

Timing of Intubation and ICU Mortality in COVID-19 Patients: A Preplanned Retrospective Analysis of 4198 Critically Ill Patients

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Abstract

Background

Optimal time to intubate patients with SARS-CoV-2 pneumonia is controversial. Whereas some authors recommend trying noninvasive respiratory support before intubate, others argue that delaying intubation can cause patient-self-induced lung injury and worsen the prognosis. We hypothesized that delayed intubation would increase the risk mortality in COVID-19 patients.

Methods

This preplanned retrospective observational study used prospectively collected data from adult patients with COVID-19 and respiratory failure admitted to 73 intensive care units between February 2020 and March 2021. Patients with limitations on life support and those with missing data were excluded.

We collected demographic, laboratory, clinical variables and outcomes.

Intubation was classified as 1) Very early: before or at ICU admission; 2) Early: < 24 hours after ICU admission; or 3) Late: ≥ 24 hours after ICU admission. We compared the early group versus those intubated late, using chi-square tests for categorical variables and the Mann-Whitney U for continuous variables. To assess the relationship between early versus late intubation and mortality, we used multivariable binary logistic regression. Statistical significance was set at $p < 0.05$.

Results

We included 4198 patients [median age, 63 (54–71) years; 70.8% male; median SOFA score, 4 (3–7); median APACHE score, 13 (10–18)], and median $\text{PaO}_2/\text{FiO}_2$, 131 (100–190)]; intubation was very early in 2024 (48.2%) patients, early in 928 (22.1%), and late in 441 (10.5%). ICU mortality was 30.2% and median ICU stay was 14 (7–28) days. Although patients in the late group were younger [62 vs. 64, respectively, $p < 0.05$] and had less severe disease [APACHE II (13 vs. 14, respectively, $p < 0.05$) and SOFA (3 vs. 4, respectively, $p < 0.05$) scores], and higher $\text{PaO}_2/\text{FiO}_2$ at admission (116 vs. 100, respectively, $p < 0.05$), mortality was higher in the late group than in the early group (36.9% vs. 31.6%, $p < 0.05$). Late intubation was independently associated with mortality (OR 1.83; 95%CI 1.35–2.47).

Conclusions

Delaying intubation beyond the first 24 hours of admission in patients with COVID-19 pneumonia increases the risk of mortality.

Trial registration: clinical-Trial.gov (NCT 04948242)

Background

Patients with COVID-19 pneumonia can develop severe hypoxemia and acute respiratory distress syndrome (ARDS) that can increase the risk of death. Although ARDS has been studied for decades, the optimal timing for the initiation of invasive mechanical ventilation (IMV) remains unknown. Whether early or late intubation is better remains controversial, partly due to adverse effects of IMV such as ventilator-induced lung injury and ventilator-associated pneumonia^{1,2}. In patients with COVID-19 pneumonia, especially during the first wave of the pandemic, the decision of when to intubate was also influenced by a lack of ventilators and by concerns about an increased risk of contagion of healthcare personnel arising from the generation of aerosols in noninvasive respiratory support.

Various guidelines recommend early intubation in patients with severe COVID-19 pneumonia because a large proportion of these patients develop respiratory failure requiring emergency orotracheal intubation, which entails a higher risk of viral transmission to healthcare workers^{3,4,5,6}, and some experts also recommend early intubation to prevent patient-self-induced lung injury (P-SILI)^{7,8}. However, others argue that there is insufficient evidence for P-SILI and caution against adopting this rationale for making decisions about mechanical ventilation in patients with COVID-19 pneumonia⁹. A recent meta-analysis including more than 8,000 critically ill patients with COVID-19 suggested that the timing of intubation may have no impact on mortality¹⁰; however, the heterogeneity of the studies analyzed precludes definitive conclusions. We hypothesized that delayed intubation is associated with higher mortality in COVID-19. To test this hypothesis, we aimed to determine the impact of intubation timing on ICU mortality from data collected prospectively in a large population of critically ill COVID-19 patients.

