# Investigating the relationships among lung function variables in chronic obstructive pulmonary disease in men

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**Background:** In patients with chronic obstructive pulmonary disease (COPD), the independent contributions of individual lung function variables to outcomes may be lower when they are modelled together if they are collinear. In addition, lung volume measurements may not be necessary after spirometry data have been obtained. However, these hypotheses depend on whether forced vital capacity (FVC) can predict total lung capacity (TLC). Moreover, the definitions of hyperinflation and air trapping according to lung function variables overlap and need be clarified. Therefore, the aim of this study was to evaluate the relationships among various lung function parameters to elucidate these issues. **Methods:** Demographic data and 26 parameters of full lung function were measured in 94 men with COPD and analyzed using factor and correlation analyses. **Results:** Factor analysis revealed five latent factors. Inspiratory capacity (IC)/TLC and residual volume (RV)/TLC were most strongly correlated with all other lung volumes. IC/TLC, RV/TLC, and functional residual capacity (FRC)/TLC were collinear and were potential markers of air trapping, whereas TLC%, FRC%, and RV% were collinear and were potential markers of hyperinflation. RV/TLC >0.4 (or IC/TLC <0.4) was comparable with the ratio of forced expiratory volume in one second ($FEV_1$) and FVC <0.7. FVC% and $FEV_1$% were poorly correlated with TLC%. The correlation study showed that TLC%, RV/TLC, and $FEV_1$% could be used to represent individual latent factors for hyperinflation, air trapping, inspiration, expiration, and obstruction. Combined with diffusion capacity%, these four factors could be used to represent comprehensive lung function. **Conclusions:** This study identified collinear relationships among individual lung function variables and thus selecting variables with close relationships for correlation studies should be performed with caution. This study also differentiated variables for air trapping and lung hyperinflation. Lung volume measurements are still required even when spirometry data are available. Four out of 26 lung function variables from individual latent factors could be

used to concisely represent lung function.

1 **Investigating the Relationships among Lung Function Variables in Chronic**

2 **Obstructive Pulmonary Disease in Men**

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24 **Abstract**

25 **Background:** In patients with chronic obstructive pulmonary disease (COPD), the independent

26 contributions of individual lung function variables to outcomes may be lower when they are

27 modelled together if they are collinear. In addition, lung volume measurements may not be

28 necessary after spirometry data have been obtained. However, these hypotheses depend on

29 whether forced vital capacity (FVC) can predict total lung capacity (TLC). Moreover, the

30 definitions of hyperinflation and air trapping according to lung function variables overlap and

31 need be clarified. Therefore, the aim of this study was to evaluate the relationships among

32 various lung function parameters to elucidate these issues.

33 **Methods:** Demographic data and 26 parameters of full lung function were measured in 94 men

34 with COPD and analyzed using factor and correlation analyses.

35 **Results:** Factor analysis revealed five latent factors. Inspiratory capacity (IC)/TLC and residual

36 volume (RV)/TLC were most strongly correlated with all other lung volumes. IC/TLC, RV/TLC,

37 and functional residual capacity (FRC)/TLC were collinear and were potential markers of air

38 trapping, whereas TLC%, FRC%, and RV% were collinear and were potential markers of

39 hyperinflation. RV/TLC >0.4 (or IC/TLC <0.4) was comparable with the ratio of forced

40 expiratory volume in one second ($FEV_1$) and FVC <0.7. FVC% and $FEV_1$% were poorly

41 correlated with TLC%. The correlation study showed that TLC%, RV/TLC, and $FEV_1$% could

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42   be used to represent individual latent factors for hyperinflation, air trapping, inspiration,

43   expiration, and obstruction. Combined with diffusion capacity%, these four factors could be used

44   to represent comprehensive lung function.

45   **Conclusions:** This study identified collinear relationships among individual lung function

46   variables and thus selecting variables with close relationships for correlation studies should

47   be performed with caution. This study also differentiated variables for air trapping and lung

48   hyperinflation. Lung volume measurements are still required even when spirometry data are

49   available. Four out of 26 lung function variables from individual latent factors could be used to

50   concisely represent lung function.

