Original Article

The Natural History of Severe Chronic Obstructive Pulmonary Disease: The SPOCCAT Study Protocol

Jessica González [a,b], Dan Sánchez [c], Daniel Ross-Monserrate [d], Elena Miguel [e], Marc Miravitlles [f], Roser Costa [g,h,*], on behalf of the SPOCCAT study [◊]

[a] Translational Research in Respiratory Medicine, University Hospital Arnau de Vilanova and Santa Maria, IRBLleida, Lleida, Spain
[b] CIBER of Respiratory Diseases (CIBERES), Institute of Health Carlos III, Madrid, Spain
[c] Pneumology Service, Hospital Municipal de Badalona, Spain
[d] Pneumology Service, Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Spain
[e] Pneumology Service, Hospital Universitari de Igualada, Igualada, Spain
[f] Pneumology Service, Hospital Universitari Vall d'Hebron, Vall d'Hebron Institut de Recerca (VHIR), Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain
[g] Pneumology Service, Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain
[h] Institut de Recerca i Innovació en Ciències de la Vida i de la Salut a la Catalunya Central (IRIS-CC), Vic, Spain

A R T I C L E   I N F O

A B S T R A C T

Introduction: Patients with severe chronic obstructive pulmonary disease (COPD) are often underrepresented in cohorts, creating uncertainty about the natural history and prognostic factors of this subgroup. Our goal was to describe the SPOCCAT (Severe COPD: Prospective Observational study of COPD in Catalonia) study protocol.
Material and methods: SPOCCAT is a non-interventional, multicenter, prospective cohort study of patients with severe COPD (FEV$_1$% predicted < 50%). The study aims to: (1) establish a five-year prospective cohort; (2) identify demographic and clinical characteristics; (3) describe treatment patterns; (4) better understand the natural history of severe COPD, including lung function decline, exacerbation rates, and mortality; and (5) identify prognostic factors for poor outcomes.
Recruitment began in January 2024, and the cohort will be followed for a minimum of five years (or until death or lung transplant) with follow-up visits every 12 months. Baseline data include demographics, laboratory analyses, comorbidities, lung function, respiratory symptoms, respiratory disease exacerbations and etiology, quality of life, physical activity, chest computed tomography, and treatment. Annual follow-up visits will assess changes in treatment, exacerbation frequency and severity, microbiological outcomes, complementary tests, and mortality. Participation requires written informed consent from all patients, with data collected in an anonymized electronic Case Report Form.
Results: The results of the SPOCCAT study will provide relevant information about the characteristics, treatment, and prognostic factors of severe COPD.
Conclusions: SPOCCAT has the potential to enhance understanding of severe COPD, exploring innovative aspects and establishing a robust research framework for future COPD-related projects.

La historia natural de la enfermedad pulmonar obstructiva crónica grave: el protocolo del estudio SPOCCAT

R E S U M E N

Introducción: Los pacientes con enfermedad pulmonar obstructiva crónica (EPOC) grave a menudo están infrarepresentados en las cohortes, lo que genera incertidumbre sobre la historia natural y los factores pronósticos de este subgrupo. Nuestro objetivo fue describir el protocolo del estudio de EPOC grave: estudio observacional prospectivo de la EPOC en Cataluña (SPOCCAT)

* Corresponding author.
  E-mail address: mdrcosta@althaia.cat (R. Costa).
◊ A list of the researchers participating in the Organization of the SPOCCAT study is provided in Appendix.

Material y método: El SPOCCAT es un estudio de cohorte prospectivo, multicéntrico y no intervencionista de pacientes con EPOC grave (volumen espiratorio forzado en un segundo [FEV1] % previsto < 50%). El estudio tiene como objetivo: 1) establecer una cohorte prospectiva de cinco años, 2) identificar características demográficas y clínicas, 3) describir patrones de tratamiento, 4) comprender mejor la historia natural de la EPOC grave, incluida la disminución de la función pulmonar, las tasas de exacerbación y la mortalidad, y 5) identificar factores de pronóstico de malos resultados. El reclutamiento comenzó en enero de 2024 y se seguirá a la cohorte durante un mínimo de cinco años (o hasta la muerte o el trasplante de pulmón) con visitas de seguimiento cada 12 meses. Los datos basales incluyen datos demográficos, análisis de laboratorio, comorbilidades, función pulmonar, síntomas respiratorios, exacerbaciones y etiología de enfermedades respiratorias, calidad de vida, actividad física, tomografía computarizada de tórax y tratamiento. Las visitas de seguimiento anuales evaluarán cambios en el tratamiento, frecuencia y gravedad de las exacerbaciones, resultados microbiológicos, pruebas complementarias y mortalidad. La participación requiere el consentimiento informado por escrito de todos los pacientes, con datos anonimizados recopilados en un cuaderno de recogida de datos electrónico.

Resultados: Los resultados del estudio SPOCCAT aportarán información relevante sobre las características, el tratamiento y los factores pronósticos de la EPOC grave.

Conclusiones: El estudio SPOCCAT tiene el potencial de mejorar la comprensión de la EPOC grave, explorando aspectos innovadores y estableciendo un marco de investigación sólido para futuros proyectos relacionados con la EPOC.

