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Original

Prognosis of Covid-19 elderly patients to inform discussions of values-based care

Prognóstico de pacientes idosos com Covid-19 para fundamentar discussões de cuidado baseado em valores

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ABSTRACT

Objective: To investigate the prognosis of elderly patients in a large elderly cohort with Covid-19. We evaluated additional predictors of mortality beyond age in these elderly patients. **Methods:** The study was a retrospective analysis of data from a major Covid-19 referral center in São Paulo, Brazil. We included all patients aged 75 or above and were admitted to the hospital with Covid-19 from March 2020 to May 2021. We used regression to identify independent factors for mortality. Statistical analyses were carried out using R. **Results:** About 49% of these patients were intubated. Intubated patients had an 80% mortality rate compared to a 22,7% for non-intubated patients. For intubated male sex patients, higher Simplified Acute Physiology Score 3, higher heart rate and an unwell apparent state of health contributed to a worse prognosis. For the non-intubated patients, a lower peripheral oxygen saturation at presentation, higher heart rate, older, dementia and a history of mialgia at presentation as well as an unwell apparent state of health contributed to a worse prognosis. **Conclusion:** Elderly Covid-19 patients have a poor prognosis when intubated and this should be considered at the outset. Therefore, intubation in this population should probably not be considered standard practice, especially if for the individual patient under consideration, their functional independence is a priority over extending life span.

Keywords: Covid-19; Respiratory insufficiency; Intubation; Aged

RESUMO

Objetivo: Investigar o prognóstico de pacientes idosos em uma ampla coorte de idosos com Covid-19. Avaliamos preditores adicionais de mortalidade, além da idade, nesses pacientes idosos. **Métodos**: O estudo foi uma análise retrospectiva de dados de um importante centro de referência para Covid-19 em São Paulo. Incluímos todos os pacientes com 75 anos ou mais internados no hospital com Covid-19 de março de 2020 a maio de 2021. Utilizamos regressão para identificar fatores independentes de mortalidade. As análises estatísticas foram realizadas usando o *software* R. **Resultados:** Aproximadamente 49% desses pacientes foram intubados. Pacientes intubados tiveram taxa de mortalidade de 80% em comparação com

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22,7% para pacientes não intubados. Para pacientes intubados, sexo masculino, *Simplified Acute Physiology Score 3* mais alto, frequência cardíaca mais alta e um aparente estado de saúde debilitado contribuíram para um pior prognóstico. Para pacientes não intubados, menor saturação de oxigênio periférico na admissão, frequência cardíaca mais alta, idade mais avançada, demência, histórico de mialgia na admissão e um aparente estado de saúde debilitado contribuíram para um pior prognóstico. **Conclusão:** Pacientes idosos com Covid-19 apresentam prognóstico ruim quando intubados, o que deve ser considerado desde o início. Portanto, a intubação nessa população provavelmente não deve ser considerada uma prática padrão, especialmente se, para o paciente individual em consideração, a independência funcional for prioridade em relação à extensão da vida útil.

Descritores: Covid-19; Insuficiência respiratória; Intubação; Idoso

INTRODUCTION

The coronavirus disease 2019 (Covid-19) pandemic brought into the spotlight a major problem we see every day in emergency departments – the decision to intubate or not intubate elderly patients. In general, hospital admissions age is a powerful predictor of mortality and adverse events.[1] For Covid-19, specifically, age was also confirmed as an independent predictor of mortality.[2] Elderly patients who are intubated have not only a higher risk of death but also of significant disability and loss of independence.

The purpose of this paper is to challenge the notion that age can be used as a sole predictor of prognosis and for setting the standard for what could be futile care.[3,4] Patients in the same age group can be heterogenous in terms of apparent state of health, sarcopenia, functional status, and frailty. Further stratification of the patient's prognosis would be very helpful for shared decision-making.[5]

Since the prognosis for Covid-19 was uncertain in the beginning of the pandemic, most patients were intubated despite their age. The objective of this study was to investigate the prognosis of elderly patients in a large elderly cohort with Covid-19. We evaluated additional predictors of mortality beyond age in these elderly patients.

METHODS

Study design and participants

On March 2020 the *Hospital das Clínicas* of the *Faculdade de Medicina* of the *Universidade de São Paulo* (USP) was designated to receive Covid-19 patients at the beginning of the Covid-19 pandemic. All Covid-19 patients received from March 30th, 2020 to May 22nd, 2021 were included in a hospital wide database. For the purposes of this study, we selected all the patients 75 years old or older. We divided these patients into two groups considering whether they had been intubated for Covid-19 or not.

The study protocol was approved by the Research Ethics Committee of (protocol number CAAE 30417520.0.0000.0068). Written informed consent was deemed not necessary. In this report, we conformed to all STROBE guidelines.[6]

Data collection

Data from patients 75 years old or over was extracted from their electronic health records and imported into RedCap.

