Original Article

Mortality Rate and Associated Factors in Critically Ill Intubated Patients with Coronavirus Disease 2019 (COVID-19) at Pranangklao Hospital

Natthika Yurakate, M.D.[1*], Muthita Phanasathit, M.D.[2]

Abstract

Introduction: In the epidemic wave of the ongoing coronavirus disease 2019 (COVID-19) pandemic in April 2021. This study aimed to explore the 30-day mortality rate and its associated factors and anesthetic practice in critically ill COVID-19 patients who received intubation.

Methods: This retrospective cohort study was collected data from medical records in critically ill COVID-19 patients who received intubation and admitted to Pranangklao Hospital (PNKH) from April 1 to June 30, 2021.

Results: A total of 73 patients were admitted and intubated with the median age was 65 years (IQR = 18), 43 (58.9%) were male, 37 (50.7%) were body mass index (BMI) $\geq$ 30 kg/m^2, and 60 (82.2%) had underlying diseases. The most common underlying diseases were hypertension (63.00%) and diabetes (47.90%). The 30-day mortality rate was 79.50%. Compared between the survivors (n = 15) and non-survivors (n = 58), the mortality significantly increased with age (P = .002), more underlying diseases (P = .007), having cough (RR_{adj} 31.90, 95% CI = 1.67-610.65, P = .021), and more complications (RR_{adj} 2.58, 95% CI = 1.02-6.51, P = .045). The anesthetics were used as follows: midazolam (80.95%), thiopental (40.48%), propofol (26.19%), and ketamine (23.81%). The muscle relaxants used in intubation included succinylcholine (90.48%) and rocuronium (9.52%).

Conclusions: Critically ill intubated COVID-19 patients showed a very high mortality rate that significantly increased with age, underlying diseases, and complications. Intubation treatment in vulnerable populations should be done cautiously to avoid adverse events.

Keywords: Anesthetics, Critical illness, Coronavirus, COVID-19, Mortality rate, Intubation, SARS-CoV-2

Received: 26 November 2021 **Revised: 8 April 2022** **Accepted: 20 April 2022**

[1] Department of Anesthesiology, Pranangklao Hospital, Nonthaburi, Thailand
[2] Department of Psychiatry, Center of Excellence of Applied Epidemiology, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand
***Corresponding author:** Natthika Yurakate, M.D., Department of Anestheology, Pranangklao Hospital, Nonthaburi, Thailand
Email: natthika.yk@gmail.com

Introduction

The novel coronavirus disease-2019 (COVID-19) is a respiratory disease emerging in December 2019 in Wuhan, Hubei Province, China.[1,2] Its severity ranges from no symptoms to severe pneumonia and rapid death. Thailand is the first country to detect a confirmed case of COVID-19 outside of China in January 2020 thru immigration screening.[3,4] Pranangklao Hospital (PNKH), Nonthaburi Province has been prepared to deal with the COVID-19 epidemic. The Department of Anesthesiology has readied its personnel and guidelines for caring for COVID-19 patients. Throughout the year 2020, the spread of the COVID-19 epidemic was well under control.[5] At PNKH, the Department of Anesthesiology was consulted for intubation for the first time in January 2021, after which the other case was found again on April 21, 2021.

In Thailand, the information about demographics, clinical characteristics, factors associated with mortality, and incidence of mortality in intubated critically ill patients with COVID-19 remains insufficient. Identifying populations at increased risk of death is needed for anesthesiologists, who may be consulted to manage patients' airways. Therefore, to investigate demographic data, mortality rate, and clinical characteristics of critically ill COVID-19 patients who received intubation to construct a database for planning patient care. The medical chart reviewed anesthetics agents, intubation treatment, and problems in intubation practice were recorded. The research data would be applied to develop a body of knowledge in caring for critically ill COVID-19 patients in PNKH.

Methods

Study Method

This retrospective cohort study reviewed and collected data from medical records in critically ill patients with COVID-19 who were diagnosed with SARs-CoV-2 infection by real-time polymerase chain reaction (RT-PCR) method and underwent invasive ventilation in PNKH, single-center, from April 1 to June 30, 2021. The participants were recruited from critically ill COVID-19 patients who received intubation by anesthesiologists in PNKH and by unknown specialties in other hospitals in Nonthaburi, including Bang Yai Hospital, Bang Buathong Hospital, Pak Kret Hospital, Sai Noi Hospital, Busrakham Hospital, Bang Kwang Central Prison Hospital, and Nonthaburi Field Hospital referred to PNKH for further treatment. The exclusion criteria were patients who did not have patient status on the 30-day after intubation; however, none of the participants were excluded. The study was endorsed by the Human Research Ethics Committee, PNKH (EC27/2564). The Thai Clinical Trials Registry Committee registration was approved (TCTR20220315003).

