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The prognosis in extremely elderly patients receiving orotracheal intubation and mechanical ventilation after planned extubation

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Abstract

The main objective of this study was to evaluate the outcomes of extremely elderly patients receiving orotracheal intubation and mechanical ventilation after planned extubation. This retrospective cohort study included extremely elderly patients (>90 years) who received mechanical ventilation and passed planned extubation. We reviewed all intensive care unit patients in a medical center between January 1, 2010, and December 31, 2017. There were 19,518 patients (aged between 20 and 105 years) during the study period. After application of the exclusion criteria, there were 213 patients who underwent planned extubation: 166 patients survived, and 47 patients died. Compared with the mortality group, the survival group had lower Acute Physiology and Chronic Health Evaluation II scores and higher Glasgow Coma Scale (GCS) scores, with scores of 19.7 ± 6.5 (mean ± standard deviation) vs 22.2 ± 6.0 ($P = .015$) and 9.5 ± 3.5 vs 8.0 ± 3.0 ($P = .007$), respectively. The laboratory data revealed no significant difference between the survival and mortality groups except for blood urea nitrogen (BUN) and hemoglobin. After multivariate logistic regression analysis, a lower GCS, a higher BUN level, weaning beginning 3 days after intubation and reintubation during hospitalization were associated with poor prognosis. In this cohort of extremely elderly patients undergoing planned extubation, a lower GCS, a higher BUN level, weaning beginning 3 days after intubation and reintubation during hospitalization were associated with mortality.

Abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation, BMI = body mass index, BUN = blood urea nitrogen, CIs = confidence intervals, GCS = Glasgow Coma Scale, ICU = intensive care unit, MEP = maximal expiratory pressure, MIP = maximal inspiratory pressure, ORs = odds ratios, RSBI = rapid shallow breathing index, SBT = spontaneous breathing trial, SD = standard deviation, TISS = therapeutic intervention scoring system.

Keywords: extremely elderly patients, mechanical ventilation, prognosis

1. Introduction

Oral tracheal intubation with mechanical ventilation is a common treatment for respiratory failure. Increased longevity and improved medical care have led to rapid growth of the elderly population worldwide. An increasing number of elderly patients with respiratory failure receive mechanical ventilation treatment. Post extubation respiratory failure after weaning and elective extubation is a common event associated with significant morbidity and mortality.[1] Our previous study presented the prognostic factors and outcomes of unplanned extubation[2] and predictors for successfully planned endotracheal extubation.[3] If respiratory failure recurs extubation, reintubation may lead to an unfavorable outcome, including clinical deterioration before reintubation, complications related to reintubation per se, and increased cardiac and respiratory complications. Reintubation prolonged the length of intensive care unit (ICU) stay and hospital stay, prolonged mechanical ventilator support, increased medical costs, and increased mortality.[4,5] Older adults can be more vulnerable to disease for a variety of reasons. However, there are limited data about the factors associated with mortality after extubation in the extremely elderly population (>90 years old). Therefore, this lack of information justified the present study to determine the outcome and risk of mortality among an extremely elderly population who were electively extubated following current criteria for weaning.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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We used a retrospective cohort of mechanically ventilated very elderly patients in a tertiary medical center in Taiwan to observe the prognosis after extubation in extremely elderly patients and assess their risk factors related to mortality before extubation.

2. Materials and methods

2.1. Patients and hospital setting

We retrospectively reviewed all medical and surgical adult patients in Chi Mei Medical Center in Taiwan, which has 1288 bed and 96 ICU beds for adults, between January 1, 2010, and December 31, 2017. The study data were retrospectively collected and analyzed. Therefore, no informed consent was needed, and the requirement was specifically waived by the Institutional Review Board of Chi Mei Medical Center. Ethics approval was also obtained from the institutional review board. (IRB: 10806–010)

The ICU staff included clinical pharmacists, physical therapists, dietitians, respiratory therapists, nurses, residents, and attending physicians. Attending physicians and respiratory therapists bore the responsibility for the ventilator setting and weaning process.