Methods

Design

This preplanned retrospective observational study used prospectively collected data from consecutive COVID-19 patients admitted to 73 ICUs (71 in Spain, 1 in Andorra, and 1 in Ireland) between February 22, 2020 and March 11, 2021. Data were retrieved from the Spanish Society of Intensive Care Medicine and Coronary Units' (SEMICYUC) registry of COVID-19 patients. The study was registered at Clinical-Trials.gov (NCT 04948242).

We selected all consecutive patients ≥ 15 years old who met the criteria for COVID-19 pneumonia and acute respiratory failure. We excluded patients with limitations on life support and those with missing data. Patients were followed up from ICU admission to ICU discharge or death.

Data collection

Patients' demographic and clinical data were recorded on a case report form, anonymized, and sent to the coordinating center, where all the information was entered in the COVID-19 registry, as reported elsewhere¹¹. Collected data included demographic characteristics (age, sex, and body mass index), comorbidities, time course of the illness (dates of symptoms onset, diagnosis, hospital admission, and

ICU admission), laboratory tests, microbiologic results, radiological findings, time to intubation, noninvasive respiratory support (oxygen, high-flow nasal cannula [HFNC], noninvasive ventilation [NIV], and IMV) at ICU admission and 24 hours after admission, complications, organ-support measures, treatments administered, and outcomes. Disease severity was evaluated 24 h after ICU admission using the Acute Physiology and Chronic Health Evaluation (APACHE) II score and the Sequential Organ Failure Assessment (SOFA) score.

Clinical decisions (e.g., indicating intubation, respiratory support, and treatments) were not protocolized and were left to the discretion of attending physicians. COVID-19 diagnoses were confirmed by reverse transcription-polymerase chain reactions positive for SARS-CoV-2 in specimens from the upper (nasal / oropharyngeal swabs) or lower respiratory tract (tracheal aspirate or bronchoalveolar lavage), and COVID-19 pneumonia was diagnosed through clinical signs of pneumonia with acute respiratory failure and lung infiltrates on chest imaging^{12,13}.

Outcome

The primary outcome was all-cause ICU mortality.

Secondary outcomes included hospital mortality, ICU and hospital LOS, and time under IMV.

Analysis plan

We classified intubation time as 1) very early: before or at ICU admission; 2) early: < 24 hours after ICU admission; or 3) late > 24 hours after ICU admission. We compared patients in the early group versus those in the late group. The very early group was used as a reference for comparisons between groups.

Statistical analysis

Rather than calculate the sample size a priori, we included all patients admitted to the participating ICUs during the study period. Categorical variables are expressed as frequencies and percentages, and continuous variables are expressed as medians and Q1 and Q3 interquartile. To compare baseline characteristics between groups, we used chi-square or Fisher's exact tests for categorical variables and the Mann-Whitney U for continuous variables. All tests were two-tailed, and significance was set at $p < 0.05$. To compare mortality between groups, we used binary logistic regression, including in the model variables that were significant in the univariate analysis and reporting the results as odds ratios (OR) with their 95% confidence intervals (CI). To investigate possible hospital-level or inter-hospital variation in ICU mortality (as random effects), we used multilevel logistic regression analysis with a conditional random intercept model¹¹, classifying hospitals according to the total number of beds (< 200, 200 – 500, or > 500). Regression coefficients are summarized as the variance with standard deviation and the interclass correlation coefficient (ICC).

We used SPSS version 24 (IBM Corp. Armonk, NY, USA) and R software (cran.r-project.org) for statistical analyses.

Results

Study population

During the study period, 4,266 patients were admitted to the participating ICUs with COVID-19 pneumonia; 51 (1.2%) were excluded from the analyses due to decisions to limit life support during their ICU stay and 17 (0.4%) were excluded due to missing data (Figure 1). Thus, we analyzed data from 4,198 patients [median age, 63 (54–71) years; 70.8% men; median SOFA score, 4 (3–7), median APACHE II score, 13 (10–18); and median PaO₂/FiO₂ ratio at ICU admission, 131 (90–190)].

