The Association Between Comorbid Illness, Colonization Status, and Acute Hospitalization in Patients Receiving Prolonged Mechanical Ventilation

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BACKGROUND: Long-term acute care (LTAC) hospitals provide specialized care for survivors of critical illness who require prolonged mechanical ventilation. These chronically ill patients often have multiple comorbidities and are colonized with antibiotic-resistant organisms. We investigated the association of comorbidities and colonization status with outcomes in patients requiring prolonged mechanical ventilation in an LTAC facility. We hypothesized that comorbidity burden and colonization with multiple drug resistant organisms would be associated with worse clinical outcomes. METHODS: We performed a retrospective, cohort study of 157 mechanically ventilated subjects in an urban LTAC facility admitted from January 2007 to September 2009. Comorbidity burden was documented from pre-admission data using the Charlson Comorbidity Index. Colonization data were obtained from surveillance cultures. Outcomes studied included transfer back to acute care facilities, stay, and ventilator weaning status. RESULTS: Within 60 days, 58.6% of subjects were transferred back to an acute care facility. The most common reason for transfer was infection/sepsis (37%). The Charlson Comorbidity Index of subjects transferred to acute care, versus those who were not, was 4.9 ± 3.1 versus 3.6 ± 2.7 ($P = .01$), an odds ratio of 1.1 for each 1-point increase in Charlson Comorbidity Index (95% CI 1.03–1.71, $P = .02$). Colonization with acinetobacter was associated with higher incidence of transfer (71% vs 51%, $P = .01$). The odds ratio for transfer to acute care was 1.3 for each additional organism colonizing a subject (95% CI 1.11–1.53, $P = .006$). CONCLUSIONS: Higher comorbidity burden and colonization status were associated with increased risk of transfer to acute care. Further investigation is needed to clarify this relationship between comorbidity burden and colonization with change in clinical status. *Key words: long-term care; infection; artificial respiration; severity of illness index; comorbidity; acinetobacter.* [Respir Care 2013;58(2):250–256. © 2013 Daedalus Enterprises]

Introduction

Patients treated in critical care units often require prolonged mechanical ventilation (PMV) after recovering from catastrophic critical illness. PMV, defined as ventilator dependence for > 21 days,[1] is associated with increased hospital morbidity and mortality.[2] A multidisciplinary approach involving specialized care teams, high nurse to patient ratios, protocolized weaning practices, and sedation protocols has been shown to reduce duration of mechanical ventilation, morbidity, and mortality.[3-7]

Recently, long-term acute care (LTAC) hospitals have emerged to provide specialized care required for patients recovering from sequelae of critical illness such as PMV, severe malnutrition, physical deconditioning, and decubitus wounds.[8-10] Chronically critically ill patients, such as those admitted to LTAC hospitals, often have high acuity of illness, multiple comorbidities, long hospitalizations,

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and frequent readmissions to acute care facilities, which increases their risk of colonization and infection with antibiotic-resistant organisms.[11,12] These characteristics are associated with poor long-term outcomes and high mortality rates.[13,14]

Colonization of hospitalized patients with multidrug-resistant (MDR) organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci, and *Acinetobacter baumannii* is increasing. Estimated prevalence of MRSA and acinetobacter colonization is estimated to be as high as 30%.[13] Chronically ill patients in LTAC hospitals often have high acuity of illness, multiple comorbidities, prolonged hospitalizations, and frequent readmissions to acute care facilities, subjecting them to increased risk of colonization and subsequent infection with MDR organisms.[14-17]

To date there are few studies predicting adverse outcomes in patients admitted to LTAC facilities.[14,18] We performed a retrospective cohort study investigating the association between comorbidities and colonization status with clinical outcomes of patients requiring PMV treated at an LTAC facility. We also examined factors affecting ability to wean from PMV. We hypothesized that comorbidity burden and colonization with MDR organisms would be associated with worse clinical outcomes, specifically transfer to acute care setting and successful weaning from PMV.

