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Comparison of the Outcomes of Patients Starting Mechanical Ventilation in the General Ward Versus the Intensive Care Unit

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Objective: Mechanical ventilation is sometimes initiated in the general ward (GW) due to the shortage of intensive care unit (ICU) beds. We investigated whether invasive mechanical ventilation (MV) started in the GW affects the patient's prognosis compared with its initiation in the ICU.

Methods: From January 2016 to December 2018, medical records of patients who started MV in the GW or ICU were collected. The 28-day mortality, ICU mortality, ventilator-free days, and complications related to the ventilator and the ventilator-free days were analyzed as outcomes.

Results: A total of 673 patients were enrolled. Among these, 268 patients (39.8%) started MV in the GW and 405 patients (60.2%) started MV within 24 hours after admittance to the ICU. There was no difference in 28-day mortality between the 2 groups (27.2% versus 27.2%, $P = 0.997$). In addition, there was no difference between ventilator-related complication rates, ventilator-free days, or the length of hospital stay. A high Acute Physiology and Chronic Health Evaluation II score, the presence of solid tumor, the absence of chronic kidney diseases, and low platelet count were associated with higher 28-day mortality. However, the initiation of MV in the GW was not associated with an increase in 28-day mortality compared with the initiation in the ICU.

Conclusions: Starting MV in the GW was not a risk factor for 28-day mortality. Therefore, prompt application of a ventilator if medically indicated, regardless of the patient's location, is desirable if a skilled airway team and appropriate monitoring are available.

Key Words: assessment, patient outcome, general ward, intensive care unit, mechanical ventilation, rapid response team

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The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2, is rapidly spreading around the world.[1] The number of critically ill COVID-19 patients is also increasing, leading to a serious shortage of intensive care unit (ICU) beds and ventilators.[2–4] The COVID-19 pandemic has raised issues about ICU capacity and robustness and collateral damage. Many ICUs have had to seek ad hoc solutions to surge capacity problems, for example, taking care of ventilated patients outside the ICU.

The limited ICU resource has always been an ongoing problem, and for this reason, there have been many studies on ICU triage criteria.[5–8] The number of patients in need of treatment in an ICU has been steadily increasing worldwide.[9] Many of these patients require mechanical ventilation (MV) and are treated only in the ICU in most countries.[10] A ventilator is one of the most helpful treatments for maintaining oxygenation while recovering from respiratory failure. In most countries, the number of ICU beds is insufficient, so MV is sometimes started in the general ward (GW).[11–15]

Previous studies reported that mortality related to MV in the GW is higher than that in the ICU.[11–15] Iwashita et al[12] found a higher hospital mortality (41.4% versus 38.8%, $P < 0.001$) and a longer duration of ventilation (11.7 versus 9.5, $P < 0.001$) in mechanically ventilated patients in the non-ICU setting. Hersch et al[11] showed that the group who initiated MV in the medical ward had lower survival rates (20% versus 38%, $P < 0.05$) and higher endotracheal tube–related inadvertent events (62% versus 20%, $P < 0.05$). However, there was a study that showed no differences in adverse events related to ventilator use in the GW.[13]

There are only a few articles on ventilation conducted in the GW, and the differences in prognosis and complications of MV initiated in the GW versus the ICU are not well known. In this study, we compared the prognosis and complications between patients starting MV in the GW versus the ICU to assist clinicians in their decision making about intubation.

METHODS

Study Design and Patients

This retrospective single-center cohort study was conducted in a tertiary care hospital in Seoul, Korea. Patients who were screened by the rapid response team (RRT) and started MV in the GW and those who started MV in the ICU were included in this study. A total of 2223 patients were screened from January 1, 2016, to December 31, 2018. Among them, 673 patients were included, excluding patients who did not undergo MV (n = 517), patients who were started on a ventilator in the emergency department (n = 605), patients who received a ventilator 24 hours after admittance to the ICU (n = 115), and patients with a hematologic malignancy (n = 313).

