Original Article

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Clinical Risk Factors of Extubation Failure in Adult Patients with Mechanical Ventilation in Medical Intensive Care Unit

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Objective: To screen for risk factors that might predispose to extubation failure, we investigated potential risk factors associated with mechanical ventilation (MV) including basic demographic profiles, comorbidity, disease severity, MV dependence, and mortality.

Methods: There were 232 patients admitted to our intensive care unit (ICU) from April to December 2017. In addition to demographic characteristics, information on body mass index (BMI), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Glasgow Coma Scale (GCS), renal function, electrolytes, and blood gas measured at the time of acute respiratory failure before intubation was collected. Comorbidities including type II diabetes and hypertension, the duration of MV, outcomes of MV (e.g., successful extubation), MV dependency, and mortality were also analyzed.

Results: Extubation was successful in 125 patients (53.9%), while MV dependence and fatality were noted in 24 (10.3%) and 83 (35.8%) patients, respectively. Acute respiratory failure of pulmonary origins was found in 112 (48.3%) and non-pulmonary origins in 120 (51.7%) patients. The rate of successful extubation was 1.9-time higher in the latter than in the former ($p = 0.077$). MV dependence was noted in 16 patients (66.7%) with acute respiratory failure of pulmonary origins and 8 patients (33.3%) of non-pulmonary origins ($p = 0.05$). The APACHE II score and GCS scores were significantly associated with extubation outcome ($p < 0.001$). Besides, BUN, Creatinine, and pH on blood gas analysis were significantly different between survivors and non-survivors.

Conclusion: Patients receiving MV showed higher risk of MV dependence if they were subjected to prolonged MV of over 7.8 days and spend more time in the ICU.

Key words: mechanical ventilation, intubation care, extubation failure, intensive care unit

Introduction

Mechanical ventilation (MV) is a common life-sustaining strategy for patients admitted to the intensive care unit (ICU), especially for those experiencing acute respiratory failure and requires endotracheal intubation. However, intubation or extubation are not risk-free even when the procedures are performed

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based on the established criteria. Emergency intubation in the ICU is frequently required for hypoxic patients with acute respiratory failure or unstable hemodynamics.[1,2] Consistently, a previous study has reported a probability of life-threatening complications such as hypotension and respiratory failure in up to 20 – 50% of patients in the ICU, especially in those with difficult intubation.[3]

The clinical outcomes of patients receiving MV have been reported in the ICU setting. A report recruiting 139 adults showed no significant difference in successful extubation rate between patients with and those without spontaneous breathing trials.[4] Despite the demonstration of an over 90% successful extubation rate in both groups, the reintubation rate was close to 10% regardless of the implementation of spontaneous breathing trials.[4] The result was consistent with that of another study that further identified reintubation as a poor prognostic factor.[5] Although most studies evaluating patients at low risk for extubation failure demonstrated a reintubation rate from about 10 to 15%, ssome authors reported an extubation failure rate exceeding 25% or 30% in high-risk patients.[6] Strategies for identifying patients at high risk for extubation failure are essential to the implementation of improvement programs for weaning program and extubation.

To identify potential predictors of extubation failure in patients receiving MV, we focused on basic patient profiles, comorbidities, disease severity, rate of successful extubation, incidence of MV dependence, and mortality.

Materials and Methods

Study design and setting and participants

This retrospective study enrolled patients admitted to the ICUs at a tertiary referral center in Taiwan from April to December 2017. All patients were older than 18 years and under invasive mechanical ventilation because of acute respiratory failure. Exclusion criteria included patients with age less than 18 years, those receiving endotracheal intubation anesthesia for operation, and those using invasive or noninvasive ventilator at home.

Patients with mechanical ventilation was cared under the direction and guideline of critical care physicians, respiratory therapists, and nursing staff in our ICU. There was pulmonary or critical care fellowship program involved as a MV care team. Certified attending physicians provided standard MV care protocol and standard hospital weaning protocol included requirements for hemodynamic stability, improvement in underlying medical conditions, reaching a threshold in three respiratory parameters including: FiO_2 < 40%, $PaO_2 \geq 60$ mmHg, arterial oxygen tension/fractional inspired oxygen ratio ≥ 200 mmHg, positive end-expiratory pressure < 5 – 8 cmH_2O, minute ventilation volume > 10 L/min, and respiration rate 6 – 30/min, and having a satisfactory cough in our ICU. The decision to extubate was made by the MV care team. Criteria for considering reintubation and the same criteria used to evaluate weaning trial for the secondary extubation.