QUICK LOOK

Current knowledge

Long-term acute care hospitals provide specialized care for survivors of critical illness requiring prolonged mechanical ventilation. These patients often have multiple comorbidities and are colonized with multiple drug resistant organisms. The relationship of this comorbidity burden and multiple drug resistant colonization on outcomes has not been established.

What this paper contributes to our knowledge

When accounted for cumulatively, the total comorbidity burden, as represented by the Charlson Comorbidity Index and acinetobacter colonization, is independently associated with a higher likelihood of readmission to an acute care facility.

SEE THE RELATED EDITORIAL ON PAGE 383

Methods

This study was approved by the University of Maryland School of Medicine institutional review board.

Study Design and Subject Selection

We performed a retrospective cohort study of mechanically ventilated in-patients at the University Specialty Hospital, an urban, long-term acute care (LTAC) facility affiliated with the University of Maryland Medical Center. University Specialty Hospital is a 180 bed, LTAC hospital operated by the University of Maryland Medical System. The Ventilator Unit has 60 beds and a patient-nurse ratio of 6.5:1, a respiratory therapist-patient ratio of 9:1, 24-hour hospitalist coverage, hemodialysis unit, and multidisciplinary support team consisting of physical, occupational, recreational, and speech therapists, and clinical pharmacist services, social worker, psychiatric liaisons, and nutritionists. Physical rehabilitation efforts consisted of passive range of motion exercises for ventilator dependent patients. Criteria for transfer from acute care hospitals to the ventilator unit included hemodynamic stability, tracheostomy, $F_{IO_2} \leq 60\%$ with $S_{pO_2} \geq 90\%$, PEEP ≤ 10 cm H_2O, and no need for cardiac monitoring, intravenous vasoactive medications, or continuous intravenous drips.

All subjects included in this study were ventilator-dependent with a tracheostomy (Shiley, Nellcor Puritan Bennett, Pleasanton, California). The subjects studied were identified from a ventilator weaning database kept for quality improvement purposes, admitted between January 2007 and September 2009. To eliminate possible violation of the assumption of independence of observations, subjects who were discharged to an acute care facility or another location and subsequently readmitted to University Specialty Hospital were excluded from the study upon readmission.

Data Collection

Data were extracted from electronic medical records, including demographic data, presence of indwelling lines (central venous catheters, Foley catheters), enteric access tubes, and colonization with MDR organisms. All comorbid illnesses were recorded per subject, and comorbidity burden was characterized from pre-LTAC admission data using the Charlson Comorbidity Index with the Deyo modification.[19,20] The Charlson Comorbidity Index is a weighted scoring system that estimates 1-year mortality based on prior comorbid conditions, using the Internal Classification of Diseases (Ninth Revision) codes, with greater values representing greater comorbidity burden. Colonization data were obtained from routine rectal, nasal, and sputum surveillance cultures, collected from each subject on admission to the facility, and when clinically warranted (ie, fever, change in sputum consistency/color, change in oxygen requirements, suspected infection, or

hemodynamic instability). Colonization data of interest included cultures found positive either on admission or during the LTAC stay, with MRSA MDR *Pseudomonas aeruginosa*, extended spectrum β lactamase producing *Klebsiella pneumoniae*, and MDR *Acinetobacter baumannii*.

