



EDITORIAL

An Integrated therapeutic approach: do COPD comorbidities justify it?

Uma abordagem terapêutica integrada: as comorbilidades na DPOC justificam-na?

Chronic obstructive pulmonary disease (COPD) remains a major public health problem, causing considerable morbidity and mortality; it has risen from the fourth most common cause of death in 1990 to the third from 2010.¹ This dark prognostication is consistent with US data showing a progressive age-specific rise in mortality from COPD in both males and females over the last 50 years.²

Previous studies in Portugal have also identified an increase in the prevalence of COPD from 5.3% in 2002³ to 14.2% in 2013,⁴ although they were measured by somewhat different methods,⁵ and the number of deaths in the country accounts for up to 2,743 COPD patients per year.⁶ The same source⁶ states that 800 000 Portuguese people suffer from COPD nowadays, yet more than 660,000 are still undiagnosed.⁵

It is increasingly recognised that COPD often coexists with other chronic diseases and that these comorbidities contribute to patient health status and prognosis.^{7,8} Comorbidities and also exacerbations were introduced into the COPD definition in the second GOLD revision⁷ as they have a role in the severity of the disease in individual patients. Extrapulmonary manifestations of COPD are typically believed to be linked to progression of the disease; examples such as skeletal dysfunction, lean mass depletion, and osteoporosis and osteopenia.^{9,10} In other comorbidities such as cardiovascular diseases (CVD), systemic inflammation has been proposed as an explanation for the association between them and COPD.¹¹ In fact, epidemiological data suggest that COPD patients are at a greater risk of CVD compared with age- and sex- matched controls.¹²

Autonomic imbalance, vascular endothelial dysfunction and lower arterial compliance may be implicated in this association.¹¹ Also the decreased physical activity observed in all severity stages of COPD patients¹³ may increase CVD and other comorbidities risks.

Furthermore, pulmonary neoplasms, anxiety and depression are highly prevalent in COPD patients^{7,8}, the former

because of sharing the same main risk factor- tobacco smoke, and the latter because of social isolation and physical impairment.

A recent study¹⁴ showed that comorbidities are predominantly present in “symptomatic” GOLD groups B and D.

The presence of comorbidities in these patients certainly requires proper diagnosis, quantification, and allocation of therapeutic means. It is interesting that all COPD multi component indices until very recently incorporated many domains but not comorbidities.¹⁵ However, two new indices, COTE and CODEX have explicitly incorporated co morbidities as added dimensions in the assessment of COPD severity and prognosis^{16,17}.

In this issue of the Portuguese Journal of Pulmonology, Areias V *et al*¹⁸ report on the distribution of comorbidities in patients with old COPD GOLD 4, that is FEV₁% predicted < 30% and/or chronic respiratory failure. The authors conclude that their high prevalence justifies the need for a comprehensive and integrated therapeutic approach.

This is a well conducted cross-sectional study with a retrospective analysis, in a well defined patient population, but it has some limitations: The absence of a control group prevented the authors from evaluating the effect of age and gender properly as well as other factors possibly implicated in the prevalence of comorbidities; the limited sample size (n = 89) could have reduced the power of sub-analyses and the importance of the results; furthermore, including only GOLD Stage 4 patients, does not allow for generalizing about the prevalence of comorbidities in the whole COPD population.

Nevertheless the results are important and similar to those reported in previous studies¹⁹⁻²¹ in relation to the prevalence of comorbidities in COPD patients.

The increased risk of lung carcinoma in the studied population are similar to that described by other authors¹⁵ and certainly might make health authorities reconsider the

importance and utility of creating a lung cancer screening program in COPD patients.

The finding that frequent exacerbators were associated with an increased risk of presenting with at least two comorbidities should point to a better way of preventing exacerbations through effective management of comorbidities.

COPD prevalence in Portugal is comparable to that of some European countries like Germany (13.2%) and Sweden (16.2%), which implies that the economic investment in COPD treatment in our country should be similar to that in those countries mentioned.

Projections and health planning regarding COPD are based on its current prevalence together with demographics, and national studies aimed at determining each of them are of crucial interest. However, a holistic estimate of the burden of COPD might include quantifying comorbidities, their severity, and therapy requirements. If this is not done, the burden of COPD will always be underestimated, and the resources allocated to disease control will remain insufficient.

