Comparison of Proportional Assist Ventilation plus, T-Tube Ventilation, and Pressure Support Ventilation as Spontaneous Breathing Trials for Extubation: A Randomized Study–Reply

In reply:

We appreciated the comments from Mathews et al regarding our article in RESPIRATORY CARE.[1] We would like to add some comments and clarify some issues about their opinions.

The study was randomized (as described in the methods section), and because of its characteristics, it could not be blinded. Therefore, the small differences between the groups were a result of randomization. However, the number of subjects included was enough to answer the main question and achieve our conclusions.

In the cited article, table 1[1] shows that the distribution of the subjects was broad, including neurological (trauma or non-trauma), medical, and surgical patients. The proposed classification by Mathews et al for "neurologic and non-neurologic" diseases sounds artificial, since it does not consider important clinical situations (such as COPD) and the fact that the neurological population can include young patients with traumatic brain injury and elderly patients with stroke.

According to the study protocol (see methods section), all subjects with COPD were placed on noninvasive ventilation immediately after extubation. This approach is reasonably well described in the literature.[2–4] The 15% extubation rate is in line with the international literature.[5] We should not compare oranges with apples: In Esteban et al[6] the failure rate was 25% of the total number of subjects, which is comparable with that found in our study.

The statistical analysis shows that all methods had comparable abilities to predict extubation success or failure, with values comparable with those in the literature.[7,8] The fact that the incidence of tracheostomy was larger in a group does not mean greater efficiency in predicting extubation failure or success: The decision to perform tracheotomy includes several issues, like consciousness level, underlying medical conditions, and etiology of respiratory failure.[9]

Therefore, Mathews et al share our conclusions, that proportional assist ventilation plus is a safe method and is efficient to perform a spontaneous breathing trial, comparable with other existing methods (T-tube and pressure support ventilation), and a clinical option for clinicians and respiratory practitioners in the ICU.

Erica F Osaku PT PhD
Intensive Care Unit
Western Paraná State University Hospital
Cascavel, Paraná, Brazil

Cláudia RLM Costa PT PhD
Intensive Care Unit
Western Paraná State University Hospital
Cascavel, Paraná, Brazil

Sandy N Teixeira PT
Intensive Care Unit
Western Paraná State University Hospital
Cascavel, Paraná, Brazil

Péricles AD Duarte MD PhD
Intensive Care Unit
Western Paraná State University Hospital
Cascavel, Paraná, Brazil

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FEV_1/FEV_6 May Misdiagnose Patients With COPD

To the Editor:

We read with great interest the paper by Wang et al[1] proposing the use of FEV_1/FEV_6 as a reliable index for diagnosing COPD. Although the utility of FEV_6 has been demonstrated in some clinical scenarios,[2,3] we are concerned that the current study reaches conclusions that may result in the misclassification of patients as having COPD.

Our main cause for concern is the authors' use of the fixed ratio of $FEV_1/FVC < 0.70$ as the standard against which the FEV_1/FEV_6 was compared. The authors recognize the potential problem of using the fixed cutoff to diagnose COPD, but this is of extreme importance in preventing misdiagnosis of COPD in older adults. Although there has been ongoing debate regarding the use of the fixed ratio, numerous studies have identified the problem of misclassification of older adults when the natural history of the decline in FEV_1 and FVC are not taken into account.[4-6] In addition, this paper used an $FEV_1 < 80\%$ predicted in conjunction with the faulty fixed ratio to define subjects who had COPD. For this purpose, the study used a predicted set derived from whites rather than from the local population. Defining the presence of moderate airway obstruction as an $FEV_1 < 80\%$ has been shown to misclassify subjects because of age, sex, and ethnicity biases, depending on the reference equations chosen.[7] Kim et al[8] showed that applying the third National Health and Nutrition Examination Survey (NHANES III) FEV_1 reference

equations to Asians misclassified 30% of never-smokers when compared with an ethnically specific equation.

In the data presented, there was very little difference between the *mean* values for FEV_6 and FVC in males and females; however, there were no comparisons made for the youngest or oldest subjects. The exhalation times associated with FVC were not reported, although the authors reported that "obtaining 99% of the FVC in 6.64 s is sufficient." They also report that FEV_6 was obtained in >80% of the tests, suggesting that up to 20% of the tests did not achieve the 6 s criterion. It is therefore not surprising that this study found significant agreement between the FEV_1/FEV_6 and the FEV_1/FVC with likelihood ratios approaching 100% for a fixed cutoff of 0.72.

