



Peeping at COPD through the keyhole: time to broaden the view to the complexity of the disease by the heterogeneity of symptoms

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The assessment of co-occurring nonrespiratory symptoms in COPD allow us to explore the true complexity of the disease and to plan specific integrated, multidimensional care strategies <https://bit.ly/4dwdnBQ>

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The approach to COPD has evolved significantly over time. Whereas initially, diagnosis, prognosis and therapy of COPD were almost entirely assessed and guided by respiratory function alone, particularly forced expiratory volume in the first second (FEV₁) [1], over time, there has been an increasing awareness of the importance of considering other factors of the disease, such as the respiratory impact and the risk of exacerbations. This three-dimensional approach, which has led to the current use of the “ABE” algorithm and the degree of airway obstruction, has represented an essential step towards personalised therapy [2]. However, this approach observes COPD from only one point of view and perhaps limited one: respiratory. The complexity and heterogeneity of COPD may involve some aspects that are not purely respiratory.

Houben-Wilke *et al.* [3] investigated the occurrence of 20 symptoms (respiratory and nonrespiratory) in a sample of >500 patients with COPD recruited in different settings, comparing them with those of a control group. Notably, sex distribution and mean age were comparable between patients and non-COPD subjects, as was the prevalence of comorbidities reported (except for, of course, the reported COPD, and malignancies, which were lower in COPD); therefore, every valuable finding may produce disease-specific considerations. Symptom intensity was measured using a visual analogue scale (VAS), which is accessible and immediately applicable in clinical practice, with a cut-off (VAS ≥30 mm) used to define the presence of symptoms and the related prevalence. The possibility of performing a clustering analysis with different symptom severity associated with various outcomes, including care dependency, has finally explored some unknown aspects (nonrespiratory) of the disease. Other than dyspnoea, fatigue and cough, the authors reported that COPD patients generally have more nonrespiratory symptoms than non-COPD subjects, with some relevant prevalences in the cohort that merit note, such as muscle weakness (53%), muscle cramps (37%), insomnia (36%), night micturition (27%), depression (24%) and thirst (24%) [3].

For severity of symptoms, they identified three clusters of COPD patients: the first, defined as “least symptom burden”, reporting mainly mild fatigue and respiratory symptoms; the second, “medium symptom burden”, with higher symptom intensity but predominantly respiratory symptoms again; and the third, “high symptom burden”, exhibiting the greatest variability of symptoms and severity. It is noteworthy that FEV₁, risk of exacerbations (moderate and severe) and dyspnoea score on the modified Medical Research Council scale were similar between the second and third clusters, although the cluster 3 had a higher burden of symptoms, with 11 symptoms present in ≥50% of the patients. For the nonrespiratory symptoms reported above in the total COPD cohort, in cluster 3, the prevalence of muscle weakness was 78%, muscle cramps 70%, insomnia 76%, night micturition 56%, depression 59% and thirst 56%. Cluster 3,



moreover, represented COPD patients with a greater care dependency (35% of patients had a Care Dependency Scale score ≤ 68 , indicating that the patient is dependent on care from others) and this despite the low comorbidity burden (median Charlson Comorbidity Index total score of 2). Finally, although cluster 3 included patients deriving prevalently from tertiary care (66%), in line with the prevalence in the total cohort of COPD (63%), 22% and 12% referred to the secondary and primary care setting, respectively, such that there were more symptomatic COPD patients in non-severe settings [3]. In a few words, HOUBEN-WILKE *et al.* [3] have identified a cluster of symptomatic COPD patients that is uncommon to define as severe, uncommon to classify and uncommon to find in a specific setting.

It is also likely that, rather than being a manifestation of a disease, symptoms are epiphenomena of a reduction in the body's physiological reserve that makes the individual vulnerable to adverse events, a condition known as frailty. Frailty not only increases the risk of disability but also of hospitalisation and death, even in nonobstructive respiratory diseases [4], making early recognition essential, considering that it is partly reversible [5, 6]. Symptoms thus pose a challenge because, in this kaleidoscope of possibilities, clinicians are prompted to discern their nature on a case-by-case basis, not to overlook the diagnosis of diseases and frailty, but also to address the symptoms in the best way to offer an actual tailored treatment.