Study parameters

Demographic variables were also collected from existing medical records to describe patients under the care program of MV. The variates for risk analysis were body mass index (BMI), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Glasgow Coma Scale (GCS), renal function, electrolytes (Na, K, and Ca) and blood gas measured at the time acute respiratory failure before intubation. Smoking, comorbidity including type II diabetes and hypertension, the duration of MV and their outcome including successful extubation, MV dependency and mortality were enrolled for study.

Definitions

An extubation failure is defined as the

need for reintubation within 48 hours of tube removal and the most recent consensus on weaning defined success as the absence of mechanical assistance for 48 hours after extubation.[7,8] For the current study, MV dependence is defined as the need for mechanical ventilation for more than six hours per day for more than 21 days (Chang et al).

Statistical analysis (software, statistical methods for categorical and continuous variable, definition of statistical significance)

The variates were expressed as mean ± SD for the univariate and laboratory data. Univariate, bivariate and multivariate analyses were performed and we used with a 95% CI and a significance of less than 5% in the odd ratio analysis. In the univariate analysis, for the categorical variables, the distributions of absolute and relative frequencies (percentages) were used for the numerical variables, Student's t-test was used for those with a normal distribution and the Mann-Whitney U test was used for un-normal distribution. For the multivariate analysis, the logistic regression model was used for obtaining the odd ratio (OR). The study protocol was approved by the Ethics Committee of E-Da Hospital (EDAH IRB No. EMRP-106-092).

Results

Demographics

There were 232 patients (160 male and 72 females) a mean age of 66.0 ± 16.1 (49 to 83) years as shown in Table 1. Etiology of acute respiratory failure for the need of MV were classified into two group; lung diseases primary (n = 112, 48.3%) including the broncho-pneumonia and chronic obstructive pulmonary disease, and the non-lung primary diseases (n = 120, 51.7%) such as stroke, septic shock, hemorrhagic shock and un-expected cardiac arrest etc.

The outcome of MV patients

Outcome of our MV patients, there were extubation success in 125 (53.9%), MV dependence in 24 (10.3%) and death in 83 (35.8%). Demographic variables of each group and etiology of acute respiratory failure was classified as shown in Table 1. The etiology of acute respiratory failure due to lung origin was found in 112 (48.3%) and non-lung origin in 120 (51.7%) totally. MV dependence was found in 16 (66.7%) in lung origin and 8 (33.3%) in non-lung origin MV patients ($p = 0.05$). In case of BMI ≤ 18.5 (n = 43) and > 24.1 (n = 75), the successful extubation were found in 17 (39.5%) and 44 (58.7%), but MV dependence were found in 8 (18.6%) and 5 (10.6%) respectively without significant difference. The APACHE II and GCS score had relation with the outcome of MV patient ($p < 0.001$). There was no difference in the risk factors of smoking, diabetic and hypertension shown in Table 1.

Laboratory test profile of MV patients of each group

The results of laboratory test of MV patients demonstrated that renal function blood urea nitrogen (BUN), Creatinine and pH value have a significant difference ($p < 0.001$ for renal function and $p = 0.002$ pH acidity) at the time of acute renal failure as shown in Table 2. Level of $PaCo_2$ of the death group had the higher than other two group but without significance.

Risk factor and odd ratio of significant variates

The successful extubation was found 1.9 times in the non-lung origin diseases than that of lung origin ($p = 0.077$). The higher GCS and had a better outcome and the duration of usedness of MV also had an influence on results as Table 3. The usedness of MV were found 7.8 ± 5.3, 19.4 ± 7.8, and 12.8 ± 12.0 days in extubation, MV dependence and death group respectively ($p = 0.001$).

Table 1. The outcome of MV patients and their basic profiles and risk variates of each group.

