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Retrospective Assessment of Home Ventilation to Reduce Rehospitalization in Chronic Obstructive Pulmonary Disease

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Background: Healthcare systems are attempting to reduce hospital readmissions due to chronic obstructive pulmonary disease (COPD).

Methods: A retrospective study of a quality improvement (QI) program performed at a single center whose multifaceted intervention included nocturnal administration of advanced positive airway pressure (PAP) modality (or noninvasive positive pressure ventilation [NIPPV]) called averaged volume assured pressure support (AVAPS-AE) initiation by a respiratory therapist (RT), medication reconciliation by a pharmacist, adequate provision of oxygen, and ongoing RT-led care. In this QI program, consecutive patients who had been hospitalized twice in a single year with an acute COPD exacerbation underwent such interventions after they met specific selection criteria.

Results: Three-hundred ninety-seven consecutive patients were eligible for the program because they had two or more hospitalizations in the previous year. The proportion of patients who were readmitted on two or more occasions decreased from 100% (397 of 397) in the year prior to initiation of intervention to 2.2% (9 of 397) in the following year (χ^2 = 758, p < 0.0001). Seventy patients died over the one year following initiation of the multifaceted intervention. A composite outcome of rehospitalization and death was associated with inhaled steroids (adjusted odds ratio [adjOR] of 2.13; 95% confidence interval [CI] 1.09, 4.17; p = 0.02), whereas inhaled antimuscarinics tended to be associated with less risk for rehospitalization or death (adjOR 0.56; 95% CI 0.34, 1.03; p = 0.06).

Conclusion: In a retrospective cohort study of a QI initiative undertaken at a single center, we have observed that a multifaceted intervention that involved initiation of nocturnal advanced PAP (NIPPV) modality, RT-led respiratory care, medication reconciliation, appropriate oxygen therapy initiation, and patient education led to significant reduction in rehospitalization.

Keywords: chronic obstructive pulmonary disease, hospitalization, readmission, positive airway pressure, Intermittent Positive-Pressure Ventilation

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In an effort to improve the quality of care in patients with chronic obstructive pulmonary disease (COPD), the Center for Medicare & Medicaid Services (CMS) has now included COPD-related 30-day hospital readmissions to the prior CMS readmission measures that were already in place for acute myocardial infarction, heart failure, and pneumonia.[1] Such measures are reported on Hospital Compare, a database with information about the quality of care at over 4,000 Medicare-certified hospitals across the country; the COPD 30-day readmission measure went into effect as of October 1, 2014.[1] Moreover, the Agency of Healthcare Research and Quality (AHRQ) has identified COPD as an ambulatory care-sensitive condition (ACSC), which is defined by AHRQ as a condition for which good outpatient care can potentially reduce hospitalization, prevent complications, and reduce disease severity.[2]

Initiation of noninvasive positive pressure ventilation (NIPPV) in patients with severe stable COPD with arterial partial pressure of carbon dioxide ($PaCO_2$) greater than 52 mm Hg has been shown to reduce mortality, but in the same study an effect on hospitalization was not discerned.[3] Conversely, there is prospective observational data that continuous positive airway pressure (CPAP) is associated with reduction of hospitalization and mortality in patients with COPD and co-existent obstructive sleep apnea (OSA).[4] However, the routine use of NIPPV or CPAP therapy in patients with COPD with

BRIEF SUMMARY

Current Knowledge/Study Rationale: Healthcare systems are attempting to reduce hospital readmissions due to chronic obstructive pulmonary disease (COPD). Although there are European studies that continuous positive airway pressure (CPAP) may reduce hospitalization and mortality and non-invasive positive pressure ventilation (NIPPV) may reduce mortality in patients with stable severe COPD, whether NIPPV initiation in US Hospitals can reduce re-hospitalization in an "at-risk" COPD population is unclear.

