

Effect of early versus delayed or no intubation on clinical outcomes of patients with COVID-19

Ilias Siempos (✉ isiempos@yahoo.com)

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Elena Xourgia

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Theodora K. Ntaidou

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Dimitris Zervakis

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Eleni E. Magira

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Anastasia Kotanidou

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Christina Routsi

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Spyros G. Zakynthinos

First Department of Critical Care Medicine and Pulmonary Services, Evangelismos Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece

Research Article

Keywords: acute respiratory distress syndrome, ARDS, acute respiratory failure, coronavirus, viral pneumonia, critically ill

Posted Date: August 4th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-52647/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Optimal timing of initiation of invasive mechanical ventilation in patients with acute hypoxic respiratory failure due to COVID-19 is unknown. Thanks to early flattening of the epidemiological curve, ventilator demand in Greece was kept lower than supply throughout the pandemic, allowing for unbiased comparison of the outcomes of patients undergoing early intubation versus delayed or no intubation.

Methods: We conducted an observational study including all adult patients with laboratory-confirmed COVID-19 consecutively admitted in Evangelismos Hospital, Athens, Greece between March 11, 2020 and April 15, 2020. Patients subsequently admitted in the intensive care unit (ICU) were categorized into the “early intubation” versus the “delayed or no intubation” group.

Results: During the study period, a total of 101 patients (37% female, median age 65 years) were admitted in the hospital. Fifty-nine patients (58% of the entire cohort) were exclusively hospitalized in general wards with a mortality of 3% and median length of stay of 7 days. Forty-two patients (19% female, median age 65 years, 62% with at least one comorbidity, 14% never intubated) were admitted in the ICU; all with acute hypoxic respiratory failure. Early intubation was not associated with higher ICU-mortality (21% versus 33%), fewer ventilator-free days (3 versus 2 days) or fewer ICU-free days than delayed or no intubation.

Conclusions: A strategy of early intubation was not associated with worse clinical outcomes compared to delayed or no intubation. Given that early intubation may presumably reduce virus aerosolization, these results may justify further research with a randomized controlled trial.

Background

Management of acute hypoxic respiratory failure associated with coronavirus disease 2019 (COVID-19) often includes mechanical ventilation [1,2]. Optimal timing of initiation of invasive mechanical ventilation remains unknown. On the one hand, early initiation of invasive mechanical ventilation (i.e., early endotracheal intubation) has been advocated to avoid alternate means of oxygenation (such as high-flow nasal oxygen or non-invasive mechanical ventilation) associated with aerosolization of virus [3]. Also, early intubation may prevent induction of harmful self-inflicted lung injury in patients who breath spontaneously and have large transpulmonary pressure swings [4]. On the other hand, delaying intubation, by trying alternate means of oxygenation, may mean that some patients may not be intubated at all and therefore will be protected from the adverse events of invasive mechanical ventilation. The latter strategy may also address the shortage of ventilators to meet the increased demand of treating patients with COVID-19.

Ventilator supply-demand mismatch could have affected clinical decision-making regarding application of early versus delayed or no intubation in several epicenters of the pandemic [5]. It could also have affected clinical outcomes [6]. Therefore, ventilator supply-demand mismatch may act as a confounder

when attempting to estimate the effect of early versus delayed or no intubation on clinical outcomes of patients with COVID-19 in several epicenters of the pandemic. This might not be the case for Greece where early implementation of social distancing measures and flattening of the epidemiological curve reduced burden of health-care system, constantly maintaining ventilator demand lower than supply. This fact allowed for an unbiased estimation as to whether early intubation as opposed to delayed or no intubation affects prognosis of patients with COVID-19. We hypothesized that early intubation is not associated with worse clinical outcomes, including mortality, than delayed or no intubation among patients with acute hypoxemic respiratory failure due to COVID-19.

Methods

Study design

We conducted an observational cohort study including all adult (≥ 18 years old) patients with laboratory-confirmed COVID-19, consecutively admitted in Evangelismos Hospital (Athens, Greece) between March 11, 2020 (the day of hospital admission of the first patient with COVID-19) and April 15, 2020. Evangelismos, the biggest tertiary-care hospital in Greece, serves as one of the three reference medical centers for treating patients with COVID-19 in Athens. In response to the pandemic, 72 ICU beds (from the initially available 30), never concomitantly occupied during the study period, were made available for inpatients.

