



Case Series

Predictive factors of mortality related to COVID-19: A retrospective cohort study of 600 cases in the intensive care unit of the university hospital of Oujda

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ABSTRACT

Introduction: Although the corona virus is responsible in the majority of cases for mild symptoms, there are sometimes severe and even lethal forms of this disease. Our study aimed to identify clinical and para-clinical predictors of mortality related to COVID-19.

Materials and methods: This is a single-center retrospective cohort study conducted from March 2020 to December 2020 at intensive care unit department of Mohamed VI University Hospital Oujda, Morocco including 600 patients with COVID-19.

Results: We included 600 patients, the mortality rate was 32.50%, the predictors of mortality identified in our study were: associated heart disease (RR: 1.826; CI: [1.081–3.084]; p:0.024), high D-dimer level at admission (RR:1.027; CI: [1.011–1.047]; p:0.001), need for mechanical ventilation (RR: 4.158; CI: [2.648–6.530]; p: <0.0001).

Conclusion: Based on these results, we were able to identify 3 predictors of COVID 19 mortality (associated heart failure, high D-dimer level on admission, and need for mechanical ventilation). These predictors could help clinicians to identify early patients with high risk of lethality in order to reduce mortality related to corona virus.

1. Introduction

Since its identification in China in January 2020, the new coronavirus (SARS-COV 2) has spread rapidly throughout the world with more than 900,000 deaths which has led the World Health Organization to declare this disease as a pandemic since March 2020 [1] [2],

Although the majority of COVID-19 cases are benign, predictive factors for the occurrence of critical or fatal forms have been well documented in the literature. Age between 60 and 69 years, presence of comorbidity, male gender, increased oxygen requirement on admission and biological markers (C-reactive protein level, procalcitonin, interleukin 6 level, CD4 level, cardiac troponin, hypoalbuminemia) and

smoking have been identified as predictive factors for the occurrence of severe forms of COVID-19 [3,4].

This study was conducted to identify the predictive factors of mortality in patients with COVID-19 managed at the intensive care department of Mohammed VI University Hospital of Oujda -Morocco.

2. Objectives

The objective of this 10-month retrospective study was:

To determine the predictive factors for the occurrence of severe forms and mortality related to COVID -19 in the intensive care unit of CHU MED VI- OUJDA.

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3. Materials and Methods

3.1. A-type of study

We conducted a retrospective cohort study, mono-centric, in the intensive care unit of CHU MED VI- OUJDA, spread over ten months (from March to December 2020).

Patients were informed of their inclusion in this study.

3.2. B- Inclusion criteria and data collection

All patients hospitalized in the intensive care unit of CHU MED VI-OUJDA for the management of a COVID-19 infection confirmed by a real-time reverse transcription polymerase chain reaction (RT-PCR) test on nasal swab during the study period spread over 10 months, between March 2020 and December 2020 were included in the study.

3.3. C-Data collection

For each patient, clinical, anamnestic, and biological data, as well as treatment and evolution, were collected from the patients' medical records.

The term "death due to COVID-19" according to WHO: "is a death resulting from a clinically compatible disease, in a probable or confirmed case of COVID-19, in the absence of any other obvious cause of death unrelated to the coronavirus disease" this definition was used in this work [5].

3.4. D-Statistical analysis

The demographic data (age, height, weight, body mass index, sex ...), as well as all analyses were analysed in descriptive statistics using the Statistical Package for Social Science (SPSS 25).

Descriptive analyses of variables were expressed as median or percentage (%). Categorical data were compared using the Chi2 test. Cox model regression was used to determine predictors of mortality related to covid-19.

This study does not require a formal ethical committee approval. Access to patient data was authorized by the Mohammed VI university hospital and approved by the head of the department, taking into account the retrospective design of this study. The requirement of patient consent has been lifted. Data anonymity was respected in accordance with national and international guidelines.

3.5. E-research registration

This research is registered with the number: [Researchregistry6573](#).

This case series has been reported in line with the PROCESS Guideline [6].

