Prevalence, Clinical Characteristics, and Outcomes of Intensive Care Unit Patients Requiring Prolonged Mechanical Ventilation in a Tertiary Hospital in the Philippines: A Single-Center Retrospective Cross-sectional Study

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ABSTRACT

Background and Objective. Epidemiology data on prolonged mechanical ventilation (PMV) and PMV patient features in the Philippines is lacking. This retrospective cross-sectional study aimed to determine the prevalence of PMV among intubated patients, describe patient characteristics and outcomes, and identify risk factors associated with PMV.

Methods. A retrospective review of records was done on adult intubated patients admitted under the Medical Intensive Care Unit Service from July 2022 to June 2023. Various clinical characteristics and outcomes of PMV and non-PMV patients were collected, compared, and analyzed. PMV was defined as having MV for ≥6 hours per day for >21 days.

Results. Among 261 intubated ICU patients admitted, 75 (28.7%) required PMV. PMV patients were older (62 vs. 53.5), had higher Charlson Comorbidity Index scores (4 vs. 3), and required vasopressors (81.33% vs. 54.84%) and blood products (93.33% vs. 51.08%) more often. Nosocomial infections (86.67% vs. 45.70%), ventilator-related (30.67% vs. 12.37%) and in-hospital (66.22% vs. 32.97%) complications developed more frequently. Outcomes such as ICU length of stay (29.5 vs. 7 days) and hospital mortality (61.33% vs. 41.94%) were longer. Vasopressor use (OR 2.25, 95% CI 1.06-4.76), development of nosocomial infections (OR 6.20, 95% CI 2.64-14.56), and development of in-hospital-related complications (OR 2.20, 95% CI 1.13-4.30) were independent predictors of PMV.

Conclusion. In this single-center investigation, 28.7% of ICU patients required PMV. Knowledge of patient characteristics and risk factors aid in the development of interventions that improve outcomes and reduce PMV prevalence. Larger studies are recommended to assess nationwide PMV epidemiology and provide data on the need for step-down units for weaning.

Keywords: ventilator, mechanical, intensive care unit, ventilator weaning, critical illness/epidemiology

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INTRODUCTION

Prolonged mechanical ventilation (PMV) is defined as mechanical ventilation (MV) for at least 6 hours per day for greater than 21 days according to the National Association for Medical Direction of Respiratory Care (NAMDRC) consensus conference in 2005.[1] Due to improved clinical care in acute and critical care settings, there is an increasing proportion of patients requiring immediate mechanical ventilation that survive the acute phase of respiratory failure and critical illness that will require more prolonged ventilatory support. An estimated 5 to 13% of patients who undergo invasive MV eventually require prolonged support.[2] A single-center retrospective study in Japan by Nagata et al. estimated the incidence of PMV at 7.3%, with a median duration of 37 days.[3] Similarly, single-center studies in Taiwan and Korea have reported incidences of 6.58% and 5.1%, respectively.[4,5]

Multiple factors have been associated with PMV. Emergency ICU admission and steroid use during MV were identified by Nagata et al. in Japan.[3] In Brazil, a multicenter study revealed that PMV patients have higher APACHE II scores within 24 hours of ICU admission, vasopressor use, renal replacement therapy, and parenteral nutrition compared to non-PMV patients. Furthermore, development of complications such as pressure ulcers, infections, and pulmonary embolism increased the risk for PMV.[6] A study by Li et al. in China revealed that an age of >74 years and chronic congestive heart failure were associated with weaning failure.[7]

The I-TRACH score, consisting of six variables (ICU intubation, heart rate, BUN, pH, creatinine, and bicarbonate), was validated in a prospective observational study to predict the need for MV >7 and >14 days from the time of intubation.[8] However, this scoring system still requires validation from a multicenter trial for the aforementioned durations, and remains to be validated for durations longer than 21 days.

In the Philippines, there is a lack of step-down medical facilities such as respiratory care centers, long-term acute care centers, and weaning units that can accommodate patients requiring only ventilatory support. Hence, most ICU patients remain long-term in the ICU or are transferred out to ward beds until they are successfully weaned. Consequently, resources are directed to patients whose sole indication for ICU admission is invasive ventilatory support, rather than to those needing more intensive and urgent medical care.[9]

Furthermore, despite the best quality of care and maximum lifesaving interventions, critically-ill patients are generally discharged with worse quality of life and functional capacity; patients on PMV being identified as having one of the worst reductions in quality of life.[10] A study by Ho et al. on outcomes of patients with PMV revealed that 26.1% of discharged patients required assistance for activities of daily living while 28.3% were bedbound on discharge.[11] Additionally, patients on PMV have greater mortality rates post-discharge, increased healthcare costs, and higher resource utilization compared to non-PMV patients.[12] Although a proportion of these patients improve over time with rehabilitation,[13] the amount of resources and medical expenses directed to these patients are often disproportionate compared to the expected outcomes.[14]

Currently, there is a dearth of knowledge on the epidemiology of prolonged mechanical ventilation in the Philippines as well as the characteristics of Filipino patients that require PMV. Knowledge of prevalence and factors associated with prolonged mechanical ventilation allows physicians to provide realistic expectations for families to effectively facilitate resource planning and determining goals of care. Additionally, empiric knowledge on factors which contribute to PMV such as pressure ulcers and nosocomial infections will in turn drive further studies that seek to address these potentially correctable factors in the ICU setting. Furthermore, it will inform administrative decisions regarding the establishment of step-down facilities and the use of cost-effective management for this subset of patients.[14]

The study aimed to determine the prevalence of PMV and describe the clinical characteristics and outcomes of PMV among intubated patients admitted in the Medical Intensive Care Unit (MICU). Furthermore, it aimed to identify risk factors associated with PMV among intubated patients admitted in the MICU.

METHODS

Study Design and Setting

This study was a cross-sectional review and was limited to the review of medical records of patients admitted to the MICU. The study was conducted in the University of the Philippines - Philippine General Hospital (UP-PGH), the national university teaching hospital and a tertiary referral center in Manila, Philippines.

The Department of Medicine admits critically ill patients to the MICU, a 14-bed ICU catering to service patients. Admission is prioritized based on bed availability, disease severity, ICU admission indication, prognosis, and other factors, as determined by the ICU consultant-in-charge and residents-in-charge among the pool of referred patients. All admitted service patients are managed primarily by the ICU service, consisting of the service consultants and residents-in-charge but are managed in collaboration with the Cardiology, Pulmonary Medicine, Infectious Diseases, and Nephrology services as part of a blanket-referral system. Patients are referred additionally to other specialties and subspecialties as deemed necessary by the ICU service.

Study Population

The study included all patients admitted to the MICU service from July 1, 2022 to June 30, 2023 that fulfilled the following inclusion criteria: patients aged ≥19 years, admitted under the Internal Medicine service as a service patient, and

received invasive MV initiated during the admission, whether through endotracheal intubation or through an advanced airway such as a tracheostoma. The following patients were excluded: those under the primary service of other departments, those transferred to or from another service or department, or those transferred to or from the Pay services. Patients who were also on mechanical ventilation prior to hospital admission were not included. Furthermore, patients who received noninvasive forms of advanced ventilation (i.e., bilevel positive airway pressure, high-flow nasal cannula) and patients that were not intubated but admitted in the ICU were excluded. However, patients initially admitted to the ICU on non-invasive ventilation but were subsequently intubated were included.