There was a difference in the rate of hematologic malignancy (29.3% in the GW group versus 22.9% in the ICU group, $P = 0.029$) in the initial baseline characteristics, so patients with a hematologic malignancy were excluded to equalize the underlying diseases between the groups. Because the condition of the underlying disease, rather than MV itself, usually determines the prognosis, it was excluded from the analysis.[16–18]

Staffs on GW are composed of residents, fellows, and professors and manage only patients in the ward that belongs to their department. In the GW, oxygen therapy such as high flow nasal

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cannula and noninvasive ventilation and monitoring are available. The GW patient group was defined as the group of patients who started MV in the GW due to a lack of ICU beds, although they met the criteria for admission to the ICU. The ICU patient group was defined as the patients who started MV within 24 hours of admission to the ICU to compare them with the GW group, because it is thought that the GW group would have been admitted to the ICU and started MV there if the number of ICU beds was sufficient.

This study was approved by the institutional review board of Asan Medical Center (IRB no. 2019-0297), and informed consent was waived due to the retrospective nature of the study.

Rapid Response Team

We operate an RRT named the medical emergency team (MET) at our hospital and have full-time coverage of the entire ward. The MET consists of 9 dedicated trained nurses with experience working in the critical care unit, 2 ICU residents (internal medicine second or third grade), 1 ICU fellow, and 1 ICU intensivist. These medical staffs dedicate to RRT and work in 2 shifts or 3 shifts for 24 hours a day, 7 days a week. In addition, 2 ICU staff and 3 ICU fellows working in the ICU cover some portion of night duty. The physician' schedules change every month.[19] In the GW, the MET team manages the critically ill patients with the same protocol, similar to ICU setting.

Data Collection and Outcomes

All study data were retrieved from the Electronic Medical Records (Asan Medical Information System 2.0, Seoul, Korea). Basic demographic characteristics, including sex, age, type of admission (medical, surgical) and ICU admission diagnosis, need for invasive support (MV and renal replacement therapy) and vasopressors on ICU admission and during the ICU stay, and the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were analyzed. The 28-day mortality rate was the primary outcome. Intensive care unit mortality, length of hospital stay, length of ICU stay, ventilator-free days at 28 days,[20] and complications related to the ventilator (ventilator-associated pneumonia, barotrauma, unplanned extubation, airway/breathing circuit damage, gas supply issues) were collected as secondary outcomes. In the GW group, in-hospital mortality was additionally analyzed as a secondary outcome.

APACHE II scores for mortality predictions were also assessed during the first 24 hours on MV.

Statistical Analysis

All values are expressed as the mean ± standard deviation for continuous variables or as percentages for the categorical variables. Student *t* test or the Mann-Whitney *U* test was used for continuous data, and Pearson χ^2 test or Fisher exact test was used for categorical data. Survival was evaluated by Kaplan-Meier survival analysis and the log-rank test. Risk factors for mortality were analyzed using a Cox proportional hazards model with backward, stepwise elimination, and variables with $P < 0.1$ in the univariate analysis were entered into the multivariate models. All *P* values were 2-tailed, with statistical significance set at $P < 0.05$. All statistical analyses were performed using SPSS software (version 22.0; IBM Corporation, Somers, NY).

RESULTS

Patient Characteristics

A total of 673 patients were included in this study. Among these, 268 patients (39.8%) started MV in the GW and 405 patients (60.2%) were intubated within 24 hours after the patient was admitted to the ICU (Fig. 1). In the GW group, 35 patients (13.1%) underwent MV only in the ward. The GW group underwent MV for an average of 9.7 ± 11.2 hours in the ward. Because of clinical improvement, 11 patients underwent extubation within 48 hours of application of the ventilator, and 24 patients died within 48 hours after application of the ventilator. The ICU group underwent MV for an average of 11.9 ± 15.7 hours in the ICU. In the ICU group, 14 patients underwent ventilator weaning within 48 hours of application of the ventilator and 15 patients died within 48 hours of application of the ventilator.