Compared groups

Following collection of demographic and clinical data for the complete patient population, patients with acute hypoxemic respiratory failure admitted in the ICU were categorized into the “early intubation” and the “delayed or no intubation” group. Acute hypoxemic respiratory failure was defined as the requirement for more than 5L/min nasal oxygen (or Venturi mask more than 40%) to keep a pulse oximeter measured arterial blood oxygen saturation (SpO_2) of equal to or more than 95%. “Delayed or no intubation” group consisted of patients receiving non-rebreather mask for equal to or more than 24 hours or high-flow nasal oxygen for any period of time or non-invasive mechanical ventilation for any period of time in an attempt to avoid intubation. The remaining intubated patients comprised the “early intubation” group. The decision of early versus delayed or no intubation rested with the treating clinician.

Study outcomes

ICU-mortality, ventilator-free days and ICU-free days were the outcomes of the study. ICU-mortality was censored at 28 days after the occurrence of acute hypoxemic respiratory failure. Ventilator-free days were calculated starting at the first 24 continuous hours without invasive mechanical ventilation. The day of acute hypoxemic respiratory failure occurrence was considered as day 0 of the 28-day period for which ventilator-free days were calculated. Periods of extubation lasting for equal to or less than 48 hours before re-intubation were not calculated in the sum of ventilator-free days [7]. ICU-free days were calculated starting at the first 24 continuous hours outside the ICU in the post-ICU discharge period. The

day of ICU admission was considered as day 0 of the 28-day period for which ICU-free days were calculated. Occurrence of septic shock (defined according to Sepsis-3) [8] and need of continuous renal replacement therapy also served as outcomes of the study.

Statistical analysis

Study population included all patients treated during the study period. Continuous variables are presented as median and interquartile range (IQR). Mann-Whitney rank sum test was used to compare continuous variables. Categorical variables are presented as number of patients (percentage). χ^2 or Fisher exact test was used to compare categorical variables. A binary logistic regression analysis was carried out to isolate the contribution of early intubation and sex (independent variables) to mortality (categorical dependent variable). All statistical tests were 2-tailed and statistical significance was defined as $p<0.05$. Statistical analyses were performed using SPSS software ver. 22.0 (IBM, Armonk, NY, USA).

Results

During the study period, a total of 101 patients [37% female, median age 65 (IQR 53-73) years] were admitted in the hospital (**Figure 1**). Fifty-nine patients (58% of the entire cohort) were exclusively hospitalized in general wards. Their mortality rate was 3% (only two patients, who opted out ICU admission, died) and median length of stay was 7 days (IQR 5-13). None of the health-workers of the hospital tested positive for COVID-19.

Table 1 summarizes the baseline characteristics and outcomes of 42 patients admitted in the ICU (all with acute hypoxic respiratory failure) during the study period. The median time from hospital to ICU admission was 0 (IQR 0-3) days. Of those admitted in the ICU, 19% were female and 62% had at least one comorbidity. Their median age was 65 (IQR 58-71) years. None of those had a do-not-intubate order and 36 (86%) patients were indeed intubated. ICU-mortality among patients admitted in the ICU was 26%. Data for 13 of those patients have been included in a previous report focusing on the application of positive end-expiratory pressure [9].

Table 1 also summarizes the baseline characteristics and outcomes of patients undergoing early versus delayed or no intubation. Four patients (all transferred intubated from another hospital) were not categorized into the early versus delayed or no intubation group due to unavailability of relevant data. Baseline characteristics [including age, comorbidities and organ failure, as assessed by the Sequential Organ Failure Assessment (SOFA) scores, on the day of occurrence of acute hypoxic respiratory failure] were comparable between the two groups with the exemption of sex. Regarding means of oxygenation, non-rebreather mask was used by all but one patient (who belonged in the delayed or no intubation group), while high-flow nasal oxygen and non-invasive mechanical ventilation was used by 11 and two patients, respectively. Regarding outcomes, early intubation was not associated with higher ICU-mortality (21% versus 33%), fewer ventilator-free days (3 versus 2 days) or fewer ICU-free days (0 versus 0 days) than delayed or no intubation. Early intubation was associated with lower (albeit statistically non-

significant) need for continuous renal replacement therapy (29% versus 50%) than delayed or no intubation. The above findings persisted when comparing the baseline characteristics and outcomes of patients undergoing early versus delayed intubation, i.e., after exclusion of six ICU patients who were not intubated (**Supplemental Table**).

