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Palliative Sedation at the End of Life: A Comparative Study of Chronic Obstructive Pulmonary Disease and Lung Cancer Patients

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Keywords
Chronic obstructive pulmonary disease · Lung cancer · Palliative care · Sedation · End-stage disease

Abstract
Background: Although patients with chronic obstructive pulmonary disease (COPD) receive poor-quality palliative care, information about the use of palliative sedation (PS) in the last days of life is very scarce. ***Objectives:*** To compare the use of PS in hospitalized patients who died from COPD or lung cancer and identify factors correlating with PS application. ***Methods:*** In a retrospective observational cohort study, from 1,675 patients died at a teaching hospital between 2013 and 2015, 109 patients who died from COPD and 85 from lung cancer were compared. Sociodemographic data, clinical characteristics, health care resource utilization, application of PS and prescribed drugs were recorded. ***Results:*** In the last 6 months of life, patients who died from COPD had more hospital admissions due to respiratory causes and less frequent support by a palliative home care team (PHCT). Meanwhile, during their last hospitalization, patients who died from COPD had fewer do-not-resuscitate orders and were subjected to more intensive care unit admissions and cardiopulmonary resuscitation maneuvers. PS was applied less frequently in patients who died from COPD than in those who died from lung cancer (31 vs. 53%, $p = 0.002$). Overall, previous use of opioid drugs, support by a PHCT, and a diagnosis of COPD (adjusted odds ratio 0.48, 95% CI: 0.26–0.89, $p = 0.020$) were retained as factors independently related to PS. In COPD patients, only previous use of opioid drugs was identified as a PS-related factor. ***Conclusion:*** During their last days of life, hospitalized COPD patients receive PS less frequently than patients with lung cancer.

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive life-limiting condition and a major cause of mortality worldwide [1]. The Global Burden of Disease has identified COPD as the third most common cause of death in the world [2], and according to the European COPD Coalition, this disease is expected to increase from 270,000 deaths in Europe in 2005 to 338,000 deaths by 2030 [3]. Mortality in COPD patients depends on disease severity, the number of comorbidities, and the number of exacerbations in the last year of life [4].

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The trajectory of COPD patients typically involves slow functional decline with acute life-threatening exacerbations. In their last months of life, COPD patients often experience increased dyspnea, fatigue or weakness, severe physical disability, low mood, and pain [5, 6]. In these circumstances, palliative or end-of-life care is an important component in the treatment of patients with severe COPD [7]. However, the unpredictability regarding the prognosis of COPD and the use of life-sustaining treatments in COPD patients poses different challenges in end-of-life decision-making [3], and there is strong evidence to suggest that patients with COPD receive poor-quality palliative care compared with cancer patients [8–11]. Several population-level database analyses have shown that people dying from COPD compared to those from lung cancer are more likely to die in a hospital and are less likely to receive specialized palliative care [12–15].

Although it is a controversial procedure, for the extremely dyspneic, agitated, hypoxic patient, palliative sedation (PS) therapy may be needed as an appropriate palliative treatment [16, 17]. PS is defined as intentional sedation in the last phase of life to alleviate intolerable refractory symptoms when there is no effective treatment, in an acceptable time frame, or if the treatment is intolerable [18]. Importantly, PS includes continuous deep sedation as well as superficial, short, and intermittent sedation, where the goal is not the loss of consciousness until death but an adequate alleviation of symptoms [19, 20]. When appropriately indicated and correctly used, PS does not accelerate death [21–23].

Although there are international clinical guidelines for the management of PS [19, 20] and its application has been analyzed in patients who died from lung cancer [24], to our knowledge there are no data available for palliative end-of-life sedation in patients with COPD. Therefore, the purpose of the present study was to compare the application of PS in patients with advanced COPD who died in a tertiary hospital versus patients who died of lung cancer. In addition, we intend to compare the characteristics of the applied sedative treatment and to identify the factors related to the application of sedation in patients with advanced COPD.

Materials and Methods

Study Population

We performed a retrospective observational cohort study of consecutive patients who had died at Hospital Universitario de Fuenlabrada in Fuenlabrada, Madrid, Spain, from January 2013 to December 2015, whose primary cause of death was either COPD or lung cancer. This medical center, where all medical entries are made in electronic medical records, provides care for 110,151 inhabitants and has access to teams of palliative care specialists. The center has a PS procedure aimed at admitted patients without response to specific treatment or intensive care unit (ICU) criteria, in whom there are refractory symptoms and intolerable suffering with a very short life expectancy. Decision-making is done by consensus of at least 2 doctors who care for the patient. In addition, to obtaining consent and registering the intervention, the procedure includes the induction, preparation of the infuser with different combinations and doses of drugs, as well as the patient follow-up.