Study Impact: In a retrospective cohort study of a QI initiative undertaken at a single center, we have observed that a multi-faceted intervention that involved initiation of nocturnal AVAPS-AE (a form of NIPPV), RT-led respiratory care, medication reconciliation, appropriate oxygen therapy initiation, and patient education led to a reduction in rehospitalization. Future studies need to undertake multi-center, adequately powered randomized controlled trials to assess the efficacy of such interventions.

or without OSA in this setting in the United States remains controversial due in part, to a lack of conclusive evidence that it improves clinical outcomes and in part, to logistical difficulties in implementing PAP or advanced PAP modality such as NIPPV in hospitalized patients.

A 2013 Cochrane review that critically reviewed the body of literature of NIPPV in patients with COPD recommended that, "future research should focus on adequate patient selection, ventilator settings, training and length of ventilation, as well as exacerbation frequency, admissions to hospital and survival."[5] Our objective was to test the hypothesis that an advanced PAP modality—a form of NIPPV mode—called averaged volume assured pressure support with auto-expiratory positive airway pressure (AVAPS-AE), which is capable of treating hypoventilation due to COPD, could reduce rehospitalizations in an "at-risk" COPD population. To address this question, we performed a retrospective review of a quality improvement (QI) program instituted at a single institution that was aimed at reducing rehospitalizations of patients with COPD who had suffered at least two or more hospitalizations in the previous year. This is a retrospective study assessing the rehospitalization rates of patients with COPD both before and after the institution of a multifaceted intervention that included the use of AVAPS-AE, and consequently it may suffer from inherent biases of such a study design performed at a single center. However, we believe that such information identifies a potential intervention that could reduce COPD-related hospitalizations and could inform the need and design for a rigorous prospective multicenter randomized controlled trial aimed at reducing rehospitalizations.

METHODS

We performed a retrospective analysis of the QI program at Barnes Healthcare Services (Valodsta, GA) from 2010 to 2014 whose multifaceted intervention included (a) medication reconciliation by a pharmacist, (b) the (continued) provision of oxygen, (c) AVAPS-AE initiation by a respiratory therapist, and (d) ongoing respiratory therapist-led care. In this QI program, consecutive patients who had been hospitalized twice in a single year with an acute COPD exacerbation were screened for eligibility and admitted into this program if they had (a) COPD GOLD[6] stages 2, 3, or 4; (b) Bode Index[7] Score ≥ 5; and (c) one of the following: $PaO_2 \leq 60$ mm Hg, $PaCO_2 \geq 52$ mm Hg, or FEV1 $\leq 40\%$. The arterial blood gas was performed when the patients were clinically stabilized and close to hospital discharge. Patients were excluded from the program if their home did not have electric power or had an insect infestation. This multifaceted program was commenced in 2010 and was new to all patients reported here. Although medication reconciliation was performed, the RT-led program with home visits was not available prior to the commencement of this QI program.

Multi-faceted Program

(a) Medication reconciliation was performed by a pharmacist at the time of hospital discharge.

(b) Oxygen Therapy: Due to the severity of their COPD, most patients had been initiated on either nocturnal or 24-h oxygen therapy by their hospital physician prior to their enrollment into the QI program. Those patients who had not received oxygen were given a prescription if they had oxygen saturation $\leq 88\%$ at rest.

(c) All patients were placed on AVAPS-AE (using Trilogy 100, Philips Respironics, Inc. Monroeville, PA), or switched from CPAP or bilevel PAP therapy to AVAPS-AE, using a target tidal volume V_T mode. AVAPS-AE can automatically titrate expiratory positive airway pressure (EPAP) to treat obstructive events of OSA if present; automatically adjust pressure support (PS) to achieve a physician-defined target tidal volume, based on ideal body weight (set at 5–7 mL/Kg IBW); and maximize expiratory time to help avoid breath-stacking by adjusting the back-up rate based on the patient's spontaneous rate. The device was set with EPAP range from a minimum of 5 cm H_2O (EPAPmin) to a maximum of 15 cm H_2O (EPAPmax); PS range from a minimum of 2 cm H_2O (PSmin) to a maximum of 26 cm H_2O (PSmax); automatic back-up rate and entrained with oxygen based upon the wakefulness determination through a t-connector and oxygen concentrator. Mask fitting and therapy initiation were done by an RT either at the hospital prior to discharge, or, if the referral was not received in time before discharge by a home medical company at the patient's home.