Successful liberation was defined as being liberated from MV for at least 48 consecutive hours.[3] Patients that were not successfully liberated (i.e., reintubated due to self-extubation, reintubated due to failure of extubation, etc.) were included in the analysis for PMV. For patients with multiple admissions to the ICU, each admission was considered separately. Readmissions of the same patient in the MICU were recorded and analyzed as separate data points. The review included all cases admitted during the aforementioned period and records of cases from 30 days prior if available.

Power analysis was performed using G*Power version 3.1. A sample size of 300 achieved 52% power in a multivariable logistic regression analysis to determine significant factors associated with PMV among intubated ICU patients. The analysis detected a small-to-medium effect size (OR of 1.7) with 5% two-sided level of significance in a multivariable regression with an R-squared of at most 0.40.

Study Variables

Data were extracted retrospectively from electronic medical records of patients admitted to the ICU during the study period. The following data were obtained on ICU admission: age, sex, smoking history,[15] comorbidities,[14] Charlson Comorbidity Index,[16] history of prior hospitalization in the past 30 days, functional status on admission, diagnosis on ICU admission, source of ICU admission, Acute Physiology and Chronic Health Evaluation (APACHE) II score,[17] Sequential Organ Failure Assessment (SOFA) score,[18] and Glasgow Coma Score on ICU admission. Other data collected on ICU admission included number of medications, presence of infection (both pulmonary and non-pulmonary), whether the patient was ventilated on the first day of hospital admission, and clinical and laboratory parameters derived from the I-TRACH score: (tachycardia (HR >110), elevated BUN (BUN >25 mg/dL), acidemia (pH <7.25), creatinine >2 mg/dL, HCO3 <20 meq/L).[8] Variables included in the analysis were selected based on previous literature, data availability, and clinical relevance.

Data during ICU admission were also collected, namely: vasopressor use, renal replacement therapy, blood transfusion, and the development of nosocomial infections, MV-related complications, and in-hospital-related complications.[14] Nosocomial infections are infections needing antibiotics that developed within 48 hours of hospitalization. Mechanical ventilator-related complications on the other hand were limited to pneumothorax, mucus plug, and atelectasis. The development of nosocomial infections and mechanical ventilator-related complications were identified based on the assessment of the attending physician as written in the chart. Time metrics included time from admission to ICU referral, time from ICU referral to ICU admission, duration of MV use, duration of non-invasive ventilation, tracheostomy rate, time from intubation to day of tracheostomy, ICU length of stay, ER length of stay, and hospital length of stay. Clinical outcomes such as ICU mortality, hospital mortality, ICU discharge, and hospital discharge were also obtained. The variables, their operational definitions, and the type of data obtained are described in the Appendix.

Data Collection

Data collection involved reviewing the medical charts of patients included in the study. This was done by the study investigators and one additional research assistant (RA). Prior to actual data collection, the RA was also trained by the investigators on procedures for data extraction and collection.

After ethical approval of the University of the Philippines Manila Research Ethics Board (UPMREB 2023-0599-01), permission to conduct research was requested from the Expanded Hospital Research Office. A request for access to the medical charts was then sent to the Medical Records Division of the Philippine General Hospital. Access to records were requested for all cases admitted to the Medical ICU during the study period and cases from 30 days prior to the start of the study period to allow for additional review of prior admissions/hospitalizations. Access to this information was requested for the authors of the study and the RA.

Once the approval was obtained, data extraction and encoding were done by the study investigators and RA. The anonymity of patients' information in the data collection form was observed through assigning a code number to each admission. Information regarding demographic variables were obtained from the patient's case record. Information regarding the clinical profile, diagnosis, and relevant information on the variables of inquiry were obtained from the inpatient medical record. All data extraction and encoding were done on standardized electronic data collection forms (via Google Forms).

Validation of 20% of total collected data against the source medical records was done through separate data collection by a third party (i.e., one of the study investigators). The collected data of the assigned data collector and the third party were compared. The medical records were selected randomly using a list randomizer which was done until the 20% of total collected data was validated.

Data Analysis and Statistical Methods

Data collected through the electronic forms platform were exported to spreadsheets for analysis. Categorical data were analyzed using descriptive statistics such as frequencies and percentages. Continuous and discrete variables were summarized using median and interquartile range. The prevalence of PMV was calculated and expressed as frequency, point estimate, and 95% confidence intervals. Characteristics of PMV and non-PMV patients were compared using Mann-Whitney U-test for quantitative data and Chi-square for qualitative data. Outcomes describing the PMV and non-PMV patients were similarly compared using the above tests.

Multiple logistic regression analysis was done to assess association between the dependent variable (PMV) and the independent/marginally associated variables of interest determined through literature review, which included age, comorbidities (stroke, heart failure, COPD, previous tuberculosis), APACHE score on ICU admission, vasopressor use, renal replacement therapy, nosocomial infections, in-hospital-related complications, and tachycardia (HR >110), elevated BUN (BUN >25), acidemia (pH <7.25), elevated creatinine (>2 mg/dL), and decreased bicarbonate (<20 meqs/L). The effect sizes from the multivariate analysis were reported as odds ratios. Confidence interval was set at 95% and statistical significance was based on p-value <0.05.[19] Model fit was assessed by comparing Akaike Information Criterion (AIC) and Bayesian Information Curve (BIC) among all specifications. For the AIC and BIC, the model with the lowest values was adopted.

RESULTS

From July 1, 2022, to June 30, 2023, 348 patients were admitted to the MICU. After selection criteria screening, 261 were included, while 87 were excluded, as shown in Figure 1. All patients had complete outcome data based on the chart review. The prevalence of PMV in the study population was 28.7% [n=75, 95% CI (23.32, 34.64)].

Table 1 shows the clinical characteristics of patients included in the study group. Compared to patients who did not require PMV, patients who were on PMV were noted to be older (62 vs. 53.5; p<0.004) and scored higher in the