ICU patients who needed invasive mechanical ventilation through an oral endotracheal tube continuously over 24 hours for acute respiratory failure were enrolled. The criteria used to define patients who were considered ready to wean from ventilators were tidal volume higher than 5 ml/kg of ideal body weight, patient breathing slower than 30 breaths/minute, and a rapid shallow breathing index of less than 105 breaths/minute/L. After meeting the above criteria, attempts were made for the patient to perform spontaneous breathing for 2 hours before planned extubation.

We excluded patients who were younger than 90 years, who died before extubation, who underwent tracheostomy, who underwent endotracheal tube dislodgement, who underwent transfer to another hospital and who underwent palliative extubation.

2.2. Variables measured

Data were collected on each patient after he/she had received mechanical ventilation for more than 24 hours: age (years), sex, body mass index (BMI), Acute Physiology and Chronic Health Evaluation (APACHE) II score, Therapeutic Intervention Scoring System (TISS) scale, and Glasgow Coma Scale (GCS).

We recorded comorbidities including cardiovascular disease, pulmonary disease, renal disease, hepatic disease, endocrine disease, neurogenic disease, and malignant disease. The cause of respiratory failure was assessed during the course of mechanical ventilation and included cerebrovascular accident, poor airway hygiene or protective airway, pneumonia, cardiovascular disease, shock (not associated with pneumonia), chronic obstructive pulmonary disease, and intubation in the operating room.[6]

The laboratory data, respiratory parameters and corresponding ventilator settings were recorded before extubation. In our hospital, the process of ventilator discontinuation was driven by a weaning protocol. Patients who received ventilation underwent daily screening of respiratory function by respiratory therapists to identify patients ready to perform a 2-hour spontaneous breathing trial (SBT), namely, either pressure support ventilation or a T-piece for 2 hours, after the clinical condition improved and the hemodynamic status became stable. Physicians were notified of patients passing the SBT.

After successful completion of an SBT, the weaning parameters, including the respiratory rate, tidal volume, minute ventilation, maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), and rapid shallow breathing index (RSBI), were recorded when the patients were prepared for extubation. The length of stay in the ICU and hospital, total medical costs, and in-hospital mortality were also recorded. The primary endpoint comprised factors that predicted mortality. Patients were observed after planned extubation, and we recorded their condition after extubation, including successful reintubation or mortality. The definition of difficult weaning in patients was the requirement for up to 3 SBTs or as long as 7 days from the first SBT to achieve successful weaning. The definition of prolonged weaning was the requirement for more than 3 SBTs or more than 7 days of weaning after the first SBT.[7]

2.3. Statistical analysis

Continuous variables are reported as the mean with standard deviation (SD). Categorical variables are presented as frequencies with percentages. The differences in baseline characteristics and clinical variables between the survival and mortality extubation groups were evaluated using Students t test for continuous variables and Pearsons Chi-Squared test or Fishers exact test for categorical variables. For the variables with statistically significant differences ($P < .05$), univariate and multivariable logistic regression analyses were used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) to determine the association between risk factors and mortality. The final model was established using the stepwise approach to select the potential mortality risk factors. SPSS 26.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all analyses. Significance was set at P value $<.05$ (2-tailed).

3. Results

Between January 1, 2010, and December 31, 2017, there were 19,518 ICU patients aged between 20 and 105 years. We considered only the first episode of extubation for analysis. After exclusion of age younger than 90 years, death before extubation, tracheostomy, hospice care, endotracheal dislodgement, transfer to another hospital, and mechanical ventilation for fewer than 24 hours, there were 213 patients who underwent planned extubation, and among them, 166 patients survived and 47 patients died (Fig. 1).

Among 213 patients, the average age was 92.3 ± 2.6 years old, and 98 patients (46%) were men. The mean BMI was 21.0 ± 3.9, and 75.6% of patients were from the medical ICU. The survival group had lower APACHE II scores and higher GCS scores, with scores (mean $\pm$ SD) of 19.7 ± 6.5 vs 22.2 ± 6.0 ($p = 0.015$) and 9.5 ± 3.5 vs 8.0 ± 3.0 ($p = 0.007$), respectively. The comorbidities between the survival and mortality groups had no significant differences (Table 1).