Variate		Outcome: Extubation n = 125	Outcome: MV dependence n = 24	Outcome: Death n = 83	p	Total N = 232
Sex (n, %)	Male	81 (64.8%)	19 (79.2%)	60 (72.3%)	0.271	160 (69.0%)
	Famale	44 (35.2%)	5 (20.8%)	23 (27.7%)		72 (31.0%)
Age (mean ± sd)		65.9 ± 16.0	70.0 ± 14.3	65.0 ± 16.7	0.411	66.0 ± 16.1
Etiology (n, %)	Lung origin	60 (48.0%)	16 (66.7%)	36 (43.4%)	0.132	112 (48.3%)
	Non-lung	65 (52.0%)	8 (33.3%)	47 (56.6%)		120 (51.7%)
BMI (mean ± sd)		23.3 ± 6.0	21.7 ± 5.7	22.2 ± 4.9	0.201	22.8 ± 5.6
BMI (n, %)	≤ 18.5	17 (13.6%)	8 (33.3)	18 (21.7%)	0.128	43 (18.5%)
	18.6 – 24	64 (51.2%)	8 (33.3)	42 (50.6%)		114 (49.1%)
	≥ 24.1	44 (35.2%)	8 (33.3)	23 (27.7%)		75 (32.3%)
APACHE II score (mean ± sd)		26.2 ± 8.4	26.1 ± 6.8	31.5 ± 8.9	< 0.001*	28.1 ± 8.8
GCS (mean ± sd)		9.4 ± 2.3	7.9 ± 2.9	6.5 ± 2.9	< 0.001*	8.2 ± 2.9
Smoking (n, %)	yes	51 (40.8%)	11 (45.8%)	37 (44.6%)	0.819	99 (42.7%)
	no	74 (59.2%)	13 (54.2%)	46 (55.4%)		133 (57.3%)
Diabetic (n, %)	yes	48 (38.4%)	11 (45.8%)	33 (39.8%)	0.792	92 (39.7%)
	no	77 (61.6%)	13 (54.2%)	50 (60.2%)		140 (60.3%)
Hypertension (n, %)	yes	66 (52.8%)	12 (50.0%)	37 (44.6%)	0.509	115 (49.6%)
	no	59 (47.2%)	12 (50.0%)	46 (55.4%)		117 (50.4%)
MV day (mean ± sd)		7.8 ± 5.3	19.4 ± 7.8	12.8 ± 12.0	< 0.001*	10.8 ± 9.3
ICU day (mean ± sd)		11.1 ± 7.1	23.3 ± 10.2	14.3 ± 11.9		13.4 ± 10.0
Total Hospital day (mean ± sd)		22.4 ± 16.3	47.5 ± 21.0	17.6 ± 16.2	< 0.001*	23.6 ± 19.2

* $p < 0.05$. APACHE II: Acute Physiology and Chronic Health Evaluation II; BMI: body mass index; GCS: Glasgow coma scale; ICU: intensive care unit; MV: mechanical ventilation.

Table 2. Laboratory test profile at the time of acute respiratory failure of each group.

Variate	Outcome: Extubation n = 125		Outcome: MV dependence n = 24		Outcome: Death n = 83		p	Total N = 232	
	mean	sd	mean	sd	mean	sd		mean	sd
WBC	913.1	4,187.2	1,699.2	4,567.5	1,476.8	10,444.4	0.801	1,193.6	7,039.5
Hb	11.4	3.2	10.7	3.0	10.4	2.5	0.057	11.0	3.0
CRP	80.7	88.6	126.5	101.1	111.5	96.3	0.167	97.7	93.8
BUN	34.7	28.5	24.9	18.3	52.5	35.2	< 0.001*	39.6	31.4
Cr	2.0	1.9	1.4	0.8	2.9	2.3	< 0.001*	2.2	2.0
Na	136.9	7.6	138.0	6.0	136.3	16.3	0.681	136.8	11.3
K	3.9	1.0	4.0	0.7	4.1	1.3	0.464	4.0	1.1
Ca	7.6	3.2	4.6	4.2	7.5	2.9	0.126	7.4	3.2
pH	7.4	0.1	7.3	0.1	7.3	0.2	0.002*	7.3	0.2
PaO_2	131.3	93.4	111.3	51.0	185.3	512.2	0.398	148.4	313.3
$PaCo_2$	45.5	26.0	50.3	23.9	55.7	68.1	0.288	49.6	45.7

* $p < 0.05$. BUN: blood urea nitrogen; CRP: C-reactive protein; Hb: haemoglobin; MV: mechanical ventilation; $PaCO_2$: arterial carbon dioxide tension; PaO_2: arterial oxygen tension; pH: hydrogen ion concentration; WBC: white blood cell.

