Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Research Paper

Early versus late intubation on the outcome of intensive care unit-admitted COVID-19 patients at Addis Ababa COVID-19 treatment centers, Addis Ababa, Ethiopia: A multicenter retrospective cohort study

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) has resulted in severe acute respiratory failure, requiring intubation and an invasive mechanical ventilation. However, the time for initiation of intubation remains debatable. Therefore, this study aimed to compare early and late intubation on the outcome of COVID-19 patients admitted to the intensive care unit (ICU) of selected Addis Ababa COVID-19 treatment centers, Ethiopia.
Methods: A multicenter retrospective cohort study was conducted on 94 early and late intubated ICU-admitted COVID-19 patients from October 1, 2020, to October 31, 2021, in three selected COVID-19 treatment centers in Addis Ababa, Ethiopia. A simple random sampling technique was used to select study participants. An independent *t*-test, Mann Whitney *U* test and Fisher's exact test were used for statistical analysis, as appropriate. A P value < 0.05 was used to declare a statistical significance.
Results: A total of 94 patients participated, for a response rate of 94.68%. There was a statistically insignificant difference in the rates of death between the early intubated (47.2%) and the late intubated (46.1%) groups ($P = 0.678$). There was no difference in the median length of stay on a mechanical ventilator (in days) between the groups ($P = 0.11$). However, the maximum length of stay in the ICU to discharge was significantly shorter in the early intubated (33.1 days) than late intubated groups (63.79 days) ($P < 0.001$).
Conclusion: Outcomes (death or survival) were similar whether early or late intubation was used. Early intubation did appear to improve length of ICU stay in ICU-admitted COVID-19 patients.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1,2]. It has spread very rapidly around the world, resulting in severe acute respiratory failure with less known pathophysiology [2–5]. It has increased its rate of transmission and critical illness with a higher risk of intensive care unit (ICU) admissions, producing a wide spectrum of mortality rates [6]. It resulted in the development of severe disease in 14% of patients that required hospitalization, and 5% required admission to ICU [7].

It has no definitive treatment except giving supportive treatments for multi-system complication [8]. COVID-19 patients with severe hypoxic respiratory failure require prolonged supportive care, requiring intubation and an invasive mechanical ventilation [9,10]. According to a meta-analysis in 18 observational studies, the rate of intubation in hypoxic COVID-19 patients was 28% [11]. However, the threshold for intubation is controversial because many patients had normal work of breathing despite severe hypoxemia [12,13], precluding the decision time to intubate.

Furthermore, timing of intubation remains controversial, partly due to ventilator induced lung injury and ventilator-associated pneumonia associated with an invasive mechanical ventilation, and complications associated with intubation [14,15]. A previous study reported that

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; COVID-19, Coronavirus Disease 2019; ICU, Intensive Care Unit; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; SILI, Self-induced lung injury.

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COVID-19 patients underwent late intubation had markedly higher mortality rates compared to those who were intubated early [16]. Another study also recommended early intubation in case of worsening of respiratory status in COVID-19 patients [17].

An observational study of patients with COVID-19 also found higher mortality in late intubated patients [18]. Some experts also recommend early intubation to prevent patient-self-induced lung injury [19]. However, a systematic review suggested that the timing of intubation may have no effect on mortality in ICU-admitted critically ill COVID-19 patients [20]. Another study, however, found a mortality benefit in the early intubated ICU-admitted COVID-19 patients [21]. Therefore, data regarding timing of intubation on the outcome of ICU-admitted COVID-19 patients are needed to inform decision-making and care of patients. Therefore, this study aimed to compare the time of intubation on the outcome of ICU-admitted COVID-19 patients in selected Addis Ababa COVID-19 treatment centers, Ethiopia. In addition, we examined the impact of time of intubation on secondary clinical outcomes, including ICU length of stay and duration of mechanical ventilation.