Inclusion criteria for COPD group were: (1) COPD reported on the death certificate as the underlying, intermediate, or associated cause of death (International Classification of Diseases 10th Revision [ICD-10] codes J40–J44 and J47); (2) absence of evidence of cancer (ICD-10 code C) as an underlying cause of death; and (3) very severe airflow limitation (GOLD IV) [5] before the last hospitalization. In contrast, for the lung cancer group, we selected patients in whom lung cancer was the underlying cause of death (ICD-10 codes C33–C34).

Exclusion criteria were subjects under the age of 40, no spirometry-confirmed diagnosis of COPD, or when death had been "sudden and completely unexpected." The study was approved by the local ethics committee (APR 16/21).

Data Extraction

From the patients' electronic medical records, data for sociodemographic and clinical variables, including gender, age, BMI, smoking status, household composition, and receipt of government support for health care, were collected. For information about the baseline clinical status before the last hospitalization, we collected the dyspnea level (modified Medical Research Council [mMRC] scale), Charlson comorbidity index, last values of forced expiratory volume in 1 s, oxygen arterial blood pressure (PaO_2) and carbon dioxide arterial blood pressure ($PaCO_2$), as well as the current treatment, including the need for long-term oxygen therapy and opioid drugs. The ECOG scale of performance status was assessed only in patients with lung cancer.

Measurements of health care resource utilization during the last 6 months of life included hospitalization, emergency room visits, noninvasive ventilation, intensive care unit admissions, and support by a palliative home care team (PHCT). During the last hospitalization, the time from admission to death and the weight of the diagnosis-related groups were also recorded, as well as the presence or absence of a living will, goals-of-care document and do-not-resuscitate (DNR) order, and the incidence of cardiopulmonary resuscitation (CPR).

Finally, we recorded the application of PS (defined as the use of adequate doses of sedatives to relieve intolerable suffering from refractory symptoms, without the aim to end life) [18], including prescription information from the standardized prescription form used at the institution and the specialty of the prescribing physician.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range), depending on their normal distribution. Categorical variables were reported as absolute numbers and percentages. Comparisons between groups were performed using the Student *t*, Mann-Whitney U, or χ^2 tests.

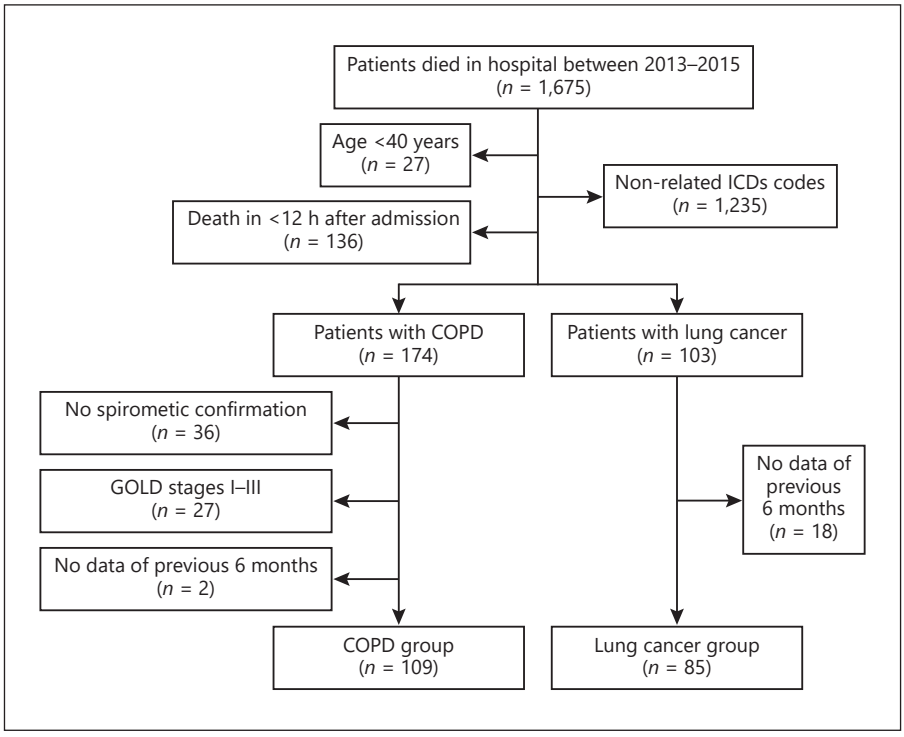

Fig. 1. Flowchart of study selection.