We compared the FEV_1 and FEV_1/FVC (predicted and lower limits of normal) for males and females at age 80 y, since older patients are at a higher risk of being misdiagnosed with COPD. Table 1 lists these comparisons based on the Knudson 1983 reference equations[9] along with those from the Global Lungs Initiative[10] published in 2012. (Predicted and lower limits of normal for FEV_6 are not available for Knudson[9] or the Global Lungs Initiative.[10]) Since Shaanxi province lies near the dividing line used for Northeast Asians and Southeast Asians in the Global Lungs Initiative, we included predicted values based on both groups. Except for Northeast Asian males, the lower limits of normal for FEV_1 are all <80% of the predicted, and the lower limits of normal for the FEV_1/FVC are all <0.70. The authors' methodology indicates a high incidence of COPD in female never-smokers. For example, if the 24 current and former female smokers in the authors' study[1] are assumed to have COPD, 53 (11%) never-smokers would be diagnosed with COPD using their methodology. The prevalence of COPD in female never-smokers in China has been shown to be ~5% when using the lower limit of normal for FEV_1/FVC.[11]

The American Thoracic Society/European Respiratory Society guidelines recommend using the lower limit of normal for both the FEV_1/FVC and FEV_1 for interpretation of spirometry.[12] Using fixed cutoffs for the ratio, whether FEV_1/FVC or FEV_1/FEV_6, risks misclassifying older adults. In addition, grading severity using 80% of the predicted FEV_1 as the lower limit of normal introduces age, sex, and ethnicity biases as well. Most modern spirometers can report lower limits of normal using up-to-date reference equations. Spirometric determination of airway obstruction is just one tool in assessing whether a patient has COPD. Primary care practitioners who encounter patients with signs and symptoms suggesting COPD should apply statistically valid methods when interpreting spirometry data.

Gregg L Ruppel MEd RRT RPFT FAARC
Division of Pulmonary, Critical Care and Sleep Medicine
Saint Louis University School of Medicine
St. Louis, Missouri

Jeffrey M Haynes RRT RPFT FAARC
Pulmonary Function Laboratory
St. Joseph Hospital
Nashua, New Hampshire

David A Kaminsky MD
Pulmonary and Critical Care Medicine
University of Vermont College of Medicine
Burlington, Vermont

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Table 1. Comparison of Predicted Values for Males and Females 80 y of Age and Mean Height From Wang et al[1]

Study	Male (80 y, 170.1 cm)			Female (80 y, 158.6 cm)		
	Predicted	Lower Limit of Normal	% Lower Limit of Normal*	Predicted	Lower Limit of Normal	% Lower Limit of Normal*
Knudson[9]						
FEV_1	2.46	1.60	65	1.75	1.13	65
FEV_1/FVC	0.78	0.68	NA	0.77	0.65	NA
NE Asian[10]						
FEV_1	2.52	2.01	80	1.81	1.27	70
FEV_1/FVC	0.76	0.64	NA	0.78	0.65	NA
SE Asian[10]						
FEV_1	2.39	1.63	68	1.63	1.10	68
FEV_1/FVC	0.77	0.64	NA	0.79	0.67	NA

* Expressed as a percentage of the predicted value.
Knudson = predicted values for Caucasians[9]
NA = not applicable
NE Asian = Northeast Asian from the Global Lungs Initiative derived from healthy subjects living north of the Huaihe River and Qinling Mountains[10]
SE Asian = Southeast Asian from the Global Lungs Initiative derived from healthy subjects living south of the Huaihe River and Qinling Mountains[10]

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FEV_1/FEV_6 May Misdiagnose Patients With COPD—Reply

In reply:

We thank Ruppel and colleagues for their thoughtful letter and excellent points regarding the possibility of misdiagnosing COPD using the fixed ratio. We are in clear agreement that FEV_1/FEV_6, as well as FEV_1/FVC, may overdiagnose COPD. In fact, we were always concerned about the agreement between the Global Initiative for Chronic Obstructive Lung Disease (GOLD) standard and the lower limit of normal standard for the diagnosis of COPD. In another study,[1] we focused on the difference between GOLD and lower limit of normal. The results showed that the 2 criteria were both effective and consistent for detecting COPD in subjects age 40–69 y. Subjects >70 y old were overdiagnosed by GOLD standards. However, subjects age 40–69 y were the main target population. Furthermore, the final diagnosis was not made in the primary care unit but required further confirmation in the superior hospital.

COPD has become a major disease in China because most people smoke; however, it still does not arouse enough people's attention. Our other study showed that 68.1% of asymptomatic participants were undiagnosed by GOLD standards.[2] Underdiagnosis of COPD in many countries was also found to be substantial, ranging from 5 to 60%.[3,4] The main problem related to COPD in China is underdiagnosis, not overdiagnosis. Overdiagnosis provides possible benefits, by improving lifestyle, because our people do not regularly receive health checks.

As for the reference equation, it was indeed a problem we did not address. The study showed that there was a difference in reference values from 6 areas in China.[5] This geographic factor may be a possible cause of COPD overdiagnosis in our study. However, spirometry with Chinese reference values is not common and does not suit our population. This issue needs further study to obtain reference equations suitable for people in China. In summary, early detection of COPD is very critical in the primary unit, and the final diagnosis of COPD requires the combination of history, physical signs and symptoms, and lung function tests.

Shengyu Wang MD
Pulmonary and Critical Care Medicine
First Affiliated Hospital of Xi'an Medical University
Shaan Xi, China

Jing Zhou MD
Pulmonary and Critical Care Medicine
First Affiliated Hospital of Xi'an Medical University
Shaan Xi, China

Xin Diao MD
Pulmonary and Critical Care Medicine
First Affiliated Hospital of Xi'an Medical University
Shaan Xi, China

The authors have disclosed no conflicts of interest.

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