Table 3. Logistic regression for odd ration of variates as a risk factor.

Variate		Extubation			MV dependence			Death		
		OR	95% CI of OR	*p*	OR	95% CI of OR	*p*	OR	95% CI of OR	*p*
Etiology	Lung origin	1.000			1.000			1.000		
	Non-lung	1.902	0.934 – 3.876	0.077*	0.058	0.002 – 1.616	0.094	0.794	0.376 – 1.680	0.547
BMI	≤ 18.5	NA			1.000			NA		
	18.5 – 24	NA			0.099	0.005 – 2.155	0.141	NA		
	≥ 24.1	NA			0.887	0.071 – 11.060	0.926	NA		
APACE		1.006	0.962 – 1.052	0.800	NA			0.999	0.952 – 1.049	0.978
GCS		1.233	1.079 – 1.410	0.002*	NA			0.740	0.647 – 0.848	< 0.001*
Hb		1.084	0.964 – 1.220	0.177	NA			-		
BUN		0.990	0.978 – 1.002	0.095	1.016	0.943 – 1.096	0.675	1.018	1.004 – 1.031	0.008*
Cr		NA			0.297	0.026 – 3.370	0.327	1.018	0.826 – 1.254	0.868
Ca		NA			0.689	0.445 – 1.067	0.095	NA		
PH		11.524	1.175 – 13.056	0.036*	NA			0.048	0.004 – 0.558	0.015*
MV (day)		0.902	0.856 – 0.951	< 0.001*	1.051	0.924 – 1.195	0.449	1.042	1.001 – 1.085	0.043*

* $p < 0.05$.

Discussion

This study demonstrates that failed extubation had an adverse impact on clinical outcomes in patients recovering from acute respiratory failure in our pre-medical center hospital ICU. Without question, extubation failure would increase ICU and hospital length of stay, and total hospital costs as well. In our patients, the length of ICU stay was found 11.1 ± 7.1 and 23.3 ± 10.2 days for success extubation and MV dependence respectively ($p = 0.001$). Therefore, the intensive care of MV patients need to pay more attention than that of others. Epstein and coworkers[9] found that 247 (85%) were successfully extubated, and 42 (15%) required MV dependence of 289 intubated patients totally. Similar to our results, in our survived patients, the successful extubation and MV dependence were found in 125 (83.9%) and 24 (16.1%) respectively. Epstein et al.[9] reported that MV dependence prolonged ICU stay by 17 days after initial extubation, which is greater than the additional 9 days needed. In this study, variations in MV dependence patients are known to correlate with the etiology of lung original and prolong the length of stay (LOS) in ICU and hospital ward, but extubation failure with worse outcomes associated with non-airway etiology from the study of Epstein et al.[9] On the contrary, failed extubation did not increase post-ICU discharge LOS from the Quintard review study,[10] despite the increased frequency of transfer to a step-down respiratory care center or ward, this may be explained by the increased mortality found in re-intubated patients and resulted from no opportunity for extubation.

MV dependence patients will prolong the stay in ICU and cause an increasing the rates of morbidity and mortality.[11] This has as a consequence; with the longer resulting hospital stay, other complications increase, such as the need for tracheotomy, the incidence of pneumonia and pulmonary damage induced by MV and finally, costs increase as well.[7,12] Additionally, a study conducted in Chile discovered an association between extubation failure and the time on MV and the length of stay in the ICU.[13] In our results, the MV dependence factors had strongly associated with the lung etiology as a primary, GCS and renal function. In an analysis study by Huapaya,[14] overall in-hospital mortality of initial lung disease was available in 15 studies on mixed initial lung disease (62% in 2001 – 2009 and 48% in 2010 – 2017) and 15 studies on idiopathic pulmonary fibrosis (79% in 1993 – 2004 and 65% in 2005 – 2017). Follow-up mortality rate at 1 year ranged between 53% and 100%. In respective of initial lung disease etiology, mechanical ventilation is associated with increased mortality.

