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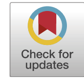

# Management of patients with COPD in the emergency department and treatment compliance with clinical guideline recommendations at discharge

Mónica Sachi Martínez Mihara [a,b], Isabel Pérez Pañart [a], María Sánchez Salamero [a], Eva Campos Picontó [a], Sara Patricia Canales Villa [a], Víctor Latorre [c], Daniel Sáenz Abad [a,b,d,*]

[a] Servicio de Urgencias. Hospital Clínico Universitario Lozano Blesa, Zaragoza, España
[b] Instituto de Investigación Sanitaria Aragón (IIS Aragón), Zaragoza, España
[c] Evidenze Health España S.L.U., Spain
[d] Universidad de Zaragoza, Zaragoza, España

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ABSTRACT

*Background:* Chronic obstructive pulmonary disease (COPD) exacerbations are a frequent cause of emergency department visits and are associated with high morbidity, mortality, and healthcare costs. These visits represent an opportunity to optimize patient management and align treatment with guideline recommendations, particularly regarding inhaled triple therapy.

*Objectives:* To describe the clinical characteristics and management of COPD patients in the emergency department and to identify factors associated with inhaled triple therapy prescription at discharge.

*Methods:* Retrospective observational study including patients aged >18 years attended at the emergency department of the Hospital Clínico Universitario (Zaragoza, Spain) between July and December 2022, with a diagnosis of COPD exacerbation at discharge. Demographic, clinical, laboratory, and therapeutic variables were analyzed. Logistic regression identified independent predictors of inhaled triple therapy prescription at discharge.

*Results:* A total of 227 patients were included (mean age: 74.4 years; 70.9% male). Most (93.4%) had a prior COPD diagnosis, and 41.0% were already on maintenance inhaled triple therapy. At discharge, inhaled triple therapy was prescribed in 53.8% of the cases. Independent variables associated with triple therapy prescription included prior use of inhaled triple therapy (odds ratio [OR]:9.4), long-term home oxygen therapy (OR:4.3), and influenza vaccination (OR:3.1). Six months after discharge, 36.0% of patients required hospital admission for COPD exacerbation.

*Conclusions:* One-third of COPD patients discharged from the emergency department do not receive guideline-recommended inhaled triple therapy. Interventions aimed at standardizing and optimizing emergency department management are needed to improve adherence to clinical guidelines and improve patient outcomes.

## Introduction

Chronic obstructive pulmonary disease (COPD) is a lung condition characterized by persistent respiratory symptoms such as dyspnea, cough, and sputum production, and chronic airflow limitation.[1] The main factors causing COPD are smoking, exposure to contaminants,

*Abbreviations:* CEICA, Comité Ético de Investigación Clínica de Aragón (Clinical Research Ethics Committee); CI, Confidence interval; COPD, Chronic obstructive pulmonary disease; COVID-19, Coronavirus disease; ED, Emergency Department; FEV1, Forced expiratory volume in one second; FVC, Forced vital capacity; GesEPOC, Guía Española de la EPOC (Spanish COPD Guidelines); GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, Inhaled corticosteroids; ICU, Intensive care unit; IQR, Interquartile range; LABA, Long-acting beta-agonist; LAMA, Long-acting muscarinic antagonist; mMRC, Modified Medical Research Council; NIV, Non-invasive ventilation; OCS, Oral corticosteroids; OR, Odds ratio; PCR, Polymerase chain reaction; RSV, Respiratory syncytial virus; SABA, Short-acting beta-agonist; SAMA, Short-acting muscarinic antagonist; SD, Standard deviation; TT, Triple therapy.

* Corresponding author at: Hospital Clínico Universitario Lozano Blesa, C. de San Juan Bosco, 15 50009, Zaragoza, España.
*E-mail address:* 303222@unizar.es (D. Sáenz Abad).

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genetic factors, and infections.[2,3]

COPD is one of the major causes of mortality and was the fourth leading cause of death in the world in 2021.[4] According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), in 2019 more than 390 million people aged 30-79 years worldwide were affected by COPD, representing a prevalence of 10.3%.[2] In Spain, a study published in 2021 estimated a prevalence of 11.8% in the adult population over 40 years of age.[5]

The diagnosis and determination of COPD severity are based on the use of spirometry and the determination of the ratio of forced expiratory volume in one second to forced vital capacity ($FEV_1$/FVC), according to the GOLD criteria.[6,7]

The course of COPD includes episodes of acute worsening of respiratory symptoms, known as exacerbations or flare-ups, which are associated with increased airway inflammation and are more common in patients with moderate and severe COPD.[3,8] COPD exacerbations are a major health problem. They are associated with increased morbidity and mortality, poorer patient quality of life and survival, and a greater use of resources and associated costs, both direct due to hospitalizations and drug treatment, and indirect due to productivity losses, which are higher in patients with flare-ups.[9–11]