The conditional random intercept model found no effects on ICU mortality attributable to the center (variance 0.39, SD 0.63; ICC 0.10) or to hospital size (variance 0.001, SD 0.04; ICC 0.0004). ICU mortality was 30.2% (n=1260/4198) and hospital mortality was 31.6% (n=1327/4198), with a median ICU length of stay (LOS) of 14 (7–28) days and hospital LOS of 29 (18–46) days. **Table 1** reports the baseline characteristics, complications, and outcomes of the entire sample.

At ICU admission, 2,024 (48.2%) patients were on IMV or immediately intubated (very early group). Additionally, 928 (22.1%) patients were intubated during the first 24 hours after ICU admission (early group), and 441 (10.5%) were intubated >24 hours after ICU admission (late group). Thus, a total of 3,393 (80.8%) received IMV during the ICU stay (Figure 1).

Very early intubation group versus non-ventilated patients at ICU admission

Compared to patients who were not intubated at ICU admission, patients in the very early group were older [65 vs. 62 y, p<0.001], had more severe disease [APACHE II: 15 vs. 12, p<0.001, and SOFA: 6 vs. 4, p<0.001], had longer LOS in both the ICU [19 vs. 10 days, p<0.001] and hospital [37 vs. 22 days, p<0.001], and had higher mortality in both the ICU [38.9% vs 21.8%, p<0.001] and hospital [41.4% vs 23.6%, p<0.001] (Supplementary material , Table 2). In the multivariate analysis, very early intubation was associated with a high risk of ICU mortality [OR: 1.73; 95%CI 1.45-2.07, Supplementary material, Table 3].

Very early intubation group versus patients who required IMV (early and late intubation groups)

Among patients who required IMV during their ICU stay (n=3393), those in the very early group had more severe disease [APACHE II: 15 vs. 13, p<0.001, and SOFA: 6 vs. 4, p<0.001] and greater mortality in both the ICU [38.8% vs. 33.3%, p<0.001] and hospital [40.71% vs. 35.43%, p<0.05] than those in the other two groups (Supplementary material Table 4). However, in the multivariate analysis included only patients who were intubated, very early intubation was not associated with a higher risk of ICU mortality (OR=1.19, 95%CI 0.99-1.43, Supplementary material Table 5).

Early intubation group versus late intubation group

Compared to patients in the early group, those in the late group were younger [62 vs. 64, p<0.05], had less severe disease [APACHE II: 13 vs. 14, p<0.05, and SOFA: 3 vs. 4, p<0.05], and had higher PaO₂/FiO₂ ratios

at ICU admission [116 vs. 100, $p=0.03$]. However, a higher proportion of patients in the late group died in the ICU [36.9% vs 31.6%, $p<0.05$] and in the hospital [39.9 vs. 33.3%, $p<0.05$] (Table 2). In the multivariate analysis, late intubation was associated with a higher risk of ICU mortality [OR= 1.83; 95%CI 1.35-2.47] regardless of the type of noninvasive respiratory support (Table 3). No differences were observed between the early and late groups regarding the LOS in the ICU (25 vs. 19, $p=0.97$) or hospital (41 vs. 35, $p=0.7$) or in the days under IMV (15 vs. 15, $p=0.62$) (Table 2).

