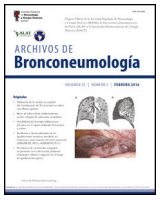
Archivos de Bronconeumología 57 (2021) 593–610

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE
Bronconeumología

www.archbronconeumol.org



Scientific Letters

Time-based Register and Analysis of COPD Endpoints (TRACE) Project: Methodology and Workflow

Registro y análisis en el tiempo de resultados clínicos en EPOC (Proyecto TRACE): metodología y procedimiento

Dear Editor,

Over the last few decades, several observational prospective cohorts have added to our understanding of the clinical presentation and the progression of chronic obstructive pulmonary disease (COPD). Although the different studies available have provided valuable information on specific aspects of the disease over a fixed period of time,[1,2] its direct implications for daily clinical practice have been less profound than expected partly due to the use of specific advanced diagnostic tools, which are not always routinely available in clinical practice. Accordingly, it would be desirable to conduct a prospective observational cohort study evaluating the tools normally available to the clinician in their daily clinical practice.

The *Time-based Register and Analysis of COPD Endpoints* (TRACE) cohort (clinicaltrials.gov NCT03485690) is a single-center, prospective cohort study aimed at evaluating COPD patients prospectively using tools normally used in the clinic. The study starts from the hypothesis that is possible to identify different patient types with different clinical behavior who show a different response to treatment by using common clinical tools available at all health centers attending patients with respiratory diseases. The protocol has been approved by the Local Ethical Health Authorities (Portal de Ética de la Investigación Biomédica de Andalucía, approval actas 08/2015 and 07/2017). Due to the observational and non-interventional nature of the study, an informed consent was waived. The ethical committee was notified of this circumstance and approved the procedure clearly recorded in the protocol.

The objective of the study is to accomplish three specific aims: (1) to describe the variation over time of different clinical variables and the results of the complementary tests routinely used in the clinic, (2) to define the different behavior patterns of the disease, and (3) to evaluate the impact of different therapeutic approaches on this behavior in the different patient types in terms of lung function improvement, perception of symptoms and exacerbation frequency. The primary endpoint is survival. The secondary endpoints include dyspnea, measured by modified Medical Research Council scale, the number of moderate or severe exacerbations, forced expiratory volume in one second (FEV_1) annual decline, forced expiratory flow at 25–75% of expiration, peak expiratory flow, peripheral blood eosinophils count, serum alpha1-antitrypsin, total IgE, bronchial colonization, and inhaled and oral COPD-related medication use.

The study population is composed solely of COPD patients recruited from specialized COPD-dedicated outpatient clinics in a tertiary university hospital. Estimated sample size was 1440 cases. Adult patients with a diagnosis of COPD according to current guidelines[3] receiving routine follow-up in our dedicated COPD outpatient clinic have been selected for inclusion. The protocol does not pre-specify any exclusion criteria, except for the complete reversibility of lung function testing during follow-up. The inclusion of patients was piloted study since 2012, a procedure that was completed in 2015.

After identification of cases, the patients are followed up at yearly visits *sine die* until they die or are lost to follow-up. The study is guided by a Steering Committee, consisting of six academic respiratory physicians who attend patients regularly. All the subjects receive their prescribed medication and therapeutic interventions throughout the study with any changes in medication being ordered by the physician in charge, according to the patient's clinical status. During the yearly visits, clinical, functional, radiological and analytical information is recorded using a standardized questionnaire.

All the clinical variables were obtained from the patient and included: socio-demographics (gender, age), tobacco history, comorbidities, clinical presentation during the previous year in a stable state (including dyspnea evaluation, cough and sputum production, color of the sputum if present, wheezing and symptoms suggestive of asthma), exacerbations and hospitalization in the previous year, current pharmacological and non-pharmacological treatment. Complementary tests, included, at least, chest radiology, pre- and post-bronchodilator spirometry and analytical results (blood eosinophils, alpha1-antitrypsin, total IgE). With this information, the patients are initially categorized according to the different versions of the Global Initiative of Obstructive Lung Disease (GOLD) document[3] and the Spanish national guidelines for COPD (GesEPOC),[4] and the classification is adapted to the successive updates of these documents during the follow-up, whenever possible.

Asthma-like symptoms are also recorded, including the presence of rhinitis, variability of respiratory symptoms during the year and worsening of respiratory symptoms when exposed to non-specific triggers. The comorbidities are recorded following different comorbidity composite scores, including the Charlson comorbidity index,[5] the COPD specific comorbidity test (COTE),[6] the COMorbidities in Chronic Obstructive Lung Disease (COMCOLD) index,[7] and the Functional Comorbidity Index.[8]

Exacerbations are recorded at each yearly clinical visit. For the present study, an exacerbation is defined as any increase in perceived respiratory symptoms which requires additional medication to control them. To consider two exacerbations as different episodes, a time lapse between episodes of at least 4 weeks from the end of the exacerbation or 6 weeks from the beginning is required.[9] The information provided by the patient regarding exacerbation frequency is matched with the information in the clinical record. Emergency ward visits and hospital admissions due to exacerbations are also noted.

Non-pharmacological treatments over the previous year are noted at every visit, including the persistence of active smoking, daily exercise, and influenza and pneumococcal vaccinations. Oral and inhaled pharmacological therapies for COPD are also noted,

as is the use of home-based therapies, including home mechanical ventilation, long-term oxygen therapy and nebulizers.