Data Collection

Demographic data and clinical features including age, sex, weight, height, body mass index (BMI), underlying diseases, complications, and presenting symptoms of all patients were collected. The date of symptom onset, date of admission, date of intubation, date of extubation, date of referral, date of discharge, date of death, and patient status on the 30th-day after intubation was recorded. The primary outcome of this study was the 30-day mortality rate, and the secondary outcome was factors associated with mortality and anesthetic practice.

In the patients undergoing tracheal intubation in PNKH by the anesthesiologist, additional information was acquired, including anesthetic agents, and intubation technique. A total of five anesthesiologists performing intubation at PNKH were invited to complete an online questionnaire regarding intubation in critically ill patients with COVID-19 two weeks after the last case to collect data on guidelines for patient care, selection of intubation apparatus, and problems in intubation practice, concerns, and on-duty infection. This was carried out anonymously through Google Forms.

Statistical Analysis

The sample size was estimated using the infinite population proportion formula[6,7] according to the primary objective to find the mortality rate. The calculation was done using the values from the study of Tu Y, Yang P, Zhou Y, et al.[8] with proportion (p) = 0.81, error (d) = 0.10, alpha (α) = 0.05, and Z (0.975) = 1.95. According to this formula, the sample size should be at least 59.

The Statistical Package for the Social Science (SPSS) version 16.0 was employed to analyze descriptive statistics such as frequency, percentage, mean, median, standard deviation (SD), interquartile range (IQR), 95% confidence intervals (95% CI), and the statistical significance was set at $P < .05$. Multiple imputation methods for missing data were not used. A Chi-square test, Fisher's Exact Test, and Mann-Whitney U test were estimated to determine the associated factors of the 30-day mortality.

According to multivariate analysis, the binary logistic regression for crude relative risk (crude RR) was performed to explore the risk or protective factors of the 30-day mortality. The associated factors including BMI, the symptom of cough, and numbers of complications were analyzed. To compute the adjusted relative risk (RR_{adj}), potential confounding factors were controlled in the binary logistic regression model. From previous study reviews,[8-11] the covariates that need to be considered as potential confounding factors of the COVID-19 death were the patients' age and the numbers of underlying diseases.

Results

Mortality Rate and Demographic Data

Seventy-three critically ill intubated patients with COVID-19 were recruited: 43 (58.90%) males. The median age was 65 years (IQR = 18, min. = 23, max. = 89). There were 58 cases of death, representing a 30-day mortality rate after intubation of 79.50%. Of the 15 survivors, 13 patients did not require an endotracheal tube (11 were discharged; 1 still received medical treatment; the other was sent back to the previous hospital). One patient was still intubated, and the other was given a tracheostomy tube and still received medical care.

The higher mortality rate was associated with an increase in age ($P = .002$). The mortality of those ≤ 60 years was 59.30%, of the 60-69-year-old group was 84.60%, and of those ≥ 70 years was 100%.

The median BMI was 27.68 kg/m^2 (IQR = 9.28, min. = 14.57 kg/m^2, max. = 66.07 kg/m^2). The patients were divided into two groups: those with BMI < 30 kg/m^2 (49.30%) and those with BMI ≥ 30 kg/m^2 (50.70%). As shown in Table 1, the patients with BMI < 30 kg/m^2 presented a death rate of 88.90% whereas the patients with BMI ≥ 30 kg/m^2 showed 70.30%. There was a significant difference in the mortality rate between these two groups ($P = .049$). Regarding BMI as the associated factor of mortality rate, stratification by age group was explored, in the group younger than 60, the patients with BMI < 30 kg/m^2 had no different mortality from those with BMI ≥ 30 kg/m^2. However, in the 60-69-year-old group, the patients with BMI < 30 kg/m^2 showed significantly higher mortality than their counterparts ($P = .014$). All patients older than 70 years old were deceased regardless of their BMI (Table 2).

Underlying Diseases

There were 60 (80.82%) and 13 (17.80%) patients with and without underlying diseases, respectively. The increase in the mortality rates among those with underlying diseases compared to those without such diseases was significant ($P = .021$). The most common underlying diseases included hypertension, diabetes mellitus, and dyslipidemia. No significant differences in mortality were found between each underlying disease. However, there was an association between the 30-day mortality rate and the number of underlying diseases, those patients with ≥ 3 underlying diseases showed a significantly higher mortality rate than those with one or two underlying diseases ($P = .007$) (Table 1).