Both in the early group and in the late group, all patients received noninvasive respiratory support to treat hypoxemia at admission. In the early group, HFNC in 510 (55%), conventional oxygen therapy in 310 (33.4%), and NIV in 108 (11.6%). In the late group, HFNC in 241 (54.6%), conventional oxygen therapy in 102 (23.1%), and NIV in 98 (22.3%) (Figure 2). The proportion of patients receiving NIV at admission was higher in the late group (22.3% vs. 11.6% in the early group, $p<0.001$) (Table 2). Median time from ICU admission to intubation was longer in patients receiving NIV than in those receiving HFNC [48 h (24-72) vs. 18 h (6-38), respectively, $p<0.05$]. In the multivariable analysis, receiving NIV at admission was independently associated with higher risk of death [OR=1.93, 95%CI 2.3-3.3] (Table 3). The proportions of patients who were eventually intubated did not differ according to the type of noninvasive respiratory support received at admission (34.3% for conventional oxygen therapy, 37.9% for HFNC, and 40.1% for NIV, $p=0.14$).

Discussion

We found that in critically ill patients with COVID-19 pneumonia who do not require intubation at admission to the ICU, intubation > 24 hours after ICU admission was associated with an increased risk of mortality. Remarkably, we found higher mortality in the late intubation group even though these patients were younger, had less severe disease, and higher $\text{PaO}_2/\text{FiO}_2$ at admission than those in the early intubation group. These findings suggest that physicians have a 24-hour window to decide whether to intubate without increasing the risk of mortality in COVID-19 patients. These findings are similar to those in patients with ARDS, where delaying intubation increases mortality^{14,15}, and guidelines indicate early intubation¹⁶.

The data analyzed here were collected during the first year of the COVID-19 pandemic, when the decreased availability of resources, including ICU beds and ventilators, resulted in delays in ICU admission and in connection to IMV. In this context, it was observed that patients could benefit from noninvasive respiratory support (e.g., HFNC or NIV) and awake prone positioning¹⁷, and that some patients with hypoxemic respiratory failure due to COVID-19 pneumonia did not have dyspnea, tachypnea, or increased work of breathing¹⁸. Avoiding intubation is desirable when possible^{1,19}; however, delaying intubation in patients who eventually require it could produce P-SILI and increase mortality^{7,20}.

In our study, nearly half the patients were intubated before or at ICU admission. The decision to intubate was left to the attending physicians' discretion, but no doubt patients in this very early intubation group had clear signs of respiratory failure or severe hypoxemia with clear indications for intubation. However,

the timing of intubation in patients who do not require emergency intubation and receive some form of oxygen therapy as the first approach to the treatment of severe respiratory failure is unclear.

The cutoff between early and late intubation is controversial. Several studies using a 24-hour cutoff found no significant differences in ICU mortality^{10,21,22}. Studies using a 48-hour cutoff have reported contradictory findings, with some observing higher in-hospital and out-of-hospital mortality rate in patients intubated after the cutoff^{23,24,25} and others finding no significant differences²⁶. One retrospective observational study including 40 patients with COVID-19 found lower mortality in patients intubated < 50 hours after admission, but the small sample precludes conclusions about the timing of intubation²⁷. Another study including 5,794 patients in five hospitals in New York City found a small but significant increase in mortality (hazard ratio: 1.03 (95% CI, 1.01–1.05) for each additional day between hospital admission and intubation²⁸.

It might be more logical to establish the cutoff according to the onset of severe hypoxemic respiratory failure. Ranieri et al.²⁹ found no significant differences in mortality, ICU LOS, or days under IMV between patients intubated 24 hours before or after the onset of ARDS diagnosed according to the Berlin criteria³⁰. In a study where patients were intubated if they developed hemodynamic instability, altered level of consciousness, or respiratory distress defined as the use of accessory respiratory muscles or inability to speak, Siempos et al.³¹ found no significant differences in mortality, ICU LOS, or ventilator-free days between a group comprising unintubated patients together with those who were intubated after receiving noninvasive respiratory support for > 24 hours to avoid intubation versus the remaining intubated patients. Finally, a prospective observational study to assess the usefulness of a protocol in which patients were intubated for increased work of breathing after HFNC and awake prone maneuver found higher mortality in patients intubated > 48 hours after admission²³.