Spirometries are performed so far with a Masterlab Pneumatic Tachograph (Erich Jaeger GHBH, Würzburg, Germany). The spirometer is calibrated daily, and the results adjusted by the atmospheric conditions. Patients are instructed to withhold their inhaler medication on the day of the test, in order to record pre- and post-bronchodilator spirometry. If this is not the case, then the spirometry is considered post-bronchodilator. The bronchodilator test is performed after the administration of 400 μg of salbutamol via a pressured metered dose inhaler with a chamber. The spirometry is performed according to current standards assessing the quality of the results. Parameters recorded in absolute values and percentage predicted values are forced vistal capacity (FVC), FEV_1, FEV_1/FVC ratio, peak expiratory flow, and forced expiratory flow between 25% and 75% of the FVC. The main limitation is in relation to the non-use of advanced diagnostic techniques beyond those recommended for clinical practice.

TRACE is a prospective cohort study is an opportunity to identify specific patients who have a specific response to various treatments using tools available to any clinician. Their results may provide new information on how to make a more personalized medicine in real clinical practice.

Final declarations

Funding. TRACE is funded by an unrestricted grant from Gebro Pharma laboratories.

Conflicts of interest

JLLC has received honoraria during the last 3 years for lecturing, scientific advice, participation in clinical studies or writing for publications for (alphabetical order): AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, Esteve, Ferrer, Gebro, GlaxoSmithKline, Grifols, Menarini, Novartis, Rovi, and Teva.

Acknowledgment

The authors are thankful to Hispamed Servicios Biomedicos (https://www.hispamed.com/) for their assistance in improving the English in the original version.

References

1. Wacker ME, Kitzing K, Jorres RA, Leidl R, Schulz H, Karrasch S, et al. The contribution of symptoms and comorbidities to the economic impact of COPD: an analysis of the German COSYCONET cohort. Int J Chron Obstruct Pulmon Dis. 2017;12:3437–48.
2. Perez de Llano L, Cosio BG, Miravitlles M, Plaza V. Accuracy of a new algorithm to identify Asthma-COPD Overlap (ACO) patients in a cohort of patients with chronic obstructive airway disease. Arch Bronconeumol. 2017.
3. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD executive summary. Arch Bronconeumol. 2017;53:128–49.
4. Miravitlles M, Soler-Cataluna JJ, Calle M, Molina J, Almagro P, Quintano JA, et al. Spanish Guidelines for Management of Chronic Obstructive Pulmonary Disease (GesEPOC) 2017. Pharmacological treatment of stable phase. Arch Bronconeumol. 2017;53:324–35.
5. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
6. Divo M, Cote C, de Torres JP, Casanova C, Marin JM, Pinto-Plata V, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2012;186:155–61.
7. Frei A, Muggensturm P, Putcha N, Siebeling L, Zoller M, Boyd CM, et al. Five comorbidities reflected the health status in patients with chronic obstructive pulmonary disease: the newly developed COMCOLD index. J Clin Epidemiol. 2014;67:904–11.
8. Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. J Clin Epidemiol. 2005;58:595–602.
9. Soler-Cataluna JJ, Rodriguez-Roisin R. Frequent chronic obstructive pulmonary disease exacerbators: how much real, how much fictitious? COPD. 2010;7:276–84.

Laura Carrasco Hernández [a] Candela Caballero Eraso [a,b]
María Abad Arranz [a] Eduardo Márquez Martín [a]
Carmen Calero Acuña [a,b] Jose Luis Lopez-Campos [a,b,*]

[a] *Unidad Médico-Quirúrgica de Enfermedades Respiratorias. Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocio/Universidad de Sevilla, Spain*
[b] *CIBER de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain*

* Corresponding author.
E-mail address: lopezcampos@separ.es (J.L. Lopez-Campos).

https://doi.org/10.1016/j.arbres.2020.10.022

Lung infection caused by *Lophomonas blattarum*☆

Infección pulmonar por Lophomonas blattarum

To the Editor:

We report a series of 6 cases, 4 women and 2 men, with a median age of 57 years, all of whom had comorbidities involving immunosuppression. They were admitted with respiratory symptoms and a chest X-ray with pulmonary infiltrates consistent with bacterial pneumonia. Empirical antibiotic treatment was administered in all cases. No response was obtained, patients deteriorated progressively, and cultures were negative.

Case 1: An 18-year-old female patient was referred from an urban area with a diagnosis of left pleural empyema. A simple chest CT scan revealed infected pulmonary sequestration in the left lower lobe. A left lower lobectomy was performed by lateral thoracotomy, without complications. An examination of the surgical piece detected *Lophomonas blattarum* infection (Fig. 1), so treatment began with metronidazole. The patient's postoperative progress was favorable and she was discharged on the fifth day with complete resolution of her respiratory symptoms.

Case 2: A 52-year-old male patient from a rural area with a history of chronic renal failure was admitted with severe acute respiratory failure. Complete blood count and chest X-ray were performed, and were consistent with community-acquired pneumonia (CAP). He received empirical antibiotic treatment and oxygen therapy but showed no improvement. In view of the lack of response, bronchoscopy was performed and samples were collected. A direct study showed flagellated parasites and intravenous metronidazole began, with great improvement. The patient completed 20 days of home treatment, with complete resolution.

Case 3: A 55-year-old male patient from an urban area with a history of pulmonary tuberculosis treated with isoniazid and

☆ Please cite this article as: Pinos Vélez N, Ordoñez Vintimilla R, Agreda Orellana S. Infección pulmonar por *Lophomonas blattarum*. Arch Bronconeumol. 2021;57:594–596.