Presenting Symptoms and Complications

The most common presenting symptoms were dyspnea (56.30%), cough (53.50%), and fever (50.70%). The most common complications included septic shock (50.00%), acute respiratory distress syndrome (ARDS; 38.90%), and acute kidney injury (AKI; 37.50%). The patients with either cough, septic shock, ARDS, or AKI showed a significantly higher mortality rate than those without these conditions (Table 1).

The Risk Factors of 30-day Mortality After Intubation

Table 3 demonstrates the risk factors of 30-day mortality after intubation; the results of the binary logistic regression model with control for potential confounder factors. Patients who were BMI ≥ 30 kg/m^2 were not likely to be increased mortality (RR_{adj} = 0.95; 95% CI 0.874-1.038).

Table 1 Demographic and clinical characteristics of critically ill patients with coronavirus disease 2019 (COVID-19) receiving invasive ventilation in Pranangklao Hospital

Characteristics	Total n = 73 (%)	Survivors n = 15 (%)	Non-survivors n = 58 (%)	*P*-value
Ages (yrs) †				.002*
< 60	27 (37.0)	11 (40.7)	16 (59.3)	
60-69	26 (35.6)	4 (15.4)	22 (84.6)	
≥ 70	20 (27.4)	0 (0.0)	20 (100)	
(median = 65, min = 23, max = 89, IQR = 18, 95% CI = 58.18, 64.77)				
Sex‡				1.000
male	43 (58.9)	9 (20.9)	34 (79.1)	
female	30 (41.1)	6 (20.0)	24 (80.0)	
BMI† (kg/m²)				.049*
< 30	36 (49.3)	4 (11.1)	32 (88.9)	
≥ 30	37 (50.7)	11 (29.7)	26 (70.3)	
(missing = 10 (13.7%))				
(median = 27.68, min = 14.57, max = 66.07, IQR = 9.28, 95% CI = 27.79, 32.45)				
Underlying diseases‡				.021*
No	13 (17.80)	6 (46.20)	7 (53.80)	
Yes	60 (82.20)	9 (15.00)	51 (85.00)	
Underlying diseases‡				
Hypertension	46 (63.00)	7 (15.20)	39 (84.80)	.229
Diabetes	35 (47.90)	4 (11.40)	31 (88.60)	.085
Dyslipidemia	27 (37.00)	3 (11.10)	24 (88.90)	.147
Chronic kidney disease	16 (21.90)	1 (6.25)	15 (93.75)	.165
Heart disease	7 (9.60)	0 (0.00)	7 (100.00)	.332
Cerebrovascular disease	4 (5.50)	0 (0.00)	4 (100.00)	.575
Respiratory disease	4 (5.50)	0 (0.00)	4 (100.00)	.575
Cancer	2 (2.70)	0 (0.00)	2 (100.00)	1.000
Others	24 (32.90)	2 (8.30)	22 (91.70)	.121
Number of underlying diseases (n = 60)‡				.007*
1-2	26 (43.33)	8 (30.80)	18 (69.20)	
≥ 3	34 (56.67)	1 (2.90)	33 (97.10)	
Presenting symptoms‡				
Dyspnea	40 (56.30)	9 (22.50)	31 (77.50)	.779
Cough	38 (53.50)	14 (36.80)	24 (63.20)	< .001*
Fever	36 (50.70)	9 (25.00)	27 (75.00)	.563
Loss of appetite	9 (12.70)	2 (22.20)	7 (77.80)	1.000
Fatigue	8 (11.30)	0 (0.00)	8 (100.00)	.189
Sore throat	7 (9.90)	1 (14.30)	6 (85.70)	1.000
Myalgia	5 (7.00)	0 (0.00)	5 (100.00)	.577
Headache	2 (2.80)	1 (50.00)	1 (50.00)	.380
Diarrhea	2 (2.80)	0 (0.00)	2 (100.00)	1.000

Table 1 Demographic and clinical characteristics of critically ill patients with coronavirus disease 2019 (COVID-19) receiving invasive ventilation in Pranangklao Hospital (Cont.)