Apparent state of health is classified into good, regular, and poor condition. This is a subjective classification that includes the general presentation of the patient their *gestalt*. In this study, the apparent state of health of the patients was classified into three categories: good apparent state of health, regular or bad. For the analysis in this study, we combined the latter two categories. Vasoactive drugs include vasopressors and inotropic medications.

Statistical analysis

To overcome missing data, we performed multiple imputation across variables and outcomes. Descriptive statistics include frequency analysis (percentages) for categorical variables and mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables. Comparisons were determined by the t test or Mann-Whitney U

test for continuous variables, as appropriate, and by the chi-square test or Fisher's exact test for categorical variables. The level of statistical significance is set at 0.05 (two-tailed). Regression models were constructed using the backward stepwise method to consider the risk of death. Statistical analyses were carried out using R.

RESULTS

From March 30th, 2020 to April 30th, 2021, we received 5,088 patients for Covid-19 treatment. Among these there were 710, patients who were 75 years and older. The mean age of this group was 81.6 years with a SD of 5.2 years **(Table 1)**. These patients stayed 13.3 ± 12.1 days in the hospital. The admission team classified approximately a third of patients as having a good apparent state of health and two-thirds as having an unwell apparent state of health. Comorbidities are prevalent in this age group as well as in this study including hypertension (75%), arrhythmias (10%), chronic obstructive pulmonary disease (10%), renal failure (13%), previous stroke (13%), dementia (11%), and obesity (8%). Almost one half of patients were either on angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blocker (ARBs). Main symptoms at presentation included dyspnea (71%), cough (63%) and fever (39%).

Table 1. Baseline characteristics of elderly patients admitted with Covid-19

Baseline characteristics	All patients (n=566)	Non-intubated (n=289)	Intubated (n=277)	p-value
Age	81,6 ± 5,1	82,53 ± 5,4	80,7 ± 4,7	< 0,001
Female sex	44%	49%	39%	0,02
Good apparent state of health	37%	47%	25%	< 0,001
Cardiovascular disease	30%	35%	27%	0,110
Hypertension	75%	74%	77%	0,491
Arrhythmias	10%	12%	8%	0,073
COPD	10%	12%	9%	0,281
Asthma	3%	3%	2%	0,499
Renal failure	13%	14%	13%	0,599
Dialysis	2%	1%	3%	0,230
Stroke	13%	15%	12%	0,576
Dementia	11%	16%	6%	< 0,001
Psychiatric condition	3%	4%	2%	0,164
Peripheral vascular disease	4%	4%	5%	0,604
Obesity	8%	6%	9%	0,212
Diabetes	46%	44%	48%	0,375
Current smoker	5%	3%	7%	0,037
Prior use of				
ACE-I	21%	25%	17%	0,021
ARB	22%	25%	18%	0,061
NSAID	3%	3%	2%	0,659
Corticosteroids	10%	8%	11%	0,309
Symptoms				
Fever	39%	43%	36%	0,097
Chills	4%	6%	1.4%	0,010
Dyspnea	71%	68%	75%	0,085