Our study has several strengths. It was conducted in 73 ICUs in different countries and included a large number of critically ill patients. Moreover, data were collected over a one-year period including different waves of the pandemic, thus avoiding possible biases related to variations in treatment arising from differences in the availability of resources and knowledge about the disease^{11,32,33}. Finally, our robust statistical analysis adjusted for demographic variables, comorbidities, and severity scores.

Our study also has some limitations. The decision to intubate was not protocolized, and the reason for intubation was not recorded. Moreover, we did not collect complementary respiratory variables (e.g., driving pressure and mechanical power) that have been related to mortality in intubated patients³⁴. Nevertheless, this epidemiological database compiled during the COVID-19 pandemic enables us to differentiate patients according to the timing of intubation in a real scenario. Our retrospective observational analysis carries the risk of selection bias, and other confounding factors cannot be excluded. For these reasons, despite the large number of critically ill patients included, our results may not be generalizable to other populations or scenarios.

Conclusions

Because delaying intubation beyond 24 hours after ICU admission can increase mortality, physicians should aim to decide whether to intubate patients with ARDS due to COVID-19 within this time window.

Abbreviations

ARDS: Acute respiratory distress syndrome, IMV: invasive mechanical ventilation, P-SILI: patient-self-induced lung injury, HFNC: high-flow nasal cannula, NIV: noninvasive ventilation, APACHE: Acute Physiology and Chronic Health Evaluation, SOFA: Sequential Organ Failure Assessment, OR: odds ratios, CI: Confidence interval, SD: standard deviation, ICC: interclass correlation coefficient, LOS: length of stay.

Declarations

Ethical approval and consent to participate

The study was approved by the ethics committee of Joan XXIII Hospital (IRB #CEIM/066/ 2020) as well as by the ethics committees at each participating center. The need for informed consent for inclusion in the database was waived because all data were de-identified by removing patient's name and medical record numbers. The need for informed consent for participation in the study was waived because this retrospective observational study had no impact on patient management.

Availability of data and materials

The anonymized database collected for the study by the SEMICYUC, and the data dictionary that defines each field in the set, will be made available to reviewers if they consider necessary prior confidentiality agreement.

Competing interests

The authors declare that they have no competing interests.

Role of funding source

The funding source had no role in the study design, data collection, data analysis, interpretation of data, the writing of the report, or in the decision to submit the paper for publication.

Authors' contributions

SM, AR, LC. MM, MB, and ED had substantial contributions to conception and design of the study.

SM, AR, ST, LC, MM, and LC had substantial contribution for data acquisition.

SM, AR, LC, MM, MB, IML, JSV, JRM, FG, ED, EBA, RGN, AAM, MV, JCB, LS and SS had substantial contribution for analysis and interpretation of data for the study.

SM, AR, IML, MM, MB, and ED drafting of the manuscript.

JRM, FG, JSV, RGN, AAM, LS, SS EBA and JCB critically reviewed the draft manuscript.

The corresponding author (SM) had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

All authors approved the final version of the manuscript. The views expressed in this article are those of the authors and not necessarily those of the SEMICYUC.

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Tables

Table 1: General characteristics of the population.