In addition, the causes of intubation and respiratory failure among planned extubation nonagenarian patients who received endotracheal intubation are presented in Table 2. Pneumonia was the major cause of intubation for all study subjects (53.5%) and had a higher distribution for mortality (70.2%).

The laboratory data before extubation revealed no significant difference between the survival and mortality groups except for blood urea nitrogen and hemoglobin (Table 3). Survival group patients had lower blood urea nitrogen levels (29.7 ± 21.4 vs 41.3

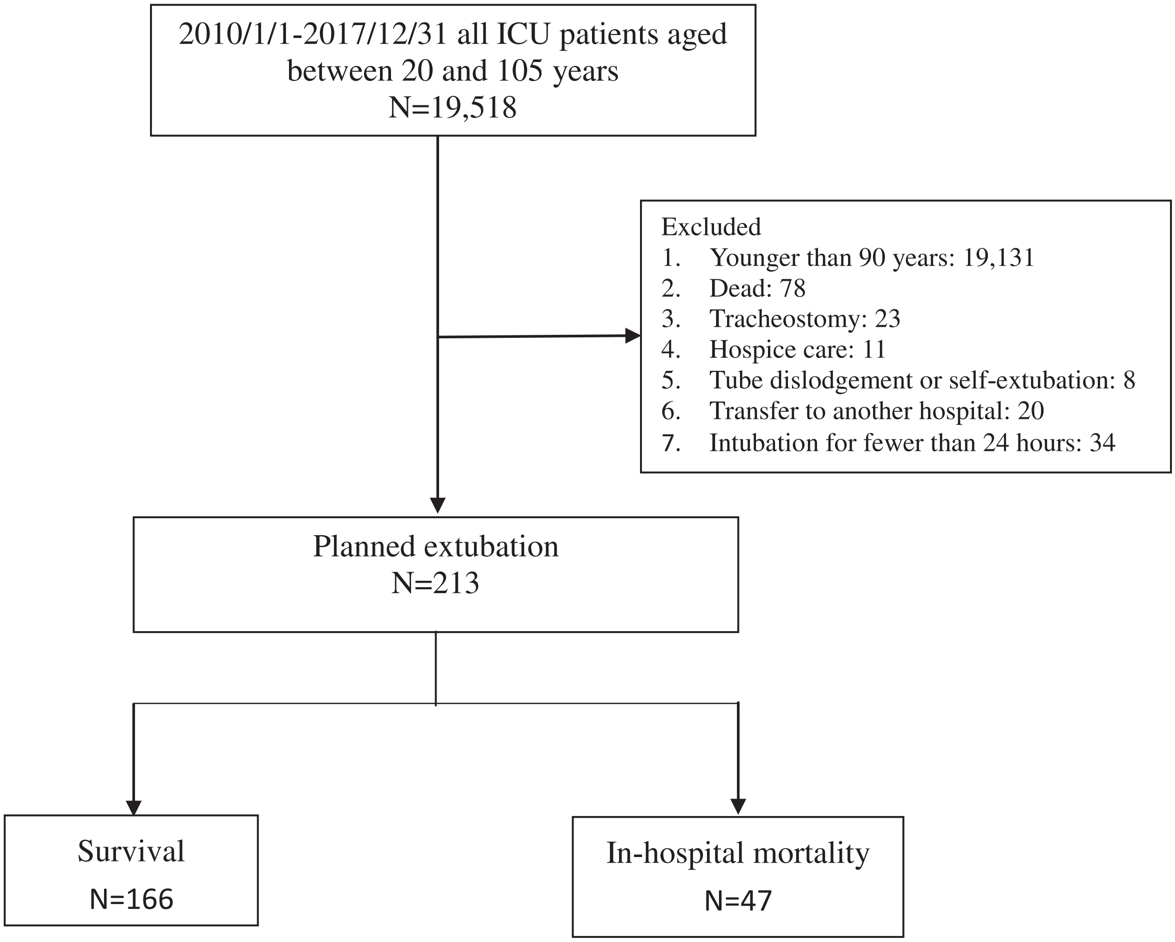

Figure 1. Flow chart of patient selection.