Clinical outcomes of interest included transfer to an acute care facility, colonization burden at 60 days, incidence of nosocomial infection, stay at the LTAC hospital, and ventilator weaning status (defined below). We had intended to include mortality at the LTAC hospital as an end point. However, overall mortality in the LTAC facility was very low (1.9%), primarily because subjects were transferred to the acute care hospital when they clinically deteriorated. Thus, mortality could not be analyzed in this study. Colonization was defined as a positive surveillance culture reflecting the presence of microorganisms (on skin, mucous membranes, open wounds, or in excretions or secretions) not causing adverse clinical signs or symptoms.[21] Nosocomial infection was defined as positive culture, with evidence of immunologic response from the infected organ (ie, pyuria in a urinary tract infection, increased number of polymorphonuclear leukocytes on sputum culture, or bacteria in body fluids that are presumed sterile) acquired > 48 hours after the subject's hospitalization to the LTAC facility, which required therapy with antibiotics.[21] These were categorized as bacteremia, urinary tract infection, pneumonia, soft tissue, and other if they did not fit into any of the other categories. Sepsis was defined according to consensus criteria as having 2 of 4 systemic inflammatory response criteria and evidence of infection, suspected or confirmed.[22]

The definition of successful weaning from PMV according to the National Association for Medical Direction of Respiratory Care guidelines is the ability to tolerate tracheostomy collar for 48 hours without mechanical ventilator support, or 7 days requiring only nocturnal ventilation for 8 or fewer hours.[1] Weaning status was recorded as "weaned" or "not weaned" according to this definition. "Weaned" refers to subjects who were no longer ventilator dependent, as defined by the above National Association for Medical Direction of Respiratory Care guidelines during their stay in the LTAC.

Statistical Analysis

Statistical analysis was performed using statistics software (GB Stat 9.0, GB Stat, Silver Spring, Maryland). Descriptive estimates of demographic and clinical characteristics are reported as mean and standard deviation and interquartile values. Frequency of distribution with percentages was calculated for categorical demographic data.

Logistic regression was performed to determine odds ratios to describe relationships between continuous variables over time. Comparisons of proportions (chi-square) were conducted when analyzing categorical variables, and comparisons of means were performed using the Student *t* test when appropriate.

Table 1. Subject Characteristics

Age, median (range) y	60 (22–97)
Male	79 (50.3)
Race/Ethnicity	
White	58 (36.9)
African-American	92 (58.6)
Asian	3 (1.9)
Other	4 (2.5)
Location Prior to LTAC Admission	
Unmonitored medical/surgical floor	1 (0.6)
Medical ICU	100 (63.7)
Surgical ICU	7 (4.5)
Trauma ICU	11 (7.0)
Other ICU	35 (22.3)
Other	3 (1.9)
Days in acute care prior to admission, median (range)*	37 (6–164)
Central Venous Access	
None	85 (54.1)
1 line	61 (38.9)
2 lines	11 (7.0)
Foley catheter	93 (59.2)
Percutaneous endoscopic gastrostomy tube	142 (90.4)
Decubitus ulcers	76 (48.4)
Frequent Comorbidities	
Hypertension	99 (63.1)
Diabetes mellitus	68 (43.3)
Cerebrovascular accident	47 (29.9)
COPD	44 (28.0)
Coronary artery disease	41 (26.1)
Chronic kidney disease	35 (22.3)
Congestive heart failure	33 (21.0)
Paraplegia/quadriplegia	24 (15.3)
Recent surgery (within 30 d)	23 (14.6)
Malignancy	16 (10.2)
Charlson comorbidity index, mean ± SD	4.3 ± 2.9

Values are number and percent unless otherwise indicated (n = 157).
* Calculated with missing data, n = 120.
LTAC = long-term acute care hospital

Results

One hundred fifty-seven subject records were reviewed. Subject characteristics are shown in Table 1. The median age of our cohort was 60 years (range 22–97 y), 58.6% were African American, and 36.9% were white. Hypertension (63.1%), diabetes mellitus (43.3%), and cerebrovascular accident (29.9%) were the most frequent comorbidities in our cohort. Most subjects (63.7%) were admitted from a medical ICU, with smaller percentages of subjects

Table 2. Outcomes of LTAC Cohort

Stay, mean ± SD, d	34.2 ± 22.7
Weaned from ventilator, no. (%)	89 (56.7)
Nosocomial infection, no (%)*	107 (68.2)
Status at 60 d, no. (%)	
Died	3 (1.9)
Discharged	8 (5.1)
Transferred to acute care	92 (58.6)
Continued care at LTAC†	54 (34.4)

* Nosocomial infection includes any infection during hospitalization, including bacteremia, urinary tract infection, and pneumonia.
† Continued care at LTAC (long-term acute care hospital) refers to subjects who remained in the LTAC beyond the 60 day observation period.