Early intubation (as opposed to delayed or no intubation) was not associated with mortality even after adjustment for sex (i.e., a baseline characteristic which differed between the two groups).

Discussion

We found that approximately one-fourth of patients admitted in the ICU with acute hypoxemic respiratory failure due to laboratory confirmed COVID-19 in Athens, Greece died during their ICU stay. We also found that early intubation was not associated with worse clinical outcomes, such as mortality, ICU-free days and ventilator-free days, compared to delayed or no intubation among those patients.

The observed mortality rate of 26% for patients with COVID-19 admitted in our ICU seems lower than the mortality rates of 62% and 51% reported by early studies from Wuhan, China and Washington State, USA, respectively [10,11]. Although the latter mortality rates might be exaggerated [12] and subsequent studies reported outcomes similar to ours [13], this finding is intriguing. It could be explained by the fact that the health-care system of Greece was not substantially burdened throughout the course of the COVID-19 outbreak. Indeed, a substantially burdened health-care system might lead to worse outcomes [6]. Thus, our finding regarding mortality rate may highlight the beneficial effect of protecting health-care systems (e.g., through early flattening of the epidemiological curve) from overwhelming on outcomes of critically ill patients with COVID-19.

We found that a strategy of early intubation, as opposed to delayed or no intubation, was not associated with worse clinical outcomes, such as mortality, ventilator-free days and ICU-free days. Rather, it seems that the difference (albeit statistically non-significant) in terms of mortality (early: 21% versus delayed or no: 33%) and ventilator-free days (early: 3 versus delayed or no: 2 days) was in favour of the early than the delayed or no intubation strategy. This finding is important because it does not seem to justify the hesitance of clinicians to perform early intubation in concern that it may inadvertently lead to otherwise preventable intubations. In the light of our finding that an early intubation strategy might not be associated with increased mortality and morbidity, one could advocate this approach when taking into consideration its potential benefit of reduced viral aerosolization. To this end, several societies indeed recommend early intubation and avoidance of prolonged use of high-flow nasal oxygen and non-invasive mechanical ventilation in the era of COVID-19 [14].

In addition to its usage as an infection control measure, early intubation could also serve as a means to prevent both emergent intubation and patient self-inflicting lung injury. Regarding emergent intubation, its avoidance could improve outcomes, including mortality [15], by reducing incidence of hypoxemia [16]. Regarding patient self-inflicted lung injury, its prevention and the subsequent pulmonary-renal crosstalk [17] might explain our finding that need for continuous renal replacement therapy was lower (albeit

statistically non-significant) in the early versus the delayed or no intubation group (29% versus 50%). The latter finding could also be explained by the relative dehydration of patients struggling to maintain normoxemia and avoid intubation through the prolonged usage of non-rebreather mask or high-flow nasal oxygen or non-invasive mechanical ventilation.

Our study has limitations. Firstly, although we included all consecutive patients admitted in our hospital, our study still has a moderate sample size. However, this is the case for several other studies involving critically ill patients with COVID-19 [13,18]. Also, the moderate sample size is the fortunate outcome of the early flattening of the epidemiological curve in Greece and eventually the reason we were able to estimate the effect of early versus delayed or no intubation on outcomes of patients with COVID-19 without the major confounding factor of the shortage of ventilators. Secondly, similar to the vast majority of studies in the field of COVID-19 [1,5,19], our study is observational and therefore subject to confounding. However, there was no difference at baseline between the compared groups in terms of variables known to affect prognosis of patients with COVID-19, such as age, comorbidities and organ failures [1]. Besides, our main finding persisted even after adjusting for sex. Finally, one could argue that the comparison of early versus delayed intubation (i.e., after exclusion of ICU patients who were not intubated) should be the primary analysis of our report. To that end, we presented the aforementioned analysis in the **Supplemental Table** and found similar results as in our main analysis. Moreover, the fact that an early intubation strategy was not associated with worse outcomes even when the comparator included never intubated patients may further strengthens the findings of our study.

Conclusion

The findings of our study suggest that early intubation, as opposed to delayed or no intubation, may not be associated with worse outcomes among critically ill patients with COVID-19. Given the observed lack of a negative effect of early intubation on mortality and morbidity of critically ill patients, such a therapeutic approach could be considered to avoid viral cross-contamination and to prevent self-inflicted lung injury. Thus, our study may justify further research with a prospective, randomized controlled trial.