4. Results

4.1. A/Demographic and clinical data

We included 600 patients between January 2020 and December 2020. The mean age of our patients was 64±18 years (1.5 years–115 years), 403 were male or 67.2% of our patients and 197 were female or 32.8%. Among our patients, 100 patients out of 600 had a body mass index (BMI) > 30 kg/m², i.e. 16.7% and the median BMI of our patients was 26.00±11.66. The most common comorbidities were diabetes 188/600, i.e. 31.30%, chronic renal failure 35/600, i.e. 5.80%, arterial hypertension 191/600 patients or 31.80%, heart failure (right or left or overall) was objectified in 79/600 or 13.20% of patients included in our study, asthma 22/600 or 3.70% and chronic obstructive pulmonary disease (COPD) 7/600 or 1.20%, obstructive sleep apnea syndrome 3/600 of our patients or 0.50%. The median duration of hospitalization

was 6 days ± 7.72. The average pulse oxygen saturation of our patients on admission was 88.29% ± 8.28 (45%–100%). 195/600 of our patients had died, i.e. 32.50%. [Tables 1–4](#).

4.2. B/paraclinical data

On admission, all our patients underwent a biological assessment. A blood count was performed in 586/600 of our patients, a blood ionogram (Na⁺, K⁺, Ca⁺⁺, Cl⁻, HCO₃⁻) and an evaluation of the renal function (urea, creatinine) were performed in 584/600 of our patients. C-reactive protein (CRP) was measured in 588/600 of our patients, Procalcitonin in 495/600 of our patients, the level of ferritinemia was measured in 495/600 and fibrinogen in 512/600 patients, while the level of D-dimer was measured in 393/600 patients and the level of LDH in 565/600 patients.

Lymphopenia was observed in 475/586 of our patients, i.e. 79.20%, with a median lymphocyte count of 840 ± 2749.91. The median platelet count was 237000 ± 156462.18. The median C-reactive protein (CRP) was 174.00 mg/l ± 113.16. Median serum ferritin was 875.00 ± 5849.12, median fibrinogen on admission was 6.70 ± 1.96, median D-dimer was 134.00±898, median LDH was 569.00 ± 515.17, median procalcitonin was 0.39 ± 15.99.

All our patients had at least one arterial blood gas measurement, the median PaO₂ was 60.00 ± 28.42, the median PaCO₂ was 34.00 ± 11.05.

In terms of radiography, 544/600 of our patients underwent a thoracic CT scan on admission, 60 patients among them had lung involvement of 10–25%, i.e. 10%, 105 patients, i.e. 17.5%, had lung involvement of 25–50%, 186 patients, i.e. 31.0%, had lung involvement of 50–75%, 193 patients, i.e. 32.2%, had lung involvement of 75%–100%.

4.3. C/the therapeutic data of the patients

On the therapeutic side 315/600 patients or 52.5% received oxygen therapy with oxygen cannula, 476/600 or 79.30% received oxygen therapy with a high concentration oxygen mask (HCM), 311/600 received high flow nasal oxygen therapy (OPTIFLOW) or 51.8%, 72/600 or 12% underwent CPAP oxygenation, 140 patients out of 600 or 23.3% benefited from oxygenation by non-invasive ventilation (NIV), 195/600 were intubated or 32.5%.

The use of the prone position was in 314/600 or 52.3% of patients.

26/604 of our patients received extracorporeal membrane oxygenation (ECMO), i.e. 4.33%.

All our patients received treatment with azithromycin for 4 days, vitamin C and zinc for 10 days, i.e. 600/600 (100%). Injectable ceftriaxone associated with injectable ciprofloxacin was administered in 181/600 (30.01%), the administration of injectable piperacillin-tazobactam associated with amikacin and injectable voriconazole in 98/600 or 16,33%, dexamethasone injection 6 mg per day for two weeks in 126/

Table 1
Demographic and clinical characteristics of patients.

Variables:	n(%)
-Age (years ± SD):	64+/-18
-Gender:	403(67,2)
-M	197(32,8)
-F	
-BMI (kg/m ² ± SD):	26 .00 (+/- 11 .66)
-Diabetes:	188(31,30)
-CKD:	35 (5,80)
-HBP:	191 (31,80)
-HF:	79(13,20)
-Asthma:	22(3,70)
-COPD:	7 (1,20)
-OSA:	3 (0,50)
-Median length of hospital stay (days ± SD):	6(+/-7.72)
-The average of pulse oxygen saturation in % (min-max):	88.29 (45%–100%)
-Deceased patients:	195(32,50)

Table 2
Paraclinical characteristics of patients.