Baseline characteristics	All patients (n=566)	Non-intubated (n=289)	Intubated (n=277)	p-value
Cough	63%	62%	63%	0,891
Coriza	10%	11%	8%	0,209
Odinofagia	2%	3%	1%	0,116
Myalgia	23%	23%	23%	0,981
Acute confusion	13%	19%	8%	<0,001
Abdominal pain	5%	8%	3%	0,013
Vomit	5%	8%	3%	0,036
Diarrhea	10%	11%	8%	0,209
Days of symptoms	8,8 ± 5,6	8,49 ± 6,11	9,25 ± 5,0	0,106
Respiratory rate	23,37 ± 5,19	22,76 ± 4,86	24,02 ± 5,45	<0,001
Heart rate	83,77 ± 17,49	83,47 ± 16,41	84,08 ± 18,58	0,922
Systolic blood pressure (mmHg)	124,76 ± 24,76	129,82 ± 23,52	119,41 ± 24,95	< 0,001
Diastolic blood pressure (mmHg)	73,33 ± 14,43	74,78 ± 13,31	71,82± 15,40	0,001
Weight	71,31 ± 17,10	70,51 ± 15,35	72,15± 18,74	0,253
Height	155,76 ± 22,58	156,29 ± 22,52	155,22 ± 22,67	0,571
Peripheral oxygen saturation	92,73 ± 5,58	92,78 ± 4,43	92,67 ± 6,58	0,814
Temperature	36,157 ± 0,88	36,40 ± 0,78	36,03 ± 0,96	< 0,001
SAPS-3	66,87 ± 17,91	57,56 ± 13,43	76,57 ± 16,83	< 0,001
Laboratory results				
Hemoglobin (g/L)	12,06 ± 2,19	11,98 ± 2,02	12,13 ± 2,35	0,429
Hematocrit	35,95 ± 6,26	35,47 ± 5,66	36,494 ± 6,79	0,063
Platelets (109/L)	218,33 ± 101,68	223,30 ± 101,82	213,15 ± 101,47	0,225
INR	1,21 ± 0,79	1,23 ± 0,85	1,19 ± 0,73	0,598
APTT (s)	33,46 ± 17,04	33,15 ± 13,89	33,78 ± 19,82	0,662
Lactate (mg/dL)	16,03 ± 9,73	15,08 ± 9,27	17,04 ± 10,11	0,016
Sodium (mEq/L)	140,61 ± 6,12	139,65 ± 6,47	141,761 ± 6,61	<0,001
Potassium (mEq/L)	4,35 ± 0,82	4,18 ± 0,73	4,53 ± 0,85	<0,001
Magnesium (mg/dL)	2,08 ± 0,39	1,98 ± 0,37	2,18 ± 0,39	<0,001
Ionized calcium (mg/dL)	4,68 ± 0,40	4,69 ± 0,42	4,66 ± 0,38	0,390
LDH (U/L)	486,01 ± 358,43	402,10 ± 211,84	573,62 ± 448,45	<0,001
C-reactive protein (mg/L)	142,51 ± 104,59	110,30 ± 83,89	176,12 ± 113,27	<0,001
AST (U/L)	66,79 ± 134,10	51,78 ± 80,52	82,44 ± 171,95	0,006
ALT (U/L)	59,66 ± 147,52	47,34 ± 61,92	76,64 ± 199,95	0,007
Troponin (ng/L)	0,17 ± 0,73	0,16 ± 0,59	0,19 ± 0,85	0,73
Urea (mg/dL)	79,00 ± 54,11	61,56 ± 39,84	97,20 ± 60,71	<0,001
Creatinine (mg/dL)	1,73 ± 1,61	1,29 ± 1,07	2,189 ± 1,93	<0,001
Lymphocytes (103/µL)	1,15 ± 1,64	1,09 ± 1,97	0,92 ± 1,19	0,212
Neutrophils (103/µL)	8,49 ± 5,51	6,45 ± 4,14	10,61 ± 5,94	<0,001

COPD: chronic obstructive pulmonary disease; ACE-I: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; NSAID: non-steroidal anti-inflammatory drug; SAPS-3: Simplified Acute Physiology Score 3; INR: international normalized ratio of prothrombin time; APTT: activated partial thromboplastin time; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

During the hospital stay, 277 underwent intubation, while 289 did not. The non-intubated patients were slightly older than intubated patients (82.5 ± 5.4 years vs 80.7 ± 4.7 years). Patients arrived at our service on average on their eighth day of symptoms. Comparing intubated and non-intubated patients there was no difference between presenting heart rate, weight, height, and peripheral oxygen saturation. There was a difference in respiratory rate, temperature and Simplified Acute Physiology Score 3 (SAPS-3). Systolic and diastolic blood pressures were 10 mmHg and 4 mmHg higher at presentation in the non-intubated patients. In the initial blood tests, we found that urea, creatinine, lactate dehydrogenase (LDH) were elevated in comparison to non-intubated patients. The non-intubated patients stayed for 11.8 ± 10.2 days at the hospital while the intubated patients for 15.5 ± 13.9 days.

In **table 2** we show that practically every intubated patient was admitted to the intensive care unit (ICU; the two exceptions are one who was treated in the emergency department and the other in the ward), compared to 40.1% of non-intubated patients. In the intubated group 95.3% received vasoactive drugs and 34.6% were submitted to dialysis, meanwhile in the non-intubated patient group 12,6% received vasoactive drugs and 1% were submitted to dialysis. We found a 22.7% mortality rate in the non-intubated group whereas an 80% mortality rate in the intubated group.

Tables 3 and 4 present the independent predictors of mortality according to intubation status. For intubated patients the predictors included male sex, a higher SAPS-3 score, a higher heart rate and an unwell apparent state of health. In the non-intubated patients, the independent predictors include a lower peripheral oxygen saturation, higher heart rate, higher age, the presence of dementia, an initial complaint of myalgia and an unwell apparent state of health.

Table 3. Predictors of mortality in elderly Covid-19 intubated patients

Multivariate predictors	OR	95%CI
Heart rate	1,024	1,008-1,041
SAPS-3	1,027	1,010-1,046
Unwell apparent state of health	1,995	1,081-3,682
Male sex	3,064	1,730-5,428

OR: odds ratio; 95%CI: 95% of confidence interval; SAPS-3: Simplified Acute Physiology Score 3.

