Predictive factors of mortality in patients admitted to the emergency department for SARS-Cov2 pneumonia

Facteurs prédictifs de mortalité des patients admis aux urgences pour une pneumopathie à SARS-COV2

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Abstract

Introduction: The overcrowding of intensive care units during the corona virus pandemic increased the number of patients managed in the emergency department (ED).
The detection timely of the predictive factors of mortality and bad outcomes improve the triage of those patients.
Aim: To define the predictive factors of mortality at 30 days among patients admitted on ED for covid-19 pneumonia.
Methods: This was a prospective, monocentric, observational study for 6 months. Patients over the age of 16 years admitted on the ED for hypoxemic pneumonia due to confirmed SARS-COV 2 infection by real-time reverse-transcription polymerase chain reaction (rRT-PCR) were included. Multivariate logistic regression was performed to investigate the predictive factors of mortality at 30 days.
Results: 463 patients were included. Mean age was 65±14 years, Sex-ratio=1.1. Main comorbidities were hypertension (49%) and diabetes (38%). Mortality rate was 33%. Patients who died were older (70±13 vs. 61±14;p<0.001), and had more comorbidities: hypertension (57% vs. 43%, p=0.018), chronic heart failure (8% vs. 3%, p=0.017), and coronary artery disease (12% vs. 6%, p=0.030).
By multivariable analysis, factors independently associated with 30-day mortality were age ≥65 years aOR: 6.9, 95%CI 1.09-44.01;p=0.04) SpO2<80% (aOR: 26.6, 95%CI 3.5-197.53;p=0.001) and percentage of lung changes on CT scan>70% (aOR: 5.6% 95%CI .01-31.29;p=0.04).
Conclusion: Mortality rate was high among patients admitted in the ED for covid-19 pneumonia. The identification of predictive factors of mortality would allow better patient management.

Key words: COVID, pneumonia, mortality, prognosis, sarscov2

Résumé

Introduction: Durant la pandémie COVID-19, le nombre de patient en détresse a augmenté dans les services d'urgence. Les facteurs de mortalité de ces patients ne sont pas bien reconnus dans la littérature.
Objectif: Définir les facteurs de mortalité à 30 jours chez les patients admis aux urgences pour une pneumonie due au coronavirus (SARS-CoV-2).
Méthodes: Étude observationnelle, prospective, monocentrique, durant 6 mois. Inclusion des patients de plus de 16 ans admis aux urgences pour une pneumonie hypoxémiante (PaO2<60 mmHg et / ou SpO2<90%) due à SARS-CoV-2, confirmée par PCR ou test rapide. Une analyse univariée et multivariée a été réalisée pour étudier les facteurs de mortalité à 30 jours.
Résultats: Inclusion de 463 patients, âge moyen =65 ±14 ans et genre ratio = 1,1. Les principales comorbidités étaient l'hypertension artérielle (49%) et le diabète (38%). La mortalité aux urgences et à 1 mois étaient respectivement 15 et 34 %. En analyse univarié, les patients décédés étaient plus âgés (p<0,001) avec plus de comorbidités : hypertension (p=0,018), insuffisance cardiaque chronique (p=0,017), coronaropathie (p=0,030) et insuffisance rénale chronique (p=0.001). En étude multivariée, les facteurs prédictifs de mortalité à 30 jours étaient : l'âge≥65 ans (aOR: 6.9, 95%CI 1.09-44.01;p=0.04), SpO2<80% (aOR: 26.6, 95%CI 3.5-197.53;p=0.001) et l'atteinte parenchymateuse>70% (aOR : 5.6% 95%CI .01-31.29; p=0.04).
Conclusion: Un âge avancé, une atteinte parenchymateuse étendue et une SpO2<80% à l'admission étaient des facteurs prédictifs de mortalité. L'identification de ces facteurs permettrait à une meilleure orientation des patients en situation de pandémie.

Mots clés: Mortalité, Urgences, Pronostic, SARS-CoV-2

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Introduction

Since its discovery in December 2019 in China, severe acute respiratory syndrome coronavirus (SARSCoV-2) has spread across the world causing devastating effects. With more than 45 million confirmed cases and 1.2 million reported deaths as of 31 October 2020 (1). Several studies have described the clinical spectrum of COVID-19. It ranges from asymptomatic to severe acute respiratory syndrome with a variety of complications. Such variability is not random as predictive factors of mortality are identified such as obesity, chronic conditions or malignancies, age > 60 years and immunocompromised hosts (2). Furthermore, geographical singularities must be considered. As disparities among populations were shaped not only by their demography. Social determinants of health material conditions, health systems (3).
The COVID-19 pandemic is putting extraordinary pressure on emergency departments (ED), clinical wards and intensive care units (ICU). Predictive factors of bad outcome and mortality have the potential to support decision making about hospital admission (4). Existing studies are either retrospective or have focused on critically ill patients admitted to the intensive care unit (5).
The aim of this study is to determine predictive factors of mortality in patients with COVID-19 admitted in the ED.