Introduction

Although several studies have been published to date, there are important gaps in our knowledge about the natural history of chronic obstructive pulmonary disease (COPD). One of the most renowned studies was published by Fletcher and Peto in the 1960s,[1] providing a pivotal contribution to the knowledge of this disease. Subsequent comprehensive studies with longer follow-up periods have reported significant insights, including the important association between tobacco and the decline in pulmonary function.[2,3]

Following these initial investigations, several research groups were established with the objective of not only examining pulmonary function but also adopting a multidimensional approach, encompassing various facets of the disease. Among these studies, cohorts of note include ECLIPSE[4] and PAC-COPD[5] which were aimed at characterizing the phenotypes of COPD. Additionally, the Hokkaido cohort in Japan[6] was focused on the study of emphysema, while the SAPALDIA 1[7] and 2[8] studies evaluated the impact of environmental pollution and gender differences. Subsequently, two of the most pivotal cohorts emerged: the BODE cohort (Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity)[9] involving multidimensional assessment, and the COPDGene (Genetic epidemiology of COPD) study,[10] aimed at exploring the genetic, functional, and radiological determinants of the disease. Along this line, the CHAIN study[11] was launched in Spain a decade ago with the objective of carrying out comprehensive, long-term assessment of COPD progression (minimum 5 years). This study included a control group consisting of smokers or former smokers without COPD. The findings of this cohort analysis have been extensive and highly influential.[12–14]

However, despite substantial advancements in understanding this disease, numerous questions remain regarding its natural history. This is particularly critical for the most severe patients, who are often underrepresented in existing cohorts and have a bleaker prognosis.[15] It is of note that only one third of the COPD patients included in the CHAIN cohort had severe or very COPD.[11] The SPOCCAT (Severe COPD: Prospective Observational study of COPD in Catalonia) study is a prospective observational registry of patients with severe COPD aimed at characterizing the population of patients with severe COPD and better understand the natural history and prognostic factors of the disease. Here, we describe the characteristics of the SPOCCAT study protocol.

Material and methods

Study objectives

The objectives of the SPOCCAT study are:

1. Establish a cohort of severe COPD patients who will be followed for at least 5 years.
2. Identify the demographic and clinical characteristics of patients with severe COPD.
3. Describe the patterns of treatment of patients with severe COPD.
4. Better understand the natural history of the disease in terms of decline of lung function, exacerbations and mortality in patients with severe COPD.
5. Identify prognostic factors of poor outcomes (decline in lung function, exacerbations and mortality) in patients with severe COPD.

Study design

SPOCCAT is a non-interventional, multicenter, prospective cohort study of patients with severe COPD followed in outpatient pulmonary clinics in Catalonia, Spain.

Patients will be managed according to the local procedures and policies without any clinical intervention from the study team. All patients will provide written informed consent to participate, and participating investigators will collect data prospectively. The following domains will be covered: demographics, laboratory analyses, comorbidities, lung function, respiratory symptoms, exacerbations of respiratory disease and their etiology in the previous year, quality of life, physical activity, chest computed tomography (CT) (when applicable) and treatment.

The cohort will be followed for a minimum period of five years with follow-up visits every 12 months. Changes in treatment, the number and severity of exacerbations, as well as microbiological outcomes and other complementary tests, will be evaluated during the yearly follow-up visits. In the event of death, the date and cause of death will be documented.

Data collection started in January 2024 in a secure electronic case report form (eCRF) developed in the REDCap (Research Electronic Data Capture) tool, sponsored by the Spanish Society of Pneumology and Thoracic Surgery (SEPAR-acronym in Spanish of the Sociedad Española de Neumología y Cirugía Torácica).
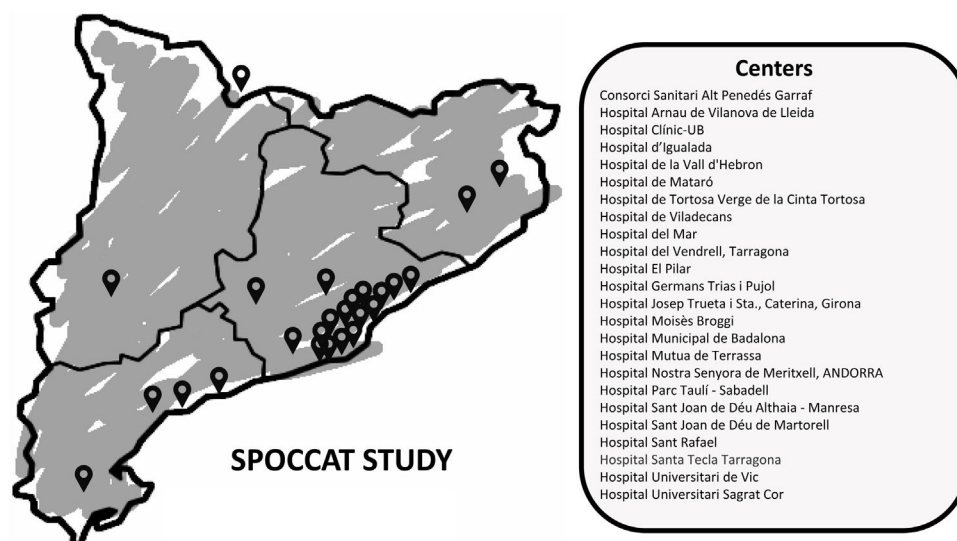
Centers