51

## INTRODUCTION

52

53      Lung function variables including residual volume (RV)/total lung capacity (TLC),

54   inspiratory capacity (IC)/TLC, RV% predicted and forced expiratory volume in one second

55   percentage predicted ($FEV_1\%$ )have been reported to be well correlated with the outcomes of

56   patients with chronic obstructive pulmonary disease (COPD) including physiological

57   deterioration, dyspnea, exercise intolerance, acute exacerbations, and mortality *(O'Donnell et al.,*

58   *2001*; *Nishimura et al., 2002*; *Casanova et al., 2005*; *Tantucci et al., 2008*; *Vassaux et al., 2008*;

59   *Zhang et al., 2013*; *Chuang et al., 2015*; *Shin et al., 2015)*. Correlations between lung function

60   variables and outcomes have been reported sporadically, such as associations between IC/TLC

61   and RV/TLC and prognostic,(*Nishimura et al., 2002*; *Casanova et al., 2005*; *Shin et al., 2015*)

62   exercise capacity, (*Vassaux et al., 2008*; *Zhang et al., 2013*; *Chuang et al., 2015*) exertional

63   dyspnea, (*Casanova et al., 2005*; *Zhang et al., 2013*; *Chuang et al., 2015*) and dynamic lung

64   expansion (*Zhang et al., 2013*; *Chuang et al., 2015*) in patients with COPD. Moreover, IC/TLC

65   and RV/TLC have been reported to have very similar Harrell's C-statistics in prognostic analysis

66   (*Shin et al., 2015*). However, as the independent contributions of IC/TLC and RV/TLC to

67   outcomes would be lower when they are modelled together if they are highly correlated, it is

68   important to investigate the relationships among lung function variables.

69      Hyperinflation and air trapping are defined using lung volumes in percentages (%)

70 combined with ratios of functional residual capacity (FRC), IC or RV and TLC (*Ruppel 1991*;

71 *Gagnon et al., 2014*; *Cohen 2017*; *Vaz Fragoso et al., 2017*). However, these definitions are

72 unclear and arbitrary and understanding the relationships among these variables may improve the

73 definitions.

74  It has also been reported that TLC measurements are not necessary after spirometry data

75 have been obtained. However, this will not be the case if forced vital capacity (FVC) cannot

76 predict TLC, as obstructive ventilatory impairment may be combined with restriction in patients

77 with COPD (*Dykstra et al., 1999*; *Nishimura et al., 2002*; *Calverley et al., 2005*; *Deesomchok et*

78 *al., 2010*; *Labbé et al., 2010*; *Shin et al., 2015*). To resolve these three issues, this study aimed to

79 thoroughly evaluate the relationships among lung function parameters using factor and

80 correlation analyses.

81 **METHODS**

82 **Study Design**

83  In this observational cross-sectional study, we analyzed lung function data from participants

84 with COPD at Chung Shan Medical University Hospital. A total of 26 lung volume and capacity

85 parameters were expressed in liters, %predicted, and ratio of TLC, FVC and SVC (Appendix 1).

86 The Chung Shan Medical University Hospital Institutional Review Board (CS11144 and

87 CS19014) approved this study, which was conducted in compliance with the Declaration of

88   Helsinki.

89   **Participants**

90       The diagnosis of COPD was made by board-certified pulmonologists according to the

91   GOLD criteria.(*GOLD Committees 2017*) Participants with other thoracic diseases such as

92   pleural diseases or thoracic cage disorders were excluded from this study. (*GOLD Committees*

93   *2017*) As few female participants meet the COPD criteria in Taiwan (e.g., 4% according to one

94   study (*Huang et al., 2018*)), they were excluded from this study. Male adult participants with a

95   post-bronchodilator $FEV_1$/FVC of <0.7 (*GOLD Committees 2017*) or 0.7-0.8 with a definite

96   obstructive pattern in spirometry were enrolled *(Johns et al., 2014)*. The latter definition was

97   used for two reasons. First, extensive small airway disease can exist before it is detectable with a

98   $FEV_1$/FVC <0.7, and thus the concavity of expiratory flow-volume curve was considered (*Johns*

99   *et al., 2014)*. Second, some participants with increased small airway compressibility had a

100  preserved $FEV_1$/FVC but a reduced $FEV_1$/slow VC ratio (*Johns et al., 2014*; *Saint-Pierre et al.,*

101  *2019 (in press)*). The exclusion criteria included a $FEV_1$/FVC of 0.7-0.8 with an equivocal

102  obstructive pattern or with a significant post-bronchodilator effect, i.e., increase in $FEV_1$ of

103  >12% and 200 mL from baseline (*GINA Committees 2017*) or bronchial asthma (*GINA*

104  *Committees 2017*) diagnosed by the board-certified pulmonologists. Bronchial asthma was

105  excluded because the proportion of lung subdivisions is different in these two diseases (*Dykstra*

106    *et al., 1999*). Informed consent was obtained from each participant by them signing the consent

107    form.

