



Care of Adults In The Acute And Critical Care Setting

A latent class analysis of prolonged mechanical ventilation patients at a long-term acute care hospital: Subtype differences in clinical outcomes[☆]

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ABSTRACT

Rationale: Patients on prolonged mechanical ventilation (PMV) at Long-Term Acute Care Hospital's (LTACHs) are clinically heterogeneous making it difficult to manage care and predict clinical outcomes.

Objectives: Identify and describe subgroups of patients on PMV at LTACHs and examine for group differences.

Methods: Latent class analysis was completed on data obtained during medical record review at Midwestern LTACH.

Main results: A three-class solution was identified. Class 1 contained young, obese patients with low clinical and co-morbid burden; Class 2 contained the oldest patients with low clinical burden but multiple co-morbid conditions; Class 3 contained patients with multiple clinical and co-morbid burdens. There were no differences in LTACH length of stay [$F(2,246) = 2.243, p = 0.108$] or number of ventilator days [$F(2,246) = 0.641, p = 0.528$]. Class 3 patients were less likely to wean from mechanical ventilation [$\chi^2(2, N = 249) = 25.48, p < 0.001$] and more likely to die [$\chi^2(2, N = 249) = 23.68, p < 0.001$].

Conclusion: Patient subgroups can be described that predict clinical outcomes. Class 3 patients are at higher risk for poor clinical outcomes when compared to patients in Class 1 or Class 2.

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Introduction

Prolonged mechanical ventilation (PMV) has been defined by researchers in many different ways, ranging from the need for 96 hours or more of mechanical ventilation with placement of tracheostomy,¹ to numbers of unsuccessful spontaneous breathing trials,² to the need for 21 days, or more, of consecutive mechanical ventilation for six or more hours a day.³ Despite the heterogeneity in the definition of PMV, the number of patients requiring PMV has grown at an alarming rate. Intensive care unit survival increased 25% between 2004 through 2009.⁴ Patients requiring PMV increased more than 5% between 2006 and 2008, and by the year 2020, it is estimated that more than 625,000 patients will require PMV in the United States.⁵ Patients who require PMV are frequently transferred from traditional intensive care units to long-term acute care hospitals (LTACHs), where they receive continued long-term medical care.^{6–8}

Using pooled data from a 2015 meta-analysis on long-term survival of PMV patients, including patients in both short-term and long-term care environments, investigators indicated that only 50% of patients are successfully weaned from mechanical ventilation.⁹ Numerous concomitant comorbid factors, which may contribute to ventilator dependence, have been identified, but relative frequency of these factors among cohorts of patients receiving PMV is not well defined.⁵ Most published research on PMV weaning has focused on identifying and analyzing a single co-morbidity as independent risk factors for ventilator dependence.^{10,11} However, patients who require PMV rarely experience a single comorbidity in isolation. It is likely that these patients experience multiple co-morbidities collectively that potentially interact, resulting in clusters of clinically distinct subgroups. Statistical advances in modeling allow for identification of subgroups of patients via cluster analysis and may be particularly useful in distinguishing those patients at risk for ventilator dependence and death in subgroups of patients receiving PMV. Therefore, the purpose of this paper is twofold: 1) to classify subgroups of patients receiving PMV at a Midwestern LTACH as identified by clinical indicators present at the time of admission and 2) examine for group differences in the outcomes of ventilator liberation, mortality, and discharge disposition amongst the subgroups.