(d) Education: Patient education was delivered during initiation of AVAPS-AE by an RT either at the hospital prior to discharge, or, if the referral was not received in time by the homecare company, at the patient's home within a week of discharge. The session took between 90 and 100 minutes and covered education about COPD and available treatments, breathing techniques, and techniques to clear mucus from the lungs; patients were also provided with an educational booklet with such information for future reference (Barnes Healthy at Home™ booklet).

(e) Respiratory therapist led care was delivered in the patients' homes. Patients were visited by the respiratory therapist twice during the first week and 6 times during the first 30 days after initiation of AVAPS-AE therapy. Subsequently, patients received monthly visits up to day 90 and visits every 3 months thereafter. Unplanned visits where scheduled at the request of the patient. Each visit took 30–45 minutes and focused on maximizing patient adherence to medications and AVAPS-AE therapy by providing information regarding the benefits of treatments and information on how to administer medications and use their NIPPV device. Additionally, patients were encouraged to quit smoking if they were active smokers. Patients were encouraged to use their NIPPV device ≥ 4 h/night on all nights. Changes to prescriptions were made following consultation with the patient's referring physician. Readmission to the hospital in the 12 months following the initiation of the QI program was retrospectively obtained by extracting information from patient charts.

Statistical Analysis

Group comparisons for proportions were made by χ^2 test or Fisher exact tests, as appropriate. All data are shown as mean and standard deviation (SD) or median and inter-quartile range. In order to assess the effect of various factors (determining variables) on rehospitalization and death, we

performed simple logistic regression with a composite outcome of rehospitalization and death as the dependent binary variable. Subsequently, we built multivariate logistic regression models with composite outcome of rehospitalization and death as the dependent variable, using significant independent variables identified by univariate logistic regression analysis with $p \leq 0.10$. All analysis was performed using SPSS v22 (IBM SPSS Inc., Armonk, NY).

RESULTS

The 397 consecutive patients who were eligible for the QI program received the multifaceted intervention. This was a quality improvement program; the patients who did not qualify were not tracked, and therefore we are unable to give an exact proportion of patients who qualified. Of the patients who qualified for the program, only 3 patients (< 1%) refused the program. Baseline characteristics of the patients enrolled in the QI program are shown in **Table 1**. Adherence to medications (oral and inhaled) for COPD, NIPPV, and oxygen was not systematically collected as part of the QI program.

Prior to the QI program, bilevel PAP therapy without back-up respiratory rate was prescribed in only 13 (3.3%); bilevel PAP therapy with back-up rate was prescribed in only 2 (0.5%); and CPAP therapy was prescribed in only 37 (9.3%) of the 397 patients. All patients in the QI program were switched to AVAPS-AE therapy after inclusion into the program. Also, prior to the initiation of the QI program, 365 (91.3%) of the patients were prescribed oxygen for 24-h use, 27 (6.8%) were prescribed oxygen for nocturnal use only, and 3 (0.8%) were not prescribed any oxygen. Following initiation of the QI program, this changed very little, with 367 (92.4%) of the patients prescribed oxygen for 24-h use, 27 (6.8%) patients prescribed oxygen for nocturnal use only, and 3 (0.8%) were not prescribed any oxygen. There was no statistical difference in the patients' oxygen prescription status before and after the QI program was initiated ($p > 0.9$, χ^2 test).