There were no statistically significant differences in age, sex, APACHE II score, or underlying disease between the 2 groups (Table 1). There were no statistically significant differences in vital signs or laboratory findings before initiating the ventilator between the 2 groups (Table 1).

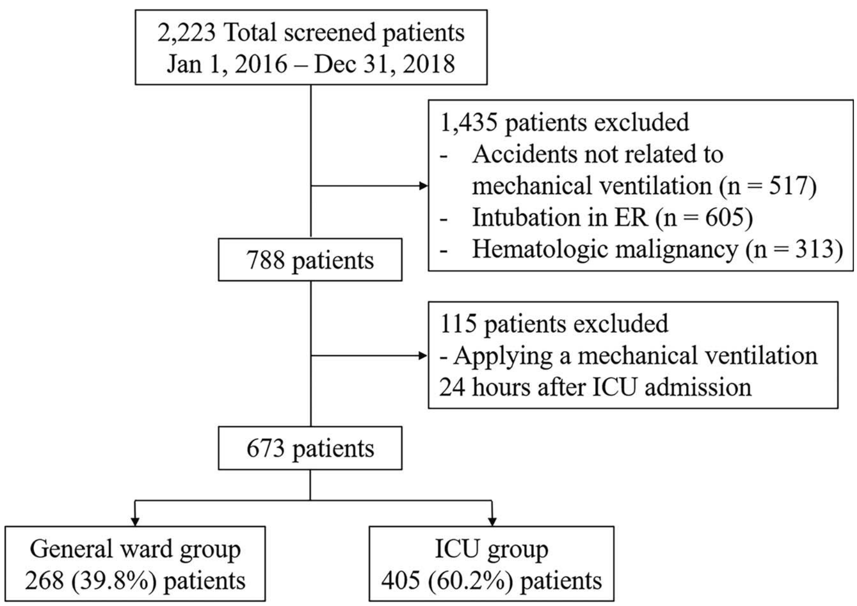

FIGURE 1. Patient flow chart. ER, emergency room.

TABLE 1. Baseline Characteristics of the Patients Between the GW Group and the ICU Group

	Total (N = 673)	GW Group (n = 268)	ICU Group (n = 405)	*P*
Age, y	64.2 ± 13.7	65.3 ± 13.1	63.5 ± 14.1	0.10
Male	460 (68.4)	181 (67.5)	279 (68.9)	0.712
APACHE II score	27.8 ± 9.5	27.9 ± 9.3	27.7 ± 9.6	0.85
Underlying disease				
Solid tumor	312 (46.4)	133 (49.6)	179 (44.2)	0.167
Chronic lung disease	152 (22.6)	63 (23.5)	89 (22.0)	0.642
Chronic heart disease	150 (22.3)	63 (23.5)	87 (21.5)	0.536
HTN	242 (36.0)	94 (35.1)	148 (36.5)	0.698
DM	195 (29.0)	88 (32.8)	107 (26.4)	0.072
Chronic liver disease	92 (13.7)	35 (13.1)	57 (14.1)	0.708
CVA	49 (7.3)	17 (6.3)	32 (7.9)	0.446
CKD	63 (9.4)	29 (10.8)	34 (8.4)	0.290
CKD on HD	43 (6.4)	19 (7.1)	24 (5.9)	0.546
Transplantation	19 (2.8)	6 (2.2)	13 (3.2)	0.457
Vital sign				
MBP, mm Hg	85 ± 27	86 ± 27	85 ± 27	0.708
HR, /min	108 ± 32	110 ± 30	107 ± 33	0.208
RR, /min	28 ± 11	28 ± 9	29 ± 12	0.242
BT, °C	36.0 ± 6.4	36.2 ± 6.0	35.9 ± 6.7	0.554
Spo_2, %	91 ± 10	91 ± 9	91 ± 12	0.743
Laboratory findings				
WBC, /mm^3	13,818 ± 16,182	14,255 ± 13,514	13,521 ± 17,776	0.568
Hemoglobin, g/dL	10.1 ± 2.4	9.9 ± 2.2	10.1 ± 2.5	0.257
Platelet, 1000/mm^3	181 ± 121	187 ± 123	176 ± 121	0.261
CRP, mg/dL	10.3 ± 8.9	10.6 ± 9.0	10.2 ± 8.9	0.585
ABGA				
pH	7.37 ± 0.14	7.36 ± 0.15	7.37 ± 0.13	0.095
pco_2, mm Hg	40.2 ± 21.0	41.7 ± 23.7	39.2 ± 18.9	0.135
P/F ratio, mm Hg	273.9 ± 186.0	262.7 ± 185.5	281.3 ± 186.2	0.206