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Methods

Design

After University of Illinois at Chicago Institutional Review Board approval (#2016–0718), a retrospective medical record review was completed of patients requiring PMV (>21 days of mechanical ventilation) admitted between January 1, 2008, and December 31, 2015, to a 48-bed free-standing Midwestern LTACH. Sample size considerations in latent class analysis are difficult as one must take into consideration design factors exclusive to latent class analysis such as class proportion, the numbers of classes, the number of measured indicator variables, the strength of the class-indicator associations, and the amount of separation between class.¹² The innovative use of latent class analysis in the LTACH population is limiting in that there are no published studies from which to estimate the population parameters necessary for power analysis. It was anticipated that class sizes would be unequal in the final sample, and as such, a larger sample size was required to achieve a power of 0.8.¹⁶ Therefore, to ensure a large sample size a convenience sample of all patients requiring PMV, who met inclusion and exclusion criteria were collected for this study (Table 1). A total of 352 paper medical records were screened for inclusion into the study by the PI (HD), and 103 were eliminated for failure to meet inclusion and exclusion criteria (Table 2). The remaining 249 records were reviewed and relevant data were extracted by the PI (HD) and two trained research assistants. Each researcher was assigned 83 medical records for extraction. Study data were collected by hand and electronically managed using REDCap research electronic data capture tools.^{13,14}

Measures

Baseline demographic data include: age, gender, marital status, weight, year and month of LTACH admission, and underlying etiology for prolonged respiratory failure. The underlying etiology for respiratory failure was coded into 1 of 9 mutually exclusive etiologic categories (Table 3).

Admission clinical indicators. Indicators of clinical status at the time of LTACH admission include: admitting vital signs; laboratory values including basic chemistries, a complete blood count, and arterial blood gasses; and short-term hospital length of stay recorded as the number of days of hospitalization. The Charlson Co-Morbidity Index, a validated index of comorbid conditions, was computed based on the medical record review.¹⁵

Outcomes

Ventilator liberation. Extracted data included ventilator weaning status and total number of LTACH mechanical ventilation days. For

Table 1
Study inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients who have received ≥ 21 total days of mechanical ventilation. <ul style="list-style-type: none"> From initiation of first day of mechanical ventilation Includes days of mechanical ventilation at the short-term acute care hospital Tracheostomy in place before, or placed during LTACH hospitalization ≥ 21 years of age at time of admission	Co-morbid neurologic conditions that would interfere with limb exercises: <ul style="list-style-type: none"> Amyotrophic lateral sclerosis Spinal cord injuries resulting in quadriplegia or paraplegia Admission to the LTACH for home ventilator training Previously known long-term/chronic ventilator patient admitted for treatment of concomitant medical condition Previous inclusion in the study from prior admission
Hemodynamically stable: <ul style="list-style-type: none"> Systolic blood pressure ≥ 90 mmHg No intravenous vasopressor medications except for inotropic medication Absence of life-threatening cardiac arrhythmias Admitted between January 1, 2008, and December 31, 2015	A LTACH length of stay ± 2 SD greater than average LTACH length of stay (<4 days or >68 days)

Table 2
Excluded patients

Criteria	n (%)
Co-Morbid neurologic condition	36 (35%)
Orally intubated ≤ 21 of MV	33 (32%)
Home MV training	4 (<1%)
Previous enrolment in study	7 (<1%)
Known chronic MV patient	5 (<1%)
LTACH LOS ≥ 68 days	11 (<1%)
Not on MV	4 (<1%)
Chart unable to be located	3 (<1%)

Note; MV = Mechanical Ventilation; LOS = Length of Stay.

Table 3
Clinical and demographic characteristics of the sample (n = 249)

Age years(\pm SD)	68.6 (\pm 14.0)
Gender n(%)	
Male	122 (49%)
Female	127 (51%)
Marital status n(%)	
Single	57 (22.9%)
Married	116 (46.6%)
Divorced	29 (11.7%)
Widowed	47 (18.9%)
Etiology of PMV n(%)	
Cardiac	27 (10.8%)
CV Surgery	52 (20.9%)
Respiratory	64 (25.7%)
Neurologic	30 (12.0%)
Trauma	21 (8.4%)
Oncologic	14 (5.6%)
GI	20 (8.0%)
Infection/Sepsis	16 (7.6%)
Renal/Endo	2 (< 1%)
Weight kg(\pm SD)	94.1 (\pm 36.6)
Charlson score (\pm SD)	5.9 (\pm 2.8)
STACH LOS days(\pm SD)	26.4 (\pm 17.0)
LTACH LOS days(\pm SD)	35.9 (\pm 16.2)
Ventilator days(\pm SD)	20.5 (\pm 15.8)
Weaned n(%)	
Yes	172 (69.1%)
No	77 (30.1%)
Deceased n(%)	
Yes	62 (24.9%)
No	187 (75.1%)