Variable	Entire population (N=4198)
<i>Demographics and severity of illness</i>	
Male, n (%)	2971 (70.8)
Age, in years, median (p25-75)	63 (54–71)
SOFA, median (p25-75)	4 (3–7)
APACHE II, median (p25-75)a	13 (10–18)
<i>Comorbidities</i>	
Hypertension, n (%)	1931 (46%)
Obesity (>30 kg/m ²), n (%)	1508 (35.9%)
Diabetes, n (%)	949 (22.6%)
Chronic heart failure, n (%)	139 (3.3%)
Chronic lung disease, n (%)	286 (6.8%)
Asthma, n (%)	262 (6.2%)
Ischemic heart disease, n (%)	256 (6.1)
Immunosuppression, n (%)	222 (5.3%)
Chronic kidney disease, n (%)	210 (5%)
<i>Laboratory findings at admission</i>	
Procalcitonin (ng/ml), median (p25-75)	0.28 (0.11–0.82)
C-reactive protein (mg/dL), median (p25-75)	14.19 (7.9–22.3)
White blood cells count (10 ⁹ /ml), median (p25-75)	8.9 (6.3–12.4)
LDH (U/L), median (p25-75)	489 (368–670)
D-dimer (ng/ml), median (p25-75)	1000 (580.5–2260)
Creatinine (mg/dL), median (p25-75)	0.76 (0.53–1.03)
Urea (mg/dL), median (p25-75)	44 (32–61)
Lactate (mmol/L), median (p25-75)	1.5 (1.1–2.1)
PaO ₂ /FiO ₂ ratio, median (p25-75)	131 (90–190)
<i>Complications and outcomes</i>	
Acute renal failure, n (%)	1123 (26.8 %)
Renal replacement therapy, n (%)	383 (9.1 %)
Acute heart failure, n (%)	376 (9 %)
ICU LOS (days), median (p25-75)*	14 (7–28) *
Hospital LOS (days), median (p25-75)*	29 (18–46) *
ICU mortality, n (%)	1270 (30.2 %)

Hospital mortality, n (%)	1327 (31.6 %)
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*Calculated on survivors.

a= Measured after 24 hours of admission.

SOFA= Sequential Organ Failure Assessment, APACHE= Physiology and Chronic Health Evaluation, LOS= Length of stay.

Table 2: Univariate analysis. Early vs. late intubation.

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Variables	Early intubation (n=928)	Late intubation (n=441)	P values
<i>General characteristics</i>			
Male, n (%)	670 (72.2)	317 (71.9)	0.9
Age, median (p25-75)	64 (56–71)	62 (50–73)	0.012
<i>Comorbidities</i>			
Hypertension, n (%)	466 (50.2)	175 (39.7)	<0.001
Obesity (>30 kg/m ²), n (%)	354 (38.1)	150 (3.4)	0.13
Diabetes, n (%)	262 (28.2)	85 (19.3)	<0.001
Chronic lung disease, n (%)	69 (7.4)	24 (5.4)	0.17
Asthma, n (%)	60 (6.5)	26 (5.9)	0.68
Immunosuppression, n (%)	60 (6.5)	28 (6.3)	0.93
Chronic kidney disease, n (%)	58 (6.2)	24 (5.4)	0.55
Chronic heart failure, n (%)	32 (3.4)	18 (4.1)	0.55
Ischemic heart disease, n (%)	64 (6.9)	27 (6.1)	0.59
<i>Severity of illness</i>			
SOFA, median (p25-75)	4 (3–7)	3 (2–6)	<0.001
APACHE II, median (p25-75) a	14 (10–18)	13 (10–14)	0.007
PaO ₂ /Fio ₂ ratio at admission, median (p25-75)	100 (75–148)	116 (90–152)	0.03
<i>Oxygen therapy at admission</i>			
Conventional O ₂ , n (%)	310 (33.4)	102 (23.1)	<0.001
HFNC, n (%)	510 (55)	241 (54.6)	0.91
NIV, n (%)	108 (11.6)	98 (22.3)	<0.001
<i>Complications and outcomes</i>			
Acute renal failure, n (%)	283 (30.5)	111 (25.2)	0.044
Renal replacement therapy, n (%)	105 (11.3%)	39 (8.9)	0.16
Acute heart failure, n (%)	104 (11.2%)	42 (9.5)	0.34
Days for IVM, median (p25-75)*	15 (8–28)	15 (8–27)	0.62
ICU LOS median (p25-75)*	19 (12–34)	25 (8–42)	0.97
Hospital LOS median (p25-75) *	35 (23–53)	41(20–64)	0.7
ICU mortality, n (%)	293 (31.6)	163 (36.9)	0.048
Hospital mortality, n (%)	309 (33.3)	176 (39.9)	0.034
<i>Treatments</i>			

Variables	Early intubation (n=928)	Late intubation (n=441)	P values
NO, n (%)	32 (3.4%)	27 (6.2)	0.026
Prone positioning, n (%)	677 (72.9%)	309 (70.1)	0.26
ECMO, n (%)	15 (1.6%)	18 (4.1)	0.005

* Calculated on survivors.

a= Measured after 24 hours of admission.