Declarations

Ethics approval and consent to participate: The Institutional Review Board of Evangelismos approved of this study (#212, 2020) and waived the need for informed patient consent.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This study was funded by a grant of Hellenic Thoracic Society (to IIS).

Authors' contributions: Study concept and design: IIS, EX, CR, SGZ; acquisition of data: IIS, TKN, DZ, EEM; analysis and interpretation of data: all authors; first drafting of the manuscript: EX, IIS; critical revision of the manuscript for important intellectual content: all authors; statistical analysis: EX; obtained funding: IIS, SGZ; administrative, technical, and material support: AK, SGZ; study supervision: IIS, SGZ. Data access and responsibility: IIS 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 read and approved the final manuscript.

Acknowledgements: The authors gratefully acknowledge the work of nurses and physicians treating patients with COVID-19 included in this study. The authors especially thank Drs Stelios Kokkoris, Prodromos Temperikidis, Ioannis Papahatzakis, Adamantia Sotiriou, Panagiotis Politis, Athina Strilakou, Panagiota Ntonia, Theodoros Tsoutsouras, Aggeliki Kanavou, Charikleia Vrettou, Sotiris Malachias, Eleni Ischaki and Vassiliki Markaki along with Alexandros Kouvarakos, RT and Sofia Kostourou, RN.

Abbreviations

COVID-19: coronavirus disease 2019, ICU: intensive care unit, IQR: interquartile range, SOFA: sequential organ failure assessment

References

- [1] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet* 2020;395:1054–62. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3).
- [2] Vetter P, Vu DL, L'Huillier AG, Schibler M, Kaiser L, Jacquieroz F. Clinical features of covid-19. *BMJ* 2020;369. <https://doi.org/10.1136/bmj.m1470>.
- [3] Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of Covid-19 in New York City. *New England Journal of Medicine* 2020;0:null. <https://doi.org/10.1056/NEJMc2010419>.
- [4] Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Critical Care* 2020;24:154. <https://doi.org/10.1186/s13054-020-02880-z>.
- [5] Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.5394>.
- [6] Ji Y, Ma Z, Peppelenbosch MP, Pan Q. Potential association between COVID-19 mortality and health-care resource availability. *The Lancet Global Health* 2020;8:e480. [https://doi.org/10.1016/S2214-109X\(20\)30068-1](https://doi.org/10.1016/S2214-109X(20)30068-1).

- [7] Finkelsztein EJ, Jones DS, Ma KC, Pabón MA, Delgado T, Nakahira K, et al. Comparison of qSOFA and SIRS for predicting adverse outcomes of patients with suspicion of sepsis outside the intensive care unit. *Crit Care* 2017;21:73. <https://doi.org/10.1186/s13054-017-1658-5>.
- [8] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:801–10. <https://doi.org/10.1001/jama.2016.0287>.
- [9] Tsolaki V, Siempos I, Magira E, Kokkoris S, Zakynthinos GE, Zakynthinos S. PEEP levels in COVID-19 pneumonia. *Crit Care* 2020;24:303. <https://doi.org/10.1186/s13054-020-03049-4>.
- [10] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine* 2020;8:475–81. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
- [11] Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA* 2020;323:1612–4. <https://doi.org/10.1001/jama.2020.4326>.
- [12] Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. *The Lancet* 2020;395:1014–5. [https://doi.org/10.1016/S0140-6736\(20\)30633-4](https://doi.org/10.1016/S0140-6736(20)30633-4).
- [13] Ziehr DR, Alladina J, Petri CR, Maley JH, Moskowitz A, Medoff BD, et al. Respiratory Pathophysiology of Mechanically Ventilated Patients with COVID-19: A Cohort Study. *Am J Respir Crit Care Med* 2020. <https://doi.org/10.1164/rccm.202004-1163LE>.
- [14] Brewster DJ, Chrimes N, Do TB, Fraser K, Groombridge CJ, Higgs A, et al. Consensus statement: Safe Airway Society principles of airway management and tracheal intubation specific to the COVID-19 adult patient group. *Med J Aust* 2020. <https://doi.org/10.5694/mja2.50598>.
- [15] Meng L, Qiu H, Wan L, Ai Y, Xue Z, Guo Q, et al. Intubation and Ventilation amid the COVID-19 Outbreak. *Anesthesiology* 2020. <https://doi.org/10.1097/ALN.0000000000003296>.
- [16] Yao W, Wang T, Jiang B, Gao F, Wang L, Zheng H, et al. Emergency tracheal intubation in 202 patients with COVID-19 in Wuhan, China: lessons learnt and international expert recommendations. *Br J Anaesth* 2020. <https://doi.org/10.1016/j.bja.2020.03.026>.
- [17] Domenech P, Perez T, Saldarini A, Uad P, Musso CG. Kidney–lung pathophysiological crosstalk: its characteristics and importance. *Int Urol Nephrol* 2017;49:1211–5. <https://doi.org/10.1007/s11255-017-1585-z>.
- [18] Elharrar X, Trigui Y, Dols A-M, Touchon F, Martinez S, Prud'homme E, et al. Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxic Acute Respiratory Failure. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.8255>.