Note: STACH LOS = Short-Term Acute Care Hospital Length of stay; LOS = Length of Stay.

this study, the last day of mechanical ventilation was defined as the last day the patient received any invasive mechanical ventilator support via tracheostomy tube, including fully assisted mechanical

ventilation or pressure supportive modes which persisted until hospital discharge. Non-invasive positive pressure ventilation via face-mask was not considered mechanical ventilation in this study and therefore was not included as a mechanical ventilation day.

Discharge disposition. Survival status at the time of discharge and discharge disposition, if discharged alive, was documented. Discharge disposition was categorized into one of four options: home, inpatient rehabilitation, skilled nursing facility, or transfer to a higher-level short-term acute care hospital. LTACH length of stay was recorded as the number of days of LTACH hospitalization, calculated by using the LTACH date of admission and date of discharge.

Data analysis

IBM SPSS Statistics for Macintosh, Version 24 software (SPSS Inc. 2016, Armonk, NY, USA) was used to analyze individual variables, and descriptive statistics were calculated for each variable. All continuous variables are expressed as mean and standard deviation. Categorical variables are presented as percentage and frequency. Tests for normality of continuous variables were completed and included Shapiro–Wilk, Shapiro–Francia, skewness and kurtosis testing, and visual inspection of p-plots, q-plots, and histograms. The data were cleaned using frequency distributions to identify data entry errors and bivariate relationships were examined with Pearson's correlation.

Latent Gold® 5.1 was used to perform latent class analysis in this study, identifying parsimonious classes of patients on PMV at a Mid-western LTACH using clinical indicators present at the time of admission. Models were run evaluating the relative fit from one to five classes using the smallest Bayesian Information Criteria value was used as the primary fit indicator to determine the optimal number of latent classes. Additional fit statistics taken into consideration included the following classification statistics: proportion of classification errors, pseudo R²-squared statistics, and entropy (Table 4).

One-way analysis of variance (ANOVA) was used to determine whether significant differences existed amongst the subgroups in demographic, clinical indicators, the total number of mechanical ventilation days, and LTACH length of stay. Chi-square tests of independence were used to examine the relationship between the subgroups and nominal outcome variables of mortality and ventilator liberation status. Post hoc ANOVA TUKEY or Games-Howell tests of significance were completed as appropriate to determine the significance of the parameters between the clusters.

Reliability testing

At the completion of primary data collection, a subsample of 50 patient charts was randomly selected and rescreened by the PI and the two research assistants for calculation of inter and intra-rater reliability scores. Inter and intra-rater reliability scores were calculated via intraclass correlation for ordinal and continuous level variables, and Cohen's Kappa for nominal level data, to quantify the degree of agreement between the three data extractors.¹⁶

Results

Complete data were available for analysis of 249 older patients on PMV with an average age of 68.6 ± 140 years, 122 (49%) were male, and 127(51%) were female (Table 3). The average length of short-term hospitalization before LTACH transfer was 26.4 days. The average LTACH hospitalization was 35.9 ± 16.2 days, or 5.1 weeks (Table 3). One-hundred seventy-two patients (69%) were successfully weaned from mechanical ventilation. Successful weaning from mechanical ventilation did not ensure survival. Sixty-two (25%) patients died during hospitalization. Of the 172 (75%) patients who successfully weaned from the ventilator, 20 (11.6%) died after 17.7 ± 12 days of independent breathing via tracheostomy collar. The three most common etiologies of PMV were respiratory disease [64 (25.7%)], cardiovascular surgery [52(20.9%)], and neurologic conditions [30(12%)] (Table 3).

Reliability testing

Cohen's Kappa for inter-rater reliability was found to range from 0.96 to 0.98, while intraclass correlation for inter-rater reliability ranged from 0.82 to 1.0. Cohen's Kappa for intra-rater reliability ranged from 0.90 to 0.96, while intraclass correlation for intra-rater reliability ranged from 0.77 to 1.0.

