GOLD-2023's new exacerbation of chronic obstructive pulmonary disease severity grading is inconsistent with severity for assessing the risk of future exacerbations

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There has never been a universally agreed strict definition for an exacerbation of chronic obstructive pulmonary disease (ECOPD) and its severity. Symptom-based definitions and healthcare resource utilization (HCRU) definitions (event-based) are commonly adopted. ECOPD is graded according to the required treatment i.e., with short-acting beta-agonists (SABAs) is considered mild, SABAs plus antibiotic and/or oral steroids therapy is considered moderate, and requiring hospitalization and emergency care is considered severe (1). Furthermore, severe patients requiring hospitalization are often associated with respiratory failure (2). In the past, there were no objective and scientific criteria for grading ECOPD, and patients' utilization of healthcare resources after exacerbation varied in different countries and regions. For example, there are no standardized criteria for ECOPD hospitalization in China, and many inpatients are not severe exacerbations (3).

Since the past grading methods could not scientifically assess the severity of ECOPD, the Global Initiative for Chronic Obstructive Lung Disease (GOLD)-2023 (4) for the first time used six objectively measured variables: dyspnea, oxygen saturation (SO_2), respiratory rate, heart rate, serum C-reactive protein, and arterial blood gases, to grade ECOPD. The new severity classification also categorized ECOPD into three grades: mild, moderate, and severe. However, the severity is significantly greater than the event-based definitions. For example, the new criteria for moderate ECOPD are SO_2 <92%, partial pressure of arterial oxygen (PaO_2) ≤60 mmHg, and/or partial pressure of arterial carbon dioxide ($PaCO_2$) >45 mmHg, but without acidosis. That is, type I respiratory failure coexists with

moderate ECOPD. ECOPD with respiratory failure was formerly categorized as severe (2).

Since 2011, GOLD has used event-based ECOPD severity grading to assess a patient's risk of future exacerbations, with evidence from the ECLIPSE study. The ECLIPSE study defined a moderate acute exacerbation as one that did not require hospitalization and required only oral steroids and/or antibiotic therapy for ECOPD. The ECLIPSE study found that the history of two moderate exacerbations was the best predictor of frequent exacerbation (5). GOLD-2023 updated the severity grading criteria for ECOPD. The new criteria are mainly suitable for real-time assessment use at the onset of ECOPD, providing a more objective measurable indicator for the management of exacerbations. It, however, may not be applicable for assessing a patient's risk of exacerbation. This is because it is difficult to capture objective clinical variables of a patient's previous exacerbations using a retrospective approach. In addition, there is no scientific evidence for the validity of a new grade of severity in assessing a patient's risk of future exacerbations, rigorous clinical studies are needed for validation.

However, reporting ECOPD using HCRU events has its drawbacks and often may underestimate ECOPD (6). However, the recall method using HCRU events is still simple and practical. The ECLIPSE study also demonstrated the effectiveness of recalling past exacerbations in predicting frequent exacerbations in patients (5).

The new ECOPD classification has made significant advances in science and objectivity. However, the new

grading criteria differ significantly from the severity defined by the event-based method in the past. Moreover, this approach is still recommended in GOLD-2023 for the assessment of a patient's risk of exacerbation. The new criteria for "moderate" are for patients with respiratory failure requiring hospitalization, which is roughly equivalent to "severe" in the past. The new criteria of two "moderate" exacerbations as an indicator of frequent future exacerbations significantly underestimate patient risk, and GOLD-2023 recommends that a history of one hospitalization puts a patient at high risk for future exacerbations. The same problem exists in GOLD-2024, which is not updated.

Although the application scenarios for these two grading the severity of ECOPD are different, the two grading criteria should still be the same. Otherwise, it will create confusion in clinical practice.

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Footnote

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