of airflow obstruction in individual patients with COPD requires some caution.

FEV_1 is a reasonably good metric of the "fast" component of lung emptying, that is, that related to the airflow across the middle and large(r) airways. In contrast, the "slow" component is strongly influenced by the functional characteristics of the small(er) airways, being critical to determining the residual volume (RV). Air trapping (high RV) worsens in tandem with disease severity because of either progressive small airway disease or loss of alveolar attachments caused by widespread emphysema (3).

In this context, it is rather axiomatic that unless TLC increases (hyperinflation) in tandem with, or out of proportion to, RV, FVC would tend to decrease as COPD evolves to its later stages, increasing (or at least stabilizing) the FEV_1:FVC ratio despite disease worsening. For instance, two patients with similar TLC and FEV_1 impairment may show widely different RVs and RV:TLC ratios (respectively, 140% and 0.50 in patient A and 200% and 0.65 in patient B). The consequences will be a substantially lower FVC and a higher FEV_1:FVC ratio (and thus a lower STAR stage) for patient B, who shows worse air trapping. The authors report that within each Global Initiative for Chronic Obstructive Lung Disease stage, increasing STAR stage was associated "with monotonic increases in hyperinflation and air trapping." In fact, it seems more appropriate to state "with monotonic increases in TLC and RV," as their sample with lung volume measurements (the University of Alabama cohort) showed an unusually low burden of air trapping (RV 78.9 $\pm$ 19.7%) and hyperinflation (TLC 76.3 $\pm$ 36.9%). In any case, as RV:TLC ratios and their impact on FVC and FEV_1:FVC were not shown, it is still possible that STAR confers an advantage to individual patients with higher RVs at a given TLC (or lower TLCs at a given RV), both decreasing FVC and increasing FEV_1:FVC at iso-FEV_1. The corollary is that despite proving useful to discriminate a group of subjects at greater risk of a negative outcome (4), STAR may end up underestimating the severity of airflow obstruction in individual patients showing worse air trapping and more advanced COPD (i.e., those more frequently seen by pulmonologists).

The authors correctly argue that coexistent restriction may relatively worsen the severity of obstruction as indicated by percentage predicted FEV_1, as part of the FEV_1 variance can be explained by FVC. Conversely, it might be contended that by increasing FEV_1:FVC, restriction would underestimate the severity of obstruction as indicated by FEV_1:FVC.

Overestimation of disease severity by FEV_1:FVC may occur in the subset of patients with only mildly reduced FEV_1 who present with higher than expected FVC because of an undue increase in TLC (3). The causes of their lung overdistension beyond that anticipated by the emphysema burden remain unknown, being probably more common in subjects born with particularly compliant lungs. Whether dysanapsis also contributes to this pattern remains to be demonstrated.

The FEV_1:FVC conundrum in COPD (5) is an excellent example of the enduring potential of pulmonary function tests beyond simple spirometry to deeply phenotype patients with such a heterogeneous disease. Exactly because of the multifaceted nature of COPD, every attempt to encapsulate the severity of dysfunction in a single domain (such as airflow obstruction) has faced limitations when applied to the care of individual subjects (6). Perhaps future research will bring us some sort of multidimensional index geared to jointly gradate the abnormalities in **g**as transfer (e.g., transfer factor), **a**irflow (e.g., percentage predicted FEV_1 or FEV_1:FVC, whichever is lower), and **l**ung volumes (e.g., percentage predicted inspiratory capacity or ratio of inspiratory capacity to TLC) to be used with metrics of **e**mphysema extension and **s**ymptom severity (dyspnea burden). Hopefully, such "GALES" would bring fresh wind to our sails toward a more holistic understanding of this fascinating disease. ■

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Novel FEV_1/FVC-based Diagnosis and Severity Classification of Chronic Obstructive Pulmonary Disease: How about FEV_1 % Predicted Basing?