Variables:	number of patients tested (N)	Median(+/-SD)
BIOLOGY:		
CBC:	586	840.00 ± 2749.91
- Lymphopenia (< 1500 cell/mm ³)		237000 ± 156462.18
- Platelets:		
CRP (NV: <10 mg/l)	588	174.00 + /- 113.16
PCT (NV:<0.5 ng/ml)	495	0.39 ± 15.99
Ferritinemia (NV: 20–280 µg/ml)	495	875.00+ /-5849.12
fibrinogen (NV:2-4 g/l)	512	6.70 ± 1.96
D-dimer (NV:<500 µg/ml)	393	134.00±898.00
LDH (NV:140–245 U/l)	565	569.00 ± 515.17
Creatinine (NV: <10 mg/l)	584	8.75 ± 22.40
ARTERIAL BLOOD GAS TEST:	600	60.00 ± 28.42
- PaO ₂ (NV:80–105mmhg):		34.00 ± 11.05
- PaCO ₂ (NV: 35–45mmhg):		
THORACIC CT SCAN:	544	10.0%
- 10–25%:	60	17.5%
- 25–50%:	105	31.0%
- 50–75%:	186	32.2%
- 75–100%:	193	

CBC: Complete blood count; LDH: Lactate Dehydrogenase; NV: normal value; CRP:C-reactive protein; PCT: procalcitonin; M:male; F: female; HBP: high blood pressure; BMI: body mass index; HF: heart failure; CKD: chronic renal failure; SD: standard deviation COPD: chronic obstructive pulmonary disease; OSA: obstructive sleep apnea syndrome.

Table 3
Therapeutic data of patients.

Variables	number of patients (N):	(%):
Oxygen therapy:	315	52.50
Oxygen cannula: HCM: Optiflow: CPAP: NIV:	476	79.30
Mechanical ventilation: ECMO VV:	311	51.80
	72	12.00
	140	23.30
	195	32.50
	26	4.33
Prone position:	314	52.30
Azithromycin:	600	100.00
Zinc:	600	100.00
Vitamin C:	600	100.00
Ceftriaxone + ciprofloxacin:	181	30.01
Tazocillin + amikacin + voriconazole:	98	16.33
Dexamethazone injection:	126	21.00
LMWH:	403	67.10

LMWH: low molecular weight heparin; VV ECMO: Extracorporeal veno-venous membrane oxygenation; CPAP: Continuous Positive Airway Pressure; HCM: high concentration mask; NIV: non-invasive ventilation; MV: mechanical ventilation.

600 (21.00%), and low molecular weight heparins (LMWH) in 403/600 patients (67.10%).

4.4. D/factors associated with patient mortality

Among the 600 patients included in our study, 195 patients died, i.e. a mortality rate of 32.50%. The median age of the deceased patients was 65 years ([59–73]; p:0.012). The majority of our deceased patients were male, 133/403 (33.00%) compared to female, 62/197 (31.50%) (33.00% vs 31.50%; p = 0.707). The mortality rate was higher in diabetic patients, 65/188 (34.60%) compared to non-diabetic patients, 130/412 (31.60%) (34.60%vs 31.60%; p:0.464). The deceased patients were also more obese (BMI>30kg/m²) i.e. 43.80% (39/89) compared to patients with a BMI < 30 kg/m² 154/503 i.e. 30.60% (43.80% vs 30.60%; p: 0.014). The mortality rate was also higher in patients with

Table 4
Factors associated with patient mortality in univariate and multivariate analysis (COX model).