The QI program using a multifaceted intervention reduced the number of hospital admissions in the year following their enrollment (**Table 2**, $\chi^2 = 758$, $p < 0.0001$). Seventy patients died during the one year following initiation of the multifaceted intervention and none were lost to follow-up. Of these 70 patients, 14 were transferred to hospice before they died and 4 were transferred to skilled nursing facilities or nursing homes. Considering that the deaths would reduce the number of available patients who are at risk for rehospitalization, we performed sensitivity analysis in the following manner: We excluded the 70 patients who died from the data analysis. Additionally, we assumed that the 49 patients who were re-hospitalized following the program initiation did not die during such hospitalization. Despite such assumptions, the proportion of patients who were readmitted on ≥ 2 occasions decreased from 100% (327 of 327) to 2.7% (9 of 327).

We performed simple logistic regression of the covariates that were associated with a composite outcome of death or rehospitalization (**Figure 1**, **Table 3**). Inhaled corticosteroids were associated with an increased risk for rehospitalization or death, whereas long-acting β-agonist therapy and history of hypertension were associated with a tendency for rehospitalization or death. Interestingly, inhaled antimuscarinics, oral steroids, and previous positive airway pressure

Table 1—Patient demographics.

Variable	Mean (SD)
Age (years)	66.9 ± 10.3
Male	161 (40)
Race, n (%)	
Black or African American	95 (23.9)
White	297 (74.7)
Asian	1 (0.3)
Not known	4 (1.1)
Ethnicity, n (%)	
Hispanic or Latino	4 (1)
Not Hispanic or Latino	393 (99)
COPD severity, n (%)	
GOLD 1	0 (0)
GOLD 2	9 (2.3)
GOLD 3	292 (73.6)
GOLD 4	96 (24.2)
Smoking, n (%)	
Active	128 (32.2)
Past	167 (42.1)
Never	102 (25.7)
Pack years	36.0 ± 27.6
Comorbidities, n (%)	
CAD	118 (29.7)
HF	149 (37.5)
DM	139 (35.0)
Hypertension	294 (74.1)
Depression	86 (21.7)
Anxiety	104 (26.2)
Oral medications, n (%)*	
Corticosteroids	271 (68.3)
Antibiotics	247 (62.2)
Inhaled medications, n (%)	
Corticosteroids	256 (64.5)
Muscarinic agents	322 (81.1)
SABA	355 (89.4)
LABA	218 (54.9)
Oxygen, n (%)	
24-hour	367 (92.4)
Nocturnal	27 (6.8)

SD, standard deviation; GOLD, Global Initiative for Chronic Obstructive Lung Disease; PAP therapy, positive airway pressure therapy; CAD, coronary artery disease; HF, heart failure; DM, diabetes mellitus; HTN, hypertension; SABA, short-acting β-agonists; LABA, long-acting β-agonists. *Antibiotics and steroids were prescribed as inpatient and continued as outpatient.

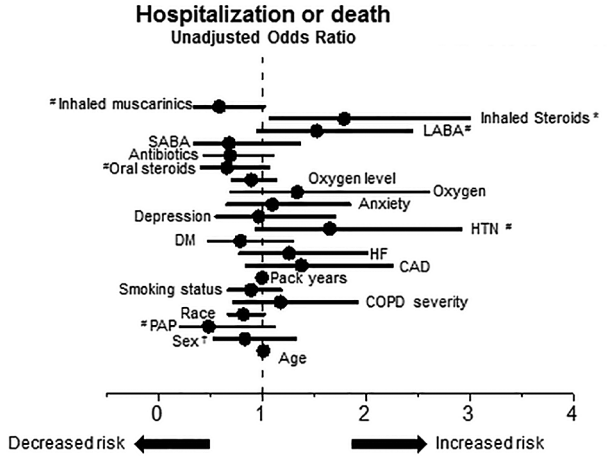
Table 2—Hospital readmissions following initiation of quality improvement program.

