Migration Letters

Volume: 20, No: S1 (2023), pp. 2867-2876

ISSN: 1741-8984 (Print) ISSN: 1741-8992 (Online)

www.migrationletters.com

Association Between Daily Average Of MobilityAchieved During Physical Therapy Sessions And Hospital-Acquired Or Ventilator-Associated Pneumonia Among Critically Ill Patients

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Abstract

Purpose: Hospital-acquired and ventilator-associated pneumonias (HAP and VAP) are associated with increased morbidity and mortality. Immobility is a risk factor for developing ICU-acquired weakness (ICUAW). Early mobilization is associated with improved physical function, but its association with hospital-acquired (HAP) and ventilator-associated pneumonias (VAP) is unknown. The purpose of this study is to evaluate the association between daily average of highest level of mobility achieved during physical therapy (PT) and incidence of HAP or VAP among critically ill patients. Materials and Methods: In a retrospective cohort study of progressive mobility program participants in the medical ICU, we used a validated method to abstract newdiagnoses of HAP and VAP. We captured scores on a mobility scale achieved during each inpatient physical therapy session andused a Bayesian, discrete time-to-event model to evaluate the association between daily average of highest level of mobility achieved and occurrence of HAP or VAP. Results: The primary outcome of HAP/VAP occurred in 55 (26.8%) of the 205 participants. Each increase in the daily average of highest level of [1]mobility achieved during PT (0-6 mobility scale) exhibited a protective association with occurrence of HAP or VAP (adjusted hazard ratio [HR] 0.61; 95% CI 0.44, 0.85). Age, baseline ambulatory status, Acute Physiology and Chronic Health Evaluation (APACHE) II, and previous day's mechanical ventilation(MV) status were not significantly associated with the occurrence of HAP/VAP. Conclusions: Among critically ill patients in a progressive mobility program, a higher daily average of highest level of mobility achieved during PT was associated with a decreased risk of HAP or VAP.

Keywords *critical care, critical illness, mechanical ventilation, complications, outcomes.*

Introduction:

Hospital-acquired and ventilator-associated pneumonias (HAP and VAP, respectively) together

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account for 21.8% of all healthcare-associated infections.[1] Both HAP and VAP are associated with protracted hospital length-of-stay (LOS), higher overall health care costs, and increased morbidity and mortality.[2]High HAP and VAP incidence rates have been reported in patients with older age, dysphagia, and structural lung disease.[3,4] Prolonged mechanical ventilation (MV), underlying medical comorbidities, and severity of illness are important risk factors for VAP development.[4,5] Strategies such as head-of-bed elevation, subglottic secretion drainage, endotracheal cuff pressure monitoring, and selective oral and digestive decontamination have shown inconsistent results in lowering VAP rates and shortening intensive care unit (ICU) LOS.[6–9] VAP prevention bundles that include practices such as minimizing sedation, daily spontaneous breathing trials, and early mobilization, on the other hand, are associated with improved outcomes.[4] Evidence for the prevention of HAP is more limited. Oral care is the most studied intervention and is associated with decreased incidence of HAP.[3] Other interventions such as early mobilization, dysphagia programs, and head-of-bed elevation have shown inconsistent results.[3] Although there are some encouraging data from HAP prevention bundles that included breathing exercises, mobility, and oral care in post-stroke, surgical, and medical ward patients, less is known about these bundles in the heterogenous medical intensive critical care population.[10–13]

Prolonged immobilization is a known risk factor for developing ICU-acquired weakness (ICUAW), a diffuse, symmetric, and generalized neuromuscular weakness that occurs early and rapidly during critical illness and can persist for years after dis-

charge from the ICU.[14–18] ICUAW is extremely common, with prevalence ranging from 25–80%.[16,19,20] It has been implicated in a broad-range of ICU-acquired complications, such as swallowing and diaphragmatic dysfunction and diminished cough strength, which can in turn lead to pneumonia.[21] The implementation of early mobility in the ICU has been shown to be safe and feasible even in the critically ill, mechanically ventilated patient.[22,23] Earlier studies that demonstrated the potential benefits of early mobility, including increased return to ambulation, improved muscle strength and physical functioning, decreased hospital and ICU LOS, shorter duration of MV and reduced healthcare costs, have helped to drive the paradigm shift toward early mobilization in the ICU.[24–27] Additionally, recent systematic reviews have shown that early mobilization led to greater muscle strength and higher probability of walking without assistance at hospital discharge, and reduced restriction in participation of normal daily activities at 6 months.[28]