Characteristics	Total n = 73 (%)	Survivors n = 15 (%)	Non-survivors n = 58 (%)	*P*-value
Presenting symptoms‡ (Cont.)				
Drowsiness	2 (2.80)	0 (0.00)	2 (100.00)	1.000
Contact case	15 (21.10)	1 (6.70)	14 (93.30)	.166
(missing = 2 (0.27%))				
Complications‡				
Septic shock	36 (50.00)	1 (2.80)	35 (97.20)	< .001*
ARDS	28 (38.90)	2 (7.10)	26 (92.90)	.035*
AKI	27 (37.50)	2 (7.40)	25 (92.60)	.037*
Electrolyte imbalance	25 (34.70)	4 (16.00)	21 (84.40)	.548
VAP/HAP	19 (26.40)	4 (21.10)	15 (78.90)	1.000
AF	11 (15.30)	0 (0.00)	11 (100.00)	.105
Pneumothorax	7 (9.70)	0 (0.00)	7 (100.00)	.332
UGIB	7 (9.70)	2 (28.60)	5 (71.40)	.630
PE	6 (8.30)	0 (0.00)	6 (100.00)	.333
CHF	4 (5.60)	0 (0.00)	4 (100.00)	.573
DIC	4 (5.60)	0 (0.00)	4 (100.00)	.573
(missing = 1 (0.13%))				
Time (days); Median time (IQR)$				
LOS	15 (16)	24 (24)	13.5 (15)	.001*
Time from symptoms onset to hospital admission *(missing = 17 (23.30%))*	3 (4)	4.5 (4)	3 (5)	.164
Time from symptoms onset to intubation *(missing = 17 (23.30%))*	6.5 (6)	5.5 (5)	7 (7)	.764
Time from admission to intubation	3 (6)	1 (4)	3 (6)	.172
Staff performed intubation‡, £				.007*
PNKH staff	47 (64.38)	42 (89.40)	5 (10.60)	
Other hospital staff	26 (35.62)	16 (10.60)	10 (38.50)	

† analyzed by Pearson Chi-square, ‡ analyzed by Fisher's Exact Test, $ analyzed by Mann-Whitney U test, £ Staff performed intubation were divided into 2 groups; 1) five anesthesiologists in PNKH and 2) unknown specialties in other hospitals in Nonthaburi, including Bang Yai Hospital, Bang Buathong Hospital, Pak Kret Hospital, Sai Noi Hospital, Busrakham Hospital, Bang Kwang Central Prison Hospital, and Nonthaburi Field Hospital

Acute respiratory distress syndrome; ARDS, Acute kidney injury; AKI, Ventilator-associated pneumonia; VAP, Hospital-acquired pneumonia; HAP, Atrial fibrillation; AF, Upper gastrointestinal tract bleeding; UGIB, Pulmonary embolism; PE, Congestive heart failure; CHF, Disseminated intravascular coagulation; DIC

Table 2 BMI as the associated factor of mortality rate, stratification by age group

Age Group	Total n = 73 (%)	Survivors n = 15 (%)	Non-survivors n = 58 (%)	*P*-value‡
< 60 years	27 (36.99)			.675
BMI < 30	8 (29.63)	4 (50.00)	4 (50.00)	
BMI ≥ 30	19 (70.37)	7 (36.80)	12 (63.20)	
60-69 years	26 (35.62)			.014*
BMI < 30	16 (61.54)	0 (0.00)	16 (100.00)	
BMI ≥ 30	10 (38.46)	4 (40.00)	6 (60.00)	
≥ 70 years	20 (27.39)			
BMI < 30	12 (60.00)	0 (0.00)	12 (100.00)	n/a
BMI ≥ 30	8 (40.00)	0 (0.00)	8 (100.00)	

‡ analyzed by Fisher's Exact Test, n/a; non applicable

Table 3 Multivariable analysis showed risk factors of 30-day mortality after intubation

Associated Factors	Relative Risk (RR)¥				*P*-value
	Crude RR	(95% CI)	Adjusted RR§	(95% CI)	
BMI (kg/m^2)					
< 30	ref.				
≥ 30	0.93	(0.86-1.02)	0.95	(0.87-1.04)	.270
Presenting symptom: Cough					
- No	ref.				
- Yes	31.42	(2.06-78.20)	31.90	(1.67-610.65)	.021*
Number of complications	2.87	(1.35-6.18)	2.58	(1.02-6.51)	.045*

¥ analyzed by binary logistic regression (entered technique), § adjusted for age (years), the number of underlying diseases
ref. = reference

The presenting symptom of cough (RR_{adj} = 31.90; 95% CI 1.67-610.65) and the numbers of complications (RR_{adj} = 2.58, 95% CI 1.02-6.51) were risk factors for 30-day mortality after intubation.

Duration of Treatment

The median time length from symptom onset to hospital admission, from symptom onset to intubation, and from hospital admission to intubation were 3 days (IQR = 4), 6.5 days (IQR = 6), and 3 days (IQR = 6), respectively.