2. Materials and methods

2.1. Study design, period and setting

This multicenter retrospective cohort study was conducted in three governmental purposely selected COVID-19 treatment centers in Addis Ababa: Saint Paul's Hospital Millennium Medical College (SPHMMC), Eka Kotebe General Hospital, and Saint Peter Specialized Hospital (SPSH) COVID-19 treatment centers, from October 1, 2020, to October 31, 2021. These hospitals were among the governmental hospitals which provide COVID-19 treatment services in the capital of Ethiopia with an estimated population of more than ten million.

2.2. Population and eligibility criteria

The source population was all COVID-19 positive patients who were admitted to the ICU and intubated in the selected COVID-19 centers during the study period. The study population was COVID-19 positive patients who were admitted and intubated in the ICUs of selected centers, who fulfilled the inclusion criteria and selected for the sample, during the study period.

Adult COVID-19 positive patients above 18 years, who were admitted and intubated in the ICUs of selected COVID-19 treatment centers were included. Pediatrics and adult COVID-19 positive patient, who were intubated before ICU admission, and patents who were referred to other hospitals without knowing their outcome (survival or death), were excluded from the study. This study has been registered on the Research Registry and has received a UIN "researchregistry8272", which can be accessed through https://www.researchregistry.com/browse-the-registry#home/. This study is reported according to the STROCSS 2021 guideline [28].

2.3. Study variables

The primary outcome variable was death in the ICU, and the explanatory variables were sociodemographic factors, clinical characteristics, respiratory parameters and vital signs of patients, interventions performed at ICU and time of intubation.

2.4. Operational definitions

Outcome: Survival or death of intubated ICU-admitted COVID-19 patient in the ICU.

Early intubation: The intubation of an ICU-admitted COVID-19 positive patient within 24 h of ICU admission.

Late intubation: The intubation of an ICU-admitted COVID-19 positive patient after 24 h of ICU admission.

Intubation: A technique of inserting endotracheal tube in the tracheal to provide an artificial airway and ventilation.

2.5. Sample size and sampling technique

Sample size was calculated using comparison of proportion with equal sample size for two independent cohort sample size formula using the proportion of mortality among early and late intubated ICU-admitted COVID-19 positive patients obtained from previous study [18] and by assuming a 5% margin of error at a 95% confidence interval. And power of 80%.

$$n1 = n2 = \frac{\left(Z_{\frac{\alpha}{2}}+ZB\right)^2 * ((p1(1-p1)+p2(1-p2)\right)}{(p1-p2)^2}$$ where, p1 = 1.46%, p2 = 18.46%, $\left(Z_{\frac{\alpha}{2}}+ZB\right)^2 = 7.84$. Therefore, the calculated sample size was (n1 = n2≈ 45). By adding 5% contingency, the total sample size was 94; 47 patients in each group.

Study subjects for each selected center were allocated equally by dividing calculated sample size (n = 94) by the selected study centers. Study participants for each COVID-19 center were selected using a simple random sampling technique using the card number of patients obtained from the logbook registry as a sampling frame, who were admitted during the study period, until the required numbers of samples reached at each center.

2.6. Data collection procedures and data quality control

Before the study, ethical approval was obtained from the Institutional Review Board (IRB) of the funding institution. Then, a permission letter was submitted to each of the selected study hospital. Then, data collection begun after ethical clearance was obtained from each study hospital. Since this is a secondary data, informed permission was not required from each client.

Data were collected by reviewing patient chart using a structured questionnaire prepared in English. Two BSc anesthetists and one nurse collected the data under the supervision of one MSc anesthetist at the selected centers.

To ensure the quality of data, pre-test was done on 5% of the total sample size at a hospital other than the study site. The data collectors and supervisors were trained on the study objective and how to review the document for a half day, and collected data were checked for completeness, accuracy, and clarity on daily basis.

2.7. Data processing and analysis

Data were manually checked for completeness, coded and entered into Epi-Info version 7.0. Then, the data were transported to SPSS version 25 (IBM® statistics) for analysis. The normality distribution was checked using histogram and Shapiro-Wilk test. Continuous variables were presented in mean and standard deviation or median and interquartile range. Normally distributed data were analyzed using an independent *t*-test, and Mann-Whitney *U* test was used for non-normally distributed data. Categorical variables were presented as a number and percentage and compared using Chi-square or Fisher's exact test. A P-value <0.05 was considered a statistically significant.