Univariate analysis:				
Factors:	N(%):	RR:	CI:	p-value:
-Age (years):	65[59–73]	1.002	[0.983–1.022]	0.012
Median [IQR]				
-Sex:	133(33.00)	1.057	[0.781–1.429]	0.707
M:	62 (31.50)			
F:				
-Diabetes:	65(34.60)	1.169	[0.866–1.578]	0.464
Yes:	130 (31.60)			
No:				
-BMI(kg/m ²):	39(43.80)	1.067	[0.746–1.528]	0.014
>30:	154(30,60)			
<or = 30:				
-HBP:	66(34.60)	1.083	[0.802–1.462]	0.463
Yes:	129 (31.50)			
No:				
-Heart Failure:	33(41.80) 162 (31.10)	1.561	[1.071–2.275]	0.059
Yes:				
No:				
-Renal failure:	10(28.60)	0.864	[0.457–1.634]	0.609
Yes:	185(32.70)			
No:				
-Asthma:	9(40.90)	0.993	[0.508–1.941]	0.391
Yes:	186(32.20)			
No:				
-COPD:	1(14.30)	0.375	[0.053–2.678]	0.301
Yes:	194(32.70)			
No:				
-Lymphopenia: (<1500/mm ³)	165(34.70)	1.056	[0.702–1.588]	0.055
Yes:	28(25.20)			
No:				
-D dimers:	3020[780–9050]	1.027	[1.012–1.047]	<0.0001
Median in ug/l [IQR]				
-Ferritinemia:	1591.50 [677.50–2594.75]	1.0004	[1.0001–1.0009]	<0.0001
Median in ug/ml [IQR]				
-Fibrinogen:	6.50[4.90–7.60]	1.992	[0.918–1.071]	0.783
Median in g/ml [IQR]				
-LDH:	751.000 [542.50–962.50]	1.001	[1.000–1.002]	<0.0001
Median in U/l [IQR]				
-Platelets:	224.000 [161000–303500]	1.0002	[1.000–1.0007]	0.171
Median in cell/mm ³ [IQR]				
-CRP:	217.00 [119.12–280.00]	1.0002	[1.001–1.003]	<0.0001
Median in mg/l [IQR]				
-Procalcitonin:	0.80[0.28–2.63]	1.004	[0.997–1.011]	<0.0001
Median in ng/ml [IQR]				
- PaO ₂ :	53[45–65]	0.991	[0.984–0.998]	<0.0001
Median in mmhg [IQR]				
- PaCO ₂ :	34.00 [30.10641.00]	1.010	[0.996–1.023]	0.415
Median in mmhg [IQR]				
-Chest CT scan:	69(37.10)	2.952	[1.188–7.336]	0.020
[50–75%]:	104(53.90)	2.680	[1.089–6.594]	0.032
[75–100%]:				
-Optiflow:	119 (38.30)	1.185	[0.887–1.584]	0.002
-NIV:	60(42.90)	1.067	[0.785–1.449]	0.003
- MV:	160(82.10)	5.043	[3.469–7.332]	<0.0001
Multivariate analysis:				
Factors:	RR:	IC at 95%:	p-value:	
- Heart Failure:	1.826	[1.081–3.084]	0.024	
-D-dimers (>500 µg/ml)	1.027	[1.011–1.047]	0.001	
- MV:	4.158	[2.648–6.530]	<0.0001	

CI: confidence index; RR: relative risk; p: p value; NIV: non-invasive ventilation; IQR: the interquartile range; MV: mechanical ventilation.

hypertension (66/191), i.e. 34.60%, compared with patients without known hypertension (129/409), i.e. 31.50% (34.60% vs 31.50%; p : 0.463). Also the mortality rate in patients with heart failure was 33/79 or 41.80% compared to the unknown patients with heart failure 162/521 or 31.10% (41.80% vs 31.10%; p : 0.059). On the other hand the mortality rate was lower in patients with renal failure 10/35 or 28.60% compared to 185/565 or 32.70% in patients without renal insufficiency (28.60 vs. 32.70; p : 0.609). The mortality rate was high in asthmatic patients 9/22 or 40.90% compared to non-asthmatic patients 186/578 or 32.20% (40.90% vs. 32.20%; p : 0.391), concerning COPD patients; the mortality rate was low in COPD patients 1/7 or 14.30% compared to 194/593 or 32.70% in non-COPD patients (14.30% vs. 32.70%; p : 0.301).

Biologically, the mortality rate was higher in patients with lymphopenia on admission (165/475) or 34.70% compared to patients with normal lymphocyte count (28/111) or 25.20 (34.70% vs 25.20%; p = 0.0001,055). Median ferritinemia at admission in deceased patients was high 1591.50 ([677.50–2594.75]; p :<0.0001), median D-dimer was high at admission in deceased patients 3020 $\mu\text{g/ml}$ ([780–9050]; p :<0.0001), the median fibrinogen was elevated at admission of the deceased patients 6.50 ([4.90–7.60]; p :0.783), the median LDH was elevated at admission of the deceased patients 751.00 ([542.50–962.50]; p :<0.0001), the median platelet count at admission of the deceased patients was 224000.00 ([161000–303500]; p :0.171), the median CRP on admission of the deceased patients was elevated 217.00 ([119.12–280.00]; p : <0.0001). The median Procalcitonin was elevated on admission of the deceased patients 0.80 ([0.28–2.63]; p : <0.0001).