Although early mobilization has been shown to be associated with improved physical function at hospital discharge and 6-month follow up,[29,30] little is known about the relationship between mobility and the incidence of HAP and VAP in medical ICU patients. As HAP and VAP are common healthcare-associated infections that can lead to increased morbidity, mortality, and incur significant individual and overall socioeconomic burdens, under- standing the association between early mobility and the occurrence of HAP/VAP may help guide future studies of preventive strategies. Therefore, the objective of this study was to evaluate the association between daily average of highest level of mobility achieved and the occurrence of HAP and VAP among critically ill patients.

Study Design and Methods

Eligible Participants

Eligible participants included adult medical intensive care unit (MICU) patients Makkah hospitals who participated in a progressive mobilization program, as previously described.[31] This program of progressive, active mobility was implemented in 2015 as a hospital quality improvement initiative. In this program, all MICU patients were screened daily by their

clinical team using a standardized screeningtool (e-Figure 1) for mobilization eligibility.[32] Patients who were eligible were subsequently enrolled in a progressive mobility program with physical therapy (PT), which occurred within 24 h of eligibility. The program of progressive mobility included therapeutic exercises, bed mobility, transfer training, and gait training with increasing patient effort (Figure 1).

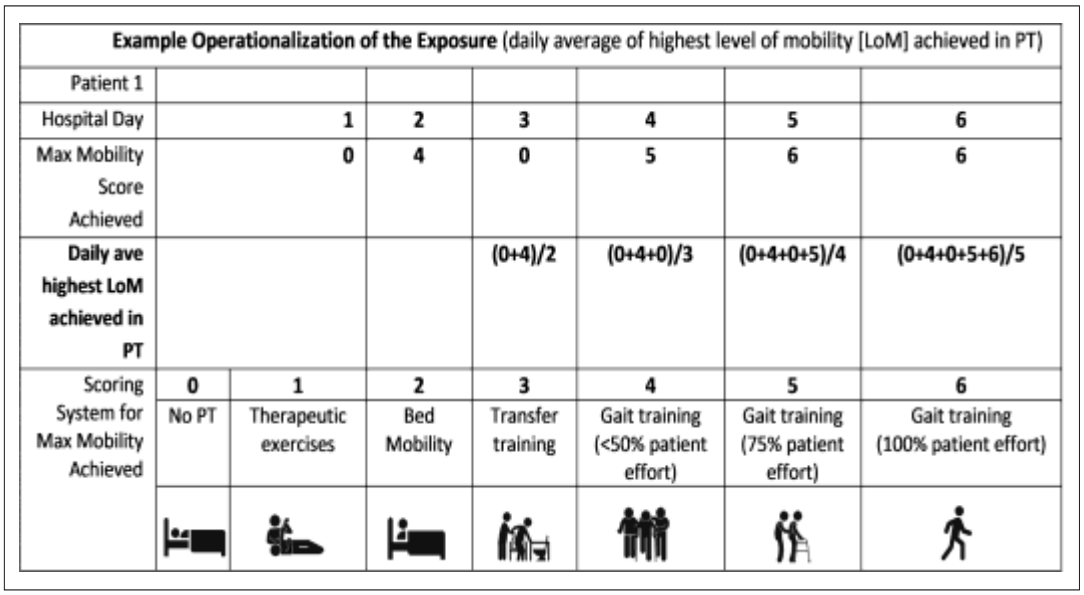

Figure 1. Illustration of the operationalization of daily average of highest level of mobility achieved. Patient 1 is assigned a score for the maximum mobility achieved (score of 0 to 6) on a given hospital day. A score of 0 represents no mobilization; a score of 1 represents therapeutic exercises, such as upper and lower extremity active range-of-motion routines; a score of 2 represents bed mobility, such as supine-to-sit exercise; a score of 3 represents transfer training including bed-to-chair and sit-to-stand exercises; a score of 4 represents gaittraining with <50% patient effort per evaluation by physical therapist; a score of 5 represents gait training with 75% patient effort per evaluation by physical therapist; a score of 6 reflects 100% patient effort during gait training. The score from each hospital day is averaged across hospitallength of stay (LOS) minus 1, from the start of eligibility through the day preceding the observation of an outcome. Incremental rise in the exposure represents an average increase of 1 level of maximum mobility achieved over all preceding days, reflecting the daily average of highestlevel of mobility achieved.