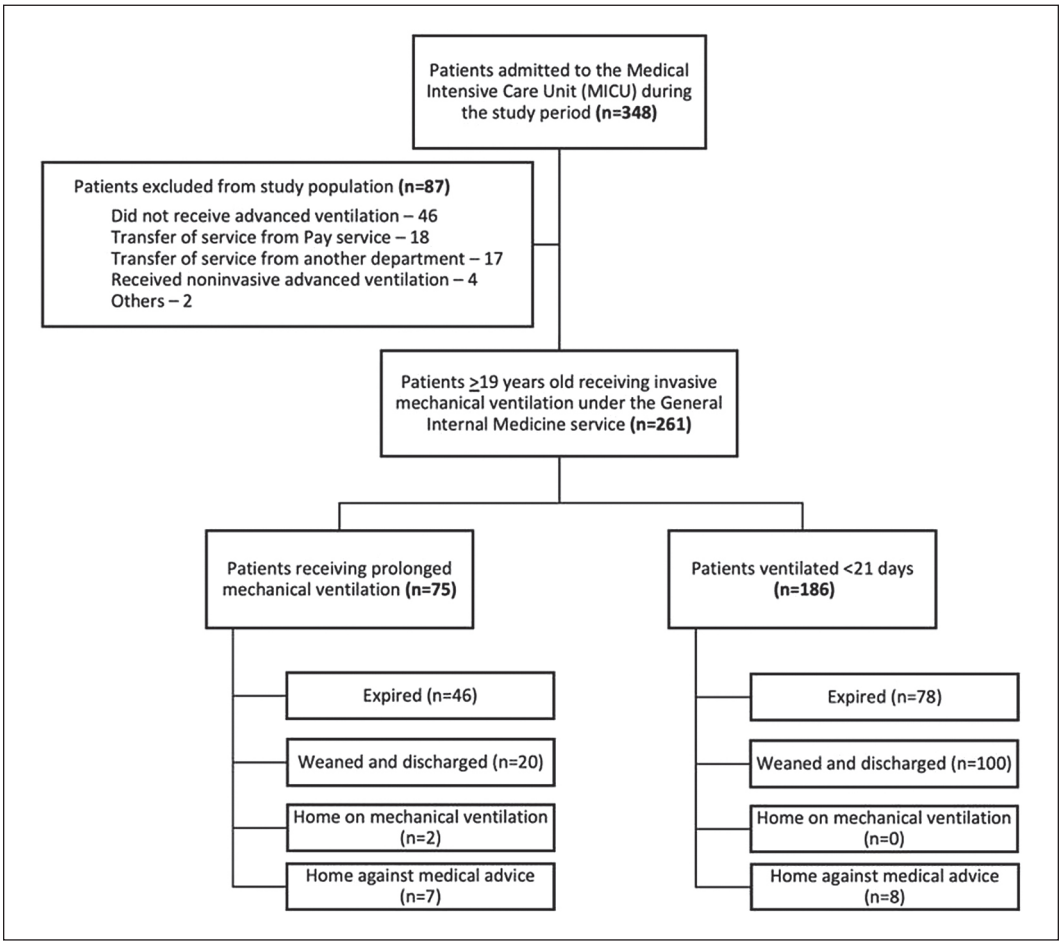

Figure 1. Flow diagram of admitted ICU patients during the study period and their corresponding outcomes on hospital discharge.

Table 1. Clinical Characteristics of Patients Requiring and not Requiring PMV

Characteristics [n=259]	PMV (n=75)	Non-PMV (n=186)	*p*-value
Age in years, median (IQR)	62 (20)	53.5 (25)	0.004
Male, n (%)	28 (37.33%)	106 (56.99%)	0.004
Smoking History			0.031
Current, n (%)	9 (12.00%)	33 (17.74%)	
Previous n (%)	17 (22.67%)	65 (34.95%)	
Never, n (%)	49 (65.33%)	88 (47.31%)	
Comorbidities			
Hypertension, n (%)	46 (61.33%)	109 (58.60%)	0.684
Type 2 diabetes mellitus, n (%)	26 (34.67%)	59 (31.72%)	0.646
Ischemic heart disease, n (%)	14 (18.67%)	39 (20.97%)	0.676
Heart failure, n (%)	31 (41.33%)	76 (40.86%)	0.944
Stroke, n (%)	10 (13.33%)	26 (13.98%)	0.891
Myocardial infarction, n (%)	3 (4.00%)	18 (9.68%)	0.127
Bronchial asthma, n (%)	8 (10.67%)	13 (6.99%)	0.323
Chronic obstructive pulmonary disease, n (%)	6 (8.00%)	21 (11.29%)	0.430
Past pulmonary tuberculosis, n (%)	18 (24.00%)	47 (25.27%)	0.830
Thyroid disease, n (%)	2 (2.67%)	4 (2.15%)	>0.999
Chronic kidney disease, n (%)	27 (36.00%)	62 (33.33%)	0.681
Malignancy, n (%)	10 (13.33%)	10 (5.38%)	0.029
HIV / AIDS, n (%)	1 (1.33%)	1 (0.54%)	0.493
Chronic liver disease, n (%)	3 (4.00%)	3 (1.61%)	0.359
Hepatitis, n (%)	0	3 (1.61%)	0.559
Gouty arthritis, n (%)	3 (4.00%)	5 (2.69%)	0.693
Osteoarthritis, n (%)	0	1 (0.54%)	>0.999
Rheumatoid arthritis, n (%)	0	0	-
Peptic ulcer disease, n (%)	0	1 (0.54%)	>0.999
Charlson Comorbidity Index, median (IQR)	4 (3)	3 (3)	0.008
History of prior hospitalization in the past 30 days, n (%)	19 (25.33%)	45 (24.19%)	0.846
Functional status on admission			0.043
Independent, n (%)	43 (57.33%)	126 (67.74%)	
Partially Assisted, n (%)	18 (24.00%)	45 (24.19%)	
Dependent, n (%)	14 (18.67%)	15 (8.06%)	
Diagnosis on ICU admission			0.033
Acute respiratory failure/disease, n (%)	68 (90.67%)	133 (71.51%)	
Cardiovascular disease, n (%)	2 (2.67%)	22 (11.83%)	
Sepsis and septic shock, n (%)	3 (4.00%)	10 (5.38%)	
Central nervous system disease, n (%)	0	1 (0.54%)	
Gastrointestinal disease, n (%)	0	7 (3.76%)	
Renal disease, n (%)	2 (2.67%)	11 (5.91%)	
Others, n (%)	0	2 (1.08%)	
Admission source			0.306
Emergency room, n (%)	54 (72.00%)	145 (77.96%)	
Ward, n (%)	21 (28.00%)	41 (22.04%)	
APACHE II Score on ICU admission, median (IQR)	15 (9.8)	15 (11)	0.790
SOFA Score on ICU admission, median (IQR)	5 (3)	6 (5)	0.149
Glasgow Coma Score on ICU admission, median (IQR)	14.7 (1.4)	14.7 (1.4)	0.866
CPR/ACLS during admission course, n (%)	33 (44.00%)	68 (36.56%)	0.264
Number of medications on admission, median (IQR)	13 (5)	14 (6)	0.745
Presence of infection on admission, n (%)			0.042
Pulmonary, n (%)	53 (70.67%)	118 (63.44%)	
Non-pulmonary, n (%)	2 (2.67%)	23 (12.37%)	
Both, n (%)	17 (22.67%)	30 (16.13%)	

Table 1. Clinical Characteristics of Patients Requiring and not Requiring PMV *(continued)*