Methods

This was a prospective, single center, observational study spanning a period of 6 months, between 1st January and 30th June 2021.

Study population

Inclusion criteria
We included all patients over the age of 16 years admitted to the emergency department for hypoxemic pneumonia due to confirmed infection with COVID-19.
- Hypoxic pneumonia was defined as respiratory symptoms associated with PaO2<60 mmHg on arterial blood gaze realized on room air and / or SpO2< 90%.
- Confirmed infection with COVID-19 was defined by the WHO (World health organization) as a person with a positive Nucleic Acid Amplification Test (NAAT) detected by real-time reverse-transcription polymerase chain reaction (rRT-PCR)

Exclusion criteria
We excluded patients with SARS-CoV-2 but admitted to ED for other reason not related to respiratory impairment, patients or relatives who declined to participate in the study and patients lost to follow up.

Data collection

We analyzed demographic, epidemiological, comorbidities collected on a specific form. We noted medical history, time from onset of symptoms, clinical condition, laboratory determinations, need for support therapy in ED (high flow oxygen, non-invasive and invasive ventilation, and oxygenation), drug therapy (steroids, antibiotics), orientation and mortality.
All patients were managed regarding to a same national protocol proposed by the time of the study by a local committee (INEAS).

Statistics

A descriptive analysis was performed on the collected data. Qualitative variables were described using frequencies and percentages. Quantitative variables were described using mean standard deviation or median according to characteristics of their distribution.
For group comparisons, Chi-square test or Fisher's exact test, and Student's t-test or Wilcoxon–Mann–Whitney test were used. A multivariate analysis was achieved with a regression logistic model including all variables with p <0.05 in the univariate analysis. All statistical tests were carried out two tailed at the 5% level of significance. The statistical analysis was performed using SPSS version 22.

Ethical approval
This study was approved by the Ethics Committee of Ben Arous Hospital. Patient consent was obtained for collection data and subsequent follow up.

Results

In the study period, 715 patients were admitted to the emergency department, 512 patients were admitted for covid-19 infection of which 481 were eligible to in this study. Thus, 463 patients were enrolled in the final analysis as 18 patients are lost to follow up at 30 days (figure 1).

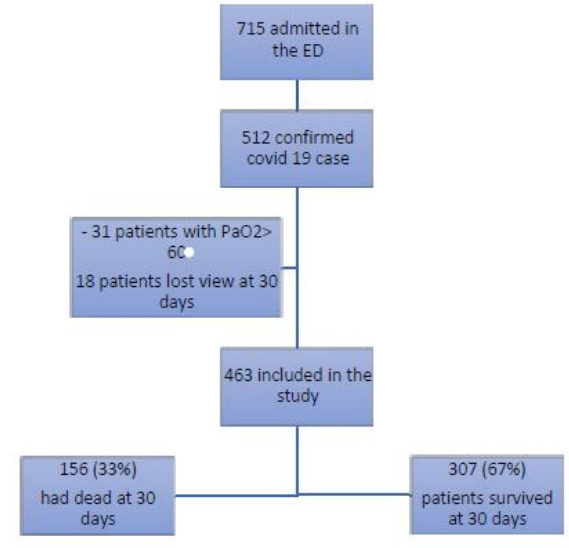

Figure 1. Flowchart of the study participants

The mean age was 65±14 years, and 244 (53%) were men (Table 1). Main comorbidities were hypertension (49%), Diabetes (38%), dyslipidemia (15%), coronary artery disease (8%) and chronic heart failure (5%). At

presentation, the most symptoms found were dyspnea (88%), cough (70%), asthenia (67%) and fever (50%).

At admission, mean Spo2 was 83±12% and mean respiratory rate was 25 bpm. The mean chest CT impairment percentage was 54±21%.