3. Results

3.1. Demographic characteristics

From a sample of 94 patients, 89 were included in this study for final analysis. Five patients were excluded from the analysis: four patients referred to other hospitals and one patient had incomplete data on the outcome. Of the 89 patients, 58.4% were male with a median age of 64.5 years (range 24–85 years). Demographic characteristics of the study

participants were comparable between the groups (Table 1).

3.2. Clinical characteristics and interventions performed at the ICU

Of the 89 patients, majority (74%) had a history of one or more comorbidities. The most common chronic comorbidity was hypertension (48.3%). There was no significant difference in the comorbidities between the groups (P value > 0.05) (Table 2).

The Mann Whitney *U* test showed that baseline vital signs at ICU admission were comparable between the groups (Table 3).

Respiratory parameters and vital signs at the immediate post intubation were also found comparable between the groups in the Mann Whitney *U* test analysis (Table 4).

Furthermore, the majority of interventions performed in the ICU were comparable between the groups. The study groups were comparable in terms of invasive mechanical ventilator support, sedation, analgesia and steroid administration (Table 5).

3.3. Survival status and ICU length of stay

The rates of death were 47.2% in early intubated and 46.1% in late intubated groups. Furthermore, survival rates were 4.5% and 2.2% in early intubated, and late intubated ICU-admitted COVID-19 patients, respectively (P = 0.678) (Table 6).

In this study, patients were followed for a minimum of 1.08 days to a maximum of 63.79 days. The maximum length of stay (LOS) on mechanical ventilation (MV) in the ICU in early intubated group was 16.56 days, while it was 16.29 days in late intubated group, with a statistically insignificant difference. However, patients intubated late had a relatively increase median LOS in the ICU than early intubated patients (P < 0.001). The minimum and maximum LOS in the ICU to discharge was statistically significant between groups (P < 0.001) (Table 6). Furthermore, there was a statistically significant difference in the median LOS in the ICU between the groups (log-rank X^2 (1) = 73.51, P < 0.001).

4. Discussion

In this study, we found a statistically insignificant difference in the survival rate of COVID-19 patients in the early and late intubated groups in the ICU. In contrast to our result, a study conducted in USA found that a higher survival rate in early intubated ICU-admitted COVID-19 patients [23]. The difference could be due to differences in the setup and critical care management of COVID-19 patients in the ICU compared to ours.

In this study, we also found a statistically insignificant difference in the mortality between early intubated and late intubated ICU-admitted COVID-19 patients. Our result is in line with a retrospective study conducted in Greece [24] and Korea [25] which found that there was insignificant difference in mortality between early and late intubated ICU-admitted COVID-19 positive patients (21% vs 33%, 56.5% vs. 33.3%); P = 0.48, 0.11), respectively. Our result is also congruent with a study performed in Atlanta that found there was no association between time to intubation and mortality (≤8 h: 38.2%; 8–24 h: 31.6%; ≥24 h: 38.1%; P = 0.7) [22]. The result of our result is also congruent with other studies, which found that no significant difference in mortality between the early intubated and the late intubated groups [23,24].

In contrast to our study, a study conducted by Bavishi1 et al. found early intubated patients had lower mortality rate than late intubated COVID-19 patients (6% vs 30%, P < 0.001) [21]. Another study also found that mortality was higher in late intubated patients compared to early intubated (43% vs 18%, P < 0.001) [18]. The possible explanation for this could be early intubation may be physiologically protective by reducing self-induced lung injury (SILI). In addition, intubation and mechanical ventilation while putting patients on muscle relaxation have protective effects by diminishing inspiratory effort and tidal volumes, thus limiting the effect of SILI [19,23,27].

The maximum length of stay on a mechanical ventilator in the ICU in early intubated patient was longer than late intubated patients in this

Table 1
Demographic characteristics of the study participants.

