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Optimizing quality of care in patients admitted with chronic obstructive pulmonary disease exacerbation

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Abstract

Objectives: Adherence to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) treatment is variable in the inpatient setting. This study evaluates appropriateness of therapy in patients admitted to an academic medical center for AECOPD. **Methods**: This was a single-center, retrospective, observational study. The primary endpoint was proportion of patients who received appropriate AECOPD treatment within 24 h. Secondary endpoints included mean length of stay (LOS) and time to administration (TTA) of pharmacotherapy, 30-day readmission rates, and proportions of various ancillary care received. Data were analyzed using descriptive and inferential statistics. **Results**: Of 533 screened admissions, 163 were included. Of those included, 55% (n = 90) received guideline-based therapy within 24 h of presentation. This group had significantly shorter mean LOS (3.48 ± 2.61 vs 4.53 ± 3.40 days, p = .026), fewer COPD-related readmissions (7 vs 14, p = .036), and numerically fewer all-cause readmissions (14 vs 19, p = .11). Mean LOS and TTA were 3.95 ± 3.02 days and 8.47 ± 12.77 h, respectively. **Discussion:** Timely and guideline-based delivery of medications was associated with shorter length of stay and fewer COPD-related readmissions. Establishing a standardized care plan through order set implementation may be one strategy to improve care and outcomes in AECOPD patients.

Keywords

GOLD guidelines, readmissions, length of stay, guideline adherence, chronic obstructive respiratory disease

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Introduction

Chronic pulmonary obstructive disease (COPD) is one of the leading causes of death globally, and exacerbation of this disease has been associated with reduced quality of life, poor health outcomes, and a greater burden on the health care system.[1,2] Acute exacerbation of COPD (AECOPD) is clinically defined as episodes of acute worsening of dyspnea, and/or cough and sputum production, and/or increased sputum purulence.[3] Appropriate management requires a multifaceted approach.

According to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, the recommended treatment for management of AECOPD includes short-acting bronchodilators and systemic corticosteroids for all patients, while antibiotic use may be indicated for select

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patients presenting with cardinal symptoms.[3] For AECOPD readmission risk reduction, transitions of care efforts should ensure patients are discharged from the hospital with both rescue (e.g., short-acting bronchodilator) and maintenance therapy. The guideline also recommends pertinent ancillary care, including inhaler technique education, tobacco cessation, referral to pulmonary rehabilitation, and pneumococcal vaccinations to prevent future COPD exacerbation.

Though a standard of care for patients with AECOPD is clearly outlined, application of treatment guidelines remains highly variable within the inpatient setting and upon transition to outpatient care. FitzGerald et al. showed that despite proven benefit of oral corticosteroids at time of exacerbation, only 71% received treatment in the hospital setting and 43% received treatment in the outpatient setting.[4] Any gaps in care may contribute to accelerated disease progression, prolonged hospital length of stay, and increased likelihood of hospital readmission.[5,6]

This study is the first part of a two-part study that will evaluate inpatient management of AECOPD prior to and following order set implementation, with a focus on timely and GOLD guideline–directed pharmacologic therapy and the associated impact on patient outcomes of hospital length of stay and readmission rates. This initial study describes the adherence to GOLD guideline recommendations pre-order set implementation and describes differences in outcomes between patients receiving prompt guideline-appropriate therapy within 24 h versus those receiving therapy beyond 24 h of presentation or inconsistent with guideline recommendations.

Methods

Study design

The University of California, Davis Medical Center (UCDMC) is an academic medical center located in Sacramento, California. The UCDMC Institutional Review Board (IRB) approved this single-center, retrospective, and observational study. Data were collected via electronic chart review. This study was given exempt status by the IRB.

