, or Fisher exact test as appropriate. ICU=intensive care unit. Obesity is defined as BMI ≥30 kg/m².

Supplemental Table 3: Odds ratios of critical COVID-19 between patients with and without obesity in Lyon University Hospital, by risk factor adjustment

	Odds ratio (95% CI) of ICU admission	p value*
Age, sex	2·16 (1·27–3·68)	0·0041
Hypertension, age, sex,	1·93 (1·10–3·39)	0·022
Dyslipidaemia, age, sex,	1·85 (1·05–3·26)	0·034
Type 2 diabetes, age, sex	1·80 (1·03–3·17)	0·040
Cardiomyopathy, age, sex	1·94 (1·11–3·40)	0·021
Chronic pulmonary disease, age, sex	2·03 (1·16–3·56)	0·013
Malignancy, age, sex	1·91 (1·09–3·34)	0·023
Immunodepression disease (including malignancy), age, sex	1·82 (1·03–3·20)	0·038

Odds ratios are calculated on all patients in Lyon University Hospital with severe COVID-19. ICU=intensive care unit. COVID-19=coronavirus disease 2019. *p value determined using multivariable logistic regression.

Supplemental Table 4: Univariate analyses of factors associated with COVID-19-ICU hospitalization in Lyon University Hospital

Variable	OR of ICU hospitalization [95 % CI]	P-value
BMI ≥30 kg/m2	2.05 [1.24, 3.41]	0.006
Age < 65	1.59 [0.99, 2.57]	0.057
Male	4.15 [2.47, 7.20]	<0.001
Hypertension	1.21 [0.76, 1.93]	0.418
Dyslipidemia	1.92 [1.16, 3.17]	0.012
Type 2 Diabete	2.09 [1.22, 3.56]	0.007
No cardiomyopathy	1.73 [0.99, 3.02]	0.046
No chronic pulmonary disease	1.19 [0.66, 2.15]	0.560
No malignancy	2.45 [0.91, 6.60]	0.056
No immunodepression	4.01 [1.53, 10.50]	0.001

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