Consorci Sanitari Alt Penedés Garraf
Hospital Arnau de Vilanova de Lleida
Hospital Clínic-UB
Hospital d'Igualada
Hospital de la Vall d'Hebron
Hospital de Mataró
Hospital de Tortosa Verge de la Cinta Tortosa
Hospital de Viladecans
Hospital del Mar
Hospital del Vendrell, Tarragona
Hospital El Pilar
Hospital Germans Trias i Pujol
Hospital Josep Trueta i Sta., Caterina, Girona
Hospital Moisès Broggi
Hospital Municipal de Badalona
Hospital Mutua de Terrassa
Hospital Nostra Senyora de Meritxell, ANDORRA
Hospital Parc Taulí - Sabadell
Hospital Sant Joan de Déu Althaia - Manresa
Hospital Sant Joan de Déu de Martorell
Hospital Sant Rafael
Hospital Santa Tecla Tarragona
Hospital Universitari de Vic
Hospital Universitari Sagrat Cor

Fig. 1. Centers participating in the SPOCCAT study.

SPOCCAT has been registered in www.clinicaltrials.gov number NCT06252805.

Population

The study population will consist of patients greater than or equal to 35 years of age, smokers or former smokers of at least 10 pack-years diagnosed with severe COPD demonstrated by spirometry showing a post-bronchodilator forced expiratory volume in 1 second (FEV_1)/Forced vital capacity (FVC) < 0.7 and an FEV_1(% predicted) < 50%. Patients will be recruited in stable state, at least 4 weeks after resolution of an exacerbation.

The exclusion criteria are: (1) Medical conditions that make it impossible to perform the usual diagnostic procedures or follow-up; (2) Another severe chronic respiratory disease that justifies impaired spirometry, such as lung fibrosis or severe bronchiectasis; (3) Active neoplasm or a diagnosis of cancer in the previous 5 years; and (4) Lack of informed consent.

Patients will be removed from the study if the informed consent is withdrawn by the patient or their legal guardian. For patients who are lost to follow-up (i.e. patients whose status is unclear because they fail to appear for study visits without stating an intention to withdraw), the investigator should report the steps taken to contact the patient, e.g. dates of telephone calls, registered letters, etc. in the eCRF.

Sample size

The sample size calculation was based on the prevalence of COPD (17%) in Catalonia among individuals older than 35 years of age,[16] with approximately 10% being classified as severe. Therefore, our target population would encompass around 130,000 individuals. Taking into account a 95% confidence interval with a standard deviation of 1.96 and a margin of error of 5%, and factoring in an expected loss of 15–20%, the final study population should include a minimum of approximately 460 patients in order to obtain valid estimates for relevant variables such as frequency of exacerbations.

Center selection

The study is promoted by the Catalan Foundation of Pneumology (FUCAP in Catalan – Fundació Catalana de Pneumologia) and will initially be implemented in Catalonia and Andorra, but if successful, it will be extended to other areas of Spain or even other

countries, providing that ethical approval is obtained in all participating sites and that the appropriate data processing agreements are established between the promoter (FUCAP) and the candidate sites.

The FUCAP extended invitations to all centers listed in its roster of hospitals before the beginning of patient recruitment. The invitation noted that participation was voluntary and unpaid. By the end of January 2024, 31 pulmonologists from a total of 24 secondary and tertiary centers (Fig. 1 and Appendix) demonstrated interest and were invited to participate in an online investigators meeting. During this launch meeting, specific topics regarding the database, logistical considerations, project initiation, and potential challenges in patient recruitment were addressed.

Baseline data collection and follow-up

The outpatient visit schedule includes a baseline visit for patient recruitment in a stable state and annual clinical visits for a minimum follow-up period of 5 years or until death or lung transplant.

The selection of variables to be collected was initially structured by the Steering Committee and agreed upon with the other participating investigators. Subsequently, all researchers interested in participating in the SPOCCAT study were invited to provide comments and make relevant changes to the database before initiating recruitment.

Given the study objectives and the multidimensional approach, the number of collected variables is extensive. Overall, the variables chosen were categorized into the following domains: sociodemographic data, comorbidities, characteristics of COPD, radiological findings on chest CT, respiratory functional tests, blood samples and gasometrical results, additional tests, and vital status.

In the section on sociodemographic data, the following are specified: year of birth, gender, height, weight, smoking history (including years of cumulative exposure and the year of cessation), vaping consumption, employment status, occupational risk exposure, and educational level. The list of comorbidities is shown in Table 1.[17]

In relation to the characteristics of COPD, this section provides a comprehensive description of the disease (Table 1), outlining symptoms (including the COPD Assessment Test questionnaire – CAT–),[18] prognostic scales such as the BODE[10] and BODEx[19] indexes, physical activity measured by the Physical Activity Vital Sign (PAVS)[20] and the mean time walked per day.[21] Furthermore,

Table 1
Baseline demographic and clinical data.