±25.3) and higher hemoglobin levels (10.4±1.4 vs. 9.6±1.4) than mortality group patients.

Table 4 shows the medical resource utilization in elderly patients who received mechanical ventilation. The significant difference in the average duration from intubation to extubation was 206.8±153.0 hours in the survival group and 306.0±250.5 hours in the mortality group ($P=.012$). Patients reintubated within 72 hours also presented a significant difference in the survival group (4.2%) compared with those in the mortality group (19.1%, $P=.001$). Patients in the mortality group also had

Table 1

Demographic and clinical variables of the planned extubation patients between survival and mortality.

	Total n=213	Survivals n=166 (77.9%)	Deaths n=47 (22.1%)	*P* value
Age (years)	92.3±2.6	92.2±2.4	93.0±3.2	.083
Male	98 (46.0%)	78 (47.0%)	20 (42.6%)	.590
BMI	21.0±3.9	20.2±3.9	20.4±4.0	.264
Medical admission	161 (75.6%)	121 (72.9%)	40 (85.1%)	.085
APACHE II	20.2±6.4	19.7±6.5	22.2±6.0	.015
TISS Scale	25.5±6.5	25.3±6.6	26.1±5.9	.422
GCS Scale	9.2±3.4	9.5±3.5	8.0±3.0	.007
Comorbidity				
Cardiovascular	57 (26.8%)	45 (27.1%)	12 (25.5%)	.829
Chest	40 (18.8%)	32 (19.3%)	8 (17.0%)	.727
Renal	3 (1.4%)	2 (1.2%)	1 (2.1%)	.636
Hepatic	3 (1.4%)	3 (1.8%)	0 (0.0%)	.353
Endocrine	48 (22.5%)	40 (24.1%)	8 (17.0%)	.305
Neurogenic	68 (31.9%)	51 (30.7%)	17 (36.2%)	.479
Malignant	51 (23.9%)	41 (24.7%)	10 (21.3%)	.627
Count of comorbidity	1.3±0.9	1.3±0.9	1.2±0.8	.517

APACHE = Acute Physiology and Chronic Health Evaluation, BMI = body mass index, GCS = Glasgow Coma Scale, TISS = Therapeutic Intervention Scoring System.

Table 2

Causes of intubation and organ failure of planned extubation patients.

	Total n=213	Survivals n=166	Deaths n=47
Causes of intubation			
Hypoventilation	8 (3.8%)	5 (3.0%)	3 (6.4%)
Airway obstruction	12 (5.6%)	10 (6.0%)	2 (4.3%)
Pneumonia	114 (53.5%)	81 (48.8%)	33 (70.2%)
Cardiogenic pulmonary edema	11 (5.2%)	8 (4.8%)	3 (6.4%)
Extrapulmonary shock	18 (8.5%)	17 (10.2%)	1 (2.1%)
Chronic obstructive pulmonary disease	6 (2.8%)	5 (3.0%)	1 (2.1%)
Surgery	44 (20.7%)	40 (24.1%)	4 (8.5%)

Table 3

Laboratory data before extubation of planned extubation patients.