The main ventilatory support used were continuous positive airway pressure (CPAP), noninvasive mechanical ventilation and high flow nasal cannula in respectively 20%, 10% and 8%. The invasive mechanical ventilation was used for 5% of patients. Seventy six percent of patients were transferred (24% in intensive care units) and 8% of them were discharged to home from ED.

The mean length of stay was 3 days. Mortality rate was 33%. The characteristics of survivors group were compared with dead patients' group.

In the table 1 and 2 we compared demographics and clinical presentation in the two groups, laboratory findings and ventilator support. Deceased were significantly older than survived patients. We noted that more patients in death group had comorbidities such as hypertension, chronic heart failure and coronary artery disease and chronic renal failure.

There was no significant difference in the incidence of diabetes, dyslipidemia, ischemic, stroke, cancer, chronic obstructive pulmonary disease, asthma and thyroid diseases in the two groups.

Table 1. Demographic characteristics and comorbidities in survivor group and Death group

Characteristics	total (n=463)	survivor (n=307)	Death (n= 156)	P value
Age, mean ±SD	65± 14	70 ± 13	61 ±14	< 0,001
Male gender n(%)	244(53)	160(52)	84(54)	0,768
Current smoking n(%)	32(7)	22(7)	10(6)	0,848
Hypertension n(%)	256(49)	137(43)	89(57)	0,018
Diabetes n(%)	175(38)	107(35)	68(44)	0,07
Dyslipidemia n(%)	69(15)	47(15)	22(14)	0,784
Coronary artery disease n(%)	36(8)	18(6)	18(12)	0,03
COPD n(%)	34(7)	23(8)	11(7)	1
Dysthyroidism n(%)	26(6)	16(5)	10(6)	0,67
Chronic heart failure n(%)	23(5)	10(3)	13(8)	0,017
Chronic renal failure n(%)	21(5)	7(2)	14(9)	0,001
Ischemic stroke n(%)	19(4)	9(3)	10(6)	0,075
Cancer n(%)	13(3)	10(3)	3(2)	0,557
Asthma n(%)	8(2)	6(2)	2(1)	0,723
Oxygen support at home n(%)	10(2)	5(2)	5(3)	0,316

Table 2. Initial clinical presentation in both groups

Clinical presentation	Total (n=463)	Survivor (n=307)	Death (n= 156)	p value
Dyspnea n(%)	405(88)	262(85)	143(92)	0,052
Cough n(%)	329(71)	230(75)	99(63)	0,013
Fatigue or malaise n(%)	308(67)	203(66)	105(67)	0,835
Fever n(%)	231(50)	153(50)	78(50)	1
Muscle pain n(%)	133(29)	99(32)	34(22)	0,019
Headache n(%)	88(19)	71(23)	17(11)	0,002
Diarrhea n(%)	90(19)	57(19)	33(21)	0,535
Vomiting n(%)	63(14)	44(14)	19(13)	0,569
Abdominal pain n(%)	24(5)	20(7)	4(3)	0,078
Loss of smell n(%)	21(5)	13(4)	8(5)	0,645
Loss of taste n(%)	15(3)	10(3)	5(3)	1
Odynophagia n(%)	13(3)	9(3)	4(3)	1

Regarding the patient's clinical presentation, the most common symptoms were dyspnea, cough fatigue or malaise or fever. We also noted that some neurologic symptoms such as headache and muscle pain are associated with a better prognosis than in death group. In fact, they are more frequent in the survived group. Moreover, vital signs at admission to the emergency room were more severe in the death group with a higher respiratory rate and a lower pulse oxygen saturation (table 3).