[19] Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *New England Journal of Medicine* 2020;382:1708–20.
<https://doi.org/10.1056/NEJMoa2002032>.

Table

Table 1. Baseline characteristics and outcomes of patients admitted in the intensive care unit.

	All (n=42)	Early intubation (n=14)	Delayed or no intubation (n=24)	p value
Age, years (IQR)	65 (58- 71)	63 (57-69)	64 (57-74)	0.68
Sex, female, n (%)	8 (19)	6 (43)	2 (8)	0.03
Race, n (%)				0.69
Caucasian	39 (93)	14 (100)	21 (85)	
Asian	2 (5)	0 (0)	2 (8)	
Middle Eastern	1 (2)	0 (0)	1 (4)	
Comorbidity, n (%)	26 (62)	8 (57)	15 (63)	0.74
Cardiovascular	20 (48)	7 (50)	11 (46)	0.80
Diabetes Mellitus	7 (17)	2 (14)	5 (21)	1
Chronic lung disease	4 (10)	1 (7)	3 (13)	1
Renal failure	1 (2)	0 (0)	1 (4)	1
Malignancy	5 (12)	0 (0)	4 (17)	0.27
SOFA score (IQR)	4 (4-6)	4 (4-5)	4 (4-6)	0.8
Respiratory	4 (3-4)	4 (4-4)	4 (3-4)	0.11
Coagulation	0 (0-0)	0 (0-0)	0 (0-1)	0.16
Hepatic	0 (0-0)	0 (0-0)	0 (0-0)	0.3
Neurologic	0 (0-0)	0 (0-0)	0 (0-0)	0.97
Cardiovascular	0 (0-0)	0 (0-0)	0 (0-0)	0.2
Renal	0 (0-0)	0 (0-0)	0 (0-0)	0.77
Usage of non-rebreather mask, n (%)	41 (98)	14 (100)	23 (96)	1
Usage of high-flow nasal oxygen, n (%)	11 (26)	0 (0)	11 (46)	0.003
Usage of non-invasive mechanical ventilation, n (%)	2 (5)	0 (0)	2 (8)	0.52

Lung mechanics at day of intubation, (IQR)				
Ppeak	NA	39 (36-41)	37 (32-42)	0.6
Pplateau	NA	28 (28-31)	28 (25-32)	0.45
PEEPtotal	NA	17 (13-19)	14 (11-19)	0.2
Pdriving	NA	13 (10-15)	13 (12-17)	0.27
Transferred intubated from another hospital, n (%)	19 (45)	12 (86)	3 (13)	<0.001
Outcomes within 28 days				
Intubation, n (%)	36 (86)	14 (100)	18 (75)	0.06
Intubation outside ICU, n (%)	21 (50)	12 (86)	6 (25)	0.004
Septic shock, n (%)	18 (43)	6 (43)	11 (46)	1
Continuous renal replacement therapy, n (%)	17 (41)	4 (29)	12 (50)	0.19
Ventilator-free days, days (IQR)	NA	3 (0-17)	2 (1-13)	0.57
ICU-free days, days (IQR)	0 (0-15)	0 (0-16)	0 (0-12)	0.59
Time from acute respiratory failure to ICU admission, days (IQR)	1 (0-1)	1 (0-1)	1 (0-2)	0.87
ICU-mortality, n (%)	11 (26)	3 (21)	8 (33)	0.48

Abbreviations: IQR: interquartile range, SOFA: sequential organ failure assessment, NA: not applicable, ICU: intensive care unit

“Delayed or no intubation” group consisted of patients receiving non-rebreather mask for equal to or more than 24 hours or high-flow nasal oxygen for any period of time or non-invasive mechanical ventilation for any period of time in an attempt to avoid intubation. The remaining intubated patients comprised the “early intubation” group.