Study Design and Outcome

We conducted a retrospective cohort study of all MICU patients who participated in the progressive mobilization program during the first quarters of 2015 and 2016. Using the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN) surveillance case definitions, we performed a retrospective chart review to abstract diagnoses of hospital-acquired and ventilator-associated pneumonias.[33–35] Allparticipant charts were reviewed beginning at hospital admission,with the first day of HAP or VAP eligibility being hospital day 3 as per NHSN definitions. According to the NHSN case definitions, a HAP case was identified by a combination of criteria consisting of clinical signs and symptoms, laboratory findings, as well as the presence of evolving chest imaging findings. A chart review HAP outcome occurrence was recorded when NHSN HAP surveillance case definition was met. Likewise, according to the Ventilator-Associated Event (VAE) framework devised by the NHSN, a combination of ventilator changes, clinical signs and symptoms, laboratory findings, chest imaging, culture data and antimicrobial usage were used to identify VAP cases. Using this

framework, a chart review VAE outcome occurrence was recorded when the corresponding NHSN criteria weremet. The primary outcome of HAP or VAP was recorded as onecomposite outcome when meeting HAP or VAP NHSN surveil-lance case definition, clinician diagnosis, or both.

Primary Exposure

We gathered detailed information about PT treatments from each hospital day, including all mobility exercises performed, reasons for mobility deferral when relevant, and adverse events as appropriate. Our primary exposure, daily average of highest level of mobility achieved during PT, was operationalized as a time-varying exposure, wherein each day's maximum mobility achieved (score of 0 to 6) was averaged across hospital length of stay (LOS) minus 1. A score of 0 represents no moblization for a specific hospital day and a score of 6 reflects 100% patient effort during gait training (Figure 1). The exposure is updated on a daily basis, from the start of eligibility through the day preceding the observation of an outcome. Each incremental rise in the exposure represents an average increase of1 on the maximum mobility score achieved during PT overall preceding days, reflecting the cumulative improvement in mobility achieved in PT. Mobilization may be deferred for reasons unrelated to the patient's ability to mobilize (eg, planned procedures, availability of staff, etc). Additionally, patients' ability to maximally mobilize may also depend on their clinical status which may vary widely between mobilized days. Therefore, daily average of highest level of mobility achieved during PT, rather than maximal mobility achieved overall, was chosen as a primary exposure to reflect the comprehensive "dose" of mobility experienced by each participant in PT.

Covariates

We gathered demographic information including age, sex, race,and body mass index (BMI; kg/m^2) via chart review of the initial PT encounter note of patients participating in the progressive mobility program. Baseline ambulatory status was also captured through chart review of the initial PT assessment, which specified if patient was independent, dependent on assis tive equipment or another person, or dependent on both. We also collected data on Acute Physiology and Chronic Health Evaluation (APACHE) II score and MV status, including dates and number of intubations. Chart abstraction began from hospital admission until HAP or VAP occurrence, death,or discharge, and censored at hospital day 16, based on prior studies demonstrating the mean duration to occurrence of hospital acquired pneumonias to be 4.2 ± 3.8 days.[36] We excluded outside hospital transfers, as well as patients with confirmed pneumonia diagnoses prior to hospital day 3 if they met the case definition for Community Acquired Pneumonia.[37]

Statistical Analysis

Descriptive statistics were expressed as the count (%) for categorical variables and the median (interquartile range [IQR]) or mean (standard deviation [SD]) for continuous variables as appropriate. After determining there were no significant differences in baseline characteristics between the two cohorts, the year 1 and year 2 cohorts were combined into one analytic sample, as previously described.[30]