SOFA= Sequential Organ Failure Assessment, APACHE= Physiology and Chronic Health Evaluation, HFNC= High flow nasal cannula, NIV= Non invasive ventilation, IMV: Invasive mechanical ventilation, NO= Nitric oxide, ECMO= Extracorporeal membrane oxygenation, LOS= Length of stay.

Table 3: Mortality in the ICU: binary logistic regression analysis

Variables	OR	IC	P values
<i>General characteristics</i>			
Male sex	1.13	0.93–1.37	0.21
Age	1.05	1.04–1.06	<0.001
Comorbidities			
Chronic lung disease	1.46	1.06–2.01	0.02
Chronic heart failure	0.97	0.62–1.53	0.99
Chronic kidney injury	1.12	0.78–1.62	0.53
Diabetes	1.1	0.9–1.34	0.35
Ischemic heart disease	1.6	1.14–2.24	0.006
Hypertension	1.04	0.87–1.25	0.67
Immunosuppression	1.65	1.16–2.33	0.005
Severity of illness			
APACHE II	1	0.99–1.02	0.7
SOFA	1.08	1.04–1.12	<0.001
Respiratory support before OTI			
Conventional oxygen therapy	1.23	0.87–1.76	0.25
HFNC	1.27	0.92–1.72	0.15
NIV	1.93	1.29–2.88	0.001
Intubation timing			
EARLY intubation	0.55	0.4–0.74	<0.001
LATE intubation	1.83	1.35–2.47	<0.001
Complications and outcomes			
Acute heart failure	2.26	1.73–2.95	<0.001
Acute renal failure	2.77	2.3–3.33	<0.001

APACHE= Physiology and Chronic Health Evaluation, SOFA= Sequential Organ Failure Assessment, OTI= Orotraqueal intubation, HFNC= High flow nasal cannula, NIV= Non invasive ventilation, IMV: Invasive mechanical ventilation, NO= Nitric oxide, ECMO= Extracorporeal membrane oxygenation, LOS= Length of stay.