References

- Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2013;380:2163-96.
- Thune MJ, Carter BD, Feskanich D, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med*. 2013;368:351-64.
- Cardoso J, Reis Ferreira J, Almeida J, Santos JM, Rodrigues F, Matos MJ. Prevalence of Chronic Obstructive Pulmonary Disease (COPD) in Portugal. *Am J Respir Crit Care Med*. 2003;A110.
- Bárbara C, Rodrigues F, Dias H, Cardoso J, Almeida J, Matos MJ, Simão P, Santos M, Reis Ferreira J, Gaspar M, Gnatiuc L, Burney P. *Rev Port Pneumol*. 2013;96-105, 1983.
- Soriano JB, Lamprecht B. No more hic sunt dracones: Portugal is in the COPD map. *Rev Port Pneumol*. 2013;19:86-7.
- Relatório ONDR 2012. Direção Geral da Saúde. <http://www.dgs.pt/>
- Vestbo J, Hurd SS, Agusti AG, et al. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: GOLD Executive Summary. *Am J Respir Crit Care Med*. 2013;187:347-65.
- Fabbri LM, Luppi F, Beghé B, et al. Complex chronic comorbidities of COPD. *Eur Respir J*. 2008;31:204-12.
- Agusti AG, Sauleda J, Miralles C, et al. Skeletal muscle apoptosis and weight loss in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2002;166:485-9.
- Vestbo J, Prescott E, Almdal T, et al. Body mass, fat free body mass and prognosis in COPD patients from a random population sample. *Am J Respir Crit Care Med*. 2006;173:79-83.
- Sin DD, Man SFP. Why are patients with chronic obstructive pulmonary disease at increased risk of cardiovascular disease? The potential role of systemic inflammation in chronic obstructive pulmonary disease. *Circulation*. 2003;107:1514-9.
- Curkendall SM, DeLuise C, Jones JK, et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease. Saskatchewan Canada cardiovascular disease in COPD. *Am J Epidemiol*. 2006;16:63-70.
- Watz H, Waschki B, Meyer T, et al. Physical activity in patients with COPD. *Eur Respir J*. 2009;33:262-72.
- Agusti A, Hurd S, Jones P, et al. FAQs about the GOLD 2011 assessment proposal of COPD: a comparative analysis of four different cohorts. *Eur Respir J*. 2013;42:1391-401.
- Marin JM, Alfageme I, Almagro P, Casanova C, Esteban C, Soler-Cataluña JJ, de Torres JP, Martínez-Cambor P, Miravittles M, Celli BR, Soriano JB. Multicomponent indices to predict survival in COPD: the COCOMICS study. *Eur Respir J*. 2013;42:323-32.
- Divo M, Cote C, de Torres JP, Casanova C, Marin JM, Pinto-Plata V, Zulueta J, Cabrera C, Zagaceta J, Hunninghake G, Celli B. BODE Collaborative Group. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2012;186:155-61.
- Almagro P, Soriano JB, Cabrera F, Boixeda R, Alonso M, Barreiro B, Diez-Manglano J, Murio C, Heredia J. Working Group on COPD, Spanish Society of Internal Medicine.*. Short- and medium-term prognosis in patients hospitalized for COPD exacerbation: The CODEX index. *Chest* 2013 Sep 26. doi: 10.1378/chest.13-1328. [Epub ahead of print].
- Areias V, Carreira S, Anciães M, Pinto P, Bárbara C. Comorbidities in patients with gold stage 4 chronic obstructive pulmonary disease. *Rev port Pneumol*. 2014 (in press).
- Chatila W, Thomashow B, Minai O, Criner G, Make B. Comorbidities in chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 2008;5:549-55.
- Agusti A, Calverley P, Celli B, Coxson H, Edwards L, Lomas D, et al. Characterisation of COPD heterogeneity in the ECLIPSE cohort. *Respiratory Research*. 2010;11:122.
- Bárbara C, Moita J, Cardoso J, Costa R, Redondo R, Gaspar M. A importância da dispneia no diagnóstico da doença pulmonar obstrutiva crónica — uma análise de uma coorte estável em Portugal (ensaio clínico SAFE). *Rev Port Pneumol*. 2011;17:131-8.

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