The median time of the total length of stay (LOS) was 15 days (IQR = 16). The cumulative number of patients whose hospital admissions were shorter than 10 days was 27.40%, and that of those treated in the hospitals ≥ 10 days was 72.60%.

The median time from intubation to decease was 10.5 days (IQR = 10). Twenty-seven patients passed sooner than 10 days after intubation (46.60%). There were 23 deaths at 10 to 19 days of intubation (36.20%) and 8 deaths after the 19th-day of the treatment (17.20%).

The median time from intubation to extubation was 10 days (IQR = 4). Six patients had their endotracheal tube removed by the 10th-day of intubation (46.20%), and 7 between the 10th and 19th-day (46.1%).

Intubation Practice by Anesthesiologists

Anesthesiologists at PNKH performed intubation in 47 patients (64.38%), divided into 42 deaths (89.40%), and 5 survivors (10.60%). Compared to the patients intubated in other hospitals, the patients who received intubation at PNKH showed a significantly higher mortality rate (P = .007).

Anesthetic agents included induction agents such as thiopental, propofol, midazolam, and ketamine. At PNKH, etomidate was not available due to its short supply. Muscle relaxants, for instance, succinylcholine, rocuronium, and cisatracurium, were in use. Resuscitation drugs were adrenaline, noradrenaline, atropine, and ephedrine. All medications were prepared.

The Department of Anesthesiology adhered to the guidelines for intubation according to the announcement entitled "Guidelines for Anesthesia Care for Patients Infected or Suspected of Being Infected with the COVID-19 Virus" released on April 2020[12] by the Royal College of Anesthesiologists of Thailand. No infected practitioners at 2 weeks after the last intubation.

Intubation Technique

Five anesthesiologists responded to the questionnaire regarding intubation practice in critically ill COVID-19 patients (Figure 1). Intubation was performed in an efficient negative pressure chamber. Another nurse anesthetist stood by outside to assist and coordinate. The most utilized equipment was a high-flow oxygen nasal cannula, used by five anesthesiologists. The second most popular apparatus was a non-rebreathing mask, in which no one employed a self-inflated bag with the face mask. All these anesthesiologists adopted the rapid sequence induction in all patients. One anesthesiologist performed cricoid pressure on some patients who were suspected of having a full stomach. Conventional CMAC was most frequently chosen by 2 anesthesiologists; McGrath and D-Blade were both most often selected by 1 anesthesiologist, and a conventional disposable laryngoscope was used once.

One anesthesiologist was tested for COVID-19 by RT-PCR once due to a sore throat and a poor N95 mask fitting while on duty, and the result was negative. All five of them were slightly anxious about on-duty infection.

Drug Selection

Drugs applied to 42 patients by 5 anesthesiologists were as follows. Induction agents: midazolam (80.95%), thiopental (40.48%), propofol (26.19%), and ketamine (23.81%). A single or combination of drugs was used for induction.