Latent class analysis

One to five class solutions were examined. Initial model development is presented in Table 5. Several parameters in the initial model did not have significant Wald statistics, indicating that there was little variation in the specific indicator in question amongst the classes and did not discriminate in a statistically significant way.^{17,18} All parameters that lacked statistical significance were removed from the initial model and the model was refit until all remaining predictor variables were statistically significant. The Bivariate Residuals were then examined to assess the assumption of local independence. Several were noted to be large, indicating correlation between the associated indicator variables remained in spite of the latent class solution. Direct correlational effects between BUN and creatinine were allowed in the model as the relationship between these two predictor variables is physiologically understood. BUN and creatinine biomarker monitoring are guideline recommendations for various medical conditions frequently encountered in the patient requiring PMV at a LTACH, including acute heart failure¹⁹ and hemodialysis,²⁰ and as such, were both included in the final model. The model was re-fit and fit statistics were analyzed for effect.

The final three-class solution identified not only had the best combination of fit-statistics but was the most parsimonious solution with the strongest theoretical and clinical distinction amongst classes when compared to 2-class and 4-class solutions. The three profiles are: a young subgroup of obese patients who had low levels of clinical burden and co-morbid conditions (Class 1 Low Morbid, $n = 73$); the oldest subgroup of patients with low levels of clinical burden but

Table 4
Model fit statistics

Number of classes	BIC	Classification errors	Reduction of errors	Entropy
1	19,266.54	0.0	1.0	0.0
2	18,851.84	0.05	0.90	29.9
3*	18,708.86	0.09	0.84	51.86
4	18,504.02	0.06	0.91	42.78
5	18,519.53	0.07	0.88	50.47

* Final model.

Table 5
Initial model

Indicator Variable	Wald Statistic	p-value
Age	66.91	<0.001
Marital Status	10.64	0.005
Etiology of PMV	1.72	0.42
Weight	8.02	0.018
STACH LOS	19.24	<0.001
Glasgow score	0.51	0.78
Temperature	0.67	0.71
Systolic Blood Pressure	1.50	0.47
Diastolic Blood Pressure	7.22	0.027
Heart Rate	4.68	0.96
Respiratory Rate	29.65	<0.001
FiO2%	19.95	<0.001
pH	26.94	<0.001
pO2	24.43	<0.001
pCO2	25.25	<0.001
Blood Urea Nitrogen	142.33	<0.001
Creatinine	88.91	<0.001
White Blood Cell Count	13.20	<0.001
Hemoglobin	15.64	<0.001
Hematocrit	19.94	<0.001
Albumin	6.50	0.039
Charlson Co-Morbidity score	27.64	<0.001

Non-significant variables in initial model highlighted in grey.

multiple co-morbid conditions (Class 2 Chronically High Morbid, $n = 113$); and an elderly subgroup of patients with high levels of clinical burden and multiple co-morbid conditions (Class 3 Acutely High Morbid, $n = 71$). Table 6 displays the total sample and individual latent class characteristics with associated means and proportions by parameters.

Subgroup description

Post hoc analysis of the three subgroups revealed similarities and differences in demographic and clinical characteristics amongst the classes (Table 6). There were differences in age, weight, co-morbidities, and clinical indicators amongst the subgroups (Table 6). Class 3 Acutely High Morbid patients had the highest FiO₂ percentage on the ventilator (46.69 ± 13.36), the highest BUN (67.36 ± 29.56) and creatinine (2.64 ± 1.47) measurements, and the highest white blood cell counts (13.25 ± 6.24). This pattern may indicate that class 3 patients were the most acutely ill.