Multivariable binary logistic regression models were constructed to determine the odds ratios of receiving PS. Independent variables used in the multivariable analyses included sociodemographic and clinical characteristics and the health care resources. Relevant confounders and covariates in the models were entered using a forward stepwise selection method with $p < 0.05$ set as an entry criterion.

Statistical analyses were conducted using IBM-SPSS Statistics version 20 (SPSS Inc., Chicago, IL, USA). All results with a p value of <0.05 were deemed to be statistically significant.

Results

Baseline Characteristics

From the 1,675 patients died at hospital during the evaluation period, 109 subjects were included in the COPD group and 85 in the lung cancer group (Fig. 1). Baseline characteristics of both groups are shown in Table 1. Compared to patients who died from lung cancer, patients who died from COPD were older, were more likely to be former smokers (although the cumulative consumption of tobacco was similar), and had more institutional support. In turn, they presented less comorbidity, but more severe dyspnea and worse pulmonary function with a higher percentage of hypercapnia (59 vs. 21%, $p = 0.001$). Regardless of the expected differences in the specific treatments for each disease, use of opioid drugs, in any of their most common administration forms, was less frequent in COPD patients.

Table 2 summarizes the health care resource utilization in the 2 study groups. In the last 6 months of life, patients who died from COPD had more hospital admissions due to respiratory causes, although fewer emergency room visits. PHCT support was also less frequent in the COPD group than in the patients who had died from lung cancer, while the advance health care directive (living will) was practically nonexistent in the 2 groups. In contrast, during the last hospitalization, patients who had died from COPD had fewer DNR orders and were subjected to more ICU admissions and CPR maneuvers.

Comparison of the PS among Patients Who Had Died from COPD or Lung Cancer

PS was applied less frequently in the patients who had died from advanced COPD than in those who died due to lung cancer (31 vs. 53%, $p = 0.002$). However, there were no differences between the 2 groups in the prescribed drugs or in the total number of drugs used to induce PS (see online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000510537). It is important to note that despite the lower use of PS

Table 1. General characteristics of the study subjects[a]

	Lung cancer patients (n = 85)	COPD patients (n = 109)	p value
Males, *n* (%)	73 (86)	99 (91)	0.198
Age, yr	66±10	78±10	<0.001
BMI, kg/m^2	26.6±4.6	27.8±7.4	0.730
Smoking status, *n* (%)			
Current smoker	39 (46)	17 (16)	<0.001
Former smoker	41 (48)	81 (76)	
Never smoker	5 (6)	8 (8)	
Packs × year	46±25	57±39	0.368
Live alone, *n* (%)	4 (5)	8 (7)	0.329
Institutional support, *n* (%)	0	20 (18)	<0.001
Charlson comorbidity index	7.2±2.5	4.7±2.2	<0.001
mMRC dyspnea scale	1.2±1.0	3.5±0.6	<0.001
FEV_1, % pred.	72±14	48±4	<0.001
Baseline PaO_2, mm Hg	59.7±16.0	56.9±20.0	0.507
Baseline $PaCO_2$, mm Hg	34.9±11.2	53.4±19.5	<0.001
ECOG scale of performance status	2.2±0.8	–	–
Current treatment, *n* (%)			
SABA	21 (25)	67 (62)	<0.001
LABA	22 (26)	80 (73)	<0.001
SAMA	6 (7)	18 (17)	0.037
LAMA	18 (21)	73 (67)	<0.001
Inhaled corticosteroids	17 (20)	84 (77)	<0.001
Oral corticosteroids	46 (54)	14 (13)	<0.001
Theophyllines	1 (1)	13 (12)	0.003
LTOT	29 (34)	79 (73)	<0.001
Therapeutic chemotherapy	33 (39)	–	–
Therapeutic radiotherapy	13 (15)	–	–
Palliative chemotherapy	16 (19)	–	–
Palliative radiotherapy	14 (17)	–	–
Antidepressant drugs	5 (6)	29 (27)	<0.001
Anxiolytic drugs	30 (35)	30 (28)	0.157
Opioid drugs, *n* (%)	41 (48)	13 (12)	<0.001
Delayed opioids	24 (29)	7 (6)	<0.001
Fast-acting opioids	26 (31)	8 (7)	<0.001
Opioid patches	14 (17)	9 (8)	0.059
Sublingual opioids	3 (4)	3 (3)	0.529