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To the Editor:

We read with interest the article by Bhatt and colleagues (1). The authors proposed a new scheme for grading the severity of

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chronic obstructive pulmonary disease (COPD): STaging of Airflow obstruction by Ratio (STAR), an FEV_1/FVC–based stratification approach (using FEV_1/FVC thresholds of $\geq$0.60 to $<$0.70, $\geq$0.50 to $<$0.60, $\geq$0.40 to $<$0.50, and $<$0.40, respectively, for stages 1–4). The predictive performance for 10-year mortality of STAR grades was comparable with that of the conventional FEV_1 % predicted ($ppFEV_1$)–based stratification, Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades (2). Moreover, STAR showed a more uniform gradation of disease severity, as it provided better ability to discriminate survival between mild COPD (stage 1) and non-COPD compared with the GOLD stages.

Recently, several studies have shown the clinical importance of preserved ratio impaired spirometry (PRISm; FEV_1/FVC $\geq$ 0.70 and $ppFEV_1$ $<$ 0.80), especially for its high incidence of COPD and poor prognosis (3, 4). Nonetheless, subjects with PRISm may be often overlooked, as it does not meet the conventional criterion for COPD (FEV_1/FVC $<$ 0.70) (2). Given the rising interest in the epidemiologic issues of PRISm, physicians today may have to investigate the implications of impaired $ppFEV_1$, including PRISm, together with COPD in clinical research.

In the study by Bhatt and colleagues (1), non-COPD was defined as FEV_1/FVC $\geq$ 0.70 regardless the value of $ppFEV_1$, which is in line with GOLD standards; subjects with PRISm were included in the non-COPD group. According to Figure 1 in Bhatt and colleagues' paper, $ppFEV_1$ in subjects without COPD was distributed unfavorably to that in GOLD stage 1 subjects, whereas $ppFEV_1$ was higher in subjects without COPD than in STAR stage 1. As a decrease in $ppFEV_1$ has been known to be a strong risk factor for COPD morbidity and mortality (5, 6), the discrepancy in overall survival between STAR stage 1 and GOLD stage 1 was considered sensible to the difference in $ppFEV_1$ between them. Therefore, to assess the impact of $ppFEV_1$ on all-cause mortality, it is crucial to stratify the entire cohort regardless of the values of FEV_1/FVC (not only subjects with COPD) according to $ppFEV_1$ (i.e., $ppFEV_1$ thresholds of $\geq$0.80, $\geq$0.50 to $<$0.80, $\geq$0.30 to $<$0.50, and $<$0.30) and to assess the mortality of each subgroup. In addition, a comparison of prognostic performance between $ppFEV_1$ and FEV_1/FVC among all subjects might make physicians reconsider not only the severity grading but also the diagnostic criteria for COPD, as the cutoff points for the diagnosis of other major noncommunicable diseases (e.g., hypertension, diabetes, dyslipidemia) were established on the evidence of morbidity and mortality.

In conclusion, the work by Bhatt and colleagues (1) is intriguing, in that FEV_1/FVC—a simply calculable biomarker without age-, gender-, height-, and race-dependent predicted values—could be helpful in evaluating disease severity as well as diagnosing COPD. We believe that this new STAR can create a STIR in clinical practice and the management of COPD. ■

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Use FEV_1/FVC *Z*-Score Staging to Minimize Sex and Age Bias in Staging Chronic Obstructive Pulmonary Disease

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To the Editor:

The staging of airflow obstruction in chronic obstructive pulmonary disease (COPD) by FEV_1/FVC (STAR) provides a more uniform gradation of disease severity than FEV_1 (1). The use of FEV_1/FVC to stage COPD is a logical approach, because a low FEV_1/FVC is a better indicator of obstruction. However, the use of fixed values of FEV_1/FVC ignores the variations attributable to sex, age, and height in the absence of pathologic effects.

Figure 1 shows how STAR staging using fixed FEV_1/FVC values captures different proportions of two example cases. The frequency distribution of FEV_1/FVC in the reference population (2) is compared between 75-year-old males of average height (176 cm) and 35-year-old females of average height (163 cm). The upper panel shows that the STAR staging would favor classifying significantly more older males than younger females as having more severe COPD for the same relative degree of airflow obstruction. The lower panel

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