In terms of haematosi, the median PaO₂ of the deceased patients on admission was low at 53 mmhg ([45.00–65.00]; p : <0.0001). The median PaCO₂ of the deceased patients was 34.00 mmhg ([30.10–41.00]; p :0.415).

The mortality rate was higher in patients with a degree of lung parenchymal involvement between [75%–100%] on the thoracic scan at admission, i.e. 104/193 (53.90%), compared with patients with a degree of parenchymal involvement [50–75%]: 37.10% (69/186). The mortality rate in patients with a degree of lung parenchymal involvement between [25–50%] was 12.40% (13/105 patients), while the mortality rate in patients with a degree of involvement of [10–25%] was 8.30% (5/60 patients).

In multivariate analysis, the Cox regression model identified that: history of heart disease (RR: 1.951; CI: [1.226–3.105]; p : 0.005); high D-

dimer level at admission (>500 $\mu\text{g/ml}$) (RR: 1.027; CI: [1.011–1.043] ; p : 0.001) and use of mechanical ventilation at admission (RR: 4.158; CI: [2.648–6.530] ; p : <0.0001) were risk factors for mortality.

Patients with a history of heart disease had on day 7 and day 15 a survival rate of 67.40% and 34.60% respectively (Fig. 1). Patients who required mechanical ventilation on admission had on day 7 survival rate of 65.0% and 28.9% at day 15 (Fig. 2). Patients with a BMI>30kg/m² on admission had on day 7 a survival rate of 69.70% and 50.80% on day 15 (Fig. 3) whereas In multivariate analysis, obesity with a BMI>30kg/m² was not strongly associated with a high case fatality rate.

5. Discussion

In this retrospective cohort study performed on 600 patients during a 10-month period (from March 202 to December 2020), 32.50% of our patients died. The methods of estimating morbidity and mortality by COVID-19 differ greatly from country to country. In China, Wuhan, a retrospective study including 548 patients of which 269 patients were severe on admission, the estimated mortality was 1.1% in non-severe patients and 32.5% in severe cases during the average of 32 days of follow-up [7]. In Lombardy/Italy, a cohort study spread over the first 2 months of the COVID-19 epidemic including 3988 patients admitted to the intensive care unit, the mortality rate of the first 1715 patients admitted to the intensive care unit was 48.8% and an in-hospital mortality of 53.4% [8]. In France, the cumulative number of deaths at the beginning of June was 28,940 for 151,325 cases confirmed by RT-PCR, i.e. an apparent case fatality rate of 19% for a mortality rate of 432 per million inhabitants [9]. In the United States of America, the case-fatality rate is 3.87%, i.e. 523.8 deaths per million population [10].

Predictors of mortality were a medical history of heart disease, high D-dimer levels on admission, and mechanical ventilation.

Our study showed that the case fatality rate was high in patients with heart failure, and a Chinese cohort study showed that cardiovascular disease was independently associated with in-hospital death [11].

Several studies have shown that advanced age over 65 years, male sex, hypertension and diabetes are predictors of mortality related to covid-19 [12,13]. While our results showed that advanced age, male sex, diabetes, hypertension were not significantly associated with an increase in mortality.

An American cohort study reported that severe obesity (IMC \geq 35 kg/m²) was independently associated with higher mortality in hospitalized patients [14]. Our results had shown that BMI>30kg/m² was not