Treatment of COPD aims to reduce and control the symptoms of the disease, as well as to reduce the frequency and severity of exacerbations.[6,7] The Spanish COPD Guidelines (GesEPOC) propose the use of inhaled treatments with long-acting bronchodilators (long-acting beta-agonist (LABA) and long-acting muscarinic antagonist (LAMA)) as first option for most patients with COPD, and their combination with inhaled corticosteroids (ICS), constituting inhaled triple therapy (TT), in the case of patients with exacerbations - especially those with high eosinophil counts.[7,12] Blood eosinophil count has emerged as a clinically useful biomarker to guide the use of inhaled corticosteroids in COPD. Eosinophilia has been shown to correlate with increased type 2 airway inflammation, which is more responsive to corticosteroid therapy. Clinical studies have consistently demonstrated that patients with higher blood eosinophil counts derive a greater reduction in exacerbation risk from ICS-containing regimens, whereas patients with low eosinophil levels obtain less benefit and may be exposed to an increased risk of adverse effects. Consequently, current clinical guidelines recommend incorporating blood eosinophil count, together with exacerbation history, into therapeutic decision-making when considering inhaled TT.[12]

COPD exacerbations are an important cause of hospital emergency department (ED) visits.[13] In this context, the scarce available evidence shows that the management of patients with COPD exacerbations in the ED is often suboptimal and not fully aligned with current clinical guidelines.[14,15] Therefore, ED visits represent an opportunity to align patient management with current clinical guideline recommendations.

In this context, the primary objective of the present study was to assess compliance with the recommendations of the Spanish GesEPOC Guidelines for treatment with inhaled TT prescribed at discharge in patients with exacerbated COPD. In addition, we describe the general management and clinical characteristics of COPD patients with exacerbations in an ED.

## Methods

### *Study design and population*

Retrospective observational study reviewing data from the medical records of patients over 18 years of age seen between 1 July and 19 December 2022 at the ED of Hospital Clínico Universitario Lozano Blesa, Zaragoza (Spain), with acute exacerbation of COPD diagnosed at discharge. No additional exclusion criteria were applied. All consecutive adult ED visits during the study period were screened, and patients were included if the ED discharge diagnosis (home discharge or hospital admission) was coded as acute COPD exacerbation or closely related COPD-exacerbation diagnoses according to the local ED coding system. Patients were evaluated and diagnosed in the ED, and were discharged home or admitted for subsequent follow-up. The diagnosis of acute COPD exacerbation was established by the attending emergency physician based on clinical presentation and review of prior medical records. In patients with a previous diagnosis of COPD, spirometric data were reviewed when available; however, spirometry was not available for all patients at the time of the ED visit.

The study was approved by the Clinical Research Ethics Committee of Aragon (*Comité Ético de Investigación Clínica Aragón*, CEICA), and was conducted in accordance with the guidelines of the Declaration of Helsinki.

Since this was a retrospective study reviewing clinical histories in which pseudonymized data were obtained, it was not considered necessary to obtain informed consent from the patients included in the study, nor was it required by the CEICA. To minimize potential sources of bias, all consecutive patients meeting the inclusion criteria during the study period were included. Data were extracted using a predefined, investigator-developed data abstraction protocol that specified the variables to be collected from the electronic medical records. This protocol was designed to ensure consistency across reviewers and was not a clinical management protocol.

### *Variables*

Demographic characteristics and vital signs at triage were recorded. Clinical data collected on arrival to the ED included a previous diagnosis of COPD and comorbidities.

A previously diagnosed COPD was defined as a documented diagnosis of COPD in the electronic medical record prior to the index ED visit and did not require the availability of spirometric data for all patients. Spirometric measurements were reviewed when available, and FEV1 values were extracted from the most recent pulmonary function test performed within the previous 12 months. As a result, recent FEV1 data were available for a subset of patients.

Information on prior ED visits and hospital admissions, symptoms related to COPD during the ED stay, previous COPD treatments, variables related to admission (including intubation, oxygen therapy, and treatment), imaging findings, diagnostic tests, laboratory results, therapies prescribed at discharge, and subsequent ED visits and hospital admissions due to COPD were also collected.

Dyspnea was assessed using the modified Medical Research Council (mMRC) dyspnea scale, which ranges from grade 0 (no dyspnea except with strenuous exercise) to grade 4 (very severe dyspnea, limiting basic activities). Dyspnea grading was based on patient-reported symptoms documented by the attending physician during the ED evaluation.