The outcome measure was time to the first occurrence of HAP or VAP during the hospital stay by either meeting NHSN criteria or diagnosis by a clinician. Daily average of highest level of mobility achieved during PT, our primary expo- sure, was operationalized as a time-varying exposure. Bayesian, discrete time-to-event multivariable models (pooled logistic regression with complementary log-log link) were used to evaluate the association between the primary exposure and discretetime (days of hospital stay) to first occurrence of HAP or VAP. This analytic strategy permits the calculation of hazard ratios (HRs).[38,39] The multivariable model

was adjusted for age, base-line ambulatory status, APACHE II score, and previous day's MV status. These covariates were chosen a priori based on their clinical significance. Results were reported as adjusted HRs with 95% credible intervals (CIs). The baseline ambulatory status covariate was included as a categorical variable in the analysis, with the independent state as reference, and both levels of dependence as separate indicators in the model. Analyses were conducted using SAS Version 9.4 where signifi cance was defined as a credible interval exclusive of 1.[40]

We conducted a series of sensitivity analyses. Although previous studies evaluating accuracy of the NHSN surveillance definition showed that pneumonia cases meeting NHSN criteriaoften corresponded with clinical diagnoses of pneumonia,[41] the positive predictive value of a clinician diagnosis of HAP has been shown to be modest at best.[42,43] Therefore, we performed a sensitivity analysis that only included cases meeting the NHSN surveillance definition. Additionally, given that theassociation of the exposure may differ between HAP and VAP, we performed a sensitivity analysis evaluating the association between primary exposure and HAP alone. Lastly, since more recent mobility levels may have greater impact on HAP/ VAP risk, we performed a sensitivity analysis in which the exposure, daily average of highest level of mobility achieved during PT, included only the 2 most recent days of mobility.

Results

Between year 1 and year 2 cohorts, a total of 371 person-admissionswere examined. Of these, 166 were excluded for having a con-firmed pneumonia diagnosis prior to hospital day 3 (reflecting community-acquired pneumonia or healthcare-associated pneumonia after a prior hospitalization) or being outside hospital transfers, resulting in a total of 205 participants in the final analysis. Participant characteristics are presented by outcome status in Table 1. The median age was 63.0 (interquartile range [IQR], 52.0-78.0) in the HAP/VAP group and 66.0 (IQR 54.0-77.0) inthe group without pneumonia. The median APACHE II score inthe HAP/VAP group was 25.0 (IQR 19.0-29.0) and 24.0 (IQR 19.0-29.0) in the group that did not develop pneumonia. Approximately half of the patients ambulated independently atbaseline in both groups (47.2% vs 51.0%). About a third of patientsrequired MV in the previous day in both groups (29.1% vs 28.0%). The mean daily average of highest level of mobility achieved in PTacross all person-days within each admission was 0.57 (standarddeviation [SD], 1.26) in the subgroup where HAP or VAP occurred, and 1.15 (SD, 1.07) in the subgroup that did not develop HAP or VAP.

The primary outcome of HAP/VAP occurred in 55 (26.8%)of the 205 participants. There were 35 cases of HAP/VAP thatmet NHSN criteria. There was a total of 48 cases of HAP, of which 13 were clinician-diagnosed HAP, and there were 7 cases of clinician-diagnosed VAP. The multivariable model results are presented in the forest plot (Figure 2). Each increasein the daily average of highest level of mobility achieved in PT(on the 0-6 mobility scale) exhibited a protective association with occurrence of HAP or VAP (HR 0.60; 95% CI 0.43, 0.84). Age, baseline ambulatory status, APACHE II, and previous day's MV status were not significantly associated with theoccurrence of HAP/VAP.

In the sensitivity analysis that only included cases of HAP orVAP meeting NHSN criteria, the association of the exposure was largely unchanged from the primary analysis (HR 0.57; 95% CI 0.38, 0.86). In a sensitivity analysis evaluating the adjusted association between the primary exposure and HAP alone, the association of the exposure was also largely unchanged from the primary analysis (HR 0.62; 95% CI 0.44, 0.86). We attempted a similar sensitivity analysis between the primary exposure and VAP alone, but the model would not con- verge, likely due to the small number (7) of outcomes. In the sensitivity analysis that focused on recent mobility by opera- tionalizing the exposure to extend back for a duration of 2 days, statistical significance and the direction of the associationwith the primary outcome were maintained,

though there was aslight reduction in the magnitude of the association (HR 0.76; 95% CI 0.60, 0.95).