Characteristics [n=259]	PMV (n=75)	Non-PMV (n=186)	*p*-value
Ventilated on Day 1, n (%)	62 (82.67%)	144 (77.42%)	0.347
Tachycardia (HR >110) on intubation, n (%)	33 (44.00%)	100 (53.76%)	0.153
Elevated BUN (BUN >25 mg/dL) on intubation, n (%)	38 (50.67%)	84 (45.16%)	0.420
Acidemia (pH <7.25) on intubation, n (%)	29 (38.67%)	89 (47.85%)	0.177
Creatinine >2 mg/dL on intubation, n (%)	34 (45.33%)	92 (49.46%)	0.546
HCO3 <20 meq/L on intubation, n (%)	37 (49.33%)	106 (56.99%)	0.261
Vasopressor use, n (%)	61 (81.33%)	102 (54.84%)	<0.001
Renal replacement therapy use, n (%)	33 (44.00%)	77 (41.40%)	0.700
Blood transfusion utilization, n (%)	70 (93.33%)	95 (51.08%)	<0.001
Development of nosocomial infections, n (%)	65 (86.67%)	85 (45.70%)	<0.001
Development of MV-related complications, n (%)	23 (30.67%)	23 (12.37%)	<0.001
Development of in-hospital related complications, n (%)	49 (66.22%)	61 (32.97%)	<0.001

Table 2. Clinical Outcomes of Patients Requiring and not Requiring PMV

Characteristics	PMV (n=75)	Non-PMV (n=186)	*p*-value
Time from admission to ICU referral, median (IQR)	1 (0)	1 (0)	0.669
Time from ICU referral to ICU admission, median (IQR)	2 (4)	2 (2)	<0.001
Duration of MV use, median (IQR)	35 (25)	8 (7)	-
Duration of non-invasive ventilation, median (IQR)	0 (0)	0 (1)	0.588
Tracheostomy rate, n (%)	40 (53.33%)	2 (1.08%)	<0.001
Time from intubation to day of tracheostomy, median (IQR)	26 (12)	0 (0)	<0.001
ICU length of stay, median (IQR)	29.5 (18)	7 (5)	<0.001
ER length of stay, median (IQR)	4 (4)	2 (2)	<0.001
Hospital length of stay, median (IQR)	42 (26)	13 (11)	<0.001
ICU mortality, n (%)	32 (42.67%)	72 (38.71%)	0.555
Hospital mortality, n (%)	46 (61.33%)	78 (41.94%)	0.005
Outcome on ICU discharge			0.317
Expired, n (%)	32 (42.67%)	72 (38.71%)	
Transferred out to ward, n (%)	35 (46.67%)	76 (40.86%)	
Discharged, n (%)	7 (9.33%)	33 (17.74%)	
Home against medical advice, n (%)	1 (1.33%)	5 (2.69%)	
Outcome on hospital discharge			<0.001
Expired, n (%)	46 (61.33%)	78 (41.94%)	
Weaned and discharged, n (%)	20 (26.67%)	100 (53.76%)	
Home on MV, n (%)	2 (2.67%)	0	
Home against medical advice, n (%)	7 (9.33%)	8 (4.30%)	

Charlson Comorbidity Index (4 vs. 3; p 0.008). Fewer males required PMV than females. Among individual comorbidities, only malignancy was shown to be significantly more frequent among patients requiring PMV. Patients who were never smokers and those with dependent functional status on admission were more often among those requiring PMV.

Patients who required PMV also more frequently had acute respiratory failure versus non-PMV patients (90.67% vs. 71.51%, p 0.033) on ICU admission. PMV patients also more frequently used vasopressors (81.33% vs. 54.84%; p <0.001) and blood transfusions (93.33% vs. 51.08%; p <0.001). Furthermore, PMV patients developed nosocomial infections (86.67% vs. 45.70%; p <0.001), in-hospital-related complications (66.22% vs. 32.97%, p <0.001), and MV complications (30.67% vs. 12.37%, p <0.001) more than patients not requiring PMV.

APACHE II Score, SOFA score, and Glasgow Coma Scale on ICU admission were not significantly different between PMV and non-PMV groups. Presence of tachycardia (HR >110), elevated BUN, acidemia, creatinine >2 mg/dL, and HCO3 <20 meq/L during the time of intubation was not significantly different between groups. Similarly, intubation

on day 1 of admission, requirement for renal replacement therapy, number of medications on admission, and presence of infection on admission did not differ between the two groups.

As shown in Table 2, patients who required PMV had longer ER (4 vs 2 days, p <0.001), ICU (29.5 vs. 7 days; p <0.001), and hospital (42 vs 13 days, p <0.001) lengths of stay. PMV patients also had higher tracheostomy rates (53.33% vs. 1.08%, p <0.000), and longer time from ICU referral to ICU admission.

As shown in Figure 2, ICU mortality among patients requiring PMV was 43% compared to 39% among patients not requiring PMV. This was not significantly different (p = 0.555) as described in Table 1.

Among patients requiring PMV, the in-hospital mortality was 61.33% (n=46) as illustrated in Figure 3. Twenty

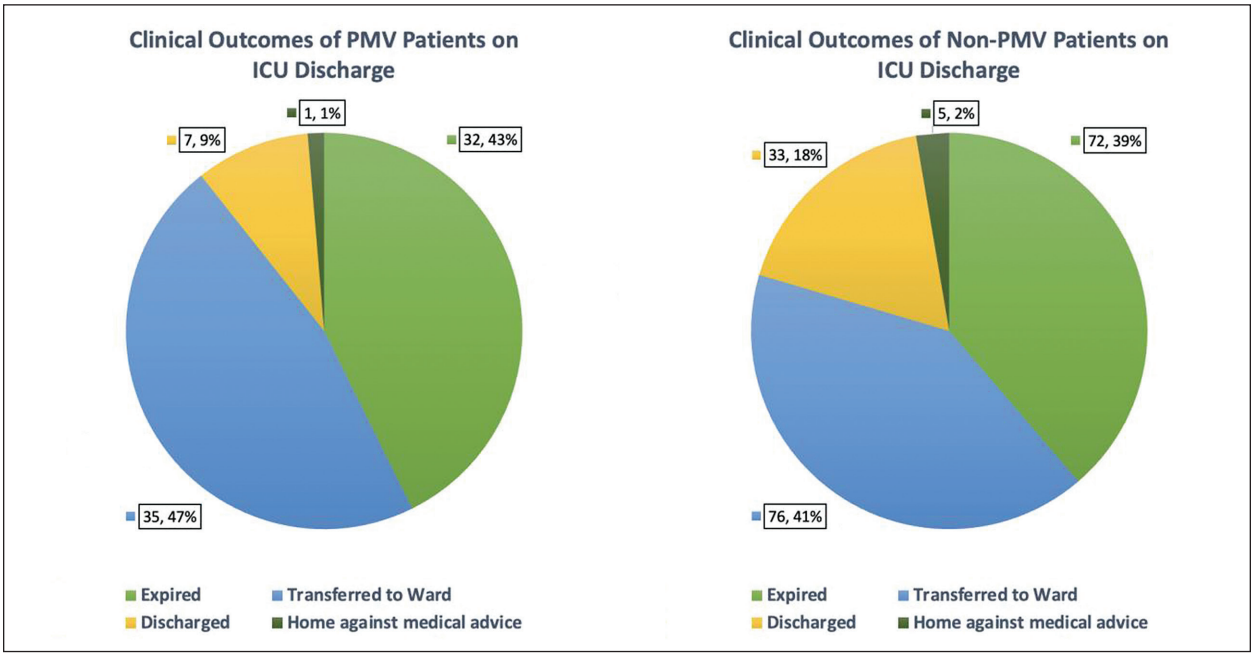

Figure 2. Clinical outcomes of PMV and non-PMV patients at ICU discharge (n, %).