Number of COPD-related Admissions	Patients with admission in the year prior to program initiation (n [%])	Patients with admission in the year post program initiation (n[%])
0	0 (0%)	348 (87.7%)
1	0 (0%)	40 (10.1%)
≥ 2	397 (100%)	9 (2.2%)

Admissions among the 397 COPD patients enrolled in the QI program. n (%), unless otherwise stated. COPD = chronic obstructive pulmonary disease

therapy (CPAP or bilevel PAP) tended to be protective against death or hospitalization (**Figure 1**, **Table 3**). In multiple logistic regressions, administration of inhaled steroids was associated with increased risk for rehospitalization, whereas inhaled antimuscarinics and previous PAP therapy (CPAP or bilevel PAP) tended to be associated with a reduction of death or rehospitalization. The presence of hypertension was associated with a tendency for increased risk for hospitalization or death (**Figure 2**, **Table 4**).

Figure 1—Unadjusted odds ratios of determining variables with a composite dependent variable of rehospitalization and death (dependent variable) are shown.



Increased risk for hospitalization and death is towards the right and reduced risk is depicted by the arrow towards the left of the vertical dashed line which indicates an odds ratio of 1.0. *p value < 0.05. #p value < 0.10. PAP therapy, positive airway pressure therapy; CAD, coronary artery disease; HF, heart failure; DM, diabetes mellitus; HTN, hypertension; SABA, short acting β-agonists; LABA, long acting β-agonists. Please see Table 3 for more details.

DISCUSSION

In a retrospective cohort study of a QI initiative undertaken at a single center, we have observed that a multifaceted intervention that involved initiation of nocturnal advanced PAP modality (AVAPS-AE), RT-led respiratory care, medication reconciliation, appropriate oxygen therapy initiation, and patient education led to significant reduction in rehospitalization (**Table 2**). In this retrospective cohort, we also found that inhaled corticosteroids were associated with an increased risk for a composite outcome of rehospitalization and death. Moreover, presence of hypertension was associated with increased risk for rehospitalization and death, whereas administration of inhaled antimuscarinics was associated with reduced risk for rehospitalization and death (**Figure 2**, **Table 4**).

Previously, Linden and colleagues performed a randomized controlled trial aimed at reducing hospitalizations in patients with COPD by promoting transitional care effected by (1) better pre-discharge patient education, discharge planning, medication reconciliation, and follow-up appointment scheduling; (2) post-discharge components such as timely follow-up,

Table 3—Univariate logistic regressions with composite outcome of rehospitalizations and death as dependent variable.

Variable	B	SE	OR	95% CI	p value
Age	0.02	0.012	1.02	0.99, 1.04	0.19
Sex	−1.07	0.18	0.84	0.53, 1.34	0.46
PAP therapy	−0.72	0.43	0.49	0.21, 1.12	0.09#
Race	−0.29	0.52	0.82	0.67, 1.03	0.09#
COPD severity	0.17	0.25	1.18	0.72, 1.93	0.51
Smoking	−0.11	0.15	0.90	0.67, 1.19	0.45
Pack years	0.002	0.005	1.002	0.99, 1.01	0.70
CAD	0.32	0.25	1.38	0.84, 2.26	0.20
HF	0.23	0.24	1.26	0.79, 2.02	0.33
DM	−0.23	0.25	0.79	0.48, 1.31	0.36
HTN	0.50	0.29	1.65	0.93, 2.90	0.085#
Depression	−0.03	0.29	0.97	0.55, 1.71	0.92
Anxiety	0.09	0.27	1.10	0.66, 1.89	0.71
Oxygen	0.30	0.34	1.34	0.70, 2.61	0.38
Oxygen supply level	−0.11	0.12	0.90	0.71, 1.14	0.39
Oral steroids	−0.41	0.25	0.66	0.41, 1.08	0.09#
Antibiotics	−0.36	0.24	0.69	0.43, 1.12	0.13
SABA	−0.38	0.36	0.69	0.34, 1.27	0.29
LABA	0.42	0.24	1.53	0.95, 2.46	0.08#
Inhaled Steroids	0.58	0.27	1.79	1.07, 3.01	0.027*
Inhaled antimuscarinics	−0.53	0.28	0.59	0.34, 1.03	0.06#

*p value < 0.05. #p value < 0.10. PAP therapy, positive airway pressure therapy; CAD, coronary artery disease; HF, heart failure; DM, diabetes mellitus; HTN, hypertension; SABA, short-acting β-agonists; LABA, long-acting β-agonists; B, regression coefficient; SE, standard error; OR, odds ratio; 95% CI, 95% confidence interval.