Data are presented as mean ± SD or number (%), unless otherwise indicated.

ABGA, arterial blood gas analysis; BT, body temperature; CRP, C-reactive protein; CVA, cerebral vascular accident; DM, diabetes mellitus; HD, hemodialysis; HTN, hypertension; HR, heart rate; MBP, mean blood pressure; pco_2, partial pressure of carbon dioxide; P/F ratio, Pao_2/Fo_2 ratio; pH, power of hydrogen; RR, respiratory rate; Spo_2, saturation pulse oxygen; WBC, white blood cell.

Complication Rates of the Mechanical Ventilator and Outcomes

The rate of unplanned extubation (4.1% versus 1.7%, $P = 0.061$) showed the increased tendency in the GW patient group, but none of the complications related to the application of MV did not show any statistically significant differences (Table 2).

In the GW group, 28-day mortality was not significantly different from the ICU group (27.2% versus 27.2%, $P = 0.997$; Fig. 2). There was no difference in ICU mortality between the 2 groups (47.0% versus 44.0%, $P = 0.434$), and the ICU length of stay (LOS), hospital LOS, and ventilator-free days did not show any statistically significant differences (Table 2).

Risk Factors for 28-Day Mortality

The results of a Cox proportional hazards analysis of factors associated with the 28-day mortality are shown in Table 3. After adjusting for confounders, independent predictors of 28-day mortality included the APACHE II score (odds ratio [OR], 1.058; 95% confidence interval [CI], 1.039–1.076; $P < 0.001$); solid tumor (OR, 1.876; 95% CI, 1.342–2.624; $P < 0.001$); chronic kidney disease (CKD; OR, 0.418; 95% CI, 0.193–0.906; $P = 0.027$)

TABLE 2. Complication Rates of Mechanical Ventilators and Outcomes

	Total (N = 673)	GW Group (n = 268)	ICU Group (n = 405)	*P*
Ventilator-associated complication				
Ventilator-associated pneumonia	2 (0.3)	0 (0)	2 (0.5)	0.249
Barotrauma	10 (1.5)	4 (1.5)	6 (1.5)	0.991
Unplanned extubation	18 (2.7)	11 (4.1)	7 (1.7)	0.061
Outcomes				
28-Day mortality	183 (27.2)	73 (27.2)	110 (27.2)	0.997
ICU mortality	304 (45.2)	126 (47.0)	178 (44.0)	0.434
ICU LOS, d	13.9 ± 18.2	15.3 ± 20.4	13.1 ± 16.6	0.129
Hospital LOS, d	48.5 ± 65.9	47.3 ± 55.5	49.2 ± 72.1	0.706
Ventilator-free days	17.8 ± 8.8	17.6 ± 8.8	17.9 ± 8.8	0.660

Data are presented as mean ± standard deviation or number (%), unless otherwise indicated.