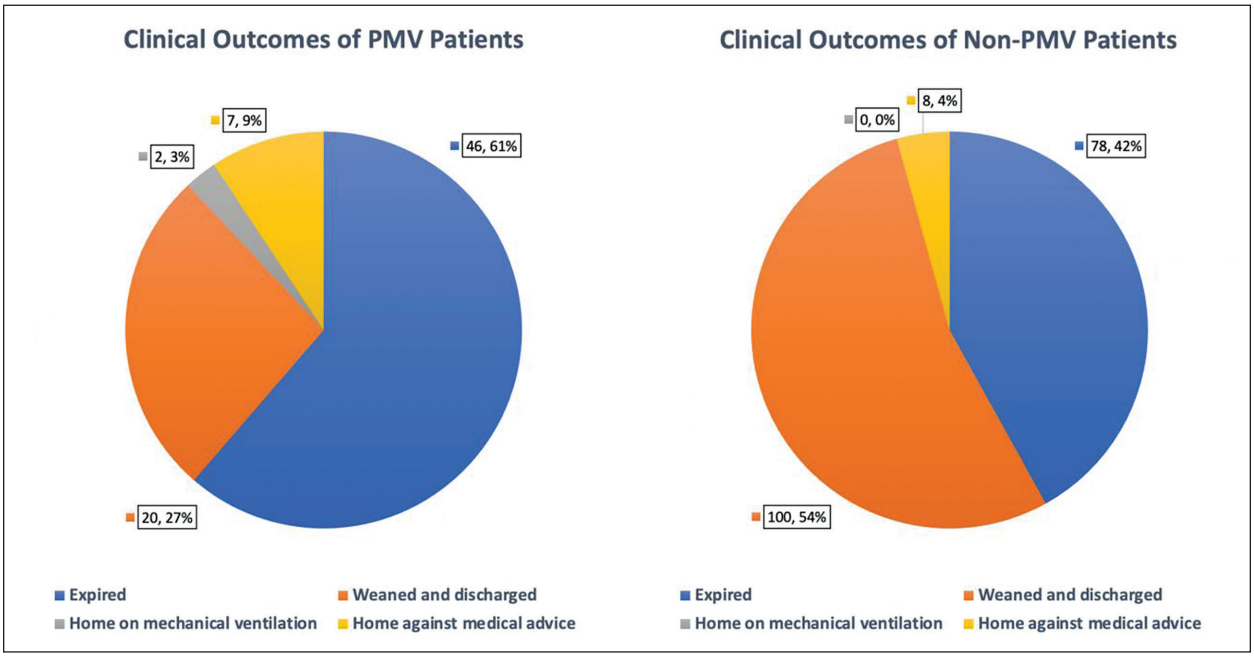

Figure 3. Clinical outcomes of PMV and non-PMV patients at hospital discharge (n, %).

Table 3. Multivariable Logistic Regression Analysis for PMV

Risk Factors	Odds Ratio	95% CI	*p*-value
Age	1.02	1.00, 1.04	0.079
APACHE score on ICU admission	1.03	0.98, 1.08	0.307
Heart failure as a comorbidity	1.09	0.57, 2.09	0.797
Chronic obstructive pulmonary disease as a comorbidity	0.50	0.16, 1.63	0.253
History of pulmonary tuberculosis	0.77	0.36, 1.65	0.499
History of stroke	0.91	0.34, 2.45	0.859
Vasopressor use	2.25	1.06, 4.76	0.034
Renal replacement therapy use	0.90	0.36, 2.21	0.816
Development of nosocomial infections	6.20	2.64, 14.56	0.000
Development of in-hospital related complications	2.20	1.13, 4.30	0.021
Presence of tachycardia (HR >110) on intubation	0.63	0.32, 1.21	0.166
Presence of elevated BUN (BUN >25) on intubation	1.65	0.72, 3.78	0.237
Presence of acidemia (pH <7.25) on intubation	0.79	0.39, 1.59	0.507
Presence of elevated creatinine (>2 mg/dL) on intubation	0.35	0.12, 1.00	0.050
Presence of decreased bicarbonate (<20 meq/L) on intubation	0.75	0.36, 1.56	0.445

(26.67%) patients were weaned and discharged, two patients were sent home on MV, and seven went home against medical advice. Among non-PMV patients, 41.94% (n=78) expired while 53.76% (n=100) were weaned and discharged. Eight went home against medical advice. In-hospital mortality was noted to be significantly higher among patients requiring PMV. These outcomes were significantly different (p <0.001) as shown in Table 2.

Table 3 shows the results of the multivariable logistic regression analysis. Controlling for all factors of interest, three significant independent risk factors for PMV were identified. First, patients who developed nosocomial infections were over six times more likely to require PMV (OR 6.20, 95% CI 2.64-14.56, p=0.000). Additionally, those who required vasopressors (OR 2.25, 95% CI 1.06-4.76; p=0.034) and patients who developed in-hospital-related complications (OR 2.20, 95% CI 1.13-4.30; p=0.021) were both more than twice more likely to require PMV in the future.

DISCUSSION

In this retrospective study, the prevalence of PMV was 28.7%. This is higher compared to most previous retrospective studies where rates of PMV are at 5.1% to 7.3%.[3,5] This difference in prevalence may be explained by differences in population size, length of study period, and number of centers. The populations of previous observational studies were greater, covered longer study periods (ranging from 26 months to 5 years),[3,6] and had multiple study centers compared to this study (N=261).[6] Differences in definitions of PMV did not significantly contribute to the differences in prevalence between our study and other retrospective studies since all studies utilized the NAMDRC consensus definition.

A prospective prevalence study in China had a PMV prevalence rate of 36% which is comparable with this study. Li et al. attribute this increased prevalence to multiple factors which include: (1) acceptance of more severely-ill patients and transfers from community hospitals and (2) lack of special care centers for patients requiring PMV.[7] These characteristics are similar to our local setting where more critically-ill patients are admitted. Furthermore, the Philippines lacks step-down facilities for chronically ventilated patients such as chronic care hospitals like in Japan and government-subsidized respiratory care centers in Taiwan.[3,4]

Previous studies revealed associations between PMV and multiple factors which were included in this study's analysis. These included age,[4,7] higher APACHE scores, renal replacement therapy use, and presence of comorbidities.[4] A review by Huang et al. identified risk factors contributing to PMV, which include: systemic comorbidities (i.e., chronic respiratory diseases, heart failure, cerebrovascular diseases, neuromuscular diseases, end stage renal disease, liver cirrhosis, malignancy), infection, malnutrition, and ventilator-induced diaphragm dysfunction.[20] In addition, Clark et al. developed a bedside model, I-TRACH, that predicts the duration of MV. In their prospective validation study, it was shown that fulfillment of at least four I-TRACH criteria predicted the need for MV >7 and >14 days from intubation.[8] All six variables included in I-TRACH were analyzed in this study, and it was noted that they did not individually predict PMV. The heterogeneity of factors associated with PMV in these studies are likely due to differences in the clinical characteristics of study populations analyzed.[9]

In this study, nosocomial infections, in-hospital complications, and vasopressor use were significant predictors of PMV. There was a variety of nosocomial infections that

developed in the study population including hospital and ventilator-associated pneumonias, complicated urinary tract infections, and skin and soft tissue infections. Similarly, there was a myriad of in-hospital complications which included pressure ulcers, muscle weakness or critical-illness neuropathy, adverse drug events, pulmonary embolism, and many others. In the study of Loss et al, these were associated with an increased risk for PMV, similar to this study.[6] However, individual analysis of these complications was beyond the scope of this study.