	Total n=213	Survivals n=166	Deaths n=47	*P* value
Laboratory data (mean±standard deviation)				
Blood urea nitrogen (mg/dl)	32.3±22.8	29.7±21.4	41.3±25.3	.006*
Creatinine (mg/dl)	1.6±3.1	1.6±3.3	1.9±2.4	.550
Sodium (mmol/L)	137.9±7.4	137.5±7.9	139.2±5.2	.177
Potassium (mmol/L)	3.9±0.5	3.9±0.5	3.9±0.7	.656
Calcium (mg/dl)	7.9±0.8	7.9±0.7	7.9±0.8	.889
Phosphate (mg/dl)	3.2±1.1	3.3±1.1	3.1±1.1	.376
Albumin (g/dl)	2.6±0.5	2.6±0.5	2.5±0.6	.573
Hemoglobin (g/dl)	10.2±1.4	10.4±1.4	9.6±1.4	.001*
Hematocrit (%)	32.4±6.3	32.8±6.0	30.9±7.0	.082
FiO_2 (%)	27.4±10.5	27.2±9.1	28.1±14.6	.589
pH	7.46±0.05	7.45±0.04	7.47±0.05	.090
PaO_2 (mm Hg)	97.3±29.6	96.6±29.6	99.4±29.7	.593
$PaCO_2$ (mm Hg)	36.5±6.4	36.5±6.6	35.4±5.5	.979
PaO_2/FiO_2 (mm Hg)	368.5±101.7	363.4±97.2	384.8±114.9	.236
Respiratory rate (breaths/minute)	18.6±5.3	21.2±17.9	18.0±5.9	.291
Heart rate (beats/minute)	80.3±18.8	86.3±13.4	81.7±14.9	.059
MAP (mm Hg)	91.5±15.9	95.3±19.0	95.8±18.2	.870
Tidal volume (ml)	364.5±140.0	371.0±144.0	341.5±123.9	.228
Minute ventilation (L/minute)	7.0±2.4	6.9±2.5	7.1±2.3	.727
MIP (cmH_2O)	31.2±11.7	31.9±12.2	28.8±9.4	.146
MEP (cmH_2O)	43.1±24.6	44.4±25.1	37.9±22.2	.144
RSBI (breaths/L)	71.2±41.1	69.4±42.1	77.4±37.1	.270
Weaning patterns, n (%)				
Difficult weaning	83 (39.0%)	72 (43.4%)	11 (23.4%)	.013*
Prolonged weaning	90 (42.3%)	64 (38.6%)	26 (55.3%)	.040*
Beginning weaning within 3days after intubation	146 (68.5%)	124 (74.7%)	22 (46.8%)	<.001*

* $P<.05$.

Continuous variables are presented as the means±standard deviation (SD).

FiO2 = fractional concentration of oxygen in inspired gas, MAP = mean arterial pressure; MIP: maximal inspiratory pressure, MEP = maximal expiratory pressure; RSBI = rapid shallow breathing index, PaCO2 = partial pressure of carbon dioxide in arterial blood, PaO2 = partial oxygen tension in arterial blood.

a higher percentage of reintubation events (31.9%) compared to patients in the survival group (9.6%) during the hospitalization period ($P<.001$). The length of the ICU stay was longer in the mortality group (15.1±7.8 vs 11.3±7.2, $P=.002$), but no significant difference was found in hospital length or medical cost.

Potential risk factors for hospital mortality in extremely elderly patients are displayed in Table 5. According to the multivariate analysis, independent variables significantly associated with hospital mortality were the following:

1. GCS,
2. blood urea nitrogen (BUN) before extubation,
3. weaning begun over 3 days after intubation and
4. reintubation during hospitalization.

Figure 2 shows the cumulative trend of 4 potential risk factors with the possible mortality rate.

4. Discussion

In this study, we focused on mortality in extremely elderly patients after planned extubation. We found that surviving patients had less severe disease according to the APACHE II score but not the TISS scale. The consciousness level was better in the surviving population. Patient respiratory failure due to pneumonia had a poor prognosis, and patients who received mechanical ventilation due to surgery had a better outcome. BUN and

Table 4

Medical resource utilization in extremely elderly patients who received mechanical ventilation.

	Total n=213	Survivals n=166	Deaths n=47	*P* value
Ventilator hours	228.7±183.2	206.8±153.0	306.0±250.5	.012*
Reintubation within 72 hours after extubation	16 (7.5%)	7 (4.2%)	9 (19.1%)	.001*
Reintubation during hospitalization	31 (14.6%)	16 (9.6%)	15 (31.9%)	<.001*
ICU length of stay	12.1±7.5	11.3±7.2	15.1±7.8	.002*
Hospital length of stay	28.1±18.0	28.0±17.0	28.2±21.4	.948
Medical cost (10,000, new Taiwan dollars)	27.9±18.1	27.3±17.3	30.2±20.7	.324

ICU = intensive care unit.

* $P<.05$.

Table 5

The odds ratio of potential mortality risk factors in planned extubation patients.