For the purposes of this study, a patient was considered an exacerbator if they had ≥2 ED visits, ≥1 hospital admission, or ≥1 intensive care unit admission due to COPD exacerbation in the previous 12 months. This operational definition primarily captures moderate-to-severe exacerbations requiring hospital-based care. According to current clinical guidelines, an ‘exacerbator phenotype’ eligible for inhaled TT is defined by the occurrence of one or more moderate or severe exacerbations, particularly in the presence of elevated blood eosinophil counts.[12]

For exploratory analyses, a “*typical patient*” candidate for inhaled TT at discharge was defined as an exacerbator patient presenting any of the following conditions: maximum historical eosinophil count ≥300 cells/$mm^3$; maximum historical eosinophil count 100–300 cells/$mm^3$ while receiving previous dual inhaled therapy without ICS; or concomitant asthma.

### *Statistical analysis*

Quantitative variables are described using measures of central tendency (mean, median) and dispersion measures (standard deviation

[SD], interquartile range [IQR]). Qualitative variables are reported as absolute frequencies and percentages.

The Student's *t*-test or Mann-Whitney *U test*, depending on the sample distribution, were used for the comparative study of continuous variables. For variables with more than two categories, analysis of variance (ANOVA) or the Kruskal-Wallis test was applied. The Chi-squared test or Fisher's exact test were used to compare qualitative variables.

A multivariate logistic regression model was constructed with inhaled TT prescription at discharge as the dependent variable and single outcome of interest. Independent variables included demographic, clinical, and laboratory characteristics, prior treatment, and previous emergency department visits or hospital admissions that showed a p-value <0.20 in bivariate analyses. Variables with ≥20% missing data or with at least one category representing <15% of the total sample were excluded from the model. Odds ratios (ORs) with 95% confidence intervals (CIs) are reported.

All analyses were performed using the SAS version 9.4 statistical package. Statistical significance between variables was considered for $p < 0.05$.

## Results

### *Patient characteristics*

The study included 227 patients with a mean (SD) age of 74.4 (10.4) years. Most (n = 161, 70.9%) patients were male, and 174 (78.0%) were current or former smokers (Table 1).

211 patients (93.4%) had a previously diagnosed COPD, with a mean (SD) of 1.3 (1.9) visits to the ED due to COPD exacerbation and 1.0 (1.7) hospital admissions due to this condition in the previous 12 months. Among those with available spirometry, the majority had moderate-to-severe airflow limitation, reflecting a clinically severe cohort (Table 1).

Considering the previous number of visits to the ED, 86 patients (37.9%) were classified as exacerbators.

With regard to previous treatment received for the management of COPD, 93 patients (41.0%) were users of inhaled maintenance TT and 113 (50.7%) had received oral corticosteroids in the previous 12 months. In addition, 74 patients (32.6%) received chronic home oxygen therapy (Table 2).

### *Clinical condition of the patient on arrival to the ED*

During examination in the ED, the degree of dyspnea was assessed in 143 patients (64.1%), of whom 93 (41.7%) had grade 4 dyspnea. In addition, 140 (64.5%) and 155 patients (75.6%) presenting to the ED reported sputum and cough, respectively. COPD severity was assessed in 139 patients (61.2%) using $FEV_1$ values obtained from the most recent pulmonary function test performed within the previous 12 months; spirometry was not routinely performed during the ED visit. Among patients with available spirometry, 64.0% had moderate-to-severe airflow limitation (GOLD stages 3–4, FEV1 <50%), reflecting a clinically severe population with a higher risk of exacerbations. In addition, a substantial proportion of patients required ventilatory support, including non-invasive ventilation, and underwent venous or arterial blood gas analysis, with a relevant proportion showing hypercapnia, further supporting the severity of exacerbations in this cohort (Table 3).

For the comprehensive assessment of COPD, an electrocardiogram was performed in approximately half of the patients (49.8%), and X-rays and blood gases were performed in almost all cases (>95%). Testing for the presence of virus (COVID-19, influenza and RSV) was performed in 118 patients (52.7%). In addition, laboratory tests showed a mean (SD) of 105.4 (173.6) cells/mm$^3$ in the eosinophil count (Table 3).