Persistent sources of inflammation such as these factors cause dysregulated immune responses, especially among critically ill patients.[21] A proportion of these patients do not recover from the initial insult and develop persistent inflammation, immunosuppression, and catabolism syndrome or PICS, which underlie chronic critical illness. There is persistent protein catabolism, elevated acute phase reactants, chronic inflammation, and immunosuppression.[22] These predispose the patient to an indolent state of inflammation and perpetuate repeated nosocomial infections, cachexia, and disproportionately slow healing.[23] Additionally, nosocomial infections and in-hospital complications contribute to the development of sepsis which contributes to diaphragm weakness.[24] These factors all preclude effective weaning and lead to PMV.

Similar to Lone et al., ICU mortality in the PMV group was not significantly different vs. non-PMV;[9] however overall hospital mortality in the PMV group was noted to be significantly higher (Table 1). The higher hospital mortality was likely due to the burden of chronic illness, which were also evident in the identified risk factors associated with PMV. The nonsignificant difference in ICU mortality between PMV and non-PMV patients may be due to the transfer of PMV patients to the wards for further weaning, as they were no longer deemed to require intensive care. This might have artificially lowered in-ICU mortality rates for PMV patients.

This study is one of the first studies in the Philippines to date that determines the prevalence of PMV and describes the clinical characteristics and outcomes of patients requiring PMV. Furthermore, a comprehensive array of clinical data were gathered in the study. The findings have several practical implications. Understanding the clinical characteristics associated with PMV enables clinicians to identify patients at risk for weaning difficulties upon ICU admission, facilitating effective triage and implementation of early intervention strategies. Additionally, recognizing risk factors for PMV can inform future research aimed at addressing these potentially treatable conditions within the ICU. From a policy perspective, the data generated from this study, along with subsequent research on PMV epidemiology from the hypotheses generated from this study, will provide a robust evidence base for advocating the establishment of dedicated weaning and step-down units in hospitals and communities.

However, several limitations were encountered. First, the study analyzed medical service (charity) patients only in a single tertiary center. Consequently, the findings may not be generalizable to a broader population of non-service (paying) patients, as selection bias could favor critically ill individuals who cannot afford timely care, potentially misestimating the prevalence of prolonged mechanical ventilation (PMV) among those with better access to interventions. This bias may skew observed associations toward more severe outcomes. However, since the study primarily focuses on charity/service patients to inform the development of public weaning and step-down units, non-service patients were excluded from the analysis. Moreover, the prevalence of prolonged mechanical ventilation might not be reflective of the prevalence in other non-tertiary care facilities. However, given that most critical cases are being referred to bigger institutions, the estimation of prevalence of prolonged mechanical ventilation in this study might only be applicable in those hospitals who cater to more critically ill patients, unable to compare it to other institutions who have ICUs but do not cater to individuals who are severely ill.

Second, the study duration was shorter than most retrospective studies analyzing PMV. However, this study analyzed the clinical profiles of patients right after the COVID-19 pandemic. Analysis of older patient profiles and inclusion of COVID-19 patients may also not be generalizable to post-pandemic contexts and patient profiles. The period wherein the study was conducted was during the COVID-19 pandemic – wherein service delivery became markedly limited due to several protocols employed which aimed to mitigate the spread of disease, such as limitation of manpower and limitations in performing procedures that risk disease spread. Ultimately, this may have hampered more effective service delivery, which might have contributed to the increase in prevalence of prolonged mechanical ventilation.

The study also focused on patient clinical characteristics. A more comprehensive analysis would have included measures of intensive care (such as the Therapeutic Intervention Scoring System or TISS Score), facility- or provider-related factors, and cost analysis of PMV.[5,9] Fourth, considering the suboptimal statistical power and the constrained sample size of 261 participants, the study's ability to identify independent predictors of PMV may be significantly limited. Additionally, subgroup analyses, interaction testing, and sensitivity analyses were not performed for this study. Furthermore, possible confounders, effect modifiers, and predictors were not identified as limited literature exists to support classification of variables into these factors. Given the limited power of the regression model, the identified predictors of PMV should be interpreted as preliminary and hypothesis-generating. Future research would benefit from larger sample sizes and extended study durations, as well as a more focused selection of potential predictors informed by the findings of this investigation.

Given the results, it is recommended to conduct prospective studies that describe the clinical characteristics and outcomes of mechanically ventilated patients over the course of admission. Furthermore, recruitment of additional tertiary

centers in private and public hospital settings may further characterize PMV patients in the Philippines at a larger scale. Additionally, cost-analysis may further help in evaluating the cost-effectiveness of establishing step-down facilities for patients with chronic critical illness. Interventions that target identified factors leading to PMV should be proposed and tested in further studies.

CONCLUSION

In this study, 28.7% of mechanically ventilated ICU patients required PMV. Multiple clinical characteristics were noted to be more common among PMV patients. PMV patients experienced significantly longer ER, hospital, and ICU lengths of stay, higher rates of nosocomial infections and complications, and higher in-hospital mortality. Vasopressor use, development of nosocomial infections, and development of in-hospital complications were found to be predictors of PMV. Knowledge of these characteristics and risk factors allow development of interventions that improve outcomes and reduce PMV prevalence. Studies on improving ICU process flows and quality can also be undertaken using information from this study. Due to the study's retrospective design and limited generalizability, larger studies are also recommended to assess the epidemiology of PMV on a nationwide scale and provide more robust data on the need for step-down units for weaning and care for chronic critical illness.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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REFERENCES