Despite being the oldest (76.74 ± 8.25) subgroup, Class 2 Chronically High Morbid patients had superior respiratory physiologic parameters with clinically normal respiratory rates (20.04 ± 4.48), the lowest set FiO₂ percentage on the ventilator (40.41 ± 4.19), and the highest measured PaO₂ in arterial blood gas measurement (107.45 ± 37.23). The only clinical derangements amongst Chronically High Morbid Class 2 patients were a slightly alkalotic pH (7.46 ± 0.05) and mild elevations in BUN measurements (39.88 ± 20.91).

Low Morbid Class 1 and Chronically High Morbid Class 2 patients were differentiated less by clinical indicators, and to a greater extent by Charlson Co-Morbidity scores. Low Morbid Class 1 patients had the lowest number of co-morbid conditions (3.85 ± 2.31), while the oldest Chronically High Morbid Class 2 patients had the highest recorded number of co-morbid conditions (6.86 ± 2.57).

The etiology for prolonged respiratory failure also differed amongst the subgroups (Table 7). Low Morbid Class 1 patients had the most extensive amount of respiratory diagnoses (37%) and neurologic diagnoses (17.8%). The Chronically High Morbid Class 2 is composed primarily of patients with a cardiovascular surgical history (29.5%). Acutely High Morbid Class 3 also contains patients with a cardiovascular surgical history (25.4%) and respiratory diagnoses (21.1%), but interestingly is further distinguished by a substantial representation of patients who are post-cardiopulmonary arrest (8.5%) and patients with cancer diagnoses (9.9%).

Validation analysis

Ventilator liberation and mortality. There was no difference amongst the subgroups in number of ventilator days [F (2246) = 0.641, $p = 0.528$]. There were differences in ventilator weaning amongst the classes. Acutely High Morbid Class 3 patients were much less likely to wean from mechanical ventilation [χ^2 (2, $N = 249$) = 25.478, $p < 0.001$, Cramer's $V = 0.320$] and more likely to die [χ^2 (2, $N = 249$) = 23.677, $p < 0.001$, Cramer's $V = 0.308$] than those patients in Low Morbid Class 1 or Chronically High Class 2 (Table 8).

Table 6
Final model with latent classes

Class 1 (n = 73)	Class 2 (n = 105)	Class 3 (n = 71)	N = 249
Age	58.25 (± 13.77) ^{a,c}	76.64 (± 8.25) ^{a,b}	67.41 (± 13.73) ^{b,c}
Weight, kg	107.05 (± 52.70) ^a	82.00 (± 20.05) ^{a,b}	98.68 (± 29.73) ^b
STACH LOS	19.03 (± 8.14) ^{a,c}	29.89 (± 21.74) ^a	28.69 (± 12.97) ^c
Resp Rate	23.00 (± 5.83) ^a	20.04 (± 4.48) ^{a,b}	24.46 (± 6.32) ^b
FiO2%	41.01 (± 9.51) ^c	40.14 (± 4.19) ^b	46.69 (± 13.36) ^{b,c}
pH	7.44 (± 0.05) ^{a,c}	7.46 (± 0.05) ^{a,b}	7.41 (± 0.08) ^{b,c}
PO2	84.94 (± 25.58) ^a	107.45 (± 37.23) ^{a,b}	88.73 (± 24.36) ^b
PCO2	46.06 (9.81) ^a	41.44 (8.37) ^{a,b}	46.32 (12.34) ^b
BUN	22.00 (± 9.37) ^{a,c}	39.88 (± 20.91) ^{a,b}	67.36 (± 29.56) ^{b,c}
Creatinine	0.76 (± 0.26) ^{a,c}	1.01 (± 0.40) ^{a,b}	2.64 (± 1.47) ^{b,c}
WBC	10.59 (± 5.21) ^c	10.62 (± 4.05) ^b	13.25 (± 6.24) ^{b,c}
Charlson Score	3.85 (± 2.31) ^{a,c}	6.86 (± 2.57) ^a	6.68 (± 2.62) ^c
Gender #(%)			Total
Male	40 (54.4%)	40 (38.1%)	42 (59.2%)
Female	65 (45.2%)	33 (61.9%)	29 (40.8%)
			122(49%)
			127(51%)

Note: STACH LOS = Short-Term Acute Care Hospital Length of stay.

