J Bras Pneumol. 2021;47(5):e20210389
https://dx.doi.org/10.36416/1806-3756/e20210389

A shadow in the GOLD ABCD classification system: measurement of perception of symptoms in COPD

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"If someone separated the art of counting and measuring and weighing from all the other arts, what was left of each (of the others) would be, so to speak, insignificant."

Plato, ancient Greek philosopher

COPD is a complex disease with a heterogeneous clinical presentation,[1-3] the severity of which being related not only to functional impairment.[1] Self-reported perception of dyspnea, a subjective description of breathing discomfort, varies in intensity and derives from physiological, psychological, social, and environmental interactions[4]; a range of qualitatively different descriptors of breathing discomfort (for example, unrewarded inspiration, inspiratory difficulty, or tightness) may be however reported by COPD patients.[4] It should be noted that COPD patients with a high degree of dyspnea may also have poor maximum exercise capacity in association, regardless of the severity of airflow obstruction.[5] In addition, dyspnea is not the only symptom reported by COPD patients: respiratory health status and how COPD impacts these patients may enclose a series of clinical aspects, improving the identification of patient-reported outcomes.[1] In a nutshell, COPD may affect the patient's perception in several ways. Therefore, although COPD-related symptoms are reported as being subjective, we should find a measuring system: Plato taught us that art that is not measured is insignificant.

The modified Medical Research Council dyspnea scale (mMRC) and the COPD assessment test (CAT) have been proposed to assess symptoms quantitatively.[6] The mMRC scale is a simple clinical discriminative scale that measures the perception of dyspnea by defining the level of physical activity that provokes the symptom to appear, whereas CAT is a self-administered questionnaire that measures health-related impacts on COPD patients, exploring not only dyspnea-related aspects.[6] Both mMRC and CAT have good prognostic power, but they particularly explore daytime symptoms, although the presence of respiratory symptoms, such as nocturnal dyspnea, may have prognostic implications during the 24-hour day.[7] In order to evaluate the symptom perception of COPD patients, the GOLD 2019 report,[1] which includes the ABCD classification system, recommends using either the mMRC scale or the CAT, with no differentiation between the two. Measurements of symptoms, by using the specific cutoffs of mMRC (≥ 2 points) and CAT (score ≥ 10), define which patients have a worse perception of their symptoms; these measurements classify the risk of exacerbations into four categories.[1]

In the present issue of the Brazilian Journal of Pulmonology, the study by Montes de Oca et al.[8] reports data from a large cohort of Latin American COPD outpatients—the designated LASSYC study—and explores the value of the perception of symptoms in the context of the GOLD ABCD classification system, revealing two relevant findings. First, the patients with a worse perception of their symptoms, in accordance with the proposed cutoffs of mMRC and CAT, were distributed into different categories of risk. Second, the patients having symptoms during a 24-hour day were better identified by CAT than by the mMRC scale using the GOLD ABCD classification system. Over the years, the GOLD has shed light on several aspects of COPD, such as the importance of the disease centralizing the knowledge of specific clinical aspects of the disease. However, a subliminal question appears thanks to the study by Montes de Oca[8]: are we using suitable measurements to define different levels of COPD severity?[9] An American mathematician and computer scientist, Grace Murray Hopper, said, "One accurate measurement is worth a thousand expert opinions." When defining the patients with a higher perception of symptoms, in accordance with the GOLD ABCD classification system, there is no equivalent use of the cutoffs of the mMRC scale and the CAT score.[8] In this context, the mMRC scale and the CAT score give us information about two aspects derived from the patients' self-perception: the severity of dyspnea and the impact of the disease, although we should not forget that dyspnea is one, but not the only symptom of COPD. The GOLD classification using the CAT score is probably more sensitive to identify patients' unexplored characteristics related to the perception of symptoms during a 24-hour day.[8] Nonetheless, if these two methods of measurement are different, the GOLD groups in which we place the patients will differ, unfortunately affecting the prediction of disease progression and therapeutic revision. To characterize the disease by two different objective measures means to observe two different patients!

In the study by Montes de Oca et al.,[8] a focus needs to be placed on COPD patients perceiving more symptoms (B and D groups). In these patients, the possibility to discriminate symptoms during a 24-hour day is prevalent, and a therapeutic adjustment, according to the GOLD document,[1] needs to be made. These two groups (B

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plus D) represented 56% and 73% of the patients, respectively, using the mMRC scale and the CAT score, whereas the distribution of patients at an elevated risk of exacerbation (C plus D groups) was lower and similar (37%) regardless of the assessment tool. In a nutshell, the LASSYC study involved an excellent cohort of symptomatic COPD outpatients by evaluating the presence of symptoms during a 24-hour day. In this context, the CAT score (rather than the mMRC scale), thanks to the multidimensional assessment of the complexity of COPD, seems to be abler to identify unexplored perceptions of patients, as demonstrated by the strong correlation with the intensity of daytime symptoms.[10] Of note, the CAT score also discriminates COPD patients with small airway dysfunction.[11] However, the cutoff point of 10 for CAT cannot be used as an equivalent to the cutoff point of 2 for mMRC: there is a greater Youden index for 1 point than for 2 points on the mMRC scale. It is time to revise this aspect in the GOLD document.

A final consideration should be made. The staging of COPD patients in the GOLD document[1] starts *de facto* from the exploration of the effect of an aimed therapy (bronchodilators or inhaled corticosteroids) on a target population (COPD patients with a worse perception of symptoms or with an elevated exacerbation risk): this may define categories of patients with different needs, but it does not define the progressive levels of disease severity. Due to the complexity of COPD, an objective marker of disease progression is yet to be defined. However, the patients' ability to move (primary function, exercise, physical activity, or a muscle biological surrogate),[12] for example, might be an indirect sign of the real impact of a respiratory disease in an organism, being an important patient-derived outcome. We learned that having different results according to different measures of subjective symptoms may give us a different measure of disease.

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