1. MacIntyre NR, Epstein SK, Carson S, Scheinhorn D, Christopher K, Muldoon S. Management of patients requiring prolonged mechanical ventilation. Chest. 2005 Dec;128(6):3937–54. doi: 10.1378/chest.128.6.3937. PMID: 16354866.
2. Nevins ML, Epstein SK. Weaning from prolonged mechanical ventilation. Clin Chest Med. 2001 Mar;22(1):13–33. doi: 10.1016/s0272-5231(05)70023-x. PMID: 11315451.
3. Nagata I, Takei T, Hatakeyama J, Toh M, Yamada H, Fujisawa M. Clinical features and outcomes of prolonged mechanical ventilation: a single-center retrospective observational study. JA Clin Rep. 2019 Dec;5(1):73. doi: 10.1186/s40981-019-0284-4. PMID: 32026077; PMCID: PMC6966730.
4. Lai CC, Shieh JM, Chiang SR, Chiang KH, Weng SF, Ho CH, et al. The outcomes and prognostic factors of patients requiring prolonged mechanical ventilation. Sci Rep. 2016 Jun 14;6(1):28034. doi: 10.1038/srep28034.
5. Kim MH, Cho WH, Lee K, Kim KU, Jeon DS, Park HK, et al. Prognostic factors of patients requiring prolonged mechanical ventilation in a medical intensive care unit of Korea. Tuberc Respir Dis. 2012;73(4):224. doi: 10.4046/trd.2012.73.4.224. PMID: 23166558; PMCID: PMC3492423.
6. Loss SH, Oliveira RP de, Maccari JG, Savi A, Boniatti MM, Hetzel MP, et al. The reality of patients requiring prolonged mechanical ventilation: a multicenter study. Rev Bras Ter Intensiva. 2015;27(1). doi: 10.5935/0103-507X.20150006.
7. Li J, Zhan QY, Wang C. Survey of prolonged mechanical ventilation in intensive care units in mainland China. Respir Care. 2016 Sep;61(9):1224–31. doi: 10.4187/respcare.04295. PMID: 27460102.
8. Clark PA, Inocencio RC, Lettieri CJ. I-TRACH: validating a tool for predicting prolonged mechanical ventilation. J Intensive Care Med. 2018 Oct;33(10):567–73. doi: 10.1177/0885066616679974. PMID: 27899470.
9. Lone NI, Walsh TS. Prolonged mechanical ventilation in critically ill patients: epidemiology, outcomes and modelling the potential cost consequences of establishing a regional weaning unit. Crit Care. 2011;15(2):R102. doi: 10.1186/cc10117. PMID: 21439086; PMCID: PMC3219374.
10. Oeyen SG, Vandijck DM, Benoit DD, Annemans L, Decruyenaere JM. Quality of life after intensive care: a systematic review of the literature: Crit Care Med. 2010 Dec;38(12):2386–400. doi: 10.1097/CCM.0b013e3181f3dec5. PMID: 20838335.
11. Ho S, Lim CJ, Puah SH, Lew SJW. Outcomes of patients requiring prolonged mechanical ventilation in Singapore. J Emerg Crit Care Med. 2020 Oct;4:32–32.
12. Hill AD, Fowler RA, Burns KEA, Rose L, Pinto RL, Scales DC. Long-term outcomes and health care utilization after prolonged mechanical ventilation. Ann Am Thorac Soc. 2017 Mar;14(3):355–62. doi: 10.1513/AnnalsATS.201610-792OC. PMID: 28033033.
13. Combes A, Costa MA, Trouillet JL, Baudot J, Mokhtari M, Gibert C, et al. Morbidity, mortality, and quality-of-life outcomes of patients requiring ≥14 days of mechanical ventilation: Crit Care Med. 2003 May;31(5):1373–81. doi: 10.1097/01.CCM.0000065188.87029.C3. PMID: 12771605.
14. Besa JJV, Masamayor EMI, Tamondong-Lachica DR, Palileo-Villanueva LM. Prevalence and predictors of prolonged length of stay among patients admitted under general internal medicine in a tertiary government hospital in Manila, Philippines: a retrospective cross-sectional study. BMC Health Serv Res. 2023 Jan 18;23(1):50. doi: 10.1186/s12913-022-08885-4.
15. NHIS - Adult Tobacco Use - Glossary [Internet]. [cited 2023 Aug 25]. Available from: https://www.cdc.gov/nchs/nhis/tobacco/tobacco_glossary.htm
16. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987 Jan;40(5):373–83. doi: 10.1016/0021-9681(87)90171-8. PMID: 3558716.
17. Knaus WA, Draper E, Wagner D, Zimmerman J. APACHE II: a severity of disease classification system. Crit Care Med. 1985 Oct 13;13(10):818–29. PMID: 3928249.
18. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure: on behalf of the working group on sepsis-related problems of the European society of intensive care medicine (see contributors to the project in the appendix). Intensive Care Med. 1996 Jul;22(7):707–10. doi: 10.1007/BF01709751. PMID: 8844239.
19. Matias Castro H, Carvalho Ferreira J. Linear and logistic regression models: when to use and how to interpret them? J Bras Pneumol. 2022 Nov 24;e20220439. doi: 10.36416/1806-3756/e20220439. PMCID: PMC9747134; PMID: 36651441.
20. Huang HY, Huang CY, Li LF. Prolonged mechanical ventilation: outcomes and management. J Clin Med. 2022 Apr 27;11(9):2451. doi: 10.3390/jcm11092451 PMCID: PMC9103623; PMID: 35566577.
21. Hawkins RB, Raymond SL, Stortz JA, Horiguchi H, Brakenridge SC, Gardner A, et al. Chronic critical illness and the persistent inflammation, immunosuppression, and catabolism syndrome. Front Immunol. 2018 Jul 2;9:1511. doi: 10.3389/fimmu.2018.01511. PMID: 30013565; PMCID: PMC6036179.

22. Mira JC, Brakenridge SC, Moldawer LL, Moore FA. Persistent inflammation, immunosuppression and catabolism syndrome. Crit Care Clin. 2017 Apr;33(2):245–58. doi: 10.1016/j.ccc.2016.12.001. PMID: 28284293; PMCID: PMC5351769.
23. Hesselink L, Hoepelman RJ, Spijkerman R, De Groot MCH, Van Wessem KJP, Koenderman L, et al. Persistent inflammation, immunosuppression and catabolism syndrome (PICS) after polytrauma: a rare syndrome with major consequences. J Clin Med. 2020 Jan 10;9(1):191. doi: 10.3390/jcm9010191. PMID: 31936748; PMCID: PMC7019692.
24. Ambrosino N, Vitacca M. The patient needing prolonged mechanical ventilation: a narrative review. Multidiscip Respir Med. 2018 Dec; 13(1):6. doi: 10.1186/s40248-018-0118-7. PMCID: PMC5831532; PMID: 29507719.