**Table 1**
Patient demographic and clinical characteristics on arrival to the ED.

| Characteristics | Value |
|---|---|
| **Age** (years), mean (SD) (n = 227) | 74.4 (10.4) |
| **Sex**, n (%) (n = 227) | |
| Female | 66 (29.1) |
| Male | 161 (70.9) |
| **Smoking**, n (%) (n = 223) | |
| Smoker | 66 (29.6) |
| Ex-smoker | 108 (48.4) |
| Non-smoker | 14 (6.3) |
| **Comorbidities** | |
| **Asthma**, n (%) (n = 226) | 13 (5.8) |
| **Pulmonary thromboembolism**, n (%) (n = 226) | 6 (2.7) |
| **Pneumonia**, n (%) (n = 225) | 51 (22.7) |
| **Cardiac conditions**, n (%) | |
| Ischemic heart disease (n = 227) | 30 (13.2) |
| Heart failure (n = 226) | 40 (17.7) |
| Arterial hypertension (n = 227) | 138 (60.8) |
| Atrial fibrillation or flutter (n = 227) | 37 (16.3) |
| **Diabetes mellitus**, n (%) (n = 227) | 71 (31.3) |
| **COPD-related data** | |
| **Previously diagnosed COPD**, n (%) (n = 226) | 211 (93.4) |
| **Spirometry in the previous year**, n (%) (n = 222) | 81 (36.5) |
| **GOLD classification according to last $FEV_1$**, n (%) (n = 139) | |
| Mild (≥80) | 9 (6.5) |
| Moderate (50–79) | 41 (29.5) |
| Severe (30–49) | 62 (44.6) |
| Very severe (<30) | 27 (19.4) |
| **ED visits and previous admissions due to COPD** | |
| **Number of previous visits to the ED**, mean (SD) | |
| In the previous 6 months (n = 224) | 0.9 (1.3) |
| In the previous 12 months (n = 227) | 1.3 (1.9) |
| **Number of hospital admissions**, mean (SD) | |
| In the previous 6 months (n = 225) | 0.6 (1.1) |
| In the previous 12 months (n = 225) | 1.0 (1.7) |
| **Number of ICU admissions**, mean (SD) | |
| In the previous 6 months (n = 225) | 0.06 (0.2) |
| In the previous 12 months (n = 225) | 0.06 (0.2) |
| **Vaccines received**, n (%) | |
| Influenza (n = 226) | 190 (84.1) |
| Pneumococcus (n = 226) | 105 (46.5) |
| COVID-19 (n = 226) | 212 (93.8) |
| 1 dose | 2 (0.9) |
| 2 doses | 27 (12.1) |
| 3 doses | 111 (49.8) |
| ≥4 doses | 72 (32.3) |

COPD: chronic obstructive pulmonary disease; COVID-19: coronavirus disease; ED: Emergency Department; $FEV_1$: forced expiratory volume in one second; GOLD: Global Initiative for Chronic Obstructive Lung Disease; ICU: Intensive Care Unit; SD: standard deviation;.

**Table 2**
Previous therapy for the management of COPD.

| Treatment | N (%) |
|---|---|
| **Bronchodilator/corticosteroid**, n (%) | |
| SABA (n = 226) | 86 (38.1) |
| LAMA (n = 227) | 37 (16.3) |
| LABA (n = 227) | 2 (0.9) |
| LAMA+LABA (n = 227) | 46 (20.3) |
| ICS (n = 227) | 13 (5.7) |
| LAMA+ICS (n = 227) | 2 (0.9) |
| LABA+ICS (n = 227) | 56 (24.7) |
| LAMA+LABA+ICS (single device) (n = 227) | 93 (41.0) |
| OCS (n = 227) | 30 (13.2) |
| OCS in previous 12 months (n = 223) | 113 (50.7) |
| **Oxygen therapy/ventilatory support**, n (%) | |
| Chronic home oxygen therapy (n = 227) | 74 (32.6) |
| Home NIV (n = 227) | 47 (20.7) |

ICS: inhaled corticosteroids; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic antagonist; NIV: non-invasive ventilation, OCS: oral corticosteroids; SABA: short-acting beta-agonist.