Variable	Category	Early intubated group (n = 46)	Late intubated group (n = 43)	P-value
		n (%)	n (%)	
Sex	Male	26 (29.2)	26 (29.2)	0.706
	Female	20 (22.5)	17 (19.1)	
Age in years	18–39	3 (3.4)	5 (5.6)	0.74
	40–64	23 (25.8)	21 (23.6)	
	>65	20 (22.5)	17 (19.1)	

P-value is taken from Chi-square and Fisher's exact test; n (%) = number (percentage).

Table 2
Comorbidities of the study participants between groups.

Comorbidities	Early intubated group n (%)	Late intubated group n (%)	P-value
Bronchial asthma	2 (2.2)	3 (3.4)	0.67
Cardiac disease	5 (5.6)	0	0.056
Cancer	0	1 (1.1)	0.483
Diabetes mellitus	9 (10.1)	8 (9)	0.485
Hypertension	12 (13.5)	11 (12.4)	0.239
Chronic kidney disease	2 (2.2)	0	0.495
HIV	2 (2.2)	4 (4.5)	0.424
Anemia	2 (2.2)	0	0.495
Epilepsy	5 (5.6)	0	0.056

n (%) = number (percentage); P value is taken from Fisher's exact test.

Table 3
Baseline patient's vital signs at ICU admission between the groups.

Vital signs	Early intubated group (n = 46)	Late intubated group (n = 43)	P-value
SpO_2 (%), M (IQR)	88 (82–92)	89 (83–92)	0.348
Heart rate, M (IQR)	100 (82.75–111)	92 (86–106)	0.242
RR (beats/min), M (IQR)	31 (25–36)	29 (25–36)	0.577
SBP (mmHg), (mean ± SD)	(139.29 ± 21.1)	(132.29 ± 29.28)	0.165
DPB (mmHg), M (IQR)	80.33 (70.5, 92)	80 (60, 90)	0.208
Temperature (^{O}C), M (IQR)	36.4 (35.8,37)	36.4 (36,37.1)	0.98

M (IQR) = median (interquartile range); SD = standard deviation; SpO_2 (%): peripheral oxygen saturation; RR = respiratory rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; mmHg: millimetre of mercury; ^{O}C = degree Celsius.

Table 4
Respiratory parameter and vital signs of study participants at immediate post intubation.

Variable	Early intubation Group (n = 46)	Late intubation group (n = 43)	P-value
SpO_2 (%)	90 (80–94.25)	86 (76–91)	0.054
Heart rate (beats/min)	109.5 (99–125.5)	110 (99–130)	0.056
Respiratory rate (breaths/min)	20 (16.75–25)	20 (18–28)	0.052
FIO_2	100 (95–100)	100 (91–100)	0.996
PEEP	11 (10–12)	12 (10–12)	0.406

Variables are expressed as median and interquartile range; SpO_2 (%): peripheral oxygen saturation; FIO_2: Fraction of inspired oxygen; PEEP: positive end expiratory pressure.

Table 5
Interventions performed at the ICU for the study participants.