COPD, chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group; FEV_1, forced expiratory volume at 1 s; LABA, long-acting beta-adrenergic; LAMA, long-acting muscarinic antagonist; LTOT, long-term oxygen therapy; mMRC, modified Medical Research Council; $PaCO_2$, carbon dioxide arterial pressure; PaO_2, oxygen arterial pressure; SABA, short-acting beta-adrenergic; SAMA, short-acting muscarinic antagonist.
[a] Data are mean±standard deviation or number (percentage). Comparisons by Student's t test or χ^2 test.

among patients who died from COPD than in those died from lung cancer, the former had a higher level of refractory dyspnea (mMRC scale 3.5 ± 0.6 vs. 1.2 ± 1.0, p < 0.001) and there were no differences between the 2 groups in the respiratory failure severity (PaO_2 56.9 ± 20.0 vs. 59.7 ± 16.0 mm Hg, p = 0.507) or in the Richmond Agitation – Sedation Scale score (2.6 ± 0.7 vs. 2.5 ± 0.8, p = 0.698).

Overall Risk Factors for PS Indication

The comparison of the socio-demographic characteristics, clinical variables, and use of health care resources between patients undergoing PS and those who were not in the overall group of deceased patients is shown in online suppl. Table 2. To summarize, patients in whom PS was indicated were younger, had lower BMI, and a previous diagnosis of lung cancer, and they used more fre-

Table 2. Comparison of health care resource utilization between the 2 study groups[a]

	Lung cancer patients (n = 85)	COPD patients (n = 109)	p value
Events during the last 6 months			
Number of hospitalizations	1.95±1.00	2.23±1.38	0.107
Number of hospitalizations due to respiratory causes	1.44±0.96	1.94±1.50	0.005
Hospitalization days	19±16	25±21	0.051
ER visit, n (%)	55 (65)	60 (55)	0.028
Number of ER visits	1.42±1.63	0.97±1.20	0.034
ER visit due to respiratory causes, n (%)	24 (23)	36 (27)	0.530
Number of ER visits due to respiratory causes	0.34±0.83	0.38±0.76	0.755
ICU admission, n (%)	6 (7)	14 (14)	0.245
Number of ICU admissions	0.08±0.31	0.18±0.51	0.093
Noninvasive mechanical ventilation, n (%)	3 (4)	5 (5)	0.504
PHCT support, n (%)	20 (24)	5 (5)	<0.001
Anticipate declaration of last wills, n (%)	0	1 (1)	0.562
Events during the last hospitalization			
Time to death, days	8±7	12±11	0.008
ICU admission, n (%)	2 (2)	12 (12)	0.012
Number of ICU admissions	0.02±0.15	0.17±0.50	0.006
Noninvasive mechanical ventilation, n (%)	1 (1)	4 (4)	0.271
DNR order, n (%)	79 (93)	82 (75)	0.001
CPR, n (%)	0	7 (6)	0.016
Effective CPR, n (%)	0	3 (3)	0.176
DRG weight	2.57±1.19	3.20±4.49	0.210

CPR, cardiopulmonary resuscitation; DNR, do-not-resuscitate; DRG, diagnosis-related groups; ER, emergency room; ICU, intensive care unit; PHCT, palliative home care team. [a] Data are mean ± standard deviation or number (percentage). Comparisons by Student's t test or χ^2 test.