Demographic data
  Sex
  Year of birth
  Education level
  Employment status
  Risky occupational exposure
  Height (cm)
  Weight (kg)
  Smoking status
  Pack-years
  Year of smoking cessation
  Vaping

Comorbidities
  Arterial hypertension
  Atrial fibrillation
  Hypercholesterolemia
  Ischemic heart disease
  Heart failure
  Peripheral vascular disease
  Dementia
  Gastrointestinal ulcer
  Gastroesophageal reflux
  Anxiety
  Depression
  Periodontal disease
  Diabetes mellitus
  Organ damage due to diabetes
  Stroke
  Connective tissue disease
  Liver disease
  Hemiplegia
  Renal insufficiency
  History of cancer treated more than 5 years ago
  Type of cancer
  HIV
  Obstructive sleep apnea
  Pulmonary hypertension
  Osteoporosis

COPD characteristics
  Asthma in childhood
  Asthma today (according to clinical criteria)
  Dyspnea mMRC
  Cough
  Expectoration
  CAT
  Number of days per week usually walked
  Minutes a day walked
  Chronic bronchial infection
  Chronic hypoxemic respiratory failure
  Chronic hypercapnic respiratory failure

Exacerbations in the last year
  Microorganism
  Type and severity
  Admission to ICU
  NIMV
  IMV
  Microorganisms isolated
  Pneumonia

Abbreviations: HIV = human immunodeficiency virus; mMRC = modified medical research council; CAT = COPD assessment test; ICU = intensive care unit; NIMV = non-invasive mechanical ventilation; IMV = invasive mechanical ventilation.

Table 2
Diagnostic tests performed.

CT characteristics (within the last 5 years)
  Emphysema
  Bronchiectasis
  Location
  Type

Respiratory functional testing
  FVC (mL and %)
  FEV_1 (mL and %)
  FEV_1/FVC (%)
  Bronchodilator test
  TLC (mL and %)
  RV (mL and %)
  FRC (TGV) (mL and %)
  DLCO (mL/min/mmHg and %)
  KCO (%)
  Basal oxygen saturation (%)
  FeNO
  Six-minute walking test

Blood analysis
  Hemoglobin (gr/dL)
  Hematocrit (%)
  Leukocytes ($\times 10 \times 9$/L)
  Neutrophils ($\times 10 \times 9$/L and %)
  Lymphocytes ($\times 10 \times 9$/L and %)
  Basophils ($\times 10 \times 9$/L and %)
  Eosinophils ($\times 10 \times 9$/L and %)
  Platelets ($\times 10 \times 9$/L)
  Creatinine (mg/dL)
  Urea (mg/dL)
  Alpha-1 antitrypsin (mg/dL)
  IgE (IU/mL)
  Vitamin D (25-hydroxy) (ng/mL)
  Fibrinogen (mg/dL)
  C-reactive protein (mg/L)
  NT-proBNP (pg/mL)

Gasometry
  pH
  pCO_2 (mmHg)
  pO_2 (mmHg)
  Standard HCO_3 (mmol/L)
  BE (mmol/L)
  FiO_2 with which it was performed (%)

Additional tests
  Echocardiogram (within the last 5 years)
  LVEF (%)
  PAP (mean) (mmHg)

Abbreviations: CT = computed tomography; FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; TLC = total lung capacity; RV = residual volume; FRC = functional residual capacity; TGV = thoracic gas volume; DLCO = diffusing capacity of the lungs for carbon monoxide; KCO = carbon monoxide transfer coefficient; FeNO = fractional exhaled nitric oxide (FeNO); NT-proBNP = N-terminal pro-B-type natriuretic peptide; pH = potential hydrogen; pO_2 = partial pressure of oxygen; pCO_2 = partial pressure of carbon dioxide; HCO_3 = bicarbonate; BE = bases excess; FiO_2 = fraction of inspired oxygen; LVEF = left ventricular ejection fraction; PAP = pulmonary artery pressure; IU = international units;

detailed information is provided for each exacerbation in the previous year, including severity, tests conducted, microorganism isolated, treatment administered, and the need for hospitalization (including intensive care unit) and respiratory support.[22] The severity of exacerbations was determined based on the treatment received as follows: mild exacerbations, those treated with short-acting bronchodilators; moderate exacerbations, those treated with short-acting bronchodilators plus antibiotics or oral corticosteroids; or severe exacerbations, those requiring visits to the emergency department or hospitalization.[23]

Information regarding spirometry results, lung volumes, lung diffusing capacity and the 6-min walking test will also be collected in each visit (Table 2). Information from other tests or examinations such as blood analysis (including blood gas analysis), exhaled nitric oxide, and echocardiogram will also be collected if performed prior to the baseline visit and during follow-up (Table 2). In relation to radiological findings, data will be gathered on the presence, distribution and severity of emphysema and/or bronchiectasis if the patient has undergone a CT scan within the 5 years preceding the baseline visit or during follow-up.

Pharmacological treatment (both respiratory and non-respiratory), and non-pharmacological interventions (including the use of oxygen therapy, non-invasive mechanical ventilation, respiratory physiotherapy, etc.),[24] and adherence as well as

Table 3
Treatments for COPD and comorbidities.