The identification of a cluster with a higher symptom burden prompts us to thoroughly rethink the management of patients with COPD, which too often is limited to respiratory function tests and the assessment of exacerbations and respiratory symptoms alone. Symptoms are not directly associated with the degree of airway obstruction, number of exacerbations or healthcare setting, making the risk of underestimating the symptom burden in less severe patients non-negligible. Palliative care, which wisely has been included in the latest releases of the Global Initiative for Chronic Obstructive Lung Disease document [2], aims to prevent and treat symptoms to ensure a good quality of life for patients and their families; but too often, it is confused with end-of-life care and initiated only in the last phase of the disease.

The heterogeneity of the disease, which emerges from the assessment of symptoms reported here, requires a multidimensional evaluation of the patient, leading to the recognition of "treatable traits" [7] and, furthermore, integrated management that also considers quality of life and patient preferences. In this regard, the Comprehensive Geriatric Assessment may be helpful [8]. This is a multidimensional assessment that explores all domains of intrinsic capacity (*i.e.* physical, mental, psychological, sensory and "vitality"), which are the factors on which an individual can rely [9], integrating them with the evaluation of the external environment. It allows defining of the individual's vulnerabilities and pathologies, with their relative impact on survival, autonomy in activities of daily living, healthcare needs and quality of life, identifying the most appropriate treatments for that individual, defining a priority order and professional collaborations to be implemented, and monitoring over time the benefit of the interventions undertaken. The need to collaborate and determine a personalised care plan in COPD, not limited to purely respiratory management, is increasingly evident because, as reported by a patient in a reflection for a statement by the European Respiratory Society, the objective is to "go beyond current practice where the patient is followed by a series of clinicians. Clinicians must collaborate with each other and with the patient in order to have a 'complete' understanding of the impact of their work. In my case, I needed clinicians to better understand the psychological impact of their individual actions" [10].



FIGURE 1 St Peter's Basilica through the Aventine keyhole.

The value of the paper by HOUBEN-WILKE *et al.* [3] is that it forces the reader to broaden their view. Airway obstruction, respiratory symptoms and exacerbations are pivotal for managing COPD. However, we need to assess co-occurring nonrespiratory symptoms to explore the true complexity of the disease by the heterogeneity of symptoms, and use these symptoms to plan specific, integrated, multidimensional care strategies. Alternatively, focusing only on respiratory aspects is like peeping at St Peter's Basilica through the Aventine keyhole (figure 1), a suggestive point of view, but one that excludes most of the wonder of Rome.

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References

- 1 Rabe KF, Hurd S, Anzueto A, *et al.* Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 2007; 176: 532–555.
- 2 Agustí A, Celli BR, Criner GJ, *et al.* Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. *Eur Respir J* 2023; 61: 2300239.
- 3 Houben-Wilke S, Deng Q, Janssen DJA, *et al.* Symptom burden and its associations with clinical characteristics in patients with COPD: a clustering approach. *ERJ Open Res* 2024; 10: 01052-2023.
- 4 Scarlata S, Zotti S, Finamore P, *et al.* Frailty in the chronic respiratory patient: association with mortality and clinical features in obstructive, restrictive, and mixed spirometric patterns. *Aging Clin Exp Res* 2023; 35: 2573–2581.
- 5 Clegg A, Young J, Iliffe S, *et al.* Frailty in elderly people. *Lancet* 2013; 381: 752–762.
- 6 Scarlata S, Finamore P, Laudisio A, *et al.* Association between frailty index, lung function, and major clinical determinants in chronic obstructive pulmonary disease. *Aging Clin Exp Res* 2021; 33: 2165–2173.
- 7 Agustí A, Bel E, Thomas M, *et al.* Treatable traits: toward precision medicine of chronic airway diseases. *Eur Respir J.* 2016; 47: 410–419.
- 8 Scarlata S, Finamore P, Antonelli Incalzi R. Treatable traits: the added value of comprehensive geriatric assessment. *Eur Respir J* 2023; 62: 2301366.
- 9 Cesari M, Araujo de Carvalho I, Amuthavalli Thiyagarajan J, *et al.* Evidence for the domains supporting the construct of intrinsic capacity. *J Gerontol A Biol Sci Med Sci* 2018; 73: 1653–1660.
- 10 Osadnik CR, Brighton LJ, Burtin C, *et al.* European Respiratory Society statement on frailty in adults with chronic lung disease. *Eur Respir J* 2023; 62: 2300442.