Table 1:

Characteristic	HAP/VAP(N = 55)	No HAP/VAP(N = 150)
Age—Median (IQR)	63.0 (52.0–78.0)	66.0 (54.0–77.0)
Male sex—no. (%)	38 (69.1)	73 (48.7)
Number of comorbidities[a]—	2.0 (1.0–3.0)	2.0 (1.0–3.0)
APACHE II[b]—Median (IQR)	25.0 (19.0–29.0)	24.0 (19.0–29.0)
Baseline ambulatory status—no. (%)—Independent	25 (47.2)	76 (51.0)
Required mechanical ventilation[c]—no. (%)	16 (29.1)	42 (28.0)

Figure 2:

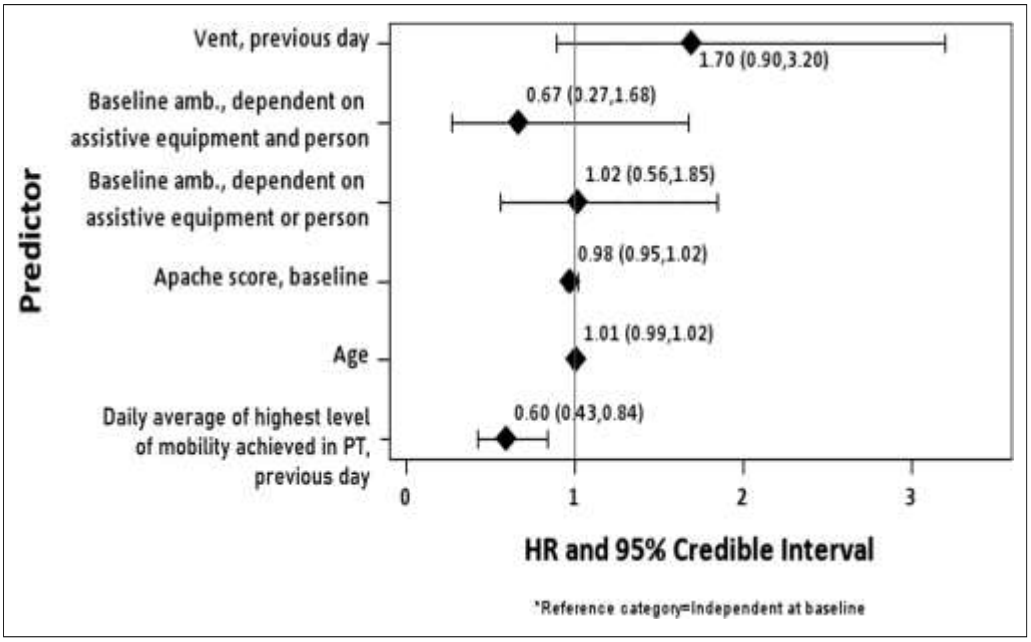

Figure 2. Factors associated with the development of HAP or VAP among critically ill patients. Daily average of highest level of mobility achieved exhibited a protective association with occurrence of HAP or VAP (adjusted HR 0.60; 95% CI 0.43, 0.84). Age (HR 1.01; 95% CI 0.99,1.02), dependent on assistive equipment or person at baseline (HR 1.02; 95% CI 0.56, 1.85), dependent on assistive equipment and person atbaseline (HR 0.67; 95% CI 0.27, 1.68), and previous day's MV status (HR 1.70; 95% CI 0.90, 3.20) were not significantly associated with the occurrence of HAP/VAP

Discussion:

In this retrospective cohort study of MICU patients in a progressive mobilization program, each incremental rise in the score achieved during PT on the 0–6 mobility scale was associated with

a nearly 40% decrease in the hazard of HAP or VAP. This protective association remained significant after adjustment for age, baseline ambulatory status, severity of illness as measured by APACHE II score, and previous day's MV status. In the sensitivity analyses evaluating only casesmeeting NHSN criteria and HAP alone, this protective association remained largely unchanged. The findings of our study contribute to the growing literature of HAP and VAP prevention by demonstrating a protective association between progressive mobility, specifically mobility achieved during PTsessions, and development of these pneumonias in the hospital.