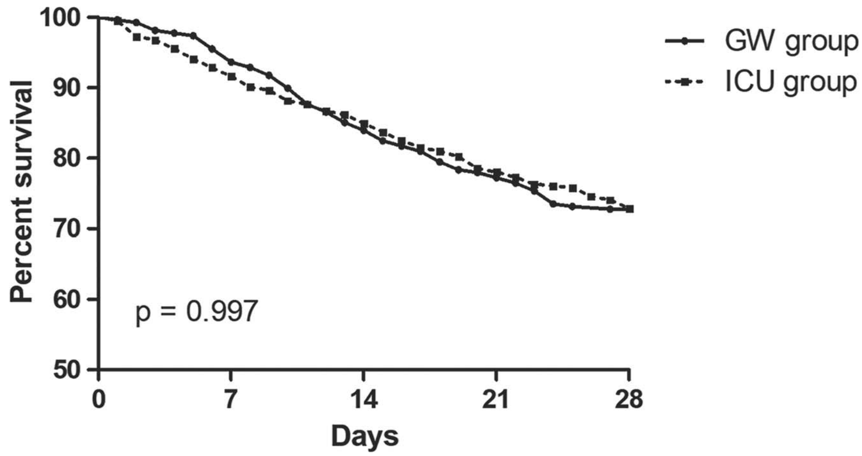

FIGURE 2. Kaplan-Meier curves of 28-day mortality in patients.

and platelet count (OR, 0.998; 95% CI, 0.996–1.000; $P = 0.009$). Ventilator initiation in the GW was not a statistically significant risk factor.

Risk Factors for In-Hospital Mortality in the GW Group

The results of a Cox proportional hazards analysis of factors associated with the in-hospital mortality are shown in Table 4. After adjusting for confounders, independent predictors of in-hospital mortality included the APACHE II score (OR, 1.040; 95% CI, 1.017–1.063; $P < 0.001$); solid tumor (OR, 1.930; 95% CI, 1.345–2.769; $P < 0.001$), cerebral vascular accident (OR, 0.299; 95% CI, 0.109–0.823; $P = 0.019$); mean blood pressure (OR, 0.990; 95% CI, 0.981–0.998; $P = 0.019$), and heart rate (OR, 1.009; 95% CI, 1.002–1.016; $P = 0.014$). Transfer to the ICU was not a statistically significant risk factor.

DISCUSSION

In this study, 39.8% of the patients requiring intubation and MV started in the ward, and monitoring was performed in the GW for an

TABLE 3. Risk Factors for 28-Day Mortality Assessed Using a Cox Proportional Hazards Model

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	1.003	0.992–1.014	0.597			
Male	1.105	0.813–1.502	0.525			
APACHE II score	1.062	1.045–1.079	<0.001	1.058	1.039–1.076	<0.001
Underlying disease						
Solid tumor	1.899	1.413–2.551	<0.001	1.876	1.342–2.624	<0.001
Chronic lung disease	0.532	0.351–0.806	0.003	0.915	0.575–1.456	0.707
Chronic heart disease	0.698	0.477–1.022	0.065	0.894	0.570–1.404	0.627
Chronic liver disease	1.375	0.935–2.024	0.106			
DM	0.986	0.715–1.359	0.930			
CKD	0.455	0.233–0.889	0.021	0.418	0.193–0.906	0.027
CVA	0.541	0.266–1.099	0.090	0.520	0.243–1.114	0.093
Transplantation	0.342	0.085–1.380	0.132			
Laboratory findings						
WBC	1.000	1.000–1.000	0.004	1.000	1.000–1.000	0.021
Platelet	0.997	0.996–0.998	<0.001	0.998	0.996–1.000	0.009
CRP	1.014	0.998–1.031	0.095	1.009	0.992–1.026	0.327
P/F ratio	1.000	0.999–1.001	0.619			
Vital sign						
MBP	0.992	0.987–0.997	0.003	0.997	0.991–1.003	0.346
HR	1.004	0.999–1.009	0.117			
RR	1.008	0.994–1.022	0.245			
Ventilator start in GW	1.001	0.744–1.345	0.997			
Ventilator-associated complication	0.682	0.302–1.538	0.356			

CRP, C-reactive protein; CVA, cerebrovascular accident; DM, diabetes mellitus; HR, heart rate; MBP, mean blood pressure; RR, respiratory rate; WBC, white blood cell; P/F ratio, PaO_2/FiO_2 ratio.