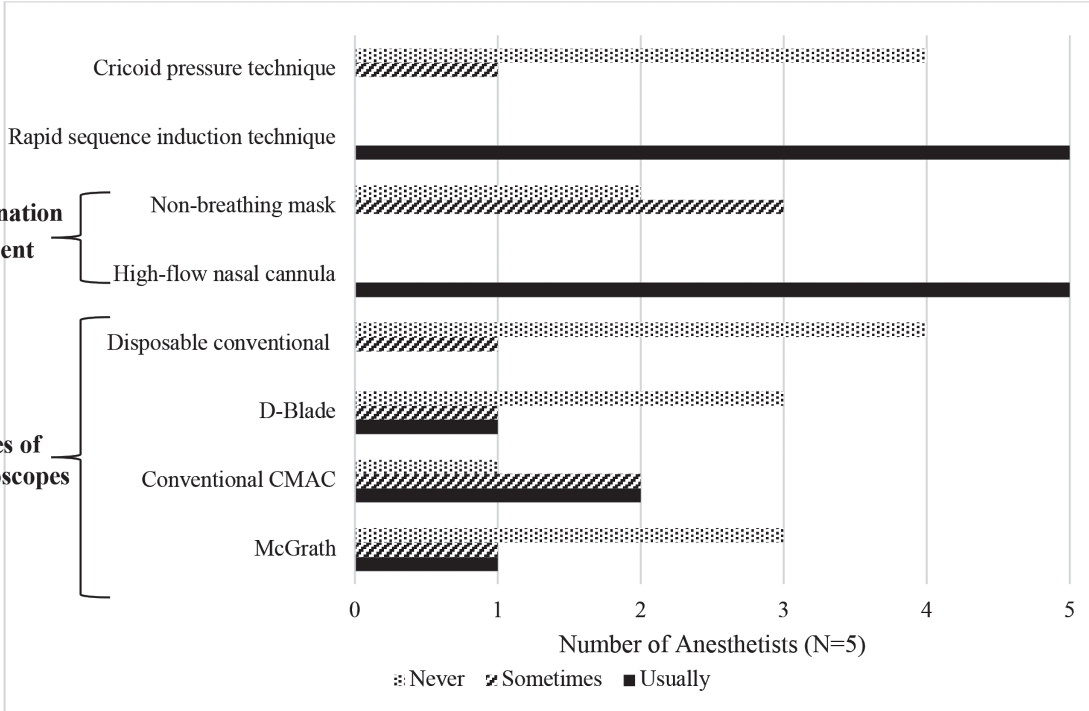

Figure 1 Anesthetic intubation practice.

Muscle relaxants chosen for intubation were succinylcholine (90.48%), rocuronium (9.52%). Other drugs were fentanyl and atropine. Either cisatracurium or rocuronium was given for mechanical ventilation.

Problems

Some problems emerged during the process of patient preparation. For example, there were no channels for injection, and no ventilators were ready for use. This was solved by making a checklist to ensure the readiness of the intensive care team before intubation. The other difficulty was that communication between medical personnel. While wearing a Powered Air Purifying Respirator (PAPR), this difficulty was resolved by having equipment and medicines well-prepared before the procedure to reduce verbal communication. In addition, the anesthetic data of five patients were nowhere to be found due to no records, which was addressed by issuing a treatment order specifically for COVID-19 patients consulted for intubation.

Discussion

This retrospective cohort study collected data, from April 1 to June 30, 2021, during the epidemic wave of COVID-19, on medical records of critically ill intubated patients representing a 30-day mortality rate after intubation of 79.50%. This result was in line with several studies.[8,10,13-15] The mortality increased with increasing age, and no survivors were older than 70.

As generally known, obesity has a negative impact on the respiratory system.[16,17] Obese patients are more at risk of developing severe COVID-19 than those with an average.[18,19] Previous studies have indicated obesity as a risk factor in severe COVID-19 outcomes, such as severe pneumonia,[18] invasive mechanical ventilation,[19] and increased hospitalizations.[9] Further studies have suggested that obesity in COVID-19 increased the risk for mortality.[20,21] This study found that BMI was neither a risk nor a protective factor of mortality. The present study provided evidence that age potential influenced the patients' BMI. Those with a BMI $\geq$ 30 kg/m^2 or obese[22,23] were more likely to be young while most aged patients had BMI less than 30 kg/m^2.[10] However, obese patients with COVID-19 of all ages still need careful care to prevent progression to severe COVID-19.

Diabetes is a common disease in the elderly. It has a negative effect on infectious diseases[24] and is also common comorbidity in patients infected with COVID-19,[8,10,25] but its effect on mortality rate remains controversial. However, it was found that COVID-19 patients with concomitant diabetes are at risk of progressing to severe COVID-19.[26-28]

From multivariable analysis, the presenting symptom of cough and the numbers of complications were risk factors for the 30-day COVID death in critically ill intubated patients. Nevertheless, the relative risk of cough had boarded 95% CI. The patients with cough may be at mortality risk should be carefully interpreted due to the small sample size or limitation of retrospective medical chart review.

On average, the non-survivors were intubated 3 days after hospitalization, of which as many as 70.20% died within 10 days later, indicating a rapid progression. Consistent with the fact that most of the deceased were elderly and had the underlying disease, considered a susceptible group. Most cases were extubated within two weeks (85.7%), with a median hospitalization time of 23-24 days. There was higher mortality among the patients who received intubation in PNKH than in other hospitals. This could be because in general, those who were admitted to PNKH were in a more severe condition. Also, intubation in other hospitals prior to referral to ensure patients' safety resulted in earlier intubation and less disease severity at the time of intubation.