Table 3. Risk factors for sedation at the end of life in the overall study patients

	Crude OR (95% CI)	p value	Multivariate analysis[a]	
			adjusted OR (95% CI)	p value
Age, yr	0.972 (0.948–0.996)	0.025	–	–
BMI, kg/m^2	0.773 (0.566–0.998)	0.048	–	–
COPD group (vs. lung cancer group)	0.403 (0.224–0.725)	0.002	0.480 (0.258–0.893)	0.020
Oral corticosteroids	2.586 (1.386–4.826)	0.003	–	–
LTOT	0.500 (0.279–0.895)	0.020	–	–
Anxiolytic drugs	1.915 (1.033–3.551)	0.039	–	–
Opioid drugs	2.804 (1.515–5.189)	0.001	2.712 (1.427–5.154)	0.002
PHCT support	2.991 (1.428–7.169)	0.014	4.721 (1.682–13.249)	0.003
DNR note	4.762 (1.751–12.952)	0.002	–	–

CI, confidence interval; COPD, chronic obstructive pulmonary disease; LTOT, long-term oxygen therapy; OR, odds ratio; PHCT, palliative home care team. [a] Stepwise multivariate model including age, sex, institutional support, Charlson comorbidity index, dyspnea, and current treatment in the last 6 months.

quently oral corticosteroids, long-term oxygen therapy, anxiolytics, and opioid drugs. In turn, they had more support of palliative home care and DNR orders were more frequently established.

Table 3 shows the odds ratios for the estimated correlation between PS indication and those variables that showed significant differences in the comparison between groups. Interestingly, when the stepwise multivar-

Table 4. Comparison of the characteristics of COPD patients who received/did not receive sedation[a]

	Patients with sedation (n = 34)	Patients without sedation (n = 75)	p value
Males, n (%)	31 (91)	38 (91)	0.620
Age, yr	76±11	79±10	0.136
BMI, kg/m^2	27.8±7.4	26.5±6.3	0.631
Smoking status, n (%)			
Current smoker	4 (13)	13 (18)	0.494
Former smoker	26 (81)	55 (74)	
Never smoker	2 (6)	6 (8)	
Packs × year	45±39	60±39	0.395
Lives alone, n (%)	2 (6)	6 (8)	0.519
Institutional support, n (%)	5 (15)	15 (20)	0.601
Charlson comorbidity index	4.3±2.1	4.8±2.2	0.247
mMRC dyspnea scale	2.6±1.4	2.4±1.4	0.505
FEV_1, % pred.	46±5	48±4	0.387
Baseline PaO_2, mm Hg	56.5±16.0	57.2±21.9	0.894
Baseline $PaCO_2$, mm Hg	50.6±18.1	54.8±20.3	0.412
Current treatment, n (%)			
SABA	26 (77)	41 (55)	0.024
LABA	26 (77)	54 (72)	0.405
SAMA	7 (21)	11 (15)	0.305
LAMA	18 (53)	55 (73)	0.031
Inhaled corticosteroids	28 (82)	56 (75)	0.265
Oral corticosteroids	7 (21)	7 (9)	0.096
LTOT	23 (68)	56 (75)	0.492
Antidepressant drugs	8 (24)	21 (28)	0.405
Anxiolytic drugs	14 (41)	16 (21)	0.029
Opioid drugs	11 (32)	6 (8)	0.002
Laxatives drugs	8 (24)	7 (9)	0.049
Health resources use during the last 6 months of life			
Number of hospitalizations	2.1±1.4	2.3±1.4	0.474
Number of hospitalizations due to respiratory causes	1.8±1.6	2.0±1.5	0.509
Hospitalization days	13±9	11±9	0.247
ER visit, n (%)	19 (65.9)	41 (54.7)	0.872
Number of ER visits	1.0±1.2	1.0±1.2	0.873
ER visit due to respiratory causes, n (%)	9 (27.3)	19 (27.1)	0.079
Number of ER visits due to respiratory causes	0.42±0.75	0.36±0.76	0.676
ICU admission, n (%)	7 (20.6)	7 (9.3)	0.018
Number of ICU admissions	0.24±0.50	0.16±0.52	0.480
Noninvasive mechanical ventilation, n (%)	4 (12)	1 (1)	0.032
PHCT support, n (%)	3 (9)	2 (3)	0.174
Health resources use in the last hospitalization			
Time to death, days	13±9	11±9	0.247
ICU admission, n (%)	7 (20.6)	5 (6.8)	0.086
Number of ICU admissions	0.09±0.30	0.01±0.12	0.075
Noninvasive mechanical ventilation, n (%)	3 (9)	1 (1)	0.089
DNR order, n (%)	29 (85)	53 (71)	0.078
CPR, n (%)	2 (6)	5 (7)	0.621
Effective CPR, n (%)	2 (6)	1 (1)	0.221

COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; DNR, do-not-resuscitate; ER, emergency room; FEV_1, forced expiratory volume at 1 s; ICU, intensive care unit; LTOT, long-term oxygen therapy; mMRC, modified Medical Research Council; $PaCO_2$, carbon dioxide arterial pressure; PaO_2, oxygen arterial pressure; PHCT, palliative home care team. [a] Data are mean ± standard deviation or number (percentage). Comparisons by Student's t test or χ^2 test.