^a $p < 0.05$ between class 1 and class 2.

^b $p < 0.05$ between class 2 and class 3.

^c $p < 0.05$ between class 1 and class 3.

Table 7
Etiology of PMV by class*

n(%)	Class 1 (n = 73)	Class 2 (n = 105)	Class 3 (n = 71)	Total
Cardiac	9 (12.3)	9 (8.6)	9 (12.7)	27 (10.8)
CV Surgery	3 (4.1)	31 (29.5)	18 (25.4)	52 (20.9)
Respiratory	28 (38.4)	20 (19)	16 (22.5)	64 (25.7)
Neurologic	13 (17.8)	14 (13.3)	3 (4.2)	30 (12)
Trauma	7 (9.6)	8 (7.6)	6 (8.5)	21 (8.4)
Oncologic	1 (1.4)	6 (5.7)	7 (9.9)	14 (5.6)
GI	5 (6.8)	11 (10.5)	4 (5.6)	20 (8)
Infection/Sepsis	6 (8.2)	6 (5.7)	7 (9.9)	19 (7.6)
Renal/Endocrine	1 (1.4)	0 (0)	1 (1.4)	2 (0.8)

CV Surgery = cardiovascular surgery.

GI = Gastrointestinal.

*Significant differences amongst the classes at $p < 0.05$.

Discharge disposition. There was no difference amongst the subgroups in LTACH length of stay [F(2246) = 2.243, $p = 0.108$]. Although the distribution of discharge dispositions vary amongst the classes, these differences were not different from each other [χ^2 (6, $N = 183) = 9.99$, $p = 0.125$, Cramer's $V = 0.125$]. Of note, the young Low Morbid Class 1 patients were the most likely to discharge to home. The sick Acutely High Morbid Class 3 patients were more likely to transfer back to a short-term acute care hospital for higher-level care. Results are reported in [Table 8](#).

Discussion

The purpose of this study was to classify subgroups of patients receiving PMV at a Midwestern LTACH as identified by clinical indicators present at the time of admission via latent class analysis, and to examine for group differences in clinical outcomes. Our results demonstrate that distinct subgroups of patients receiving PMV at LTACH's can be described that predict clinical outcomes. While this study did not find group differences in LTACH length of stay or duration of mechanical ventilation at the LTACH, we did find that high levels of clinical burden and multiple co-morbid condition at LTACH admission are associated with mortality and ventilator dependence.

Patients are transferred to a LTACH only after they are stabilized, deemed appropriate for transfer by the sending facility^{21,22} and meet clinical criteria recommended by health management guidelines.²³ Timing of transfer to LTACH is an important consideration as researchers have shown a modest mortality benefit for those patients with shorter primary short-term intensive care unit length of stays.⁴ When

Table 8
Outcomes by class

	Class 1(73)	Class 2(105)	Class 3(71)	Total (249)
Ventilator liberation #(%)*				
Weaned – Yes	61 (83.6%)	78 (74.3%)	33 (46.5%)	172 (69.1%)
Weaned – No	12 (16.4%)	27 (25.7%)	38 (53.5%)	77 (30.9%)
Mortality #(%)*				
Deceased	6 (8.2%)	27 (25.7%)	31 (43.7%)	64 (25.7%)
Alive	67 (91.8%)	78 (74.3%)	40 (56.3%)	185 (74.3%)
Discharge disposition #(%)				
Home	14 (20.9%)	7 (9%)	4 (10.5%)	25 (13.7%)
SNF	24 (35.8%)	40 (51.3%)	17 (44.7%)	81 (44.3%)
Rehab	23 (34.3%)	22 (28.2%)	9 (23.7%)	54 (29.5%)
STACH tx	6 (9%)	9 (11.5%)	8 (21.1%)	23 (12.6%)

Note: SNF = Skilled Nursing Facility; STACH tx = Transfer to short term acute care hospital; Amb = Ambulation.