Six patients admitted in the ICU were not intubated and therefore were included in the delayed or no intubation group. Four patients (transferred intubated from another hospital) were not categorized into the early versus delayed or no intubation group due to unavailability of relevant data.

Cardiovascular comorbidities included congestive heart failure, hypertension, coronary artery disease, dyslipidemia and valvular dysfunction.

Figures

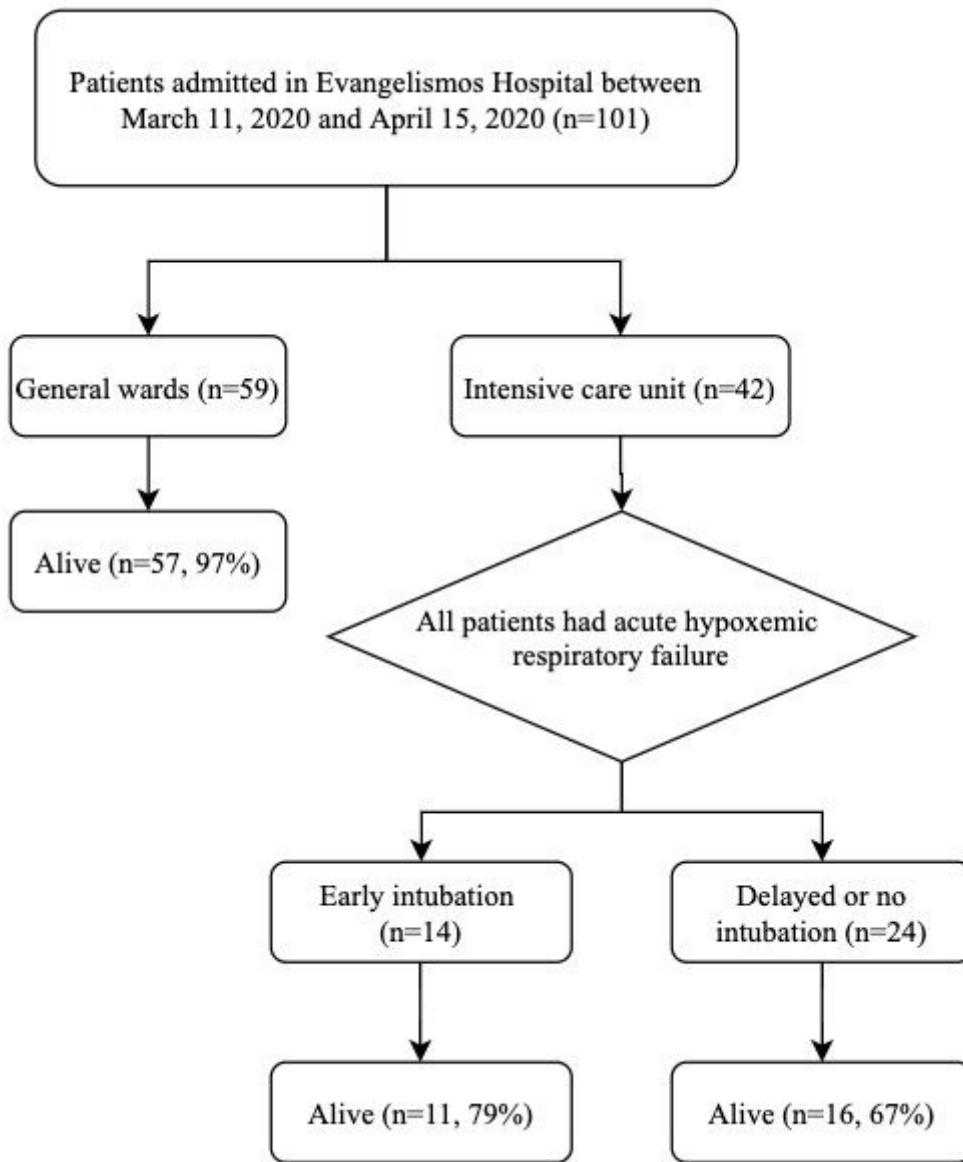


Figure 1

Patient flow diagram. Six patients admitted in the intensive care unit were not intubated and therefore were included in the delayed or no intubation group. Four patients (transferred intubated from another hospital) were not categorized into the early versus delayed or no intubation group due to unavailability of relevant data.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementalTable.docx](#)