

**PROTECTION OF HUMANS AND ANIMALS**

The authors have followed the protocols of their work center on the publication of data. The data was anonymized and none of the authors had access to patient identification. The study was conducted in accordance with the Helsinki Declaration updated in 2013.

**DATA CONFIDENTIALITY**

The authors declare having followed the protocols in

use at their working center regarding patients' data publication.

**COMPETING INTERESTS**

All authors declared no competing interests.

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**Is COPD a Cause of Premature Death?****A DPOC é Causa de Morte Prematura?**

**Keywords:** Mortality, Premature; Pulmonary Disease, Chronic Obstructive/mortality

**Palavras-chave:** Doença Pulmonar Obstrutiva Crónica/mortalidade; Mortalidade Prematura

Patients Chronic obstructive pulmonary disease (COPD) is currently the third most important cause of death worldwide.<sup>1</sup> Although absolute COPD deaths and crude mortality rates are rising in many countries, age-standardized mortality rates have been declining in many parts of the world. This has led some authors to argue that, in the future, patients will die with COPD but not from COPD.<sup>2</sup> In the present study we aimed to understand the circumstance of death in COPD patients and if COPD can be considered a cause of premature death.

A total of 303 stable COPD patients over 40 years of age, diagnosed according to the GOLD criteria, were recruited consecutively at the ambulatory pulmonology clinic of Guimarães Hospital, between March 2016 and May 2017. The exclusion criteria were refusal to participate or inability to understand simple questionnaires, such as the COPD assessment test or the Medical Research Council Dyspnoea Questionnaire. The patients were followed for 46 to 60 months, and some preliminary results are discussed in the present paper. A statistical analysis was performed with SPSS Statistics for Windows software, version 22.0. Armonk, NY: IBM Corporation. The level of significance was set at  $p < 0.05$ .

Five years after the start of recruitment, patients who had died were identified, and their ages and clinical notes, by the time of death, were recorded and analysed. The study was approved by the Ethics Committee of Guimarães Hospital.

The demographic, clinical and functional characteristics

Characteristics	n = 303
Male gender	241 (79.5)
Mean age (years)	67.5 ± 10.2
Age ≥ 65 years	186 (61.4)
Mean smoking amount (pack/years)	49.3 ± 32.4
mMRC grade ≥ 2	185 (61.1)
Frequent ECOPD (≥ 2/last year)	115 (38.0)
Post-bronchodilator FEV <sub>1</sub> %	53.2% ± 19.7
GOLD stage	
I	30 (9.9)
II	127 (41.9)
III	106 (35.05)
IV	40 (13.2)
GOLD 2017 classification	
A	70 (23.1)
B	120 (39.6)
C	7 (2.3)
D	106 (35.0)

Data shown as mean ± S/D or n (%)

mMRC: Medical Research Council Dyspnoea Questionnaire; ECOPD: COPD exacerbations; GOLD: Global Initiative for Chronic Obstructive Pulmonary Disease

of the 303 COPD patients, by the time of their recruitment, have been previously published,<sup>3,4</sup> and some are presented in Table 1.

In the meantime, 61 patients (20.13%) died. Their median and mean age of death was, respectively, 77.00 and 77.02 ( $\pm$  8.78) years, being 77.00 and 77.45 ( $\pm$  8.51) years for male patients and 76.50 and 74.13 ( $\pm$  10.6) years for female patients. The mean FEV<sub>1</sub>% of the patients who died and those still alive was 43.36 and 54.40, respectively ( $P$  = 0.032), at the time of recruitment. However, we found no statistically significant association between death and the GOLD classification nor with a history of frequent exacerbations.

Thirty-two patients presented COPD exacerbation with acute-on-chronic respiratory failure by the time of death. Pneumonia, heart failure, advanced stage lung cancer and kidney failure were the other most important causes of

death. In 27 patients, two or more different disorders contributed and were present at the time of death.

COPD exacerbation with acute-on-chronic respiratory failure was the most important cause contributing to death, suggesting that most of these patients have died, in fact, because of COPD. Taking into account the current average life expectancy of the Portuguese population<sup>5</sup> – 81.06 years, 78.07 for men and 83.67 for women – COPD was associated with a shorter life expectancy, particularly in female patients.

#### COMPETING INTERESTS

The authors have no competing interests to declare related to this study.

#### FUNDING SOURCES

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## A Case Report of Acute Hepatitis of Unknown Origin

### Caso Clínico de Hepatite Aguda de Origem Desconhecida

**Keywords:** Biomarkers; Child; Disease Outbreaks; Hepatitis

**Palavras-chave:** Biomarcadores; Criança; Hepatite; Surtos de Doenças

Dear Editor,

Since the first international alert on the 5<sup>th</sup> April 2022 and the ongoing news, probable cases of hepatitis of unknown origin have been reported in children worldwide. The etiology and pathogenic mechanisms of the disease remain under investigation, and so far the evidence suggests adenovirus or SARS-CoV-2 as being the most likely infectious causes, although toxins, drugs or environmental exposures have been considered as well. Further hypotheses point out a novel pathogen or variant of adenovirus or SARS-CoV-2.<sup>1</sup>

In Portugal, according to the most recent data from the European Centre for Disease Prevention and Control (ECDC), published on the 1<sup>st</sup> July there are only 19 suspected cases.<sup>2</sup>

We report, to the best of our knowledge, the very first suspected case of non-viral A-E hepatitis in Portugal.

The patient was a previously healthy 22-month-old female child, with a history of SARS-CoV-2 infection in January 2022. During April 2022, she presented with prolonged fever (maximum 40.2°C) that was managed with antipyretics, not exceeding therapeutic daily doses, with complete resolution after day-10. She also presented with anorexia and malaise, and on days four and five with non-bloody diarrhea. On day nine she had limited vomiting.

During the acute illness there were no signs of jaundice, choloria or acholic stools. A good general appearance was kept throughout the disease course.

With no relevant previous results, follow-up bloodwork