Concerning the obesity, there was no different, but too thin (BMI < 18.5) had poor prognosis of MV dependence in our MV patients. Obesity and mortality in ICU are inversely associated reported by meta-analyses.[15,16] The obesity paradox phenomenon has recently become apparent in the ICU.[16] O'Brien J M et al. had found no statistically significant difference between BMI categories (< 25 vs. 25 to < 30 vs. ≥ 30) in the competing risks analyses.[17] After careful matching, the data suggest that ICU mortality in obese population was higher in the medical group than in the surgical group and remains significantly higher post ICU admission. After adjustment for Simplified Acute Physiology Score II, age, category of admission, history of cardiac disease, and history of respiratory disease for category of admission, ICU mortality did not differ between obese and non-obese patients.[18]

Morbidity or mortality of MV patients were depending the severity of the primary disease and inappropriate care in ICU. By the way it is difficult to identify the primary cause of complicated or mortality patients in ICU sometimes. However, ICU mortality was significantly higher in patients who failed extubation.[9] The mortality was 35.8% (83/232) among our MV patients in this study. In addition, the hospital mortality rates were variable due to differences in the etiology or timing of reintubation, because these factors have been shown to have an important influence on patient outcomes.[7,9,19] Alternatively, severity of illness or perhaps some unrecognized aspect of the delivery of patient care, which may differ in the level hospital setting, may also account for these different results.

There is no agreement about extubation failure and how to define failure, and because there is no consensus about the time frame, reported incidences may vary. The reintubation rate for ICU patients liberated from mechanical ventilation in America. ICUs is approximately 10%[20] and they propose a time cutoff of 96 hours for reintubation definitions and it captures 90% of ICU reintubation events. Before extubation, standard hospital weaning process is absolutely necessary to perform. The prolonged weaning patients had a non-significant trend toward a higher rate of re-intubation, tracheostomy, and significantly longer length of stay and higher mortality in the intensive care unit.[21] In order to minimize the risks, discomfort, and expense of prolonged intubation, a trial of extubation is occasionally attempted, but it may be followed sometime thereafter by a risk to re-intubate. The incidence of reintubation was depended on the clinical mix of patients,[1,22] their critical acuity, critical care resources, and the threshold levels for extubation.[20,21,23] Even if reintubation is successful, patients had usually increased ICU mortality and cost of care, prolonged hospital length of stay. Therefore, experts' guidelines of intubation and extubation of the ICU patient of French Society of Anesthesia and Intensive Care Medicine (SFAR) and French-speaking Intensive Care Society (SRLF) have strongly recommend a spontaneous breathing trial before any extubation in an ICU patient ventilated for more than 48 hours to decrease the risk of extubation failure.[24] However, spontaneous breathing trial is inadequate as the sole means of detecting all patients at risk of extubation failure, we should probably take more specific causes consideration and risk factors of failure including ineffective cough, excessive tracheobronchial secretions, swallowing disorders and consciousness level which were included in our weaning protocol before extubation.

In conclusion, careful planning of tracheal extubation or tube exchange is as vital as the planning required for intubation. Many threatening circumstances can be anticipated and managed preemptively with an extubation strategy. Too early to extubate is a common mistake and reintubation strategy may include the judicious administration of oxygen by insufflation or jet ventilation; advancement of an endotracheal tube over the tube exchanger where possible. The present study found that MV patients present a higher risk of MV dependence, if they are subjected to a prolonged time on MV of greater than 7.8 days and spend more time in ICU.

Author Contributions

Study Design, Zi-Zi Guo and Yu-Ching Lu; Data Collection, Chun-Mei Huang; Statistical Analysis, Zi-Zi Guo and Yu-Ching Lu; Data Interpretation, Zi-Zi Guo and Ho-Sheng Lee; Manuscript Preparation, Yu-Ching Lu; Literature Search, Zi-Zi Guo and Chun-Mei Huang. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of E-Da Hospital (EDAH IRB No. EMRP-106-092).

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

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