Figures

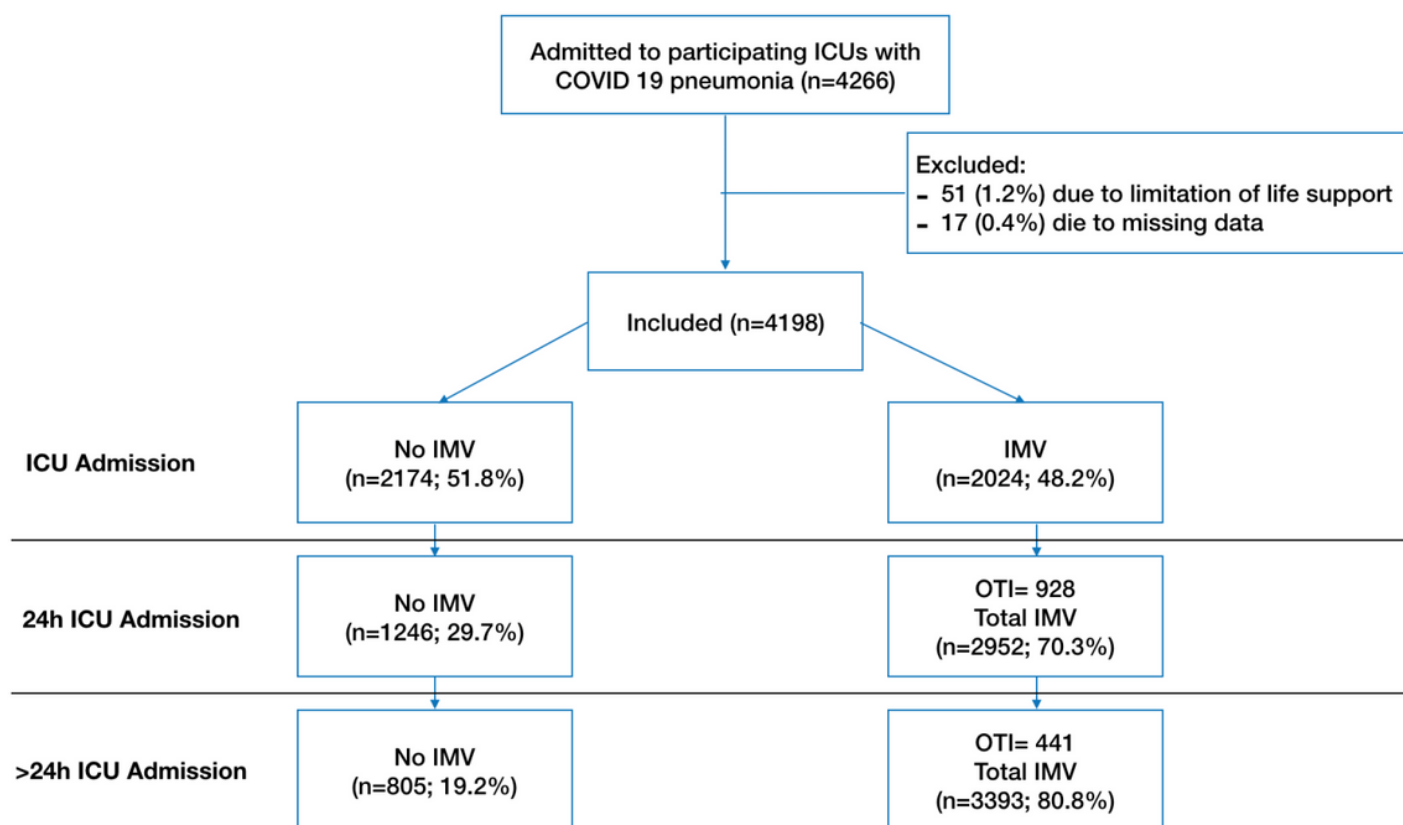


Figure 1

Flowchart of the study.

IMV= Invasive mechanical ventilation, OTI= Orotraqueal intubation

VERY EARLY GROUP 48.2% (n=2024)

Conventional oxygen therapy 17.2% (n=723)
High Flow nasal cannula (HFNC) 27.1% (n=723)
Non invasive ventilation (NIV) (n=312)

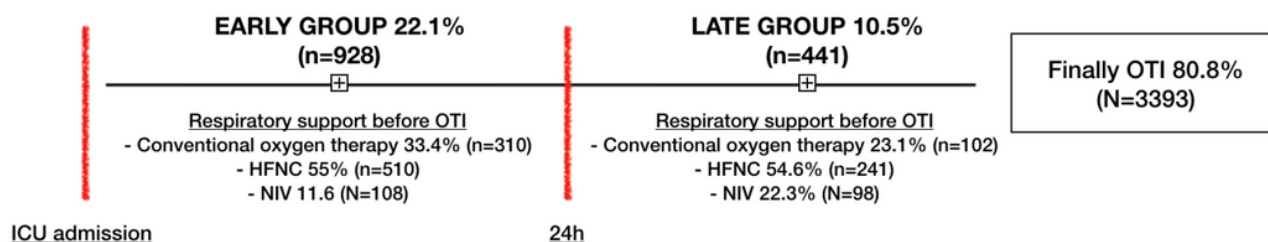


Figure 2

Ventilator support therapy evolution

OTI= Orotraqueal intubation.

Supplementary Files

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