**Table 3**
Clinical condition and tests performed during the ED visit.

| Characteristics | Value |
|---|---|
| **Dyspnea**[a], n (%) | |
| Usual dyspnea assessed (n = 109) | |
| Grade 0 | 9 (4.1) |
| Grade 1 | 16 (7.4) |
| Grade 2 | 49 (22.6) |
| Grade 3 | 28 (12.9) |
| Grade 4 | 7 (3.2) |
| Dyspnea assessed in the ED (n = 143) | |
| Grade 0 | 5 (2.2) |
| Grade 1 | 3 (1.3) |
| Grade 2 | 12 (5.4) |
| Grade 3 | 30 (13.5) |
| Grade 4 | 93 (41.7) |
| **Sputum**, n (%) | |
| Usual sputum assessed (n = 109) | 52 (47.7) |
| Sputum assessed in the ED (n = 217) | 140 (64.5) |
| Mucosal | 48 (34.3) |
| Purulent | 46 (32.9) |
| Rust-colored | 13 (9.3) |
| Hemoptoic | 4 (2.9) |
| **Cough**, n (%) | |
| Usual cough assessed (n = 121) | 55 (45.5) |
| Cough assessed in the ED (n = 205) | 155 (75.6) |
| **Fever**, n (%) (n = 204) | 64 (28.6) |
| **COPD severity assessment ($FEV_1$)**, n (%) (n = 227) | 139 (61.2) |
| **Tests performed for diagnosis** | |
| **Electrocardiogram**, n (%) (n = 113) | |
| Sinus node rhythm | 89 (78.8) |
| Atrial fibrillation/flutter | 15 (13.3) |
| Other | 9 (8.0) |
| **X-ray**, n (%) (n = 223) | |
| Normal | 125 (56.1) |
| Pneumonia without effusion | 30 (13.5) |
| Pneumonia with effusion | 6 (2.7) |
| Pneumothorax | 1 (0.4) |
| Heart failure | 3 (1.3) |
| Other | 58 (26.0) |
| **Blood gases**, n (%) (n = 217) | |
| Basal venous | 67 (30.9) |
| Basal arterial | 80 (36.9) |
| Venous $O_2$ | 8 (3.7) |
| Arterial $O_2$ | 43 (19.8) |
| **Virus PCR**, n (%) (n = 224) | 118 (52.7%) |
| Negative | 74 (33.0) |
| COVID-19 | 11 (4.9) |
| Influenza | 11 (4.9) |
| RSV | 7 (3.1) |
| COVID-19 + influenza | 0 (0.0) |
| COVID-19 + RSV | 0 (0.0) |
| RSV + influenza | 0 (0.0) |
| COVID-19 + RSV + influenza | 15 (6.7) |
| **Laboratory tests**, mean (SD) | |
| pH (n = 218) | 7.4 (0.07) |
| Partial pressure $O_2$ (mmHg) (n = 216) | 61.1 (26.5) |
| Partial pressure $CO_2$ (mmHg) (n = 218) | 49.0 (16.0) |
| Bicarbonate (nmol/L) (n = 218) | 26.9 (4.8) |
| Hemoglobin (g/dL) (n = 220) | 13.50 (1.98) |
| Leukocytes (cells/$mm^3$) (n = 221) | 11,722 (10,184.9) |
| Neutrophils (cells/$mm^3$) (n = 217) | 8774.6 (4259.3) |
| Eosinophils (cells/$mm^3$) | |
| Previous laboratory tests (n = 219) | 196.5 (205.6) |
| Current laboratory tests (n = 212) | 105.4 (173.6) |
| Historical maximum (n = 222) | 229.2 (221.9) |
| Platelets ($10^3$ x cells/$mm^3$) (n = 220) | 229.2 (95.8) |
| Glucose (mg/dL) (n = 220) | 142.7 (55.6) |
| Urea (mg/dL) (n = 219) | 36.4 (30.6) |
| Creatinine (mg/dL) (n = 221) | 1.08 (0.4) |
| C-reactive protein (mg/L) (n = 209) | 55.6 (64.8) |
| Sodium (mmol/L) (n = 220) | 138.4 (4.6) |
| Potassium (mmol/L) (n = 213) | 4.5 (0.6) |

COVID-19: coronavirus disease; ED: Emergency department; PCR: polymerase chain reaction; RSV: respiratory syncytial virus
[a] mMRC (Modified Medical Research Council) dyspnea scale

### *Treatment for COPD prescribed in the ED and factors associated with the use of inhaled TT at discharge*

The therapy most commonly prescribed at discharge after an ED visit was inhaled treatment, which was prescribed for 200 patients (88.9%). Among them, 167 patients (74.2%) received inhaled corticosteroid–containing regimens, including either dual therapy (ICS–LABA) or inhaled TT, while 121 patients (53.8%) were prescribed inhaled TT. In addition, 92 patients (40.9%) were prescribed an antibiotic (Table 4).

No statistically significant relationship was found between the treatment prescribed at discharge from the ED in the form of inhaled TT or ICS, respectively, and the classification of the patients as *"typical patients"* or not (n = 37) (Table 5).

The results of the logistic regression analysis (n = 163) showed the prior use of inhaled TT (OR [95% CI]: 9.4 [4.1–21.3], $p < 0.0001$), chronic home oxygen therapy (OR [95% CI]: 4.3 [1.9–10.1], $p < 0.001$) and influenza vaccination (OR [95% CI]: 3.1 [1.1–8.7], $p = 0.03$) to be significantly associated with the prescription of inhaled TT at discharge in patients with COPD.

### *Follow-up of patients with COPD*

The main destination after discharge was admission to the Pulmonology and Internal Medicine Departments (n = 134, 59.3%), or discharged home (n = 87, 38.5%) (Table 6).

Within 30 days of discharge, 11 patients (4.9%) died. Due to the retrospective nature of the study, cause-specific mortality could not be reliably determined, and deaths were not necessarily attributable to COPD alone. In the same period, 74 patients (33.2%) were evaluated for COPD in the Pulmonology or Internal Medicine Departments. 6 months after discharge, 138 (61.9%), 104 (46.6%) and 80 patients (36.0%) were evaluated at a specialty clinic (Pulmonology or Internal Medicine), visited the ED, or were admitted due to a COPD exacerbation, respectively.

## Discussion

This study describes the characteristics and management of a cohort of patients reporting to an ED due to COPD exacerbation. In addition, the possible factors related to the prescription of inhaled TT at discharge, a treatment recommended by the GesEPOC management Guidelines for this patient profile,[12] were evaluated.