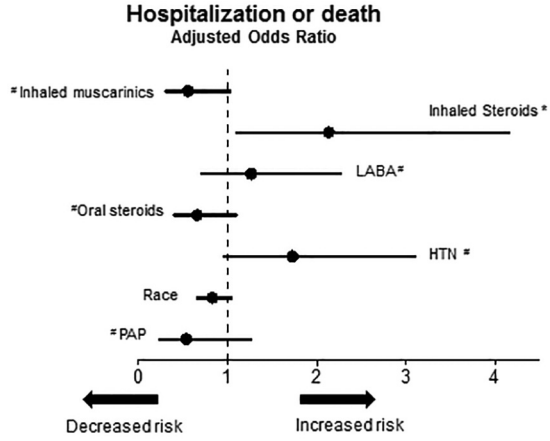
follow-up telephone call, and availability of patient hotline; and (3) patient-centered discharge instructions with motivational interviewing and interactive-voice response system to enable follow-up care after discharge. Despite implementing such care, they did not observe any reduction in rehospitalization.[8] In this report, we observed a significant reduction in rehospitalization by affecting a multifaceted intervention program that differed from that of Linden and colleagues in two key areas: first, the initiation of nocturnal ventilation with the AVAPS-AE mode of NIPPV that provided ventilator assistance in all such patients who were high risk for readmission as evidenced by two or more hospital admissions in the previous year; and second, the RT-led care that included home visits to ensure adequate medication and device-based therapy and the frequency of their home visits. A recent Cochrane review that critically reviewed the body of literature of NIPPV in patients with COPD recommended that, "future research should focus on adequate patient selection, ventilator settings, training and length of ventilation, as well as exacerbation frequency, admissions to hospital and survival."[5] Our study is responsive to such a call for research and provides compelling data that should encourage the performance of a rigorous prospective multicenter randomized controlled trial.

The mechanisms by which nocturnal ventilation with AVAPS-AE would improve COPD outcomes are unclear. There is evidence that patients with COPD suffer from insomnia, and that insomnia is independently association with mortality.[9–22] In particular, Omachi and colleagues have shown that poor sleep is cross-sectionally associated with worse COPD and is longitudinally predictive of COPD exacerbations, emergency health care utilization, and mortality.[23] Furthermore, there is recent evidence to suggest that in a population-based cohort, persistent insomnia was associated with increased risk for all-cause—particularly cardiopulmonary mortality—and was associated with a steeper increase in inflammation measures as serum C-reactive protein levels.[10] Elevated levels of CRP in individuals with COPD have been associated with increased risk of exacerbations.[24] There is evidence that NIPPV can improve sleep quality and decrease work of breathing in patients with COPD.[25–27] Conceivably, AVAPS-AE could reduce the work of breathing and thereby improve sleep quality with consequent favorable effects on inflammation and patient outcomes.[28]

Recently, the COPD Outcomes-based Network for Clinical Effectiveness and Research Translation (CONCERT) stated that research priorities in COPD should focus on studies aimed at evaluating different approaches to healthcare delivery (e.g., integrated healthcare strategies during transitions in care) rather than head-to-head comparisons of medications.[29] Specifically, integrated healthcare strategies during transitions in COPD care (e.g., early hospital discharge) were rated more than twice as important as the second-highest preferences. Our report of this QI method is responsive to such a call in that we are using a non-medication based approach to improved clinical management strategy during transition of care from hospital to home.