	Univariate analysis			Multivariable analysis for potential risk factors		
Parameters	**OR**	**95%CI**	***P* value**	**OR**	**95%CI**	***P* value**
Ventilator hours	1.003	1.001–1.004	.002			
APACHE II	1.067	1.012–1.125	.017			
GCS	0.869	0.784–0.964	.008	0.322	0.135–0.730	.007*
ICU stay	1.065	1.021–1.111	.003			
Intubation due to pneumonia	2.474	1.234–4,958	.011			
Intubation due to surgency	0.293	0.099–0.867	.027			
Hemoglobin before extubation	0.650	0.498–0.849	.002			
BUN before extubation	1.020	1.006–1.034	.004	2.702	1.277–5.716	.009*
Beginning weaning over 3 days after intubation	3.355	1.714–6.565	<.001	3.472	1.658–7.271	.001*
Difficult weaning	0.399	0.190–0.838	.015			
Prolonged weaning	1.973	1.025–3.797	.042			
Reintubation at 72 hours after extubation	5.380	1.884–15.361	.002			
Reintubation during hospital	4.395	1.972–9.791	<.001	4.447	1.845–10.719	.001*

* $P < .05$.

APACHE = Acute Physiology and Chronic Health Evaluation, BUN = blood urea nitrogen, GCS = Glasgow Coma Scale, ICU = intensive care unit.

hemoglobulin were significantly different between patients in the survival group and those in the mortality group. The length of ICU stay was greater in the mortality group, but the length of hospital stay was not different.

Our previous study identified 3 independent predictors of successful extubation, including the cuff leak test, MEP, and RSBI after multivariate analysis.[3] In this study, we found that lower GCS, higher BUN, weaning beginning more than 3 days after intubation and reintubation during hospitalization were associated with poor prognosis after multivariate logistic regression analysis. Among these 4 independent risk factors, if patients had 3 risk factors, the mortality rate was 54.5%, and if patients had 4 risk factors, the mortality rate was 100.0%.

A previous study[6] showed that many factors are associated with an increased risk of extubation failure, including advanced age (>70 years), duration of ventilation before extubation, anemia, severity of illness at time of extubation, semirecumbent positioning after extubation, use of continuous intravenous sedation, and unplanned extubation.[8] In our study, we enrolled only extremity elderly patients (>90 years) and excluded unplanned extubation. Our patients underwent spontaneous breathing attempts only under stable conditions and after management of the underlying critical condition. Our critically ill patients underwent daily interruption of sedative infusions

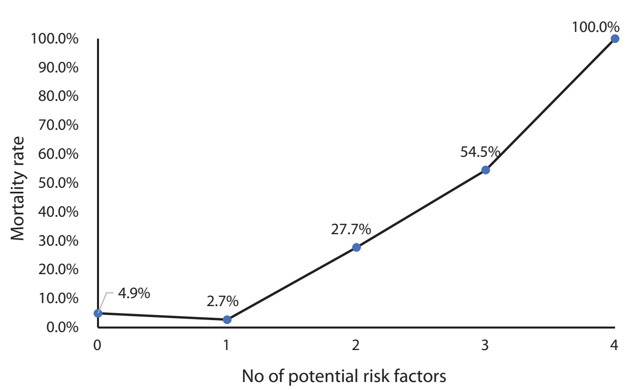

Figure 2. The in-hospital mortality of the potential risk factors in planned extubation nonagenarian patients.

when they received mechanical ventilation and discontinuation sedation when they underwent spontaneous breathing. We found that patients who were considered ready to be weaned 3 days after intubation had better outcomes, but this may imply that the patients underlying medical conditions were less severe. The hemoglobulin level was significantly different between surviving and nonsurviving patients but had no impact on mortality after multivariate logistic regression.

Frutos-Vivar el al[9] found that extubation failure was independently associated with mortality. They enrolled 180 patients who required reintubation within 48 hours after extubation and found that reintubation was independently associated with mortality (OR: 5.18; 95% CI, 3.38–7.94). Our study also has similar results. We found that patients in the mortality group had statistically significant differences in reintubation at 72 hours or reintubation during hospitalization after planned extubation. The OR of mortality for reintubation during the hospital stay was 4.156 in our study, with a 95% CI between 1.675 and 10.311.