Maintenance treatment for COPD
SABA
SAMA
LABA
LAMA
Inhaled corticosteroids
Number of devices for maintenance treatment
Pressurized device (MDI)
Dry powder device (DPI)
Respimat device
Nebulization device
Adherence to treatment
Inhalation technique
Oral corticosteroids
Immunosuppressive treatment
Statins
Oral antidiabetics
Beta blockers
Biological treatment for COPD
Roflumilast
Theophylline
Chronic mucolytics
Chronic macrolides
Chronic hypoxemic respiratory failure
Chronic hypercapnic respiratory failure
Oxygen therapy
NIMV
Nebulized antibiotic treatment
Flu vaccination last year
COVID vaccination last year
Pneumococcus vaccination
Physiotherapy/respiratory rehabilitation last year
Endoscopic or surgical treatment for emphysema

Abbreviations: COPD = chronic obstructive pulmonary disease; SABA = short-acting β_2-agonist; SAMA = short-acting muscarinic receptor antagonist; LABA = long-acting β_2-agonist; LAMA = long-acting muscarinic antagonist; NIMV = non-invasive mechanical ventilation; MDI = metered dose inhaler; DPI = dry powder inhaler.

vaccinations will be collected at baseline and at each follow-up visit (Table 3).

During each follow-up visit, the following events will be recorded: ischemic cardiovascular event, cardiovascular accident, cardiac arrhythmia, pulmonary embolism, cancer and its type. A detailed description of exacerbations including the etiology, severity and treatment will also be noted. Instances in which a patient is lost to follow-up or chooses to withdraw from the study will be recorded. Vital status and the cause of death will be specified with the date and coded as: respiratory, cardiac, lung cancer or other, and other causes. If the patient undergoes lung transplantation due to their condition, it will be reported, marking the conclusion of the patient's participation in the study.

It is important to highlight that there is no specific protocol for conducting additional tests; however, those performed as part of routine clinical practice will be registered.

Data review and database management

The eCRF is provided with filters for plausible ranges in numerical data. Missing data will generate queries to the investigators. Each researcher involved will be granted access to the eCRF and their patients' records. The SPOCCAT Scientific Committee will have comprehensive access to all the information for quality control purposes.

The services of a data manager will be enlisted to enhance communication with researchers, manage queries that may arise, maintain the database, and ensure quality control. The data manager will contact the researchers for reminders or corrections, as necessary, by email or telephone call. In addition, the data manager will periodically send researchers an email with an update on case recruitment and the status of the project.

Ethics

The study protocol has received approval from the Research Ethics Committee of the Hospital Universitari Mútua de Terrassa, as the reference center, and also from the ethics committees of the remaining participating centers. All participants will be requested to provide written informed consent to be enrolled in the study. The SPOCCAT study will adhere to the principles outlined in the Declaration of Helsinki for research projects. All participants will receive information about the nature and objectives of the study and will provide consent to participate through an informed consent process.

Data will be collected in an anonymized (eCRF), with each participant assigned a unique identifier. No personal data that could identify individuals will be recorded. The data obtained will be maintained with strict confidentiality in accordance with the regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 on General Data Protection Regulations, along with the Organic Law 3/2018, of December 5, on the Protection of Personal Data and guarantee of digital rights. Only the designated investigator at each center will have access to the data.

Discussion

The SPOCCAT study has been designed with the objective of filling the gaps in the knowledge about the characteristics, patterns of treatment and prognosis of patients with severe COPD. This study originated from the interaction among pneumologists working in day hospitals caring for severe COPD patients and has evolved into a highly ambitious project, which currently involves a total of 31 investigators across the entire Catalan territory and Andorra. SPOCCAT has the potential to enhance our understanding of the subgroup of severe COPD patients, encompassing the evaluation of innovative aspects, such as non-pharmacological interventions, radiological observations, and chronic bronchial infection. This will facilitate the characterization of the long-term trajectory of these patients, enabling the investigation of predictive factors and diverse clinical outcomes.

The SPOCCAT study has been developed considering previous successful models, such as the CHAIN Spanish cohort[11] and the EARCO (European Alpha-1 antitrypsin deficiency Research Collaboration) International Registry,[25,26] which is following +2500 patients from 90 centers in 24 countries and is currently in its fourth year of follow-up. We have replicated this structure with an eCRF that collects the most relevant information obtained in routine clinical visits and organizing yearly follow-ups that will collect information about changes in comorbidities, clinical characteristics, treatments, number, severity and characteristics of exacerbations, and eventual lung transplant or death. With this information, we aim to address the remaining gaps in severe COPD, employing a novel and contemporary approach, covering areas that other cohort studies have not explored to date. In addition to the multidimensional assessment previously described in cohorts such as CHAIN,[11] various distinct features of COPD will be evaluated. This includes the coexistence of asthma, pharmacological and non-pharmacological treatment, the presence and type of chronic bronchial infection, the etiology of exacerbations, as well as routine complementary tests, such as chest CT, blood analysis, and respiratory function tests.