**Table 4**
Treatment for COPD prescribed at discharge from the ED.

| | N (%) |
|---|---|
| **Bronchodilator/corticosteroid**, n (%) | |
| SABA (n = 224) | 71 (31.7) |
| SAMA (n = 225) | 43 (19.1) |
| LAMA (n = 225) | 25 (11.1) |
| LABA (n = 225) | 1 (0.4) |
| LAMA+LABA (n = 225) | 26 (11.6) |
| ICS | |
| Single device (n = 225) | 11 (4.9) |
| Any device (n = 225) | 167 (74.2) |
| LAMA+ICS (n = 225) | 4 (1.8) |
| LABA+ICS (n = 225) | 57 (25.3) |
| LAMA+LABA+ICS (single device) (n = 225) | 99 (44.0) |
| Inhaled therapy (n = 225) | 200 (88.9) |
| Inhaled LAMA+LABA+ICS (n = 225) | 121 (53.8) |
| OCS (n = 225) | 99 (44.0) |
| **Oxygen therapy/ventilatory support**, n (%) | |
| Chronic home oxygen therapy (n = 224) | 88 (39.3) |
| Home NIV (n = 225) | 52 (23.2) |
| **Antibiotic**, n (%) (n = 225) | 92 (40.9) |

ICS: Inhaled corticosteroids; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic antagonist; NIV: non-invasive ventilation; OCS: oral corticosteroids; SABA: short-acting beta-agonist; SAMA: short-acting muscarinic antagonist.

**Table 5**
Relationship between treatment prescribed at discharge with inhaled TT and ICS, respectively, and classification as "typical patients".

| Variable | Typical patient | | p-value |
|---|---|---|---|
| | Yes | No | |
| **Inhaled TT at discharge** | | | 0.45 |
| Yes | 22 (59.5) | 99 (52.7) | |
| No | 15 (40.5) | 89 (47.3) | |
| **ICS at discharge** | | | 0.83 |
| Yes | 28 (75.7) | 139 (73.9) | |
| No | 9 (24.3) | 49 (26.1) | |

ICS: inhaled corticosteroids; TT: triple therapy.
Typical patient group (n = 37) used as reference category.

**Table 6**
Follow-up of patients after discharge from the ED.

| | N (%) |
|---|---|
| **Destination at discharge**, n (%) (n = 226) | |
| Discharge home | 87 (38.5) |
| Observation room | 0 (0.0) |
| Admission to Pulmonology | 106 (46.9) |
| Admission to Internal Medicine | 28 (12.4) |
| ICU | 2 (0.9) |
| Death | 1 (0.4) |
| Other | 2 (0.9) |

ICU: intensive care unit.

Although COPD exacerbations are one of the main causes of visits to EDs, the available evidence on the management of these patients in the setting of Spanish emergency services is scarce.

The characteristics of our patient cohort were consistent with those reported in major COPD trials, with a predominance of current or former smokers and a mean age of approximately 70 years.[16–18] Exposure to tobacco smoke is a clearly established risk factor for COPD and a trigger for exacerbations,[19] and also increases the risk of readmission.[20] Therefore, visits to the ED are a good time to emphasize the importance of smoking cessation as a non-pharmacological treatment measure, following the recommendations of the GesEPOC,[7,12] and could contribute to reducing the number of visits to the ED and readmissions due to COPD after discharge.

Most patients reporting to the ED had previously diagnosed COPD, and approximately one previous visit to the ED and one admission due to COPD in the past year. Despite this high percentage, it is notable that less than half of the patients were users of maintenance inhaled TT, and approximately half had received oral corticosteroids in the previous 12 months. The treatment patterns of the patients in our study are similar to those reported by previous studies conducted in patients with COPD reporting to an ED. A German study reported that only 30% of patients with COPD received treatment with inhaled TT, and that the presence of dyspnea was more common in patients with a low dose of inhaled therapy as compared to those treated with the corresponding dose according to the treatment guidelines.[21] On the other hand, two studies conducted in Canada showed that the management of patients with COPD reporting to the ED is not adequate, and that only half of these individuals were prescribed appropriate treatment.[22,23] Overall, these data indicate that the management of patients with COPD presenting to ED is frequently suboptimal in terms of long-term treatment regimens. The consistency of this finding across different healthcare systems suggests that this is a global issue rather than a context-specific one. Beyond clinical factors, this phenomenon may reflect the influence of broader, multifactorial determinants, including socioeconomic and structural factors, which can affect access to care, continuity of follow-up, and implementation of guideline-recommended therapies.