In a retrospective cohort study, patients with COPD treated with NIPPV at the time of hospitalization had lower inpatient mortality, shorter length of stay, and lower costs than those treated with invasive mechanical ventilation (IMV).[30] However, they did not observe any reduction in 30-day readmission in such patients receiving inpatient NIPPV when compared to those who did not receive such therapy. However, this study did not assess the impact of home-based NIPPV on readmission

Figure 2—Adjusted odds ratios of determining variables with a composite dependent variable of rehospitalization and death (dependent variable) are shown.



Increased risk for hospitalization and death is towards the right and reduced risk is depicted by the arrow towards the left of the vertical dashed line which indicates an odds ratio of 1.0. * p value < 0.05. #p value < 0.10. PAP therapy, positive airway pressure therapy; CAD, coronary artery disease; HF, heart failure; DM, diabetes mellitus; HTN, hypertension; SABA, short-acting β-agonists; LABA, long-acting β-agonists. Please see Table 4 for more details.

Table 4—Multivariate logistic regressions with composite outcome of re-hospitalizations and death as dependent variable.

Variable	B	SE	OR	95% CI	p value
PAP therapy	−0.62	0.44	0.54	0.23, 1.26	0.15
HTN	0.55	0.3	1.73	0.96, 3.11	0.07#
Oral steroids	−0.42	0.26	0.67	0.39, 1.1	0.12
LABA	0.24	0.3	1.27	0.7, 2.27	0.43
Inhaled steroids	0.76	0.34	2.13	1.09, 4.17	0.026*
Inhaled antimuscarinics	−0.59	0.32	0.56	0.30, 1.04	0.06#

* p value < 0.05. # p value < 0.10. Model R^2 = 0.09; 394 observations. PAP therapy, positive airway pressure therapy; CAD, coronary artery disease; HF, heart failure; DM, diabetes mellitus; HTN, hypertension; SABA, short-acting β-agonists; LABA, long-acting β-agonists; B, regression coefficient; SE, Standard error; OR, Odds ratio; 95% CI, 95% confidence interval.

rates. In a recent randomized controlled trial, the initiation of NIPPV in patients with severe stable COPD with $PaCO_2 \geq 52$ mm Hg resulted in mortality reduction, but an effect on rehospitalization was not discerned.[3] Conversely, there is prospective observational data that CPAP is associated with reduction of hospitalization and mortality in patients with COPD and coexistent OSA.[4] In our study, we report that the use of CPAP or bilevel PAP prior to hospitalization tended to be associated with reduced readmissions. Conceivably, prior exposure to CPAP or bilevel PAP therapy could have acclimatized the patients to better tolerate the NPPV. However, we needed greater statistical power in order to demonstrate a significant effect of CPAP or bilevel PAP therapy on rehospitalization. In our study, the use of AVAPS-AE in association with the multifaceted intervention dramatically reduced the rehospitalization risk (**Table 2**, $\chi^2 = 758$, $p < 0.0001$). Such data could suggest that advanced PAP modes such as AVAPS-AE may be superior to other conventional PAP modalities such as CPAP or bilevel PAP. Our study suggests that a head-to-head comparison of conventional modes of ventilation—such as CPAP and bilevel PAP—versus AVAPS-AE need to be performed to assess the effect of PAP therapy on hospital readmissions.

In our study, we performed regression analysis to identify factors associated with increased risk for readmission and death in our study. Interestingly, we noted that inhaled corticosteroids were associated with increased risk for readmission whereas oral steroids tended to be associated with reduced risk for readmissions (**Figure 2**, **Table 4**). There is evidence in the literature that would support such a differential effect based upon route of administration. There is evidence that outpatient treatment with oral prednisone offers an advantage over placebo in treating patients who are discharged from the emergency department or hospitalized with an exacerbation of COPD that manifests as reduction in 30-day and 90-day relapse, and time to relapse.[31,32] Although we have attributed the effect to route of administration, duration of administration may be a factor as well. Specifically, current recommendations for duration of systemic (oral) steroids in patients with COPD does not exceed 14 days. Unlike systemic steroids, inhaled corticosteroids are prescribed long-term (over many years). Others have noticed greater risk for pneumonia in patients with COPD when they receive inhaled corticosteroids and long-acting β-agonists (LABA) when compared to LABA alone.[33,34] Our study is in line with such observations. However, others have suggested that inhaled corticosteroids with LABA combination and the inhaled antimuscarinics (such as tiotropium) can improve health status and reduce exacerbation rates and are likely to have a favorable effect on mortality.[34,35]