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iate model was applied, only the previous use of opioid drugs, the assistance by a PHCT, and the absence of a diagnosis of advanced COPD were retained as independent factors that increase the risk of indication of PS.

Factors Related to the Indication of PS in COPD Patients

Table 4 presents the comparison between patients died from COPD who received PS versus those who did not. Of all the variables explored, the indication of PS in patients who died from COPD was more frequent in those who used short-term beta-adrenergic drugs (odds ratio: 2.70, 95% CI: 1.08–6.72, $p = 0.033$), anxiolytic drugs (2.58, 1.07–6.21, $p = 0.034$), or opioid drugs (5.50, 1.83–16.54, $p = 0.002$). However, in the stepwise multivariate model adjusted for age, gender, BMI, Charlson comorbidity index, and baseline forced expiratory volume in 1 s, the only variable retained as a factor independently related to PS was the previous use of opioid drugs (adjusted odds ratio: 4.32, 95% CI: 1.31–14.21, $p = 0.016$).

Discussion/Conclusion

In addition, to confirm previous data suggesting that COPD patients have less access to palliative care, mainly at home, than patients with lung cancer, our study shows that this situation also occurs in the last days of life, since PS was less frequently used in patients who died from COPD than in those died from lung cancer. By comparing patients who died from COPD and from lung cancer, our results confirm that palliative care is used less in COPD patients. In fact, the advanced COPD patients that we have evaluated had more hospitalizations in the last 6 months of life, as well as a higher percentage of ICU admissions, mechanical ventilation or CPR maneuvers during the final hospital admission in which death occurred, along with a fewer signed DNR orders. Our results also confirm that in the final phase of their lives, patients who died from COPD were less frequently given opioid drugs or palliative care (particularly home palliative care) than patients who died of lung cancer.

These findings are consistent with the information provided by previous studies, which have reported that patients who died from COPD were admitted to ICU more frequently and had longer ICU stays, as well as greater use of mechanical ventilation, antibiotics, or diagnostic tests than patients who died from lung cancer, both during the last months of life and at the end of hospital admission during which death occurred [25–28]. Previous studies have also demonstrated that patients with advanced COPD have an extremely limited awareness of palliative care options for their condition [29] and poor access to palliative care services [30]. A recent population study conducted in Belgium has reported that patients who died from COPD received less opioid drugs, sedatives, and morphine and used fewer palliative care services than those who died from lung cancer [31]. In fact, different clinical or population studies carried out worldwide have identified that the use of formal palliative care services by patients who died from COPD ranges from 3.3 to 21.4% [8, 27, 28, 32, 33], and in all cases, their use was much lower than in patients who died of lung cancer. This situation is even more pronounced in the case of palliative home care. Thus, 5% of patients who died due to COPD at our hospital had home-based palliative care, which is higher than the 0.84% identified in the Taiwan National Health Insurance Research Database [28], 2.8% obtained in a study conducted in Canada [34], or 4% in a Swedish population study [35].

To adequately assess the limited access to palliative care services, it is important to keep in mind that this does not seem attributable to patient preferences or to better control of symptoms. In fact, the Study to Understand Prognosis and Preferences for Outcomes and Treatments (SUPPORT) found that lung cancer and COPD patients were equally likely to not be intubated and not receive CPR [25, 36]. Otherwise, compared with cancer patients, COPD patients suffered from more breathlessness and anxiety but less pain and nausea during the last week of life, and COPD patients had lower rates of complete relief from breathlessness, anxiety, and death rattle [35]. Precisely, the poor symptom control determines that many patients with COPD are hospitalized in the final phase of their disease [11, 31, 37] and that patients with COPD are much less likely to die at home than patients with lung cancer [10].