In healthcare systems with universal coverage, such as those in Spain and many European countries, limited use of guideline-recommended inhaled TT is unlikely to be primarily driven by cost or insurance barriers. Instead, this finding may reflect a combination of factors, including fragmentation of care, variability in access to respiratory specialty follow-up, therapeutic inertia, and challenges in translating guideline recommendations into routine clinical practice. In addition, ED visits often focus on acute management, and opportunities to reassess and optimize long-term maintenance therapy may be missed, underscoring the need for better integration between acute and outpatient care.

Adherence to guideline-recommended inhaled TT outside the ED setting is known to be variable, even in outpatient and specialist clinics, reflecting the complexity of COPD management in real-world practice. Although our study was not designed to assess treatment adequacy in the ambulatory setting, the low proportion of patients already receiving or newly prescribed TT at discharge suggests that suboptimal adherence to guideline-recommended treatment may extend beyond the ED setting. In this context, ED visits may represent a critical opportunity to reassess disease severity and optimize long-term treatment. Exploratory multidisciplinary strategies, such as the involvement of clinical pharmacists in the ED to support prescription of appropriate inhaled therapy, provide patient education, and ensure structured follow-up, could be valuable interventions to improve guideline adherence and continuity of care.

After diagnosis in the ED, approximately 60% and 40% of the patients were admitted to the Pulmonology or Internal Medicine Department or discharged home, respectively, and a single death was recorded during the ED visit. However, 11 patients had died 30 days after discharge. Our results align with those published in previous studies referred to patient discharge and mortality rates.[16,23–25] At 6 months, a high percentage of patients in our cohort visited the ED or were admitted due to COPD. Some studies suggest that patients with COPD who go to the ED and are discharged home have a higher readmission rate than those who are hospitalized after their stay in the ED.[22] This could at least partially explain the high percentage of patients in our cohort who returned to the ED or were admitted due to COPD 6 months after discharge. Given that treatment prescribed at discharge was frequently not aligned with guideline recommendations, suboptimal long-term management may have contributed to subsequent ED visits or hospital readmissions; however, causality cannot be established due to the observational nature of the study.

Our operational definition of exacerbator status was based on ED visits and hospital admissions and therefore primarily captures moderate-to-severe exacerbations requiring hospital-based care. As a result, moderate exacerbations managed exclusively in the outpatient setting—often treated with short courses of oral corticosteroids by primary care providers—may not have been fully captured. This is supported by the observation that a higher number of patients received oral corticosteroids in the previous 12 months compared with those classified as exacerbators based on ED utilization. This difference likely reflects exacerbations managed outside the hospital setting.

An interesting finding was the high prevalence of bronchitic symptoms, such as cough and sputum production, among patients presenting to the ED. Although these symptoms are commonly associated with a phenotype that may benefit from optimized inhaled therapy, a substantially lower proportion of patients were receiving maintenance inhaled TT. This discrepancy likely reflects the fact that symptom burden alone does not determine eligibility for TT, which is primarily guided by exacerbation history and inflammatory profile. In addition, ED visits often focus on acute symptom relief rather than comprehensive reassessment of long-term maintenance therapy, which may contribute to underutilization of guideline-recommended treatment.

The relatively small proportion of patients classified as 'typical patients' (approximately 16% of the total cohort) reflects the application of strict, guideline-based criteria to a real-world ED population. Several factors may contribute to this finding, including the high proportion of patients already receiving inhaled TT prior to the index visit and the potential suppression of blood eosinophil counts during acute

exacerbations, particularly in patients treated with systemic corticosteroids. In addition, the limited size of this subgroup reduces statistical power, which likely explains the absence of statistically significant differences between typical and non-typical patients.

From the assessment performed in the ED, inhaled treatments were prescribed for most patients, including ICS and inhaled TT, although the percentage of patients receiving these treatments cannot be considered optimal. In addition, a more detailed analysis of TT prescription at discharge in patients classified as "Typical patients" showed no statistically significant differences. Inhaled TT, ideally in a single device, has been shown to be a better treatment option for reducing exacerbations, and is the recommended fundamental therapy for the management of patients with COPD and exacerbations.[6,12,19]

However, the high proportion of patients who did not receive guideline-recommended inhaled TT at discharge suggests that treatment optimization criteria may not be consistently applied in the ED setting, highlighting potential gaps between clinical guideline recommendations and real-world practice. Given the complexity of COPD management and the acute-care focus of ED practice, these findings support the potential value of structured, multidisciplinary approaches to improve adherence to guideline-recommended therapy. Dedicated care models involving emergency physicians, respiratory therapists, clinical pharmacists, and case managers could facilitate systematic identification of patients who may benefit from treatment optimization, provide targeted education, and ensure appropriate follow-up after discharge. In this context, other studies have also shown that treatment in these patients does not conform to the recommendations of the guidelines. A Portuguese study on the management of hospitalized COPD patients after their stay in the ED showed that only 26% of the patients had a TT prescription at discharge.[17] In this regard, a review of studies reporting data on the management of patients with COPD and exacerbations in the ED showed that compliance with the recommendations of the clinical guidelines or some of their recommendations for treatment was generally low, and that corticosteroid administration is lower than recommended.[25]

This lack of alignment in the treatment regimen of patients with COPD and exacerbations was also observed on analyzing the factors associated with inhaled TT at discharge in our study. The results of the multivariate analysis identified prior use of inhaled TT, chronic home oxygen therapy and influenza vaccination as possible factors independently associated with inhaled TT prescription at discharge from the ED. The identification of prior TT use and chronic home oxygen therapy is expected, because they may be considered indicative of increased severity of COPD.