Table 3. Baseline characteristics of findings in survivor group and Death group

Characteristics	Total (n=463)	Survivor (n=307)	Death (n= 156)	p value
Heart rate, mean (bpm)±SD	97± 18	96±18	98 ± 14	0,34
Respiratory rate mean (bpm)±SD	25± 8	24± 4	28 ± 7	< 0,001
Oxygen pulse saturation (spo2) mean(%)±SD	83± 12	87±6	76±15	<0,001
PH mean ±SD	7,45± 0,09	7,46±0,06	7,41± 0,120	<0,001
Pao2, mean ±SD	47±9	49±9	45±9	0,011
Paco2 mean ±SD	32± 9	32±7	33±11	0,228
HCO3-, mean (mmol/l) ±SD	22± 9	23±10	21±5	0,005
Lactate mean (mmol/l) ±SD	2± 1,6	1,65±0,81	2,53±2,36	<0,001
White blood cell count (WBC),mean (/ml) ±SD	12700	8895±6977	10571±6419	0,01
Hemoglobin(Hb), mean (g/dl) ±SD	12±4	17±7	13±8	0,48
Lymphocytes count median (e/mm3) [IQ]	968 [700,1359]	1040 [765,1415]	875 [597,1200]	0,013
D-dimer, median (ng/ml) [IQ]	1159 [709,2152]	1032 [595,1782]	1316 [820,2715]	0,089
Prothrombin (TP),mean(%) ±SD	77± 16	79±16	74±16	0,024
Glycemia, mean(mmol/l)±SD	10,21± 6,13	9,27±5,4	12±7	< 0,001
Urea, mean (mmol/l) ±SD	6.1±3	7±5	12±10	<0,001
Creatinine, median(µmol/l) [IQ]	78 [66,101]	74 [64,88}	92 [71, 146]	< 0,001
Potassium, mean(mmol/l)±SD	4,20± 0,71	4,11±0,67	4,39±0,76	<0,001
Sodium, mean (mmol/l)±SD	135± 5	135±5	134±6	0,753
Aspartate aminotransferases (ASAT), median(UI/l) [IQ]	36 [23,52]	32 [22,49]	42 [27,60]	0,052
Alanine aminotransferases (ALAT), median(UI/l) [IQ]	24 [18,38]	24 [18,38]	24 [19,35]	0,982
Chest CT impairment (%)	54± 21	47±20	65±18	< 0,001
Chest CT impairment ≥70 % (n)	70(15)	27 (8)	43(27)	<0,001
Pulmonary embolism n(%)	26(6)	13(4)	13(8)	0,182

Arterial blood gas performed in patients on ED at admission showed a tendency to metabolic acidosis in the death group compared with the survived group and a

higher lactate level in the death.
Regarding laboratory findings, the death group had more white blood cells a reduced lymphocyte count and a lower prothrombin level than in the survived group Also the death group was characterized by a higher level of glycemia, creatinine and potassium.
Chest CT was practiced in 184 patients of all patients included in this study (40%). In the death group.
Table 4 showed the main used respiratory support in both groups.

Table 4. Respiratory support used for both groups

Respiratory support	Total (n=463)	Survivor (n=307)	Death (n= 156)	p value
Noninvasive mechanical ventilation n (%)	48(10)	9(3)	39(25)	< 0,001
High-flow nasal cannula n (%)	37(8)	10(3)	27(17)	< 0,001
Continuous positive airway pressure (CPAP) n (%)	94(20)	28(9)	66(42)	< 0,001
Invasive mechanical ventilation n (%)	21(5)	3(1)	18(12)	< 0,001

Table 5 detailed the referral of patients from the two groups.

Table 5. Referral and admissions of patients from the two groups

	Total (n=463)	Survivor (n=307)	Death (n= 156)	p value
Transferred patient n (%)	352(76)	271(88)	77(49)	< 0,001
ICU n (%)	111(24)	53(17)	59(38)	< 0,001
Medicine n (%)	241(52)	219(71)	19(12)	< 0,001
Discharged n (%)	39(8)	33(11)	6(4)	0,031

By multivariable analysis, factors independently associated with 30-day mortality were age ≥65 years aOR: 6.9, 95%CI 1.09-44.01;p=0.04) SpO2< 80% (aOR: 26.6, 95%CI 3.5-197.53;p=0.001) and percentage of lung changes on CT scan>70% (aOR: 5.6% 95%CI.01-31.29;p=0.04).