APPENDIX

Study variables and corresponding operational definitions

Variable	Operational Definition
Age	Age on admission as stated in the case record. [D]
Sex	Male or female as stated in the case record. [C]
Smoking History (current, previous, never) [18]	Defined as follows: Current smoker: Patient has smoked 100 cigarettes in their lifetime and who currently smokes cigarettes Former smoker: Patient has smoked at least 100 cigarettes in their lifetime but who had quit smoking at the time of interview/admission Never smoker: Patient has never smoked or has smoked less than 100 cigarettes in their lifetime Or as stated in the initial chart entry of the physician-on-duty or resident-in-charge of the Department of Medicine [C]
Comorbidities [17]	Comorbidities of the patient as stated in the initial chart entry of the physician-on-duty or resident-in-charge of the Department of Medicine. This is limited to the following and will be analyzed individually: hypertension, type 2 diabetes mellitus, ischemic heart disease, heart failure, stroke, myocardial infarction, bronchial asthma, chronic obstructive pulmonary disease, past pulmonary tuberculosis, thyroid disease, chronic kidney disease, malignancy, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), chronic liver disease, hepatitis, gouty arthritis, osteoarthritis, rheumatoid arthritis, peptic ulcer disease. [C]
Charlson Comorbidity Index [19]	A scoring system for classifying comorbidity and prognosticating 10-year survival using the following variables: age, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident or transient ischemic attack, dementia, connective tissue disease, peptic ulcer disease, liver disease, diabetes mellitus, hemiplegia, moderate to severe chronic kidney disease, solid tumor, leukemia, AIDS. [D]
History of prior hospitalization in the past 30 days	Presence or absence of hospitalization within the prior 30 days in the Philippine General Hospital or other hospitals. [C]
Functional status on admission (independent, partially assisted, or dependent)	Functional status as stated in the initial chart entry of the physician-on-duty or resident-in charge of the Department of Medicine. [C]
Diagnosis on ICU admission	Defined as the primary problem of the patient on ICU admission/indication for ICU admission, based on the initial entry of the Medical Intensive Care Unit resident-on-duty. The diagnoses will be classified under the following and will be analyzed individually: [C] Acute respiratory failure/disease Cardiovascular disease Sepsis and septic shock Central nervous system disease Gastrointestinal disease Renal disease Others

Study variables and corresponding operational definitions *(continued)*

Variable	Operational Definition
Admission source (ER or ward)	Defined as location of patient prior to physical admission to the Medical Intensive Care Unit [C]
APACHE II Score on ICU admission [20]	A measure of disease severity that estimates mortality among the critically ill based on physiologic measurements, comorbid conditions, and age; defined as follows: calculated from the raw data indicated in the case record upon admission to the Medical Intensive Care Unit [D]
SOFA Score on ICU admission [21]	A disease severity scoring system used to measure the degree of organ dysfunction/failure in patients, defined as calculated from the raw data indicated in the case record upon admission to the Medical Intensive Care Unit [D]
Glasgow Coma Score on ICU admission	A scoring system utilized to describe the level of consciousness upon admission to the Medical Intensive Care Unit [D]
CPR/ACLS during admission course	Presence or absence of use of cardiopulmonary resuscitation or Advanced Cardiovascular Life Support during admission irrespective of duration and day of admission [C]
Number of medications on admission	Number of medications as stated in the review of therapeutics upon admission to the Medical Intensive Care Unit [D]
Presence of infection on admission (pulmonary vs. non-pulmonary)	Presence or absence of infection as stated in the diagnosis/problem list of the Medical Intensive Care Unit physician-on-duty. Presence of pulmonary and non-pulmonary infections will be analyzed separately. [C]
Ventilated on Day 1	Defined as whether or not patients underwent invasive mechanical ventilation on the first day of admission [C]
Tachycardia (HR >110) [9]	Presence of tachycardia (HR >110) at the time of intubation [C]
Elevated BUN (BUN >25 mg/dL) [9]	Presence of BUN >25 mg/dL at the time of intubation [C]
Acidemia (pH <7.25) [9]	Presence of acidemia (pH <7.25) at the time of intubation [C]
Creatinine >2mg/dL [9]	Presence of elevated creatinine, defined as >2 mg/dL, at the time of intubation [C]
HCO3 <20meq/L [9]	Presence of decreased bicarbonate <20 meq/L at the time of intubation [C]
Vasopressor use	Use of vasopressors during course of ICU admission irrespective of indication and duration [C]
Renal replacement therapy use	Use of renal replacement therapy during course of ICU admission irrespective of indication and duration [C]
Blood transfusion utilization	Use of blood transfusion during course of ICU admission irrespective of indication and type of blood products [C]
Development of nosocomial infections [17]	Development of new-onset infections after ICU admission, which include hospital-acquired pneumonia, ventilator-associated pneumonia, catheter-related bloodstream infection, surgical site infection, skin and soft tissue infection. Hospital-acquired infections diagnosed at the time or prior to ICU admission are excluded. [C]
Development of mechanical ventilation-related complications [17]	Development of complications during ICU admission related to mechanical ventilation, namely pneumothorax and subcutaneous emphysema. [C]
Development of in-hospital-related complications[17]	Development of new medical problems after ICU admission, deemed as harmful events resulting from the process of care and treatment rather than the natural progression of disease which include falls, pressure injuries, cardiac complications, venous thromboembolism, renal failure, gastrointestinal bleeding, and adverse drug events. HAIs and mechanical ventilation-related complications will be counted separately. [C]
Time from admission to ICU referral	Number of days counted from the day that the patient was admitted as stated in the case record to the day that the patient was referred based on the entry of the Medical Intensive Care Unit physician-on-duty [D]
Time from ICU referral to ICU admission	Number of days counted from the day that the patient was referred based on the entry of the Medical Intensive Care Unit physician-on-duty to the day that the patient was physically admitted to the Medical Intensive Care Unit [D]
Duration of MV use	Duration of invasive mechanical ventilation in days [D]
Duration of non-invasive ventilation	Duration of noninvasive mechanical ventilation in days [D]
Tracheostomy rate	Calculated as the percentage of intubated patients that underwent tracheostomy surgery [Co]
Time from intubation to day of tracheostomy	Number of days from intubation to day of tracheostomy surgery [D]
ICU length of stay	Number of days of stay in the intensive care unit counted from the day that the patient was physically transferred to the Medical Intensive Care Unit to the day that the patient was physically discharged or transferred to the ward [D]

Study variables and corresponding operational definitions *(continued)*

Variable	Operational Definition
ER length of stay	Number of days of stay in the emergency room counted from the day that the patient was admitted as stated in the case record to the day that the patient was physically transferred to the ward or intensive care unit [D]
Hospital length of stay	Number of days of stay in the hospital counted from the day of admission to the day of discharge as stated in the medical record [D]
ICU mortality	Calculated as the percentage of intubated patients that died during admission in the Medical Intensive Care Unit [Co]
Hospital mortality	Calculated as the percentage of intubated patients that were admitted in the Medical Intensive Care Unit and died during admission irrespective of area of death [Co]
Outcome on ICU discharge (expired, transferred out to ward, discharged, home against medical advice)	Defined as discharged if the patient was cleared by the physician to leave the hospital after receiving inpatient care Defined as transferred out to ward if the patient was cleared by the physician to be transferred out to the medical ward after receiving ICU care Defined as expired if the patient died during admission Defined as home against medical advice if the patient decided to leave the hospital against the advice of the physician [C]
Outcome on hospital discharge (expired, weaned and discharged, home on MV, home against medical advice)	Defined as weaned and discharged if the patient was weaned off of mechanical ventilation (both invasive and noninvasive) and cleared by the physician to leave the hospital after receiving inpatient care Defined as expired if the patient died during admission Defined as home on MV if the patient was cleared by the physician to leave the hospital after receiving inpatient care, but with requirements for mechanical ventilatory support as outpatient Defined as home against medical advice if the patient decided to leave the hospital against the advice of the physician [C]

[D] – discrete variables, [C] – categorical variables, [Co] – continuous variables