Table 3. Reasons for Transfer to Acute Care Facility

	no. (%)
Infection/sepsis	34 (37.0)
Respiratory	18 (19.6)
Gastrointestinal	12 (13.0)
Cardiac	13 (14.1)
Neurologic	4 (4.3)
Other	11 (12.0)

admitted from trauma (7.0%) and surgical (4.5%) ICUs. There were one or more central venous catheters in 45.9% of the subjects.

Mean stay was 34.2 days (Table 2). Within 60 days 58.6% of subjects were transferred to an acute care facility. Organ system failures resulting in transfer are listed in Table 3, with the most common being suspected infection or sepsis (37%). Other reasons for transfer to an acute care facility included respiratory (tachypnea and/or oxygen desaturation), gastrointestinal (gastrointestinal bleed or surgical issues), cardiac (extreme tachycardia or decompensated heart failure), and neurologic (change in mental status) etiologies. Successful weaning occurred in 56.7% of the subjects.

The overall mean Charlson Comorbidity Index of our cohort was 4.3. The Charlson Comorbidity Index of subjects who were transferred to an acute care facility was 4.9 ± 3.1, compared to 3.6 ± 2.7 for those who were not ($P = .01$). An odds ratio of 1.1 for transfer to an acute care facility was calculated for each increase of one point in Charlson Comorbidity Index (95% CI 1.03–1.71, $P = .02$). No statistically significant associations between any individual comorbidity and outcomes were found.

The characteristics of subjects requiring transfer to acute care facilities are shown in Table 4. Of subjects colonized with acinetobacter in the sputum, 71.0% were transferred to acute care facilities, compared with 50.5% of subjects who were not colonized ($P = .01$). Mean stay in the LTAC was 30 days in subjects colonized with acinetobacter, compared to 37 days in subjects who were not colonized ($P = .06$). Colonization at any other site tested with MRSA, vancomycin-resistant enterococci, pseudomonas, and klebsiella did not have any statistically significant associations with transfer to acute care hospitals.

The odds ratio for transfer to acute care was 1.3 (95% CI 1.11–1.53, $P = .006$) for each additional organism colonizing a subject. Comparison of proportions using the chi-square test showed that all subjects who increased their overall colonization burden by 3 organisms in 60 days were transferred to acute care ($P < .001$).

In addition, we performed multiple logistic regression for determining predictors of transfer to an acute care facility. Included in the model were the only 2 variables predicting transfer in bivariate analysis: the age adjusted Charlson Comorbidity Index, and the presence of acinetobacter colonization at some point during the LTAC stay. Analysis showed that both variables were significant independent predictors of transfer to acute care facility ($P = .003$ for the overall prediction model). The odds ratios were as follows: for Charlson Comorbidity Index 1.154 for each 1 unit increase in Charlson Comorbidity Index (CI 1.027–1.295, $P = .02$), for the presence of acinetobacter 2.444 (CI 1.407–4.248, $P = .01$).

We determined whether the development of acinetobacter during the LTAC stay was a predictor of transfer to the acute care facility. Subjects were divided into 3 groups according to acinetobacter colonization status: those with initial cultures positive; those initially negative who remained negative during subsequent cultures (when subsequent cultures were drawn); and those initially negative who became positive during subsequent cultures (Table 5). Development of positive cultures for acinetobacter at any time was strongly associated with transfer to the acute care facility ($P = .002$).

Logistic regression analysis of age and ventilator weaning showed that the odds of successful weaning for every 5-year increase in age was 0.8 (95% CI 0.71–0.89, $P < .001$). There were no statistically significant associations between race, sex, or Charlson Comorbidity Index and ventilator weaning.