* Significant differences amongst the classes at $p < 0.05$ via chi-square analysis.

examining our results, patients in Low Morbid Class 1 had the shortest primary short-term hospital lengths of stay before LTACH transfer (19.03 ± 8.14) as compared to patients in either Chronically High Class 2 or Acutely High Morbid Class 3. The almost 10-day difference in stabilization and readiness for transfer amongst the subgroups is not entirely clear from the data. It is possible the difference exists due to the etiology of respiratory failure amongst the subgroups. The etiology of respiratory failure

in the majority of Low Morbid Class 1 patients is largely non-operative in nature and consists of respiratory diagnoses (COPD exacerbation, pneumonia, etc.) and neurologic disorders (cerebral vascular accidents, Guillian Barre Syndrome). Additionally, Low Morbid Class 1 also contained the lowest percentages of post-cardiac surgery patients (4.1%). In contrast, Chronically High Class 2 and Acutely High Morbid Class 3 both contain higher percentiles of post-cardiac surgery patients and smaller numbers of patients with a non-operative diagnosis. Previous research has suggested a negative relationship between surgical intensive care unit admissions²⁴ on hospital outcome.²⁵ This difference in outcomes between non-operative and post-operative transfer patients may continue at the LTACH level. Another possible explanation for the differences in short-term acute care hospital length of stay may reside in intensive care unit operational differences amongst medical versus surgical services, or possibly hospitals and health systems. This study did not attempt to analyze differences in patient characteristics and outcomes between patients on PMV transferred from university-level tertiary and quaternary care hospitals and those transferred from smaller,

regional primary care hospitals. Research analyzing outcome differences amongst patients transferred to higher-level care hospitals has been mixed,^{26,27} and future research analyzing differences in outcome based on previous short-term level-of-care could prove fruitful. Additionally, the transfer rates of Acutely High Morbid Class 3 patients back to a short-term acute care hospital for higher-level care from the LTACH is an important finding, as the ultimate mortality rates in this subgroup were not tracked post LTACH discharge and are likely underreported in this study.

There was an approximate 25 kg average weight difference between patients in Low Morbid Class 1 and Chronically High Class 2. While BMI data were not collected in this study, an average weight of 107 kg likely places most patients in Low Morbid Class 1 in the obese weight category. Those overweight/obese patients in Low Morbid Class 1 were approximately 11% more likely to wean from mechanical ventilation, and 20% more likely to be discharged alive than lighter patients in Chronically High Class 2. This “obesity paradox”, a noted mortality benefit despite higher morbidity amongst various cohorts of the obese, is a consistent finding in the critical care literature.^{28–32} However, there is not a significant difference between the average weights of Low Morbid Class 1 and Acutely High Morbid Class 3 patients. Obese patients in Low Morbid Class 1 were approximately 39% more likely to be discharged alive than those patients in Acutely High Morbid Class 3 even though there was no difference in average weight between these two classes. Thus, the protective effect of weight does not entirely explain mortality differences between the subgroups.

Examination of the blood chemistry results reveals distinctions amongst the subgroups. Chronically High Class 2 patients have a slightly elevated pH (7.46 ± 0.05) and BUN (39.88 ± 20.91), values likely consistent with a metabolic alkalosis pattern and is suggestive of possible over diuresis in this subgroup. Acutely High Morbid Class 3 patients have poor renal indicators despite having the lowest percentage of patients with co-morbid chronic kidney disease (2.9%), thus indicating the renal impairment seen in the Acute High Morbid Class 3 patients is acute. The mortality outcome of Acutely High Morbid Class 3, post-cardiothoracic surgical patients with acute renal failure is congruent with previously reported data documenting an increased risk of death in patients with acute kidney injury after cardiothoracic surgery.³³

Charlson CoMorbidity averages further distinguish differences amongst the subgroups. Researchers studying intensive care unit mortality have reported that concomitant chronic health problems are associated with increased hospital mortality.^{34–37} Therefore, it is not surprising that the Low Morbid Class 1 patients, who have the lowest average Charlson-Co Morbidity scores, have the lowest mortality and highest discharge to home rates. In comparison, patients in Chronically High Class 2 (6.86 ± 2.57) and Class 3 (6.68 ± 2.62) both have Charlson Co-Morbidity scores above six. Charlson Co-Morbidity scores above six have been shown to be an independent predictor of mortality in the critically ill, particularly in patients with acute kidney injury.³⁸ This co-morbidity associated mortality trend appears to continue at the LTACH level, as our findings suggest the effect of comorbidity was greatest for those with renal impairment.