The observation that the mean blood eosinophil count was close to 100 cells/mm$^3$ is clinically relevant. This finding may be partly explained by the frequent use of systemic corticosteroids among patients with recurrent exacerbations, which can transiently suppress circulating eosinophil counts and limit the usefulness of eosinophil counts measured during the ED visit for guiding long-term inhaled therapy decisions. This may partly explain why eosinophil count was not independently associated with TT prescription at discharge in our cohort, despite guideline recommendations favoring this treatment in patients with elevated eosinophil levels.

In addition, the evolving role of biologic therapies targeting type 2 inflammation in COPD introduces further complexity in interpreting eosinophil-driven treatment decisions, underscoring the need for cautious interpretation of eosinophil counts in real-world acute care settings.[7,12] In this regard, the 2025 update of the GOLD guide recommends that patients on LABA+LAMA with exacerbations and with a blood eosinophil count of $\geq$100 cells/mm$^3$ should be considered candidates for inhaled TT.[26] Incorporation of this recommendation into routine clinical practice and its consideration for future studies may contribute to the identification of eosinophil count as a factor associated with the inhaled TT regimen.

On the other hand, the number of previous visits to the ED due to COPD and previous admissions could be related to a greater number of exacerbations, but were likewise not identified as independent factors. In this context, studies with a larger number of patients could identify new factors associated with the inhaled TT regimen at discharge.

This study has some limitations. It was conducted at a single site, so the results should be interpreted with caution as they may not reflect the situation of other EDs in Spain. However, the number of patients included is large and allows relevant conclusions to be drawn in the context of the study. Although both men and women were included, male patients predominated in the study population, reflecting the real-world demographic profile of patients with COPD attending our ED during the study period. Therefore, potential sex-related differences in COPD management and outcomes could not be fully explored. On the other hand, there are limitations inherent to the retrospective study design involved. Thus, the investigators had no influence on the variables collected at the time when the patients reported to the ED. Because of the retrospective nature of the study, the data were obtained from the medical records of the patients, and therefore were not collected for research purposes, which may imply a loss of data for some of the analyses. A prospective multicenter study would be needed to validate the results obtained in our study.

## Conclusion

In conclusion, our study shows that a high percentage of patients with COPD reporting to the ED due to exacerbations do not receive inhaled TT at discharge - the treatment recommended by the GesEPOC Guidelines for this patient profile. In addition, it should be noted that eosinophil counts, previous visits to the ED, and previous admissions have not been identified as factors associated with TT prescription. It is therefore necessary to optimize the management of these patients through training and the standardization of management across the different EDs.

Future research should explore the underlying factors contributing to suboptimal adherence to guideline-recommended therapy in patients with COPD presenting to the ED, including organizational, structural, and socioeconomic determinants. In addition, prospective studies evaluating multidisciplinary and structured care models—such as the involvement of emergency physicians, respiratory therapists, pharmacists, and case managers—may help identify effective strategies to improve treatment optimization, continuity of care, and long-term outcomes in this high-risk population.

## Ethics approval and consent to participate

The study was approved by the Clinical Research Ethics Committee of Aragon (*Comité Ético de Investigación Clínica Aragón*, CEICA), and was conducted in accordance with the guidelines of the Declaration of Helsinki.

The obtention of the informed consent from the patients included in the study was not considered necessary.

## CRediT authorship contribution statement

**Mónica Sachi Martínez Mihara:** Writing – review & editing, Investigation, Formal analysis. **Isabel Pérez Pañart:** Writing – review & editing, Investigation, Formal analysis. **María Sánchez Salamero:** Writing – review & editing, Investigation, Formal analysis. **Eva Campos Picontó:** Writing – review & editing, Investigation, Formal analysis. **Sara Patricia Canales Villa:** Writing – review & editing, Investigation, Formal analysis. **Víctor Latorre:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis. **Daniel Sáenz Abad:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Daniel Saenz Abad reports statistical analysis was provided by AstraZeneca Pharmaceutical Spain. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Data Availability

The data that support the findings of this study are not publicly available due to privacy or ethical restrictions. Patient-level data contain sensitive clinical information, and sharing them is not permitted under the policies of the institution.

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