Patient population

Patients were included if they were at least 18 years of age and admitted for AECOPD between January 1 through 31 December 2018. Patients were identified using ICD-10 coding for chronic obstructive pulmonary disease with acute exacerbation (J44.1). Pregnant patients and those admitted to the ICU were excluded. Demographic information collected included sex, age, smoking status, comorbidities, illicit drug use, oxygenation dependence at home, discharge to home, mean body mass index, AECOPD treatment prior to presentation, previous admission within 30 days prior to index admission, and admitting service. Comorbidities associated with COPD exacerbation identified were defined as cardiovascular disease (chronic heart failure, hypertension, stroke, etc.), diabetes mellitus, metabolic syndrome, skeletal muscle dysfunction, osteoporosis, lung cancer, depression, and anxiety.[4–6]

Study variables

The primary endpoint was the proportion of patients who received timely guideline-appropriate therapy, which was defined as receiving all appropriate AECOPD pharmacologic treatment orders, including short-acting bronchodilators, systemic corticosteroids, and antibiotics, within 24 h of emergency department presentation.[3]

Secondary endpoints included LOS, 30-day all-cause and COPD-related readmissions, time to administration (TTA) of appropriate inpatient COPD medications, as well as transition of care outcomes related to hospital discharge: appropriate discharge COPD medication orders, receipt of pulmonary education, pneumococcal vaccination status, approval of prescription coverage assistance, and referral to outpatient pulmonary care.

Medication therapy assessment

The appropriateness of AECOPD medications was defined according to the 2018 GOLD guidelines:

- Short-acting beta-2 agonist ± short-acting anticholinergics
- Systemic corticosteroids at an equivalent dose of 40 mg of oral prednisone daily for 5 days
- Antibiotics for patients presenting with three cardinal symptoms (increase in dyspnea, sputum volume, and sputum purulence) or two of the cardinal symptoms with increased sputum purulence being one of the two symptoms.
- Azithromycin 500 mg once followed by 250 mg once daily on days 2–5 OR.
- Azithromycin 500 mg once daily for 3 days OR.
- Doxycycline 100 mg twice daily on days 1–5.

Bronchodilator, corticosteroid, and antibiotic indication, agent selection, dose, route, and frequency were collected via chart review and determined appropriate if adherent to the above GOLD recommendations.

Statistical analysis

Descriptive statistics were used to calculate the proportions, mean, and standard deviations. Data were analyzed using inferential statistics (two-sample Mann–Whitney U test for continuous variables; Fisher's exact test for categorical

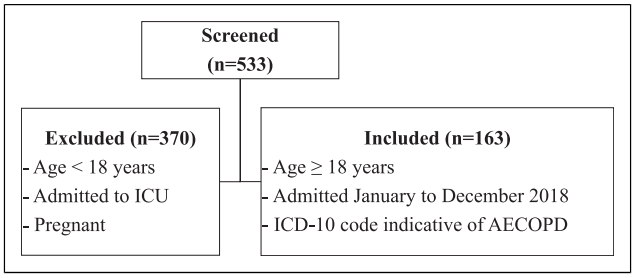

Figure 1. Screening process.

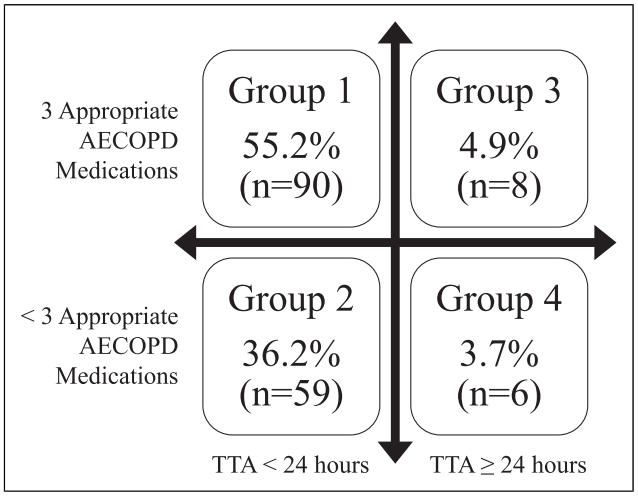

Figure 2. Proportion of admissions in which patients received AECOPD medications within or past 24 h since admission.

variables). Length of stay and readmission rates were compared between patients receiving timely and appropriate therapy to those who did not, using risk ratios and 95% confidence interval (CI). Sample size was estimated for the two-part pre-post study evaluating receipt of guideline-appropriate AECOPD therapy within 24 h before and after order set implementation. Assuming a baseline proportion of 30% patients receive appropriate treatment for COPD exacerbation within 24 h of admission, a sample size of 163 would be required for a two-sided type I error (alpha) of 0.05 with an 90% power to detect a 15% improvement in the primary outcome.