As discussed, the subgroups do vary on individual clinical parameters and clinical outcomes. Patients in the youngest subgroup (Low Morbid Class 1) are approximately 48% more likely to be discharged alive and 57% more likely to successfully liberate from mechanical ventilation than those patients in Acutely High Morbid Class 3. Yet, one of the most important findings in this study is that the association of some of these individual clinical parameter patterns is contrary to expectations. For example, the Chronically High Class 2 is the oldest subgroup, has the longest short-term hospitalizations, and also has the highest Charlson Co-morbidity scores. This combination would lead a clinician to expect a high mortality rate in this subgroup. Yet, Chronically High Class 2 patients have vastly superior rates of

ventilator liberation and mortality when compared to Acutely High Morbid Class 3 patients. Perhaps, then, it is not the individual parameters that influence ventilator liberation and mortality but the complex interplay of all of clinically significant variables combined that have meaningful impact on clinical outcomes.

Clinical implications

This study has several implications for clinical practice. Identifying patients at risk for a poor clinical outcome is the first step in the development of targeted interventions aimed at improving not only survival, but also health-related quality-of-life. Patients requiring PMV transferred to an LTACH who fit the profile for the acute, high morbid subgroup should be identified upon admission as “at risk” and monitored closely throughout their hospitalizations for clinical decline.

Limitations and recommendations for future research

To our knowledge, this is the first analysis aimed at the creation of homogeneous subgroups of patients requiring PMV transferred to a LTACH. While this is innovative and significant, there are limitations in this study. The retrospective design, using data collected for non-research purposes, is a limitation as causal inference cannot be made. Since available medical records were reviewed, results are limited to data in the records and documentation was, in some cases, incomplete. Missingness analysis of predictor variables in the final latent class model indicated that missing variables were limited exclusively to the blood chemistry values only, were missing at random, and percent of missing variable per subject was low at 1.6–6.8%. The software used to complete the latent class analysis in this study, Latent Gold® 5.1, can classify subjects with missing variables without case deletion or imputation. Complete case analysis can increase the odds of errors of inference.³⁹ Therefore, to offset against the effect of missing data, the latent class analysis in this study was completed with all study subjects regardless of missing data.

This study did not follow patients who were discharged alive to assess 1-year mortality rates. Longitudinal assessment of mortality amongst the clusters is recommended. Also, this study did not distinguish amongst renal failure patients requiring hemodialysis. Considering the effect of renal failure on outcome, future analysis of differences amongst dialyzed and non-dialyzed renal failure patients is encouraged. Additionally, this study did not investigate other LTACH hospital processes (mobilization, sedation exposure) or complications (sepsis) known to impact morbidity and mortality in the acute care setting.

Recommendations for future research include replication studies aimed at validation of this latent class solution with similar, yet distinct data set.⁴⁰ Once the presence of subgroups within the sample is validated, development of targeted interventions aimed at improving ventilator liberation rates and mortality outcomes in at-risk patients is encouraged. Finally, given the lack of consistent definition of PMV replication studies aimed at examining the stability of the latent class using a shortened duration of pre-admission duration of mechanical ventilation is warranted.

Conclusion

We found three distinct clinical profiles of PMV patients at a Midwestern LTACH that are associated with different rates of ventilator liberation and survival. Different subgroups of LTACH patients who require PMV with varying levels of clinical indicators have been defined in this study. Identification of patients at high risk for a poor clinical outcome may prove useful in ascertaining needed level of care and clinical monitoring.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.hrtlng.2019.01.001](https://doi.org/10.1016/j.hrtlng.2019.01.001).

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