**Measurements**

109    *Pulmonary function testing.* Cigarette smoking, drinking coffee, tea, or alcohol, and taking

110    medications were not permitted 24 hours before any test. Bronchodilators were not administered

111    within 3 hours for short-acting beta agonists and 12 hours for long-acting beta agonists before

112    the tests. $FEV_1$, TLC, and RV were measured using spirometry and body plethysmography

113    (MasterScreen™ Body, Carefusion, Wuerzburg, Germany) in accordance with the currently

114    recommended standards.(*Miller et al., 2005*; *Wanger et al., 2005*) The best of three technically

115    satisfactory readings was used.(*ATS/ERS 2002*; *Miller et al., 2005*; *Miller et al., 2005*) All of the

116    spirometry data were obtained before and after inhaling 400 µg of fenoterol HCl. Post-dose

117    measurements were performed 15 minutes after inhalation. Static lung volume data and diffusing

118    capacity for carbon monoxide ($D_L CO$) data measured using the single-breath technique were

119    obtained before inhaling fenoterol. For details of lung subdivision measurements, please refer to

120    Appendix 2. Simple volume calibration was conducted using a 3-L syringe before each test.

121    Accuracy checks for body plethysmograph mouth flow and pressure and box pressure were

122    conducted daily. We have previously reported the predicted values currently used at our institute.

123    The predicted values are in line with our previous report *(Chuang et al., 2001)*. The reason that

124    we did not use lower limit of normal as the criterion of airflow limitation was that we did not

125    have reference equations using post-bronchodilator $FEV_1$ and FVC for the Taiwanese population.

126

127    **Statistical Analysis**

128    All of the data were checked for normal distribution by the Kolmogorov-Smirnov test. Data were

129    summarized as mean ± standard deviation or median (25th – 75th percentiles) when appropriate.

130    We used factor analysis to evaluate the correlated pulmonary function variables and identify the

131    latent factors. We extracted the initial set of factors using the principal-component method based

132    on Kaiser criterion, then 1-more and 1-fewer factor models were also evaluated. The factors were

133    then rotated using an orthogonal transformation method (VARIMAX in SAS) to assess the

134    interpretability of the factors. The numbers of factors determined in the final model was based on

135    biological plausibility. Pearson's or Spearman's correlation coefficients were further used when

136    appropriate for quantifying the pair-wise relationships among the pulmonary function variables.

137    All statistical analyses were performed using SAS statistical software (SAS Institute Inc., Cary,

138    NC, USA). Statistical significance was set at two-sided $p < 0.05$.

139

140    **RESULTS**

141        A total of 94 male participants (mean age 68.1±7.2 years) with COPD were enrolled after

142 excluding 10 participants (Table 1 and Figure 1). Five of these 10 participants who were

143 excluded were diagnosed with bronchial asthma including three females and another five had

144 spirometry data that did not meet the inclusion criteria. Only five of the 94 participants had a

145 $FEV_1/FVC$ ratio 0.7-0.8 with a definite obstructive pattern. Most of the participants had

146 moderate airflow obstruction (Table 1).

147      Up to 26 lung function parameters were presented in absolute values, %predicted, and as the

148 ratio of lung volume or capacity and TLC or FVC for each patient. In normal participants, lung

149 volume in liters was closely related to body height, gender, and age and hence it was usually

150 presented with %predicted. Therefore, the following variables were omitted from correlation

151 analysis: TLC, FRC, IC, IRV, ERV, RV, FVC, SVC, and $FEV_1$ in liters and $D_LCO$ in

152 mL/min/mmHg.

153 *Factor analysis.* A preliminary model with four factors were selected by Kaiser criterion and

154 then the 3-factor and 5-factor models were also evaluated. The five latent factor model was

155 identified according to biological plausibility and this model explained 92% of total variation

156 (Table 2). The communalities were generally high (12 of 16 were >0.9, three were between 0.75

157 and 0.9, and only one was 0.4). Factor 1 was highly related to inspiration and moderately to air

158 trapping; factor 2 was highly related to lung volumes and moderately to air trapping; factor 3 was

159 highly related to expiration and moderately to air trapping; factor 4 was highly related to airflow

160     obstruction; and factor 5 was highly related to diffusion capacity.

161     *Pearson's or Spearman's correlation coefficients for lung volume subdivisions.* Individual

162     variables involving %predicted were strongly correlated with each corresponding variable in ratio

163     of TLC (Table 3, all $r^2$=0.38-0.85, all p<0.0001). TLC%, FRC%, and RV% were highly

164     correlated ($r^2$=0.59-0.74). RV% was the best single parameter correlated with $D_L CO$%, although

165     only with a negative moderate correlation ($r^2$=0.22, p<0.0001). FRC/TLC and IC/TLC were

166     reciprocal ($r^2$=0.98) and highly correlated with RV/TLC ($r^2$=0.37-0.38), and were most frequently

167     correlated with all of the other lung subdivisions in %predicted and ratio of TLC. IC% and IRV%

168     were approximately collinear ($r^2$=0.9). All $r^2$, the coefficient of determination for Pearson's

169     correlations, indicated the proportion of variance in one variable explained by variation in the

170     other.