The underuse of palliative care in patients with COPD has been attributed to multiple factors, such as the heterogeneity of the disease and its exacerbations, its variable clinical course, the existence of a high number of treatment options, or the lack of specific recommendations in many management guidelines for these patients. But, above all, the main justification is that determining prognosis in patients with end-stage COPD is difficult [27]. Although undoubtedly relevant, one might expect these considerations to have less influence in the last weeks of life of patients with very refractory symptoms requiring hospitalization. However, our results show that, even in

this situation, patients who died from COPD received PS less frequently than patients who died of lung cancer.

The most important finding of our study is that the underuse of palliative care is maintained in the last days of life, with less use of PS in admitted patients with respiratory failure, refractory dyspnea, and agitation-anxiety who will die in a few days when they have a previous diagnosis of COPD instead of lung cancer. The rate of PS in patients who died at our hospital due to lung cancer (53%) is similar to that identified in previous studies [38,39] . In contrast, it is more complex to compare the rate of PS in hospital of patients with terminal COPD (31%) due to limited information in this regard. By way of inference, and although the use of opioid drugs is not the same as palliative care and much less PS, Hyasat and Sriram [27] reported that 29% of 41 patients who died from COPD received morphine/midazolam infusion during their final hospitalization, during which death occurred. In turn, in a comparison of the use of palliative resources between patients who died due to COPD versus cancer in a Belgian population sample, Scheerens et al. [40] found that the treatment goal in the last week of life was less often aimed at comfort/palliation in COPD patients than in lung cancer patients. In this same study, it is striking that initial palliative measures were provided, on average, 28 days earlier for lung cancer patients than for COPD patients with regard to time of death [40].

Once adjusted for possible confounding factors, our results demonstrate that the indication for PS is higher in patients with a previous use of opioid drugs or support by a PHCT and in those with a diagnosis of lung cancer versus COPD. With regard to COPD, after adjusting for the confounding factors considered, therapeutic sedation is almost 2 times less frequent in patients who die in the hospital due to this disease than in those who die from lung cancer. Considering the consumption of resources of these patients, their functional limitation and the limited life expectancy confirmed by their death, it is not a surprise that, even in this terminal situation, palliative resources in these patients continue to be underused. In any case, our data also show that when PS is applied, the choice of drugs and dose is similar between patients with COPD and lung cancer, reflecting the application of similar sedation protocols [41, 42].

Regarding factors related to the indication of PS in patients who died from COPD, the only independent risk factor we have identified is the previous use of opioid drugs. Although our results do not allow us to identify the causes of this association, one might speculate whether it is due to the selection of patients with more intense and refractory symptoms or whether it simply reflects patients who have had previous palliative care, anticipating the conversation about decisions to be made in the final phase of life. In fact, in a cohort of 60 patients with terminal COPD enrolled in a home hospice program in our setting, 69% received PS [43].

We realize that our study presents several limitations. First of all, it is a retrospective study, so it is only possible to evaluate associations and it does not allow causal inferences to be established. Second, it is a single-center analysis, so its extrapolation to other environments must be done with caution. Nonetheless, our hospital is the only medical center in our national health care area, and the population often has very little mobility in an urban and rural setting. Furthermore, our hospital provides all levels of care, so we therefore consider the data representative of our environment. Third, the sample size is sufficient to detect differences in the frequency of the application of sedation, but it has limitations to evaluate the contribution of different risk factors. Fourth, the difference in the use of PS among patients who died due to COPD or lung cancer represents the probable underutilization of a therapeutic resource, but we do not have information on its impact on the symptoms or quality of life of patients in the hours prior to death. Finally, and although it is obvious, it is necessary to state once again that PS of terminal patients is not a practice of euthanasia, which is demonstrated by the similar survival times between patients who received PS versus those who did not. In conclusion, our study demonstrates that in addition to the underutilization of palliative care in end-stage COPD patients, what is even more striking is the underutilization of PS in the last days of life of hospitalized terminal-phase patients.

Statement of Ethics

The study was approved by the ethics committee of Hospital Universitario de Leganés-Fuenlabrada, Madrid, Spain (APR 16/21).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

E.T. and F.G.-R.: conception and design; E.T., P.P., S.S.-S., R.G., R.C., E.M.-C., and F.G.R.: development of methodology; E.T., P.P., S.S.-S., and F.G.R.: acquisition of data; E.T., R.G., R.C., E.M.-C., and F.G.R.: data analysis and interpretation of data; and all authors: wrote, reviewed, and/or revised the manuscript. All authors had full access to all the data in the study.

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