Characteristics	Early intubated group n (%)	Late intubated group n (%)	p-value
Modes of mechanical ventilation			
Pressure support ventilation	8 (9)	9 (10.1)	0.529
Assisted pressure control ventilation	1 (1.1)	0 (0)	
SIMV	7 (7.9)	12 (13.5)	
PRVC	18 (20.2)	13(14.6)	
Volume assisted control ventilation	9 (10.1)	8 (9)	
CPAP	3 (3.4)	1 (1.1)	
Prone position	1 (1.1)	4 (4.5)	0.193
Anesthesia induction drugs			
ketamine	35 (39.3)	33 (37.1)	0.563
Propofol	6 (6.7)	8 (9)	
Ketofol	1 (1.1)	1 (1.1)	
Thiopental	4 (4.5)	1 (1.1)	
Suxamethonium	46 (51)	43 (48.3)	
Drugs for sedation			
Ketamine	26 (29.2)	29 (32.6)	0.289
Propofol	12 (13.5)	9 (10.1)	0.567
Ketofol	22 (24.7)	21 (23.6)	0.924
Thiopental	1 (1.1)	2 (2.2)	0.608
Diazepam	43 (48.3)	38 (42.7)	0.4
Steroids			
Hydrocortisone	25 (28.1)	27 (30.3)	0.419
Dexamethasone	41 (46.1)	37 (41.6)	0.659
Analgesia			
Morphine	40 (44.9)	37 (41.6)	0.9
Tramadol	14 (15.7)	18 (20.2)	0.262
Fentanyl	3 (3.4)	1 (1.1)	0.617
Paracetamol	20 (22.5)	13 (14.6)	0.196
NSAIDs	0	1 (1.1)	0.483
Anticoagulant			
Unfractionated heparin	44 (49.4)	39 (43.8)	0.352
Aspirin	1 (1.1)	3 (3.4)	0.483
Rivaroxaban	0	1 (1.1)	0.483
Antihypertensive	19 (21.3)	21 (23.6)	0.475
Antidiabetic	17 (19.1)	12 (13.5)	0.363
Antiemetic	45 (50.6)	43 (483)	0.331
Diuretics	11 (12.4)	11 (12.4)	0.855

P-value is obtained from Fisher's exact test. Abbreviations: SIMV: Synchronized intermittent mandatory ventilation; PRVC: pressure release volume control; CPAP: continuous positive airway pressure; NSAIDs: non-steroidal anti-inflammatory drugs.

Table 6
The outcome and length of stay in the ICU between the groups.

Patient outcome	Early intubated Group (n = 46)	Late intubated Group (n = 43)	P value
Survived, n (%)	4 (4.5)	2 (2.2)	0.678†
Died, n (%)	42 (47.2)	41 (46.1)	
LOS on MV in days, [M (IQR)]	4.58 (2.88, 7.54)	3.67 (1.5, 5.7)	0.11‡
ICU LOS to discharge in days, [M (IQR)]	5.21 (3.503, 9.48)	10.385 (7.67, 14.79)	<0.001‡
Minimum and maximum ICU LOS to discharge	1.08 day, 33.1 days	2.5 days, 63.79 days	<0.001‡

† = P-value taken from Fisher's exact test; ‡ = P value taken from Mann Whitney *U* test; n (%) = frequency (percentage); LOS: Length of stay; M (IQR) = median (interquartile range).

study, with a statistically insignificant difference. In line with our study, a study conducted in Atlanta found that no difference in the duration of mechanical ventilation by timing of intubation [22]. Our finding is also congruent with a study performed in New York, USA that found no significant difference in the mean (SD) length of stay (in days) on a mechanical ventilator (7.7 (7.35), 6.5 (6), respectively (P = 0.28) [26]. The difference in the length of stay in days on a mechanical ventilator could be due to differences in the follow-up, setup and critical care management of intubated COVID-19 patients compared to ours.

Our study revealed that late intubated patient had longer median ICU stay than early intubated patients. This result is in line with a study conducted in Chile that found late intubated COVID-19 patients had a statistically significant longer median (IQR) ICU stay than the early intubated patients; 23 (12–39) days, 15 (9–23) days, respectively (P = 0.003) [18]. In contrast to our finding, a study conducted in Atlanta found that no difference in ICU length of stay by timing of intubation [22].

4.1. Strength

The study was conducted in a multicenter setting, and we collected data from critically ill laboratory-confirmed COVID-19-positive patients, thereby minimizing selection bias.

4.2. Limitation

Due to the retrospective nature of the study and the study design, detailed pictures of some independent predictors, such as health facility-related factors: availability of health professionals and available resources in the ICUs were not assessed. In addition. The Acute Physiological and Chronic Health Evaluation (APACHE) and Sequential Organ Failure Assessment (SOFA) were not assessed.

4.3. Relevance and implications

This study showed that length of stay on a mechanical ventilator, mortality and survival were not significantly related with time of intubation in ICU-admitted COVID-19 positive patients.