Discussion

Our study demonstrates that subjects with PMV from an LTAC hospital who had a higher total comorbidity burden, as represented by the Charlson Comorbidity Index, were more likely to require transfer to an acute care facility. Additionally, subjects who were colonized with multiple organisms were also more likely to be transferred, with acinetobacter being an organism that was independently associated with transfer. To our knowledge, this is the first study to investigate the associations between comorbidi-

Table 4. Characteristics of Subjects Transferred to Acute Care Hospitals, Compared With Those Who Were Not Transferred

	Transferred (n = 92)	Not Transferred (n = 65)	P
Charlson Comorbidity Index, mean ± SD	4.9 ± 3.1	3.6 ± 2.7	.01
Change in Colonization Number, no. (%)			< .001
0	35 (41.2)	50 (58.8)	
1	28 (73.7)	10 (26.3)	
2	21 (80.8)	5 (19.2)	
3	8 (100)	0	
Acinetobacter Colonization, no. (%)			.01
Colonized	44 (71.0)	18 (29.0)	
Not colonized	48 (50.5)	47 (49.5)	
Age, mean ± SD, y	61.1 ± 16.5	57.5 ± 16.2	.18
Race			.45
African American	53 (57.6)	39 (42.4)	
White	33 (56.9)	25 (43.1)	
Asian	3 (100)	0 (0)	
Other	3 (75.0)	1 (25.0)	
Sex			.58
Male	48 (60.8)	31 (39.2)	
Female	44 (56.4)	34 (43.6)	
Stay, mean ± SD, d	18.5 ± 15.1	56.0 ± 9.6	< .001
Central Venous Access			.61
None	49 (57.6)	36 (42.4)	
1 catheter	35 (57.4)	26 (42.6)	
2 catheters	8 (72.7)	3 (27.3)	

Table 5. Transfer to Acute Care Facility by Development of Acinetobacter Colonization

Acinetobacter Colonization Status	Subjects, no.	Transferred to Acute Care, no. (%)*
Initial positive	18	9 (50.0)
Initial and subsequent negative†	95	47 (49.5)
Initial negative, subsequent positive	44	36 (81.8)

* Comparison using chi-square test: P = .002.
† Represents results of subsequent cultures if applicable.

ties and bacterial colonization status with transfer to acute care facility in chronically ventilated LTAC patients.

Charlson Comorbidity Index was initially tested in a longitudinal study of general hospitalized patients, and subsequently validated in oncology.[23] It has more recently been validated in studies involving patients with antibiotic-resistant organisms.[24] Other scoring systems, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II), the Simplified Acute Physiology Score II (SAPS II), and the Sequential Organ Failure Assessment (SOFA), have been widely used as a measure of severity of illness and to predict outcomes in critically ill patients,[25-27] but may not be applicable in determining severity of illness in LTAC patients. We used the Charlson Comorbidity Index to measure severity of illness of our patient population because of its ease of calculation and its suitability in our population, as a less acutely ill cohort. To our knowledge, ours is the first study that demonstrates the prognostic utility of Charlson Comorbidity Index in chronically ill patients requiring PMV. Although we had intended to include mortality as an outcome in our study, the low occurrence of death at the LTAC precluded this analysis.

The results of our study suggest that Charlson Comorbidity Index can be used to predict transfer as an adverse outcome in chronically critically ill patients. Although an increased number of comorbidities represented by the Charlson Comorbidity Index was associated with increased odds of transfer to an acute care facility, when individual comorbidities were examined for association with transfer, no statistically significant associations were found. This suggests that the total comorbidity burden (or cumulative number of comorbid illnesses experienced by an individual) may have a stronger relationship with worse outcomes than any one comorbid illness alone. Our findings demonstrate that, by considering a patient's comorbidities (Charlson Comorbidity Index), it is possible to predict the need for acute care. Other scoring systems used in ICUs do not account for comorbid conditions, which may make them less useful in chronically ill patients who have multiple comorbidities. Therefore, as the number of these pa-

tients increases and research interest grows in this area, the Charlson Comorbidity Index may prove to be a simple and accurate instrument to classify the severity of illness and to predict transfer of chronically ventilated patients.