TABLE 4. Risk Factors for In-Hospital Mortality in GW Group Patients Assessed Using a Cox Proportional Hazards Model

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	0.996	0.984–1.008	0.496			
Male	1.344	0.955–1.892	0.090	1.395	0.967–2.011	0.075
APACHE II score	1.026	1.006–1.047	0.012	1.040	1.017–1.063	<0.001
Underlying disease						
Solid tumor	1.930	1.373–2.714	<0.001	1.930	1.345–2.769	<0.001
Chronic lung disease	0.641	0.423–0.971	0.036	1.019	0.638–1.627	0.937
Chronic heart disease	0.533	0.345–0.823	0.005	0.728	0.451–1.174	0.193
Chronic liver disease	0.732	0.428–1.251	0.254			
DM	0.786	0.547–1.129	0.192			
CKD	0.782	0.449–1.361	0.384			
CVA	0.326	0.120–0.882	0.027	0.299	0.109–0.823	0.019
Transplantation	0.236	0.033–1.689	0.150			
Laboratory findings						
WBC	1.000	1.000–1.000	0.088	1.000	1.000–1.000	0.153
Platelet	0.999	0.997–1.000	0.050	1.000	0.998–1.001	0.577
CRP	0.998	0.978–1.019	0.844			
P/F ratio	1.001	1.000–1.002	0.127			
Vital sign						
MBP	0.994	0.988–1.001	0.083	0.990	0.981–0.998	0.019
HR	1.005	0.999–1.012	0.087	1.009	1.002–1.016	0.014
RR	0.996	0.978–1.014	0.684			
Ventilator-associated complication	1.160	0.589–2.285	0.667			
Transfer to ICU	0.582	0.372–0.911	0.018	0.695	0.399–1.208	0.197

CRP, C-reactive protein; CVA, cerebrovascular accident; DM, diabetes mellitus; HR, heart rate; MBP, mean blood pressure; RR, respiratory rate; WBC, white blood cell; P/F ratio, PaO_2/FiO_2 ratio.

average of 9.7 ± 11.2 hours before admittance to the ICU, but there was no difference in 28-day mortality (27.2% versus 27.2%, P = 0.997) or ICU mortality (47.0% versus 44.0%, P = 0.434). Unplanned extubation was slightly higher in the GW group, but it was not statistically significant. High APACHE II score, presence of solid tumor, absence of CKD, and low platelet count were associated with an increase in 28-day mortality, but ventilator initiation in the GW did not show statistically significant values for 28-day mortality.

In this study, patient age, sex, underlying disease, laboratory data, and vital signs did not show any differences at baseline. However, Iwashita et al[12] reported that the percentage of men was lower (60.2% versus 61.3%, P = 0.025) and the age was older (72.8 versus 70.1 y, P < 0.001) in the non-ICU group. In the study by Iwashita et al,[12] quasi-ICU and GW were analyzed in a non-ICU setting. In this study, only GW was included without quasi-ICU, so this might explain why the patient characteristics are different. In addition, Hersch et al[11] showed that age (75 ± 13 versus 67 ± 20 y; P < 0.05) was older, and the APACHE II score was higher (27 ± 7 versus 24 ± 7, P < 0.05) in the wards group than in the ICU group. In the study by Hersch et al,[11] MV was divided into the ward-only group and the ICU group, but in our study, the ward-started group and the ICU-started group were divided, so this difference in study design would affect the results. Most of the studies on MV and its application in the ward were conducted in a ward alone group or in quasi-ICU, or a group not admitted to the ICU was compared with a group admitted to the ICU. In the study by Iwashita et al,[12] patients with a current history of cancer were excluded. In the study by Wongsurakiat et al,[15] an attending physician who was not skilled in critical care took care of the patients in the general medical ward without the assistance of specialized personnel, such as a respiratory therapist. In the study by Hersch et al,[11] the underlying disease was not analyzed, and the ventilators in the ward were applied by the attending physician with minimal critical care training without assistance from a respiratory therapist or RRT due to a lack of manpower. The study by Tang et al[14] included only patients who were managed by the medical respiratory team in the general medical wards. However, in our study, RRT screens and manages all patients in the GW. The RRT consists of 9 trained nurses with experience working in the critical care unit, 2 ICU residents (internal medicine second or third grade), 1 ICU fellow, and 1 ICU intensivist. These medical staffs dedicate to RRT and work in 2 or 3 shifts for 24 hours a day, 7 days a week. The RRT manages the ventilated patients in the GW independently, similar to ICU setting. In addition, there have been no prior cases of classification based on the place where the ventilator was started, as in this study.