With this study, we aim to offer an intricate overview of the standard clinical procedures involved in managing patients with severe COPD. The prospective and multicenter design, combined

with a substantial number of participants, will enable comprehensive investigation into the progression of these patients, facilitating the identification of risk factors and diverse clinical trajectories. Moreover, it will allow comparative analysis of this cohort with existing cohorts, potentially fostering collaborations on a national and international scale.

One of the most important objectives of the SPOCCAT study, that is not listed in the protocol, is the construction of a network of researchers interested in severe COPD that may participate in other initiatives in the future. The SPOCCAT database should be the basis of a collaboration that may be extended to other smaller derived protocols aimed at investigating particular aspects of patients with severe COPD.

The main limitation of this study is common to other cohorts of COPD patients and is related to the complexity involved in collecting data on such a heterogeneous disease. The collection of even more detailed and exhaustive data had to be sacrificed to make the project feasible in different clinical settings. Nevertheless, we firmly believe that all the dimensions of the disease are very specifically represented. The second limitation is the absence of a protocol for conducting complementary tests such as blood tests, respiratory function tests or chest CT scans, due to the non-interventional design of the study. Therefore, we may not have complete information on all patients or tests performed with the same frequency during follow-up. However, since these are patients with severe or very severe COPD, it is highly likely that such tests have often been performed in routine clinical practice, as recommended in guidelines.[27,28] To date, we have not planned the collection of biological samples in a biobank for molecular studies, but this will be a future objective after securing funding. Lastly, we employed the fixed ratio for diagnosing COPD primarily to streamline the process, thereby enhancing its applicability. Nonetheless, we have collected data on variables such as age, sex, height, and race for each patient, which will facilitate the application of Global Lung Initiative (GLI) equations[29] in future analyses.

Conclusions

In conclusion, SPOCCAT is a multicenter observational study of a prospective cohort aimed at gaining deeper understanding of the natural history of patients with severe COPD. The context of routine clinical practice will provide a wealth of relevant information to advance our knowledge of this condition. Furthermore, it should contribute to the establishment of a robust structure of researchers, fostering the development of numerous future projects.

Funding

Authors' contributions

R. Costa is the guarantor of the paper, taking responsibility for the integrity of the work as a whole, from inception to publication of the article. JG, DS, DRM, EM, MM, and RC were responsible for the conception, design, and drafting of the manuscript for important intellectual content.

Conflicts of interest

Marc Miravitlles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Menarini, Kamada, Takeda, Zambon, CSL Behring, Specialty Therapeutics, Janssen, Grifols and Novartis, consulting fees from AstraZeneca, Atriva Therapeutics, Boehringer Ingelheim, BEAM Therapeutics, Chiesi, GlaxoSmithKline, CSL Behring, Ferrer, Inhbrix, Menarini, Mereo Biopharma, Spin Therapeutics, Specialty Therapeutics, ONO Pharma, Palobiofarma SL, Takeda, Novartis, Novo Nordisk, Sanofi, Zambon, Zentiva and Grifols and research grants from Grifols.

Roser Costa has received speaker fees from AstraZeneca, Chiesi, GlaxoSmithKline, Zambon, Bial and Novartis.

Elena Miguel has received speaker fees from Glaxo SmithKline, AstraZeneca, Chiesi, Teva, Boehringer Ingelheim, Bial and Gebro.

Daniel-Ross Monserrate has received speaker fees from AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Faes Farma, Gebro, GlaxoSmithKline, Menarini, Novartis, Pfizer, Sanofi, TEVA and Zambon.

Dan Sánchez Berenguer has received speaker fees from AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, Faes Farma, Gebro, GlaxoSmithKline, Menarini, Novartis, Orion, Pfizer, Sanofi, Teva, and consulting fees from AstraZeneca, Bial and Gebro.

Jessica González has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Menarini and Novartis.

Appendix. Organization of the SPOCCAT study

Principal investigator: Roser Costa; *Scientific Committee*: Dan Sánchez, Elena Miguel, Jessica González, Daniel Ross-Monserrate, Marc Miravitlles.

Investigators: Cristina Aljama, Miriam Barrecheguren and Galo Granados (Hospital Universitari Vall d'Hebron, Barcelona); Nestor Soler (Hospital Clínic, Barcelona); Alicia Marin and Laura Rodríguez (Hospital Germans Trias I Pujol, Badalona); Claudia Guevara and Nuria Rodríguez (Consorci Sanitari Alt Penedés Garraf); Pilar Ortega (Hospital de Mataró); Luis Adolfo Urrelo (Hospital de Tortosa Verge de la Cinta Tortosa) Juan Antonio Lloret (Hospital de Viladecans); Sergi Pascual (Hospital del Mar, Barcelona); Minerva Sofía Ramírez (Hospital del Vendrell, Tarragona); Raquel Viana (Hospital El Pilar); Sònia Belda and Marc Bonnin (Hospital Josep Trueta i Sta., Caterina, Girona); Núria Bruguera (Hospital Moisès Broggi); Víctor Núñez (Hospital Nostra Senyora de Meritxell, Andorra); Noelia Pablos (Hospital de Martorell); Annie Navarro (Hospital Mutua de Terrassa); Eduardo Antonio Vélez and Josep Albert Martos (Hospital Sant Rafael, Barcelona); Irene López (Hospital Santa Tecla Tarragona); Fernando Ruíz (Hospital Universitari de Vic); Danny Zaya (Hospital Universitari Sagrat Cor, Barcelona).