Discussion

Most published studies about SARScov2 pneumonia have been retrospective studies including only patients admitted on intensive care units. This study by its prospective design, with more than 460 ED patients analyzed, representatively reflects the clinical profile and prognosis of several forms of clinical presentation of SARS-CoV-2 pneumonia not only critically ill patient as almost all studies until the present time. The identification of prognosis-related factors leads to optimize the use of health resources and guide better clinical management.
In this study, Mean age was 65 years old and sex-ratio=1, with hypertension and diabetes as main comorbidities. Those epidemiological characteristics are similar to almost all published studies (6,7).
One third of patients admitted to ED died. This mortality is upper that described in a meta-analysis that included more than 14,000 patients in 44 studies, which estimates mortality in all symptomatic adult patients by a percentage of 10% (8). In the same meta-analysis the mortality rate of ventilated patients admitted in intensive care units reaches 80%. Although remarkable heterogeneity was observed in the selected studies.
The analysis of a retrospective case series of 1591 consecutive patients with laboratory confirmed COVID-19 in Italy had found a mortality rate of 26% (9). An American study documented 50% mortality among patients admitted in the intensive care unit in the first wave (10).
The variability of the mortality rate can be explained by the fact that the first studies published came from Asian countries which experience a very high rate of mortality among mechanically ventilated patients (11). Secondary, the lack of international standardized guidelines in the management of Covid 19 patients can be a bias in the evaluation of the prognosis. Also, and since the outbreak of COVID-19 pneumonia, we observed a diversification of SARS-CoV-2 strains in different genetic clades with different characteristics and clinical presentations(12).
In the present study, patients in deceased group were much older than survivors, and univariate and multivariate logistic regression analysis revealed age ≥65 years as a strong predictor for death of COVID-19 pneumonia. Advanced age is arguably a high predictive factor of mortality in almost all studies.
A meta-analysis including 60 studies, with a total of more than 51,000 patients from hospitals in 13 countries proved that older age is an independent predictive factor of mortality as compared with younger adult (13).
It has been suggested that this could be due to the higher prevalence of chronic conditions and smoking and poorer immunological status in aged patients(13).
Chronic conditions and co-morbidities aren't independent predictive factors of mortality in this study but are more present among deceased.
The overall risk estimators we found are similar to those of other meta-analyses for smoking (14), chronic pulmonary disease ,cardiovascular, hypertension, cerebrovascular (15) diabetes (16), kidney and liver diseases (17).
Percentage of lung changes on CT scan was a strong predictive factor of mortality in this study.
Computed tomography (CT) of the chest is one of the main diagnostic tools for coronavirus disease 2019 COVID-19 infection. Abnormalities were variables and non-specific. In a systematic review of the literature the most common chest CT finding was vascular enlargement (84.8%), followed by ground-glass opacity (60.1%), air-bronchogram (47.8%), and consolidation (41.4%). Most lung lesions were in the lung periphery (72.2%) and involved bilateral lung (76%) (18).
In different stages of the disease, the CT manifestations are different, which are important for the diagnosis and staging of patients (19). Furthermore, the use of a semi-quantitative scoring system in some studies seems to be interesting. A multi-center paired cohort study conducted by Liu et al. (20) showed that CT changes are obvious during the acute exacerbation of COVID-19, accompanied by an increase in CT score. This indicates that an elevated CT score may predict a poor outcome. Another retrospective single-center study indicated that the CT score had a high diagnostic value in patients with severe COVID-19 (22).

In this study, we didn't find biological tools as predictive factors of mortality. In the literature, some biomarkers seemed to be interesting. Recent studies have elucidated that neutropenia and lower lymphopenia can be observed in patients with severe COVID-19 as Immune dysfunction plays an important role in the severity of COVID-19 (23). The NLR (Neutrophil-Lymphocyte Ratio) has been demonstrated by Yang et al. as an independent indicator for poor clinical outcome.

Coagulation disorders are more common in patients with severe disease than in those with mild disease A study conducted by Zhang et al. showed that a D-dimer level ≥2.0µg/mL could effectively predict the mortality of patients with COVID-19. Moreover, there are references linking high levels of LDH with the most severe forms of clinical presentation. The identification of predictive factors of mortality, leads to improve the triage and orientation of patients in the emergency department.

The strength of this study are the prospective enrollment of patients and the standardized management protocol. Another strength is the inclusion of all patients in the ED decreasing the selection bias. The limitations of the present study were the monocentric nature and small sample size.

Conclusion

Mortality rate among patients admitted in the ED for covid-19 pneumonia is 33%. Independent predictive factors of mortality were age≥65 years, SpO2<80% and percentage of lung impairment > 70% on chest CT scan.

Abbreviations list

BIPAP: Bilevel positive airway pressure
Bpm: Beats per minute
COPD: Chronic obstructive broncho-pneumopathie
CPAP: Continuous positive airway pressure
Cpm: Cycles per minute
E/mm3: Element per millimetre
ECG: Electrocardiogramme
GCS: Glasgow Coma Scale
HR: Heart rate
INEAS: Institut national de l'évaluation et de l'accréditation en santé
µmol/l: Micromole per litre
MmHg: Millimetre of mercury
Mmol/l: Millimole per liter
Ng/ml: Nanogramme per millilitre
OR: Odds ratio
PCR: Polymerase chain reaction
DS: Déviation standard
UI/l: International unit
MV: Mecanical ventilation
WBC: White blood cell

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