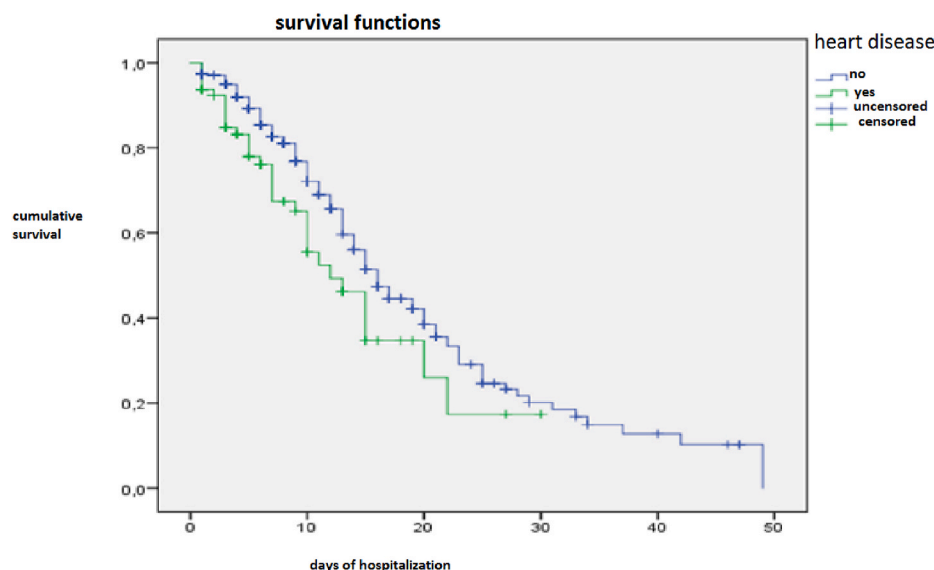


Fig. 1. Survival curve according to the history of heart disease.

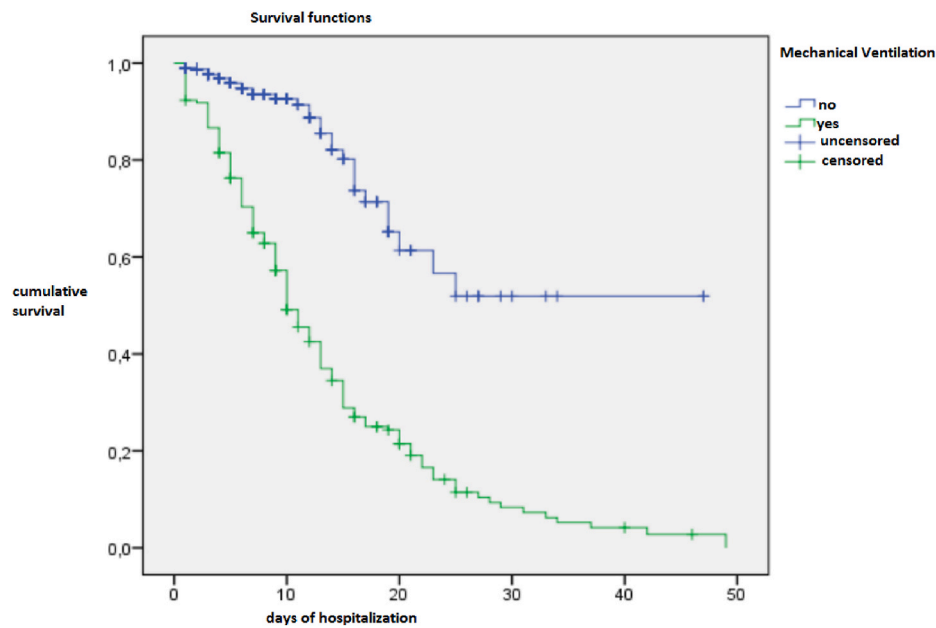


Fig. 2. Survival curve according to the necessity or not of mechanical ventilation at admission.