Results

Of the 533 admissions screened, 163 were included (Figure 1). Of all admissions in which patients received some sort of AECOPD treatment, only 55.2% received guideline-based therapy within 24 h (Figure 2).

Overall, more patients were female (55.8%), and patients had an average of 2.1 comorbidities (Table 1). A majority of patients were either current or former smokers. When comparing patients who received timely and guideline-adherent therapy (Group 1) to those who did not (Groups 2–4), there were no statistically significant differences between groups.

Nearly all patients (99.4%) received GOLD guideline–adherent short-acting bronchodilators. However, of the patients who met the criteria for and received antibiotics, 64.4% received an appropriate antibiotic dosing regimen, 25.2% received an inappropriate regimen with incorrect dose and/or duration of therapy, and 10.4% of patients did not receive any antibiotics despite an indication (Table 2). When evaluating route of administration, 41.3% and 58.7% received oral and intravenous antibiotic therapy, respectively.

Few patients (16%) received GOLD guideline–adherent steroid therapy equivalent to oral prednisone 40 mg by mouth once daily for 5 days (Table 3). Most patients received an appropriate duration of therapy (80.4%), but many received an inappropriate dose with 71.8% receiving a higher dose (mean equivalent prednisone daily dose 82.6 ± 42.0 mg).

Mean LOS for patients in Group 1 was shorter compared to those in Group 2–4 (3.5 ± 2.6 days vs. 4.5 ± 3.4 days; mean difference 1.1, 95% CI [0.12, 1.98]). Group 1 also had fewer 30-day COPD-related readmissions (7 vs 14; RR 0.41, 95% CI [0.17, 0.95]) and 30-days all-cause readmissions (14 vs 19; RR 0.65, 95% CI [0.32–1.11]).

Overall mean TTA was 8.5 ± 12.8 h, and overall mean hospital LOS was 4.0 ± 3.0 days. Thirty-day all-cause and COPD-related readmission rates were 20.2% (n = 33) and 12.9% (n = 21), respectively.

With respect to transitions of care outcomes, 63.8% received inpatient pulmonary education, 63.2% were up to date on pneumococcal vaccinations, 22.7% were referred to outpatient pulmonary care, 68.7% were discharged on appropriate COPD medications, and 18.4% received prescription coverage assistance (Table 4).

Discussion

Optimal treatment of AECOPD requires a multifaceted approach, and this study is one of the first to describe potential effects of timely, guideline-adherent pharmacologic therapy as well as components of nonpharmacological management at a single institution.

The vast majority of patients in our study received timely short-acting bronchodilators, but only 55% of patients (n = 90) received all three appropriate AECOPD medication classes within 24 h. These patients had both a shorter length of stay and fewer COPD-related readmissions.

While bronchodilator therapy was initiated quickly and appropriately for nearly all patients in this study, guideline-adherent use of corticosteroid and antibiotic therapy was less robust. The REDUCE trial showed that 5 days of

Table 1. Baseline and demographic information.

Demographics		Group 1 (n = 90)	Groups 2–4 (n = 73)
Mean age ± SD (years)		68.2 ± 12.8	67 ± 11.8
Mean comorbidities ± SD (No.)		2 ± 1.7	2.3 ± 1.6
Sex	Male, n (%)	39 (43.4)	33 (45)
	Female, n (%)	51 (56.7)	40 (55)
Smoking	Current, n (%)	38 (42.2)	27 (37)
	Former, n (%)	28 (31.1)	30 (41)
	Never, n (%)	24 (26.7)	16 (22)
Mean pack-year history ± SD (year)		31.2 ± 27.1	31.3 ± 28.9
Illicit drug use, n (%)		19 (21)	15 (21.4)
Prior COPD treatment, n (%)		9 (10)	6 (8)
O2 dependent, n (%)		31 (34)	18 (25)
Discharged to home, n (%)		80 (89)	65 (90)
Previous admission, n (%)		12 (13)	10 (14)
Mean body mass index ± SD (kg/m^2)		27.4 ± 10.3	28.7 ± 10.4
Palliative care consult, n (%)		2 (2)	3 (4)
Service	Hospitalist medicine, n (%)	48 (53.3)	46 (63)
	Internal medicine, n (%)	34 (37.8)	22 (30.1)
	Family medicine, n (%)	6 (6.7)	2 (2.7)
	Cardiology, n (%)	2 (2.2)	2 (2.7)
	Hematology/oncology, n (%)	0 (0)	1 (1.4)