References

1. Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977;1:1645–8, http://dx.doi.org/10.1136/bmj.1.6077.1645. PMID: 871704; PMCID: PMC1607732.

2. Løkke A, Lange P, Scharling H, Fabricius P, Vestbo J. Developing COPD: a 25 year follow up study of the general population. Thorax. 2006;61:935–9, http://dx.doi.org/10.1136/thx.2006.062802. PMID: 17071833; PMCID: PMC2121175.

3. Kohansal R, Martinez-Camblor P, Agustí A, Buist AS, Mannino DM, Soriano JB. The natural history of chronic airflow obstruction revisited: an analysis of the Framingham offspring cohort. Am J Respir Crit Care Med. 2009;180:3–10, http://dx.doi.org/10.1164/rccm.200901-0047OC. Epub 2009 Apr 2. PMID: 19342411.

4. Vestbo J, Anderson W, Coxson HO, Crim C, Dawber F, Edwards L, et al. Evaluation of COPD longitudinally to identify predictive surrogate end-points (ECLIPSE). Eur Respir J. 2008;31:869–73, http://dx.doi.org/10.1183/09031936.00111707. Epub 2008 Jan 23. PMID: 18216052.

5. Garcia-Aymerich J, Gómez FP, Antó JM. Caracterización fenotípica y evolución de la EPOC en el estudio PAC-COPD: diseño y metodología. Arch Bronconeumol. 2009;45:4–11, http://dx.doi.org/10.1016/j.arbres.2008.03.001. Epub 2009 Jan 3. PMID: 19186292.

6. Makita H, Nasuhara Y, Nagai K, Ito Y, Hasegawa M, Betsuyaku T, et al. Characterisation of phenotypes based on severity of emphysema in chronic obstructive pulmonary disease. Thorax. 2007;62:932–7, http://dx.doi.org/10.1136/thx.2006.072777. Epub 2007 Jun 15. PMID: 17573447; PMCID: PMC2117136.

7. Künzli N, Ackermann-Liebrich U, Keller R, Perruchoud AP, Schindler C. Variability of FVC and FEV$_1$ due to technician, team, device and subject in an eight centre study: three quality control studies in SAPALDIA. Swiss Study on Air Pollution and Lung Disease in Adults. Eur Respir J. 1995;8:371–6, http://dx.doi.org/10.1183/09031936.95.08030371. PMID: 7789479.

8. Downs SH, Brändli O, Zellweger J-P, Schindler C, Künzli N, Gerbase MW, et al. Accelerated decline in lung function in smoking women with airway obstruction: SAPALDIA 2 cohort study. Respir Res. 2005;6:45, http://dx.doi.org/10.1186/1465-9921-6-45. PMID: 15918902; PMCID: PMC1177989.

9. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350:1005–12, http://dx.doi.org/10.1056/NEJMoa021322. PMID: 14999112.

10. Regan EA, Hokanson JE, Murphy JR, Make B, Lynch DA, Beaty TH, et al. Genetic epidemiology of COPD (COPDGene) study design. COPD. 2010;7:32–43, http://dx.doi.org/10.3109/15412550903499522. PMID: 20214461; PMCID: PMC2924193.

11. López-Campos JL, Peces-Barba G, Soler-Cataluña JJ, Soriano JB, de Lucas Ramos P, de-Torres JP, et al. Chronic obstructive pulmonary disease history assessment in Spain: a multidimensional chronic obstructive pulmonary disease evaluation. Study methods and organization. Arch Bronconeumol. 2012;48:453–9, http://dx.doi.org/10.1016/j.arbres.2012.05.006. Epub 2012 Jul 4. PMID: 22766419.

12. Calle Rubio M, Rodriguez Hermosa JL, de Torres JP, Marín JM, Martínez-González C, Fuster A, et al. COPD Clinical Control: predictors and long-term follow-up of the CHAIN cohort. Respir Res. 2021;22:36, http://dx.doi.org/10.1186/s12931-021-01633-y. PMID: 33541356; PMCID: PMC7863480.

13. Cosio BG, Soriano JB, López-Campos JL, Calle M, Soler JJ, de-Torres JP, et al. Distribution and outcomes of a phenotype-based approach to guide COPD management: results from the CHAIN cohort. PLOS ONE. 2016;11:e0160770, http://dx.doi.org/10.1371/journal.pone.0160770. Erratum in: PLoS One. 2016 Nov 2;11(11):e0166257. PMID: 27684372; PMCID: PMC5042557.

14. Martínez-González C, Casanova C, de-Torres JP, Marín JM, de Lucas P, Fuster A, et al. Changes and clinical consequences of smoking cessation in patients with COPD: a prospective analysis from the CHAIN cohort. Chest. 2018;154:274–85, http://dx.doi.org/10.1016/j.chest.2018.02.007. Epub 2018 Feb 22. PMID: 29476876.