In this study, safety complications related to MV indicated a slightly higher rate of unplanned extubation in the ward group, but it was not statistically significant. Tang et al[14] showed that unplanned extubation occurred in 2.5% of patients when MV was performed in the ward. Kamio and Masamune[13] showed that there was no difference in airway/breathing circuit issues between the ICU group and the ward group (P = 0.22). However, Hersch et al[11] showed that the endotracheal tube event rate was higher in the ward group than in the ICU group (62% versus 20%, P < 0.05). In the ICU, unplanned extubation can be seen in 2% of patients[21] and is known to be associated with male sex, mental state, physical restraints, a higher GCS score, and a lower APACHE II score.[22–24] In this study, the reason why unplanned extubation was not higher in the ward than in the ICU group may be due to the presence of the RRT, which works 24 hours in this hospital, and the presence of a respiratory therapist during the day. The RRT consists of an intensivist and 2 nurses in charge, helping start intubation and ventilator treatment in the ward, and helping the nurses in charge of the ward with education and management of the ventilators. In addition, the sedation protocol and spontaneous awakening trial implemented in the GW group were equally applied to the ICU. The RRT is known to reduce in-hospital mortality and cardiopulmonary arrest.[25,26] The place where the intubation was performed is not important, and it should be carried out without hesitation if necessary. If there is an airway management team or protocol in the hospital, there is no difference in outcomes, and some patients even progressed to weaning while still in the GW in this study.

In this study, the 28-day mortality of patients who started on a ventilator in the GW was not increased. The 28-day mortality was associated with APACHE II score, solid tumor, CKD, and platelet count. Ventilator initiation in the GW was not a risk factor in the 28-day mortality. Wongsurakiat et al[15] showed that an APACHE II score greater than 22 was the only independent predictor of death (OR, 4.3; 95% CI, 1.2–15.2; $P = 0.02$) in multivariate analysis. Other risk factors for mortality related to MV include the type of respiratory failure (type I), the use of inotropes, the APACHE II score, greater than 80 years of age, lower albumin levels (<2 g/dL), required hemodialysis, or had a comorbidity, etc.[27–29] In GW group, males tended to be associated with an increase in in-hospital mortality, but no statistically significant difference in this study. Sex predominance as a risk factor for mortality in patients with ventilator is still controversial.[30–33]

Our study had several limitations. First, this study was conducted at a single center in the ICU of a private tertiary care hospital that had a very high annual volume of critically ill patients with malignancies. In the study by Tang et al,[14] cancer patients were excluded, but their mortality rate was 89.1%, which was higher than the in-hospital mortality of 52.2% in our study. This may have been influenced by the advances in cancer treatment. Second, complications related to MV could only be confirmed through medical records, so unrecorded complications could not be included in this study. However, because most records, including nursing records and vital sign sheets, were checked during the study, the excluded complications are thought to be very small. Third, this study was conducted on a group of patients who started MV after screening by the RRT. The RRT screening was not performed in the cases of intubation after admittance to the ICU from the emergency department. However, because the intensivist who decides upon intubation in the ICU belongs to the RRT, it is unlikely that there will be a major difference in determining the intubation time.

CONCLUSIONS

The 28-day mortality was not higher in the GW group compared with the ICU group. Ventilator start in the GW was not a risk factor for 28-day mortality. The decision about intubation and ventilator initiation in the GW should be made based solely on medical need, not the location, if an experienced airway team or monitoring is available for support. In addition, proper sedation should be used to avoid unplanned extubation. In preparation for an ICU shortage, it is necessary to consider the provision of a system capable of providing critical care in the ward.

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