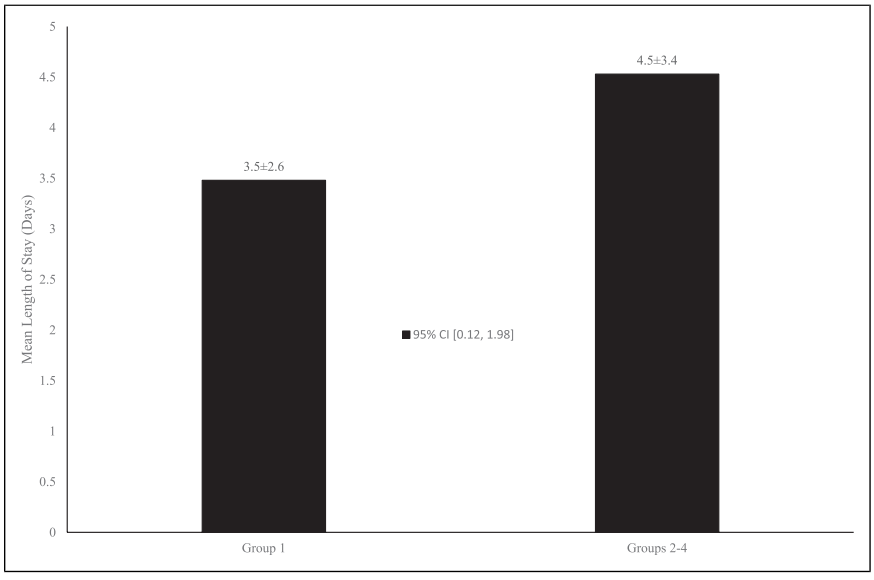

Figure 3. Mean hospital length of stay (days) in Group 1 versus Group 2–4.

prednisone 40 mg daily was noninferior to a 14-days course with respect to repeat COPD exacerbations, and additional studies have demonstrated an association of longer courses of oral corticosteroids with pneumonia and all-cause mortality.[2–8] In our study, most patients received an appropriate duration of corticosteroid therapy; however, dosing was not according to guidelines with patients being given higher doses of steroids a majority of the time. Few studies directly evaluate impact of steroid dosing in AECOPD patients, but one trial found that patients who received methylprednisolone 32 mg IV daily (equivalent to prednisone 40 mg PO daily) for 7 days significantly improved lung function, symptom scores, and oxygenation in patients admitted for COPD exacerbation compared to higher methylprednisolone doses.[9] Because steroids are not without risks, what we observed in our study suggests a need for corticosteroid stewardship regarding both dosing and route of administration.