A second important finding in our study was the relationship demonstrated between increased colonization burden and transfer to acute care hospitals. Subjects who were colonized with multiple MDR organisms had a significantly greater rate of transfer to acute care facility for medical decompensation, with the most common cause being infectious/septic in origin. All subjects who increased their colonization burden by 3 organisms in 60 days were transferred to acute care hospitals. One may infer that this association is based on the higher incidence of infection in subjects colonized with multiple organisms. This association between colonization and infection has been shown in studies with MRSA.[14]

Only colonization with MDR acinetobacter was significantly associated with transfer to an acute care facility. This may suggest that colonization with MDR acinetobacter is a marker of more severe illness, or perhaps patient frailty, requiring management in an acute care setting. Additionally, our finding that those who developed cultures positive for acinetobacter during their LTAC facility admission had a high incidence of transfer to an acute care facility is consistent with other work that has demonstrated poor outcomes in patients colonized with MDR organisms.[14,15,28]

Subjects colonized with acinetobacter were also found to have shorter stay in the LTAC hospital, presumably because they developed a deterioration of clinical status requiring transfer to acute care earlier than subjects not colonized with this organism. Although there is some subjectivity to clinical judgment, specifically the severity of patient illness or acuity that would prompt a transfer to higher level of care, the hospitalists at our LTAC uniformly practiced transfer upon recognition of severe sepsis, as defined by accepted guidelines, thus providing some clinical consistency to the reasoning behind urgent or emergency acute care transfers.

Our study also showed an approximately 20% decreased odds of successful ventilator weaning for every 5-year increase in age. This observation that older patients are more difficult to wean from the ventilator is consistent with previous studies.[29-31] Race, sex, and Charlson Comorbidity Index were not significant predictors of successful ventilator weaning.

Limitations of our study include its retrospective design, as well as the restricted generalizability of our population, which includes only chronically ventilated patients in an LTAC facility. Additionally, since overall colonization was recorded through day 60, regardless of the patient's stay in the LTAC hospital, it is possible that colonization status may have been influenced by the patients' prior stay at the acute care hospital. Patients with higher acuity that required transfer to acute care may have been more susceptible to colonization with MDR organisms. One final limitation of this study when using the Charlson Comorbidity Index to estimate severity of illness in this patient population is that, unlike other scoring systems that focus on acute illness, the Charlson Comorbidity Index cannot be quickly calculated by examination. Calculating a Charlson Comorbidity Index requires knowledge of a patient's medical history and comorbidities, which may be troublesome as chronically ill patients on mechanical ventilation are often not able to communicate this information with the physician themselves. Therefore there is strong reliance on prior medical documentation and information from the patient's family members, which may result in an inaccurate calculation of the Charlson Comorbidity Index.

Additionally, the need to transfer patients to an acute care facility from an LTAC hospital may depend on facility capabilities (ie, does the LTAC hospital have an ICU, continuous telemetry monitoring capability, and appropriate staffing and credentialing to manage more acutely ill patients?). Thus, the degree to which the results described can be generalized to all settings will depend on institutional factors such as practice culture, organization, technical capabilities of various hospital units, staffing models, and ease of access to acute care settings.

Conclusions

LTAC facilities provide care for patients requiring PMV with a high comorbidity burden and colonization with multiple MDR organisms. When accounted for cumulatively, total comorbidity burden as represented by Charlson Comorbidity Index and acinetobacter colonization is independently associated with a higher likelihood of transfer to acute care facilities. Thus, further investigation is necessary to elucidate this relationship between comorbidity burden and colonization with change in clinical status.

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