5. Conclusion and recommendation

Time of intubation had no significant difference in the outcome (death or survival) of ICU-admitted COVID-19 positive patients. Length of stay in the ICU showed a statistically significant association with intubation time. We recommend, a large-scale study with a strong study design.

Ethical approval

Ethical approval was obtained from the Institutional Review Board (IRB) of the College of Health Sciences, Addis Ababa University with a reference number: Anes 11/2021/2022 and from each of the three study institutions IRB with their protocol number: SPHMMC- 8M23/010, Eka Kotebe General Hospital- Ek/150/5/63, and SPSH- V408/14/2021.

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Author contribution

Tsehay Birhanu, Leulayehu Akalu Gemeda, Mulualem Sitot Fekede and Hirbo Samuel Hirbo contributed to study conception, design, data collection, performed statistical analysis and interpretation of the result. Mulualem Sitot Fekede and Hirbo Samuel Hirbo contributed for writing up and prepared the manuscript. All the authors read the manuscript and approved the final submission.

Registration of research studies

1. Name of the registry: Research Registry.

2. Unique Identifying number or registration ID: "researchregistry8272".
3. Hyperlink: https://www.researchregistry.com/browse-the-registry#home/

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Consent

Since this is a secondary data, informed permission was not required from each client; instead, written permission was obtained from each study hospital before data collection.

Declaration of competing interest

Declarations of interest: none.
There is no conflict of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijso.2022.100561.