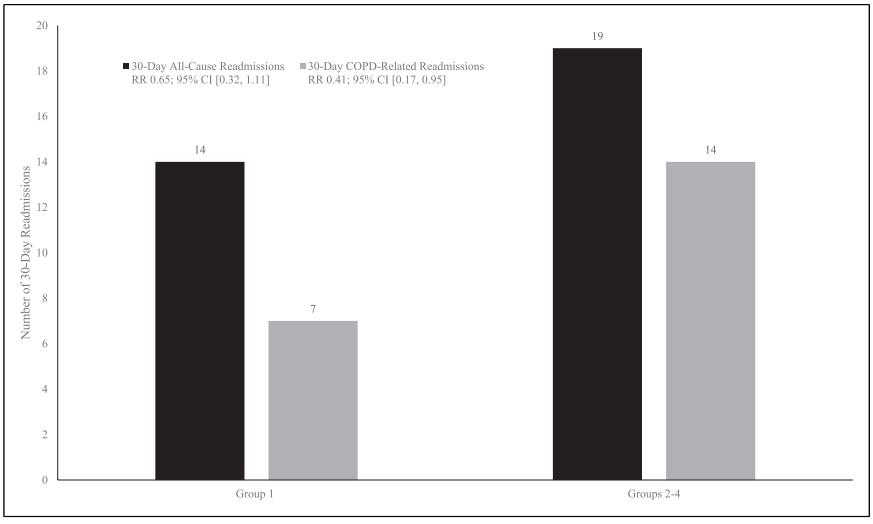

Figure 4. Number of 30-day readmissions in Group 1 vs. Group 2–4.

Table 2. Antibiotics dosing regimens.

Antibiotics	Results (n = 163)
Indicated for antibiotics, n (%)	135 (82.8)
Antibiotics given, n (%)	121 (89.6)
Regimen GOLD-guideline–adherent, n (%)	87 (64.4)
Incorrect antibiotic, dose, or duration, n (%)	34 (25.2)
Route	
Intravenous, n (%)	71 (58.7)
Oral, n (%)	50 (41.3)
Therapy omission, n (%)	14 (10.4)
Not indicated for antibiotics, n (%)	28 (17.2)
Antibiotics given, n (%)	3 (10.7)

Table 3. Systemic corticosteroids dosing regimens.

Systemic Steroids		Results (n = 163)
Oral prednisone[a] 40 mg daily for 5 days, n (%)		26 (16.0)
Therapy omission, n (%)		13 (8.0)
Oral prednisone[a] dose	40 mg daily, n (%)	29 (17.8)
	>40 mg daily, n (%)	117 (71.8)
	<40 mg daily, n (%)	4 (2.5)
Duration	5 days, n (%)	131 (80.4)
	>5 days, n (%)	12 (7.4)
	<5 days, n (%)	7 (4.3)
Route	Intravenous, n (%)	90 (55.2)
	Oral, n (%)	60 (36.8)

[a]or equivalent steroid.

Our study also demonstrated some underutilization of antibiotic therapy. A possible reason as to why some patients did not receive antibiotics when indicated could be inadequate knowledge of guidelines, specifically that indication criteria for antibiotics in AECOPD (e.g., cardinal symptoms) differ from that of other respiratory infections (e.g., fever, leukocytosis, imaging, etc.). The GOLD guidelines also discuss uncertainties about utility of antibiotics in AECOPD based upon studies that do not differentiate between bronchitis and COPD exacerbations.[3] However, a systematic review of placebo-controlled studies found that antibiotics reduce short-term mortality risk by 77% and provides evidence that supports the use of antibiotic therapy for AECOPD patients with cardinal symptoms.[10] These findings and the result of 68.7% of admissions in which patients received guideline-adherent antibiotics highlights the importance of guideline-adherence for antibiotic utilization. Furthermore, minimal data comparing oral and intravenous antibiotics exist, though the guideline prefers oral antibiotics based on the patient's oral intake.[3] Oral antibiotics are likely sufficient for management of AECOPD and should be encouraged if the patient can tolerate food or liquids. Some additional benefits of

Table 4. Transitions of care endpoints.

Secondary Endpoint	Results (n = 163)
Received inpatient pulmonary education, n (%)	104 (63.8)
Received or up to date on pneumococcal vaccination, n (%)	103 (63.2)
Received outpatient pulmonary referral, n (%)	37 (22.7)
Discharged on appropriate COPD medications, n (%)	112 (68.7)
Received prescription coverage assistance, n (%)	30 (18.4)

using oral over intravenous formulations include ease of administration, medication adherence, and cost.

In addition to evaluating the baseline standard of AECOPD pharmacotherapy, our study also investigated utilization and delivery of ancillary care. The GOLD guidelines state that evidence-based pharmacological therapy can reduce COPD symptoms, reduce frequency and severity of exacerbations, and improve health status and exercise tolerance.[3] Several studies have also demonstrated associations between decreased readmission rates and receipt of COPD inhaler teaching by inpatient respiratory therapists and outpatient pulmonologist follow-up, as well as decreased likelihood of readmissions associated with pneumococcal vaccinations.[11,12] This study identified gaps in provision of inpatient pulmonary education, outpatient pulmonary referral, guideline-adherent AECOPD discharge medications, and pneumococcal vaccinations highlighting the need to optimize transitions of care efforts to deliver guideline-based care and patient education.