15. Chen C-Z, Shih C-Y, Hsiue T-R, Tsai S-H, Liao X-M, Yu C-H, et al. Life expectancy (LE) and loss-of-LE for patients with chronic obstructive pulmonary disease. Respir Med. 2020;172:106132, http://dx.doi.org/10.1016/j.rmed.2020.106132. Epub 2020 Aug 29. PMID: 32905891.

16. Soriano JB, Alfageme I, Miravitlles M, de Lucas P, Soler-Cataluña JJ, García-Río F, et al. Prevalence and determinants of COPD in Spain: EPISCAN II. Arch Bronconeumol. 2021;57:61–9, http://dx.doi.org/10.1016/j.arbres.2020.07.024. Epub 2020 Sep 17. PMID: 32950310.

17. Lopez-Campos JL, Almagro P, Gómez JT, Chiner E, Palacios L, Hernández C, et al. Spanish COPD guideline (GesEPOC) update: comorbidities, self-management and palliative care. Arch Bronconeumol. 2022;58:334–44, http://dx.doi.org/10.1016/j.arbres.2021.08.002. Epub 2021 Sep 4. PMID: 35315327.

18. Jones PW, Harding G, Berry P, Wiklund I, Chen W-H, Kline Leidy N. Development and first validation of the COPD Assessment Test. Eur Respir J. 2009;34:648–54, http://dx.doi.org/10.1183/09031936.00102509. PMID: 19720809.

19. Soler-Cataluña JJ, Martínez-García MA, Sánchez LS, Tordera MP, Sánchez PR. Severe exacerbations and BODE index: two independent risk factors for death in male COPD patients. Respir Med. 2009;103:692–9, http://dx.doi.org/10.1016/j.rmed.2008.12.005. Epub 2009 Jan 7. PMID: 19131231.

20. Greenwood JLJ, Joy EA, Stanford JB. The Physical Activity Vital Sign: a primary care tool to guide counseling for obesity. J Phys Act Health. 2010;7:571–6, http://dx.doi.org/10.1123/jpah.7.5.571. PMID: 20864751.

21. Ramon MA, Esquinas C, Barrecheguren M, Pleguezuelos E, Molina J, Quintano JA, et al. Self-reported daily walking time in COPD: relationship with relevant clinical and functional characteristics. Int J Chron Obstruct Pulmon Dis. 2017;12:1173–81, http://dx.doi.org/10.2147/COPD.S128234. PMID: 28458527; PMCID: PMC5402919.

22. Soler-Cataluña JJ, Piñera P, Trigueros JA, Calle M, Casanova C, Cosío BG, et al. Spanish COPD guidelines (GesEPOC) 2021 update diagnosis and treatment of COPD exacerbation syndrome. Arch Bronconeumol. 2022;58:69–81, http://dx.doi.org/10.1016/j.arbres.2021.05.033. Epub 2022 Feb 14. PMID: 35971815.

23. Wedzicha JA, Ers Co-Chair, Miravitlles M, Hurst JR, Calverley PM, Albert RK, Anzueto A, et al. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2017;49:1600791, http://dx.doi.org/10.1183/13993003.00791-2016. PMID: 28298398.

24. Cosío BG, Hernández C, Chiner E, Gimeno-Santos E, Pleguezuelos E, Seijas N, et al. Spanish COPD guidelines (GesEPOC 2021): non-pharmacological treatment update. Arch Bronconeumol. 2022;58:345–51, http://dx.doi.org/10.1016/j.arbres.2021.08.010. Epub 2021 Sep 17. PMID: 35312554.

25. Greulich T, Altraja A, Barrecheguren M, Bals R, Chlumsky J, Chorostowska-Wynimko J, et al. Protocol for the EARCO Registry: a pan-European observational study in patients with α1-antitrypsin deficiency. ERJ Open Res. 2020;6:181–2019, http://dx.doi.org/10.1183/23120541.00181-2019. PMID: 32154291; PMCID: PMC7049712.

26. Miravitlles M, Turner AM, Torres-Duran M, Tanash H, Rodríguez-García C, López-Campos JL, et al. Clinical and functional characteristics of individuals with alpha-1 antitrypsin deficiency: EARCO international registry. Respir Res. 2023;23:352, http://dx.doi.org/10.1186/s12931-022-02275-4. Erratum in: Respir Res. 2023 Feb 18;24(1):57. PMID: 36527073; PMCID: PMC9756677.

27. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. Arch Bronconeumol. 2023;59:232–48, http://dx.doi.org/10.1016/j.arbres.2023.02.009. Epub 2023 Mar 1. PMID: 36933949.

28. Miravitlles M, Calle M, Molina J, Almagro P, Gómez J-T, Trigueros JA, et al. Spanish COPD guidelines (GesEPOC) 2021: updated pharmacological treatment of stable COPD. Arch Bronconeumol. 2022;58:69–81, http://dx.doi.org/10.1016/j.arbres.2021.03.005. Epub 2021 Mar 17. PMID: 33840553.

29. Stanojevic S, Kaminsky DA, Miller M, Thompson B. The new ERS/ATS standard on lung function test interpretation: some extant limitations. Eur Respir J. 2022:2201112, http://dx.doi.org/10.1183/13993003.01112-2022.