Regarding anesthetics usage, midazolam was the most popular. It was the only induction agent prescribed alone and used in combination with others for induction or used as sedatives due to its less undesirable effect on the cardiovascular system. It is mentioned that a high dose (0.2-0.3 mg/kg) of midazolam yielded a slight decrease in systemic vascular resistance.[29] For induction, much smaller doses are usually administered.[30] Etomidate has outstanding features in cardiovascular stability, but it was not used in PNKH. Its use in COVID-19 patients is said to cause hemodynamic instability, presumably related to catecholamine depletion consistent with severe sepsis.[30]

Thiopental and propofol both have an adverse effect on the cardiovascular system. They are prescribed in patients with relatively stable vital signs or used at a lower dose. In this study, ketamine was not used alone for induction. From further research, ketamine is said to be suitable for use in COVID-19 patients due to its anti-inflammatory effect,[30-33] which may reduce the risk of SARS-CoV-2 induced cytokine storm. However, it must be given with caution especially at a high dose for induction because of its negative impact on cardiovascular function, particularly in a state of catecholamine depletion.[29,30] Also, a significant increase in bronchial secretions and the need for airway suctioning were reported.[34]

The most frequently selected muscle relaxant for rapid sequence induction intubation in this study was succinylcholine because of its rapid onset and short duration properties. Succinylcholine is relatively safe for patients at risk of difficult intubation. However, in the place where sugammadex is easily accessible, rocuronium is potentially more popular than succinylcholine since it has an advantageous effect on AKI and serum potassium levels.[29,30] Nonetheless, in patients with difficult airways, there may be limitations in the safety of rocuronium.[35]

In this study, atropine has never been used to reduce secretion before intubation, but it was given to one patient with bradycardia. It was found that patients treated with a high flow nasal cannula had relatively dry airways.

This study investigated the patient data during epidemic periods of Alpha (April 2021), Gamma (May 2021), and Delta (May 2021) variants when the public still had limited access to vaccination.[36] Thus, the present study is a piece of the clinical database on COVID-19 critically ill patients in Thailand for the benefit of providing care for patients because previously demographic data, mortality rate, and clinical features were derived from internationally compiled studies that may differ in ethnicity. The accuracy of the present study will rise as more data are collected from the Thai population. Data may change as the severity of the variant alters, as the vaccine becomes more available to the population, and as the vaccine efficacy is constantly evolving.

The present study had several limitations. First, retrospective data from medical records were not all complete. Second, limited by the relatively small sample size. Since the primary object was to determine the 30-day mortality rate, the sample size was calculated by infinite population proportion. The risk factors for mortality identified in this cohort should be verified in a large-sample, multi-center, and prospective cohort. The authors did not proceed to complete a multivariate sub-group analysis with all confounding factors due to the small sample size. Thus, the significance of our results would be very weak with a widespread confidence interval.

Acknowledgements

The researchers would like to thank Busaraporn Kantakuldussadee, M.D., an anesthesiologist at PNKH for her advice and assistance in the investigation of preliminary research; Kantachart Thatsakorn, M.D., cardio-thoracic Surgeon for his encouragement and helpful comments; and Pannika Vorapaluk, M.D., anesthesiologist, Chulalongkorn Memorial Hospital, for her useful advice and support for the research review.

The authors declare that they have no conflicts of interest.

References

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *Journal of medical virology.* 2020;92(4):401-402.
2. Hui DS, E IA, Madani TA, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health-The latest 2019 novel coronavirus outbreak in Wuhan, China. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases.* 2020;91:264-266.
3. World Health Organization. Novel Coronavirus -Thailand (ex-China). World Health Organization. https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON234. Updated January 14, 2020. Accessed July 25, 2021.
4. World Health Organization. Novel Coronavirus 2019 (nCoV) Situation Report -1. World Health Organization. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf. Updated January 20, 2020. Accessed July 25, 2021.
5. Emergency Situation Center DoDC. The Coronavirus Disease 2019 Situation, Thailand situation. Emergency Situation Center DoDC. https://ddc.moph.go.th/viralpneumonia/eng/