Previously, in a retrospective database analysis, Bollu and colleagues observed that LABA therapy was associated with reduced risk for readmission.[36] While our study suggests that inhaled antimuscarinics are associated with reduced risk for hospitalization and death, we find an increased risk for such adverse consequences being associated with administration of LABA. We believe that confounding by indication is less likely to play a role in such an association, considering that antimuscarinics (which are also given for a COPD indication) tended to be associated with a reduction in rehospitalization and death (**Figure 2**). Also, it is conceivable that the LABA in the patients in our cohort study were administered in combination with inhaled corticosteroids, which are known to confer an increased risk for pneumonias in patients with COPD.[34] A history of hypertension tended to be associated with a greater risk for readmission and death. The direction of associations of various determining variables and rehospitalization risk support the internal and external validity of the findings of our study.

Limitations

We realize that our study suffers from many limitations. First, this is a retrospective before-and-after comparison following initiation of a QI program at a single center and is subject to inherent bias by the nature of such a study design. Ideally, we would need to perform a randomized controlled trial with patients receiving AVAPS-AE or usual care such as CPAP, bilevel PAP, or no PAP therapy. Second, we did not measure or adjust for adherence to the various components of our multifaceted intervention. All of the components of this multifaceted program could have been variably responsible for the observed reduction in rehospitalization that included initiation of oxygen therapy, nocturnal home ventilation with an advanced PAP (AVAPS-AE) therapy, repeated home visits, RT-led care and education that included encouragement to stop smoking, and medication reconciliation. There was no statistical difference in the patients' oxygen prescription status before and after the QI program was initiated. Therefore, initiation of oxygen therapy in 2 of the 397 patients following the implementation of the QI program was unlikely to have reduced rehospitalization. Future trials must include careful tracking of adherence to PAP therapy as well as adherence to other components of the multifaceted intervention as this is an important explanatory variable in determining patient outcomes.[37,38] Moreover, the absence of a parallel control group in this "before-and-after" study design limits our ability to ascertain the true effect of the multifaceted intervention or AVAPS-AE therapy on mortality.

CONCLUSION

In a retrospective cohort study of a QI initiative undertaken at a single center, we have observed that a multifaceted intervention that involved initiation of nocturnal AVAPS-AE, RT-led respiratory care, medication reconciliation, appropriate oxygen therapy initiation, and patient education led to a reduction in rehospitalization. Future studies need to undertake multicenter, adequately powered randomized controlled trials to assess the efficacy of such interventions.

ABBREVIATIONS

ACSC, ambulatory care-sensitive condition
adjOR, adjusted odds ratio
AHRQ, Agency of Healthcare Research and Quality
AVAPS-AE, averaged volume assured pressure support
CI, confidence interval
CONCERT, COPD Outcomes-based Network for Clinical Effectiveness and Research Translation
CMS, Center for Medicare & Medicaid Services
COPD, chronic obstructive pulmonary disease

CPAP, continuous positive airway pressure
DSM-IV, Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition
EPAP, expiratory positive airway pressure
IMV, invasive mechanical ventilation
LABA, long-acting β-agonists
LR, likelihood ratio
NIPPV, noninvasive positive pressure ventilation
OR, odds ratio
OSA , obstructive sleep apnea
$PaCO_2$, arterial partial pressure of carbon dioxide
PAP, positive airway pressure
QI, quality improvement
RT, respiratory therapist
SD, standard deviation

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