References

[1] Umakanthan S, Sahu P, Ranade AV, Bukelo MM, Rao JS, Abrahao-machado LF. Origin, transmission, diagnosis and management of coronavirus disease 2019. COVID-19; 2019. p. 753–8. 2020.
[2] Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19). WHO-China Jt Mission Coronavirus Dis 2020;1(16–24 February):1–40. 2019 [Internet], https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on. covid-19-final-report.pdf.
[3] Göker H, Aladağ-karakulak E, Demİroğlu H, Ayaz CM. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. 2020. p. 679–83.
[4] Parish Austin J, West Jason R, Caputo Nicholas D, Janus Trevor M, Yuan Denley, Zhang John, et al. Early intubation and increased coronavirus disease 2019 mortality: a propensity score–matched retrospective cohort study. Critical Care Explor 2021;3(6):e0452. https://doi.org/10.1097/CCE.0000000000000452.
[5] Parasher A. 1147. COVID-19 : current understanding of its pathophysiology, clinical presentation and treatment, vol. 97; 2021. p. 312–20. https://doi.org/10.1136/postgradmedj-2020-138577. 312–20. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgrad Med J. 2021.
[6] Twohig KA, Nyberg T, Zaidi A, Thelwall S, Sinnathamby MA, Aliabadi S. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. Lancet Infect Dis 2021;3099(21):1–9.
[7] World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance. https://apps.who.int/iris/handle/10665/331446; 13 March 2020.
[8] Shang Y, Pan C, Yang X, Zhong M, Shang X, Wu Z, et al. Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China. Ann Intensive Care 2020;10(1):1–24. https://doi.org/10.1186/s13613-020-00689-1 [Internet].
[9] Navas-Blanco JR, Dudaryk R. Management of respiratory distress syndrome due to COVID-19 infection. BMC Anesthesiol 2020;20:177. https://doi.org/10.1186/s12871-020-01095-7.
[10] King CS, Sahjwani D, Brown AW, Feroz S, Cameron P, Osborn E, et al. Outcomes of mechanically ventilated patients with COVID-19 associated respiratory failure. PLoS One 2020;15(11):e0242651. https://doi.org/10.1371/journal.pone.0242651.
[11] Cardona S, Downing J, Alfalasi R, Bzhilyanskaya V, Milzman D, Rehan M, et al. Intubation rate of patients with hypoxia due to COVID-19 treated with awake proning: a meta-analysis. Am J Emerg Med 2021;43:88–96. https://doi.org/10.1016/j.ajem.2021.01.058.
[12] Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA 2020;324(8):782–93. https://doi.org/10.1001/jama.2020.12839.
[13] Matta SK. Dilemmas in covid-19 respiratory distress: early vs late intubation; high tidal volume and low PEEP vs traditional approach? J Intensive & Crit Care 2020;6(2):1–4.
[14] Kobayashi H, Uchino S, Takinami M, Uezono S. The impact of ventilator-associated events in critically ill subjects with prolonged mechanical ventilation. Respir Care 2017. https://doi.org/10.4187/respcare.05073.
[15] Finfer SR, Vincent J-L, Slutsky AS, Ranieri VM. Critical care medicine ventilator induced lung injury. N Engl J Med 2013;369:2126–62.
[16] Kangelaris KN, Ware LB, Wang CY, Janz DR, Hanjing Z, Matthay MA, et al. Timing of intubation and clinical outcomes in adults with ARDS. Crit Care Med 2016;44:120–9.
[17] Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med 2020;65:854–87.
[18] Vera M, Kattan E, Born P, Rivas E, Amthauer M, Nesvadba A, et al. Intubation timing as determinant of outcome in patients with acute respiratory distress syndrome by SARS-CoV-2 infection. J Crit Care 2021;65:164–9. https://doi.org/10.1016/j.jcrc.2021.06.008.
[19] Cruces P, Retamal J, Hurtado DE, Erranz B, Iturrieta P, González C, et al. A physiological approach to understand the role of respiratory effort in the progression of lung injury in SARS-CoV-2 infection. Crit Care 2020;24(1):494. https://doi.org/10.1186/s13054-020-03197-7.
[20] Papoutsi E, Giannakoulis VG, Xourgia E, Routsi C, Kotanidou A. Siempos II: effect of timing of intubation on clinical outcomes of critically ill patients with COVID-19: a systematic review and meta-analysis of nonrandomized cohort studies. Crit Care 2021;25:121. https://doi.org/10.1186/s13054-021-03540-6.
[21] Bavishi AA, Mylvaganam RJ, Agarwal R, Avery RJ, Cuttica MJ. Timing of intubation in coronavirus disease 2019: a study of ventilator mechanics, imaging, findings, and outcomes. Crit Care Explor 2021;3:e0415. https://doi.org/10.1097/CCE.0000000000000415.
[22] Hernandez-Romieu AC, Adelman MW, Hockstein MA, Robichaux CJ, Edwards JA, Fazio JC, et al. Auld SC; and the emory COVID-19 quality and clinical Research collaborative. Timing of intubation and mortality among critically ill coronavirus disease 2019 patients: a single-center cohort study. Crit Care Med 2020;48(11):e1045–53. https://doi.org/10.1097/CCM.0000000000004600.
[23] Fayed M, Patel N, Yeldo N, Nowak K, Penning DH, Vasconcelos Torres F, et al. Effect of intubation timing on the outcome of patients with severe respiratory distress secondary to COVID-19 pneumonia. Cureus 2021 Nov 16;13(11):e19620. https://doi.org/10.7759/cureus.19620.
[24] Siempos II, Xourgia E, Ntaidou TK, Zervakis D, Magira EE, Kotanidou A, et al. Effect of early vs. Delayed or No intubation on clinical outcomes of patients with COVID-19: an observational study. Front Med 2020 Dec 23;7:614152. https://doi.org/10.3389/fmed.2020.614152.
[25] Lee YH, Choi KJ, Choi SH, Lee SY, Kim KC, Kim EJ, et al. Clinical significance of timing of intubation in critically ill patients with COVID-19: a multi-center retrospective study. J Clin Med 2020 Sep 2;9(9):2847.
[26] Al-tarbsheh A, Chong W, Oweis J, Saha B, Feustel P, Leamon A. Clinical outcomes of early versus late intubation in COVID-19 patients, vol. 14; 2022. p. 1–10. 1.
[27] Marini JJ, Hotchkiss JR, Broccard AF. Bench-to-bedside review: microvascular and airspace linkage in ventilator-induced lung injury. Crit Care 2003;7(6):435–44.
[28] Mathew G, Agha R, for the STROCSS Group. Strocss 2021: strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery. Int J Surg 2021;96:106165.