The association between guideline adherence and improved patient outcomes coupled with the need to incorporate transitions of care strategies provide an actionable opportunity to explore methods to standardize delivery of guideline-adherent care in AECOPD patients. Utilization of inpatient AECOPD order sets have improved physician's adherence to providing guideline- and evidence-based pharmacologic treatment, reduced in length of hospital stay, and decreased steroid exposure.[13–17] These results suggest that computerized guideline-based AECOPD order sets at admission can be a strategy to standardize the delivery of guideline-based treatment for AECOPD, and ultimately patient outcomes.

Optimization of AECOPD patient outcomes also extends to transitions of care efforts. Multiple studies that utilized AECOPD discharge care bundles, which included optimization of medication reconciliations, referral to pulmonary rehabilitation, proper education and demonstration of inhaler technique, and assessment of smoking status, during hospital admission were associated with reduced hospital readmissions at follow-up.[18–20] In addition to implementation of a guideline-adherent AECOPD order set, utilization of discharge care bundles during hospital admission may also be considered as an option to improve post-discharge outcomes in AECOPD patients.

Lastly, COVID-19 pandemic has posed new challenges to providing guideline-adherent inpatient management of AECOPD, resulting in revision of the 2021 GOLD guidelines to address the impact of the SARS-CoV-2 virus. Despite concurrent SARS-CoV-2 infection, the pharmacological recommendations for treatment of COPD exacerbations remain unchanged. The barriers of delivering GOLD guideline–optimized care in the midst of COVID-19 pandemic include limited access to therapy due to medication and hospital personnel shortages, and economic burden. Alqahtani et al. found that there was a 50% reduction in admissions for COPD exacerbations compared to pre-pandemic times possibly brought about by improved hand hygiene, social distancing and use of facial coverings reducing transmission of respiratory viruses.[21] However, the COVID-19 pandemic continues to change the healthcare infrastructure, and how management of COPD exacerbations will change in the future remains unclear.

Limitations

This study was a single-center, retrospective study with a small and underpowered sample size, as well as statistically non-significant findings. It did not account for the possibility that any patient could have been previously admitted to or had a subsequent readmission following discharge from a different hospital. COPD exacerbation was identified using coded diagnoses at discharge. However, coded diagnosis may not be fully representative of patients' baseline health. For example, baseline pulmonary function tests were rarely documented in the electronic medical record. Low baseline lung function could allude to higher risk of COPD exacerbation, and thus could have confounded data. However, of note, few studies have identified clinical significance between baseline function and exacerbation.

Furthermore, this study did not assess COPD-related and all-cause hospital readmissions beyond the 30-day post-discharge from first AECOPD admission during the study enrollment period. There is a possibility that patients who received prescription coverage assistance had delayed re-admissions that were not captured by the 30-day readmission endpoints.

In addition, inconsistent documentation about cardinal symptoms of infection upon admission could have skewed

the appropriateness of antibiotic prescribing. Last, the prior-to-admission COPD medications were not analyzed; patients who were previously on inappropriate maintenance therapy would have a higher risk of poorer outcomes unrelated to the delivery of care they received at their current admission.

Conclusion

Management of AECOPD patients in the inpatient setting should be comprehensive in both the pharmacological and nonpharmacological aspects of care. While adherence to GOLD guidelines should be encouraged, it must also be partnered with patient-centered care and multidisciplinary teams with strong clinical leadership to be effectively executed and utilized to improve patient outcomes. This study suggests that optimizing delivery of GOLD guideline–adherent care may positively impact hospital LOS and 30-day COPD-related readmissions. However, confounding factors described in the limitations section prevent drawing further conclusions more definitively. This study also identified a gap in both pharmacologic and ancillary care in AECOPD patients, implicating the need for a standardized care plan. Order set implementation may be an effective strategy to promote consistent delivery of COPD comprehensive care and guideline adherence.

Declaration of conflicting interests

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