Prior studies have shown that HAP and VAP are common hospital-acquired infections and are associated with increased hospital length of stay, higher health care costs, and increased morbidity and mortality.[41,44,45] Ventilator-associated pneumonias, for example, are one of the costliest hospital-acquired infections, with a per-case attributable cost of $40,144.[46] Other studies have shown that patients with HAP are 8 times more likely to die during hospitalization and twice as likelyto require intensive care than matched controls.[36] Given the significant clinical and economic burden of HAP and VAP, it is important to mitigate the risk of these complications and their downstream consequences. Our study suggests that mobility achieved during PT deserves further study as a potential intervention to reduce HAP and VAP rates, with possible mechanisms for our findings described in the existing literature. Prior studies have demonstrated that early mobilization improves skeletal muscle function, increases tidal volume,and decreases MV duration, which may prevent atelectasis as well as other pulmonary complications.[47–49] Rehabilitation therapy such as PT, mobility levels achieved during therapy, and mobility in general each deserve further study to better elucidate effective mobility doses, timing, and delivery models.

In prior studies, age has been associated with the development of HAP and VAP;[45] however, our study did not find this association. The relationship between baseline ambulatorystatus and the development of pneumonia has not been studied previously; our study found no significant association betweenbaseline ambulatory status and the occurrence of HAP and VAP. Other notable findings include the median durations to HAP and VAP of 5 and 10 days, respectively. The relatively short time from admission to incidence of HAP or VAP high- lights the importance of early mobilization in mitigating this detrimental complication.

A major strength of this study was its rigorous and detailed chart review, capturing comprehensive information from each PT session, allowing for a more granular calculation of the exposure variable than is often found in large datasets, such as administrative data. Additionally, our meticulous applicationof the NHSN criteria increased the rigor of pneumonia case classification. Another strength is the operationalization of the exposure variable, the daily average of highest level of mobilityachieved, which reflects the cumulative average of the score ona mobility scale. The exposure variable is updated each day, and each incremental increase reflects an average rise over all the preceding days in maximum mobility, thereby capturing the comprehensive "dose" of mobility experienced by each participant during PT sessions. Finally, while previous studies evaluated the effect of mobility as part of a care bundle in HAP andVAP prevention,[3,4,10,11] our study specifically queries the association of mobility achieved during PT and the occurrence of HAP/VAP outside the context of care bundles.

Our study also has limitations that warrant mention, including the retrospective study design and that our analyses were powered to include a focused list of covariates. Additionally, data were obtained from a single tertiary center in New Haven, CT; however, with respect to age, race, ethnicity, and education level, the demographics of the greater New Haven area are reflective of the overall population in the UnitedStates.[50] The mobility levels observed in both groups were 0.57 and 1.15 out of 6 in the HAP and VAP groups, respectively, which may appear low to account for a nearly 40% decrease in the hazard of HAP or VAP. However, the exposurevariable did not capture additional mobility efforts outside of PT sessions including, for example, nurse-driven mobility.Nurse-led mobility was far less common than mobility led by PT during the first two years of our progressive mobilization program (the time frame captured

in our study), but it is possible that patients participated in nurse-led mobility sessions not captured in our dataset. Lastly, the mobility scale used in our program incorporates two constructs (the level of mobility achieved as well as the amount of assistance required during PT), but does not reflect the frequency, duration, and total distance of ambulation, which may make this mobility scale less precise than mobility scales that incorporate these details.

Conclusion:

In conclusion, our study found a protective association between the daily average of highest level of mobility achievedduring PT and the incidence of HAP and VAP among MICU patients participating in a progressive mobility program. This protective association suggests that progressive mobilization may be a novel strategy to mitigate the risk of HAP/VAP during an ICU hospitalization. Larger, prospective studies are needed to more thoroughly evaluate the relationship between progressive mobility and hospital acquired pulmonary complications.

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