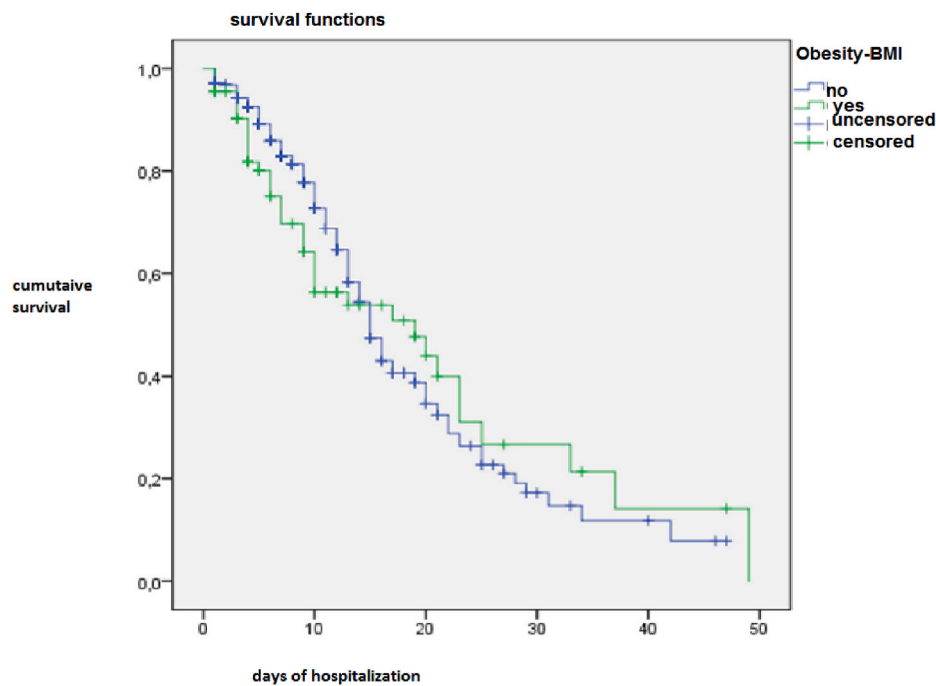


Fig. 3. Survival curve according to obesity (BMI > 30kg/m2).

significantly associated with a high case fatality rate.

Tian W, Jiang W, Yao J et al. showed in a meta-analysis involving 4659 COVID-19 patients that the risk of death was high in patients with high D dimers [15], our study confirms these results.

Tian W, Jiang W, Yao J et al. also showed that the risk of death was higher in patients with high creatinine levels [15]. Whereas our results showed that high creatinine levels on admission were not strongly associated with high case fatality.

A second Chinese meta-analysis showed that the mortality rate was significantly elevated in patients with lymphopenia and elevated procalcitonin levels on admission [12], and our results showed that lymphopenia < 1500 cells/mm³ and elevated procalcitonin levels were non-significantly associated with an increased risk of in-hospital

mortality.

One study showed that it is important to ventilate patients with severe SARS-Cov-2 pneumonia in a controlled mode, probably for at least 72 h, to avoid the occurrence of secondary lung injury (PSILI) [16]. Our results showed that the need for mechanical ventilation is a predictor of mortality related to SARS-COV 2.

This study had several limitations. First, it was a retrospective study conducted in a single center in the city of Oujda/Morocco, which involved only hospitalized patients. Therefore, these findings cannot be generalized to all COVID-19 patients in the country. Second, some key work-ups that could be associated with the severity of the disease were not (or partially achieved) in this study such as Interleukin 6.

In the future, appropriate evaluation of prognostic factors and close

monitoring were needed to provide timely interventions in high-risk patients to reduce the case fatality rate of COVID-19 in our country.

6. Conclusion

In our study, the predictors of mortality related to COVID-19 were medical history of heart failure, high D-dimer levels on admission and mechanical ventilation.

The purpose of identifying these predictors is to help health care personnel to know at an early stage any person with a high risk of lethality and thus to optimize the management of these patients in order to lower the mortality rate. Therefore, any person with COVID-19 and having these predictors of lethality should be a priority candidate for vaccination.

Provenance and peer review

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Ethical approval

This is a retrospective case series that does not require a formal ethical committee approval. Data were anonymously registered in our database. Access to data was approved by the head of the department.

Consent

This is a retrospective study.

Author statement contribution

ELKAOUINI Abderrahim: study concept, Data collection; data analysis; writing review & editing
 MERBOUH Manal: study concept, Data collection; data analysis; writing review & editing
 EL AIDOUNI Ghizlane: Study conception, data analysis contributor
 AABDI Mohammed: contributor
 EL RHALET Abdelilah: Study conception, data analysis contributor
 MAARAD Mohammed: contributor
 JEBAR Khaoula contributor
 BKIYAR Houssam: Supervision and data validation
 ABDA Naima Supervision and data validation
 HOUSNI Brahim: supervision and data validation

All authors approved the final version of the manuscript.

Registration of research studies

This research is registered with the number: Researchregistry6573.

Guarantor

Dr ELKAOUINI Abderrahim.
 Dr MERBOUH Manal.

Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.102711>.

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