file/situation/situation-no357-311263.pdf. Updated December 31, 2020. Accessed July 25, 2021.
6. Daniel WW. A foundation for analysis in the health sciences. *Biostatistics Toronto, John Wiley & Sons.* 1991;209-215.
7. Ngamjarus C, Chongsuvivatwong V. N4 Studies: Sample size and power calculations for iOS. *The Royal Golden Jubilee Ph D Program-The Thailand Research Fund & Prince of Songkla University.* 2014.
8. Tu Y, Yang P, Zhou Y, et al. Risk factors for mortality of critically ill patients with COVID-19 receiving invasive ventilation. *International journal of medical sciences.* 2021;18(5):1198-1206.
9. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ (Clinical research ed).* 2020;369:1966.
10. Halvatsiotis P, Kotanidou A, Tzannis K, et al. Demographic and clinical features of critically ill patients with COVID-19 in Greece: The burden of diabetes and obesity. *Diabetes research and clinical practice.* 2020;166:108331.
11. Du RH, Liang LR, Yang CQ, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *The European respiratory journal.* 2020;55(5):2000524.
12. The Royal College of Anesthesiologist of Thailand. Current practice guideline for anesthesia management in COVID-19 case. The Royal College of Anesthesiologist of Thailand. https://www.rcat.org/cpg?lang=en. Published April 24, 2020. Accessed September 26, 2021.
13. Cervantes J, Sureen A, Galura G, et al. Factors associated with COVID-19 severity and mortality among Hispanic patients living on the USA–Mexico border. *Journal of Investigative Medicine.* 2021;69(4):819.
14. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423, 117 patients. *BMC Infectious Diseases.* 2021;21(1):855.
15. Grasselli G, Zangrillo A, Zanella 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;323(16):1574-1581.
16. Watson RA, Pride NB, Thomas EL, et al. Reduction of total lung capacity in obese men: comparison of total intrathoracic and gas volumes. *Journal of applied physiology (Bethesda, Md : 1985).* 2010;108(6):1605-1612.
17. Dixon AE, Peters U. The effect of obesity on lung function. *Expert review of respiratory medicine.* 2018;12(9):755-767.
18. Cai Q, Chen F, Wang T, et al. Obesity and COVID-19 Severity in a Designated Hospital in Shenzhen, China. *Diabetes care.* 2020;43(7):1392-1398.
19. Simonnet A, Chetboun M, Poissy J, et al. High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation. *Obesity (Silver Spring, Md).* 2020;28(7):1195-1199.
20. Nakeshbandi M, Maini R, Daniel P, et al. The impact of obesity on COVID-19 complications: a retrospective cohort study. *International journal of obesity (2005).* 2020;44(9):1832-1837.
21. Cai Z, Yang Y, Zhang J. Obesity is associated with severe disease and mortality in patients with coronavirus disease 2019 (COVID-19): a meta-analysis. *BMC Public Health.* 2021;21(1):1505.
22. Centers for Disease Control and Prevention. Defining adult overweight and obesity. Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion. https://www.cdc.gov/obesity/adult/defining.html. Updated June 7, 2021. Accessed 20 October, 2021.
23. World Obesity Federation. Obesity. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed October 20, 2021.
24. Kim EJ, Ha KH, Kim DJ, Choi YH. Diabetes and the Risk of Infection: A National Cohort Study. *Diabetes & metabolism journal.* 2019;43(6):804-814.

25. Hur K, Price CPE, Gray EL, et al. Factors Associated With Intubation and Prolonged Intubation in Hospitalized Patients With COVID-19. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery.* 2020;163(1):170-178.
26. Kumar A, Arora A, Sharma P, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes & metabolic syndrome.* 2020;14(4):535-545.
27. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes/metabolism research and reviews*. 2020;3319.
28. Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z. Diabetes and COVID-19: A systematic review on the current evidences. *Diabetes research and clinical practice*. 2020;166: 108347.
29. Loushin MK. The Effects of Anesthetic Agents on Cardiac Function. In: Iaizzo PA, ed. *Handbook of Cardiac Anatomy, Physiology, and Devices. Humana Press*;2005:171-180.
30. Ghia S, Lazar M, Epstein J, Bhatt HV. “Anesthesia Stat” to Intubate a Coronavirus Disease 2019 (COVID-19) Patient: Implications for the Anesthesiologist. *Journal of cardiothoracic and vascular anesthesia.* 2020;34(10):2566-2570.
31. Weinbroum AA. Perspectives of Ketamine Use in COVID-19 Patients. *Journal of Korean medical science.* 2021;36(4):28.
32. Ortoleva J. Consider Adjunctive Ketamine in Mechanically Ventilated Coronavirus Disease-2019 Patients. *Journal of cardiothoracic and vascular anesthesia.* 2020;34(10):2580.
33. Hirota K, Lambert DG. Anaesthesia-related drugs and SARS-CoV-2 infection. *British journal of anaesthesia.* 2021;127(1):32-34.
34. Suri A, Sindwani G. Ketamine use in the COVID-19 era: be cautious! *Korean journal of anesthesiology.* 2020;73(6):568-569.
35. Brull SJ, Kopman AF. Clarifications on Technologies to Optimize Care of Severe COVID-19 Patients. *Anesthesia and analgesia.* 2020;131(4):192-193.
36. Ministry of Public Health. COVID-19 Vaccination Report. Ministry of Public Health. https://ddc.moph.go.th/vaccine-covid19/diaryPresentMonth/07/10/2021. Updated July 1, 2021. Accessed September 23, 2021.