Table 4. Predictors of mortality in elderly Covid-19 non-intubated patients

Multivariate predictors	OR	95%CI
Dementia	2,832	1,37-5,856
Myalgia	0,317	0,125-0,809
Unwell apparent state of health	4,605	2,299-9,226
Age	1,071	1,012-1,132
Heart rate	1,033	1,014-1,053
Peripheral oxygen saturation	0,887	0,833-0,944

OR: odds ratio; 95%CI: 95% of confidence interval

Table 2. Outcomes of elderly patients classified by intubation status

Outcomes	All patients	Non-intubated	Intubated	p-value
Death	50,0	22,7	80,0	< 0,001
ICU admission	68,1	40,1	98,7	< 0,001
Vasoactive drugs	52,8	12,6	95,3	< 0,001
Dialysis	17,3	1,0	34,6	< 0,001
Blood transfusion	12,2	4,3	20,1	< 0,001
Anticoagulation	97,4	97,1	97,8	0,768
Antiplatelets	28,8	34,6	22,7	0,007
Antibiotics	87,3	2,9	92,0	< 0,001

Results expressed as %.

ICU: intensive care unit.

In the intubated patients those with a good apparent state of health have a mortality rate of 71% compared to 83% for those with an unwell apparent state of health. In non-intubated patients those with a good apparent state of health have a mortality rate of 8% compared to 34% for those with an unwell apparent state of health.

DISCUSSION

Although this is an observational study, it is a large cohort of elderly patients with Covid-19 acute respiratory distress syndrome. Many of these patients were intubated. The mortality we found in intubated patients (76%) is in line with previous reports including 81% of mortality in 88 intubated patients.[7]

The multivariable logistic regression in this study found that low palliative performance scale, other race (non-hispanic), a previous do not intubate order and new onset dialysis were all predictive of in-hospital mortality. A pre-Covid-19 study in octogenarians or older found a mortality rate of 38.4% in general ICUs. Independent multivariate predictors of mortality were age, diagnosis, Sequential Sepsis-related Organ Failure Assessment (SOFA) score and the clinical frailty scale.[8]

In our data, of the 337 intubated patients, 76 patients survived intubation. These patients had lower SAPS-3 scores, lower heart rates and were judged to have a good apparent state of health at admission. Beyond the fact that this was a cohort of patient of 75 years or older, for the intubated patients, age was not a further independent predictor of mortality. The other two predictors were probably related specifically to the Covid-19 infection: SAPS-3, heart rate and male sex. We would like to highlight that the SAPS-3 score already includes heart rate, and therefore, the effect of an increased heart rate is counted twice as a predictor of mortality.

An interesting finding is the inclusion of the apparent state of health as an independent predictor. Apparent state of health is similar to a previously studied first clinical impression.[9] This first clinical impression was evaluated in a subjective numerical rating scale from zero to one hundred in nontrauma patients (before the Covid-19 pandemic) and was associated to morbidity and mortality.[9] This is a simple question we can ask when considering our elderly patients. In our Covid-19 cohort we found an association to prognosis and it could be used to help decide therapeutic care of elderly patients and to avoid futile care.[10]

In order to understand the apparent state of health, we can hypothesize that it might be associated to other scales such as the palliative performance scale and clinical frailty scale.[8] Our database did not include this information and we could not evaluate whether these would factor in a better or worse prediction. We did find an association to in-hospital mortality.[8,11] Apparent state of health is a subjective classification that was judged by dozens of different physicians with a wide variation in age and experience (including residents). Despite this, it behaved admirably well. If the patient looks well, the patient may do better than their age would imply, but if the patient looks ill, their prognosis may not be very good, and some therapeutic measures may be futile.

Meanwhile, in the non-intubated patients, apparent state of health was also an important predictor of mortality (with an odds ratio of 4.6) along with dementia and age, as well as characteristics probably pertaining to the Covid-19 infection: myalgia, heart rate and peripheral saturation.

CONCLUSION

When we decide the management of our patients, especially in the emergency department, we must be cognizant of multiple factors besides the patient's diagnosis such as the patients' values and their prognosis. Since conditions and diseases are heterogenous, it can be hard to pin down an accurate prognosis. Age is definitely an important element in this equation. But, as we demonstrated in this study, in Covid-19 elderly patients, the apparent state of health is an additional important element. Because of its simplicity in evaluation,

its use should be considered in clinical care and future research, for it has the potential to be a valuable tool to provide better prognosis, therefore better aligning care with the patient's values.

This study showed that elderly intubated Covid-19 patients have a generally poor prognosis, with a low likelihood of survival. In a situation of respiratory failure intubation should not be considered standard practice in this population, considering high mortality and disability rates. Instead, shared decision-making is a more reasonable approach.

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