There are certain explanations for this association between mortality and reintubation.

Reintubation may simply reflect another disease course. Once the patient is deemed ready to breathe spontaneously and capable of extubation but is then reintubated in the hospital, the underlying disease condition contributes to the major reasons. In our study, the patients severity of illness before extubation was evident by a higher APACHE II score, and disease was suspected to be more severe in the mortality group. Even though such patients improved from the condition for which they were ventilated and met the standard readiness to wean from ventilators, we believed that there was another recurrent disease, such as hospital-acquired pneumonia, stress ulcer bleeding, stroke or another episode of respiratory failure. Another explanation for the higher mortality after extubation is the development of complications associated with reintubation. Epstein et al[10] reported that these complications include arrhythmia, atelectasis/lobar collapse, myocardial infarction, and cerebrovascular accident. However, these complications were not observed in our group. Epstein et al[10] also reported the causes of death in 31 patients who died after reintubation: sepsis, multiple organ failure, respiratory failure, cardiac failure, central nervous system failure, hepatic failure, cardiac arrest, pulmonary embolism, and gastrointestinal bleeding. These conditions reflect the fact that the patient developed a new disease that required a new period of mechanical ventilation after extubation. The third explanation may relate to poor airway hygiene, as we found that patients had higher mortality with lower GCS in our study. Decreased consciousness is a common reason to protect airway hygiene. Patients are even successful in performing spontaneous breathing attempts, there is no airway protection function after extubation, and a poor level of consciousness may aggravate respiratory illnesses and result in the recurrence of respiratory failure.

Whitmore et al[11] presented a study with a total of 141 extubations and found that extubation failure was associated with a prolonged ICU stay. Their extubation failure group had a median length of ICU stay of 14.9 days vs 8.2 days in the successful group. Our study showed that the mortality group had a longer ICU stay of 15.1 ± 7.8 days vs 11.3 ± 7.2 days. Whitmore et al included all patients >18 years of age with a mean age between 57 and 58 years. All our patients aged >90 years had a slightly longer ICU hospitalization period. Swinburne et al[12] reported that elderly patients (>80 years) required more than 15 days of mechanical ventilation, which is similar to our results, and their study showed a 9% survival rate in elderly patients compared with 36% for younger patients. Our mortality rate was 22% (47/213), which was higher than that in their study because we enrolled an extremely elderly population (>90 years old).

Our patients were extubated after successful SBT and still had a risk of extubation failure. SBT evaluates the patients ability to breathe while receiving no or minimal ventilator support to identify patients who are likely to be liberated from mechanical ventilation. Despite successful completion of an SBT, the trials did not equate to tolerance of endotracheal tube removal. The association between consciousness level and extubation failure is controversial. Some studies found it a risk factor,[13] whereas others did not find an association between conscious level and successful extubation.[4,5]

Our study found that consciousness level was related to successful extubation and mortality. Decreased consciousness among elderly patients may have an impact on airway hygiene and airway protection and lead to extubation failure and mortality.

4.1. Limitations

Our study had several limitations. It was performed in a single medical center and patient population, and the clinical protocols may not be the same as those in other hospitals with respect to disease treatment or the weaning process. Therefore, our findings may not be generalizable to other hospitals. Nevertheless, an extremely elderly population was difficult to enroll. Our study enrolled only 213 patients with planned extubation during the study period, which is a small sample size for this topic. Another prospective study with a large sample size may be needed to further evaluate these risk factors.

5. Conclusion

In conclusion, our study identified 4 independent risk factors for mortality in extremely elderly patients after planned extubation. These factors included lower GCS, higher BUN level, weaning beginning more than 3 days after intubation and reintubation during hospitalization. The higher mortality in elderly patients after reintubation indicates that efforts should be preferentially focused on identifying these patients. Individualized weaning plans are necessary in these most vulnerable elderly patients, trying to prompt weaning without exposing patients to serious risks.

Author contributions

CKC and CMC designed the study, CAC collected the data, LKM, HCH, and LCC interpreted the analyses, and LKM wrote the draft of the manuscript. CAC performed the statistical analyses. CCM, CCC, CSR, and WJJ reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

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