171     *Pearson's or Spearman's correlation coefficients for spirometry variables.* FVC% and SVC%

172     were highly correlated with $FEV_1$% ($r^2$=0.38-0.74, Table 4); however, they were not correlated

173     with $FEV_1$/FVC ($r^2$=0.00-0.00). Interestingly, $FEV_1$% and $FEV_1$/FVC were related ($r^2$=0.4).

174     *Pearson's or Spearman's correlation coefficients between spirometry and lung volume*

175     *subdivisions.* FVC% and $FEV_1$% were modestly or not correlated with TLC% (Table 4, $r^2$= 0.01-

176     0.04) despite being correlated with most of the subdivisions in %predicted and ratio of TLC. Of

177     89 participants with $FEV_1$/FVC <0.7, 81 (91%) had IC/TLC <0.4 and 85 (96%) had RV/TLC

178    ≥0.4.

179    Based on these results, TLC%, RV/TLC (or $FEV_1$/FVC), $FEV_1$%, and $D_LCO$% were selected

180    from the five factors as representative of lung function.

181

182    **DISCUSSION**

183    *Factor analysis and Pearson's or Spearman's correlation coefficients.* Factor analysis is a good

184    method to identify unobservable factors from a large number of observed variables, thereby

185    allowing variables to be used to estimate a lower number of latent factors. In this study, we

186    identified five latent factors, i.e., those highly related to inspiration, expiration, lung volumes,

187    airflow obstruction, and diffusion, respectively (Table 2). However, lung volumes and

188    inspiration and expiration volumes were also mixed with air trapping, suggesting that

189    hyperinflation and air trapping overlapped (see below). In further analysis, Pearson's or

190    Spearman's correlation coefficients revealed the lung function variables associated with

191    hyperinflation and air trapping (Table 3).

192    However, it is possible that the small sample size would not meet the usual heuristics for

193    principle component analysis or factor analysis, and that this would mean it was difficult to

194    explain the implications of the non-normality and outliers in the data. Although the sample size

195    of the present study was small at 88, the influence of the small sample size depends on the data

196    characteristics. Previous studies have shown that even a small sample size of fewer than 50

197    participants can yield results with small distortions under data conditions of high loading, low

198    number of factors, and high number of variables (*de Winter et al., 2009*). When communalities

199    are high, the sample size tends to have less influence on the quality of factor solutions than when

200    communalities are low (*Hogarty et al., 2005*). We only had limited data, however the

201    communalities were generally high (12 of 16 were >0.9, three were between 0.75 and 0.9, and

202    only one was 0.4) in our final factor model. Spearman's correlation coefficients were applied for

203    the pairs involving non-normality (Tables 3 and 4) and the results were not substantially different

204    from those using the Pearson's correlations. Therefore, we assumed that the potential non-

205    normality might not substantially influence the current results of factor analysis.

206        In addition, one may argue the rationale for using the Kaiser criterion for selecting a

207    preliminary model in this study. While both the Kaiser criterion and parallel analysis use

208    information from eigenvalues of the correlation matrix, the latter can be used to determine more

209    consistently the number of factors, especially in small samples. As appropriate factor retention

210    would depend on biological plausibility rather than purely on statistical consideration, we used

211    the Kaiser criterion to determine the preliminary model, and then selected a five-factor final

212    model (as stated in the previous sections). One of the purposes of this study was to explore

213    different domains (latent factors) related to individual lung function parameters. Rotation makes

214    latent factors more interpretable. We used VARIMAX, an orthogonal rotation that did not

215    change the communalities, and the total variance explained (still 92%) while preserving

216    correlations between variables (*Rencher et al., 2012*).

217    *Lung volume subdivisions.* It has been frequently reported that both IC/TLC and RV/TLC are

218    related to prognostic, exercise capacity, exertional dyspnea, and dynamic lung expansion in

219    patients with COPD. Similarly, IC/TLC and RV/TLC have been reported to have very similar

220    Harrell's C-statistics in prognosis analysis (0.81 and 0.80, respectively, Table 4 of reference

221    (*Shin et al., 2015*)). We hypothesize that IC/TLC and RV/TLC have similar Harrell's C-statistics

222    because of their collinearity.

223        RV% was the largest and the most frequent responder following bronchodilation in a

224    previous report *(Deesomchok et al., 2010).* In the present study, it showed the best inverse but

225    moderate correlation of all lung function variables with $D_LCO\%$.

226        Definitions of pulmonary hyperinflation and air trapping of the lung are inconsistent in the

227    literature, for example: static hyperinflation = hyperinflation at rest (*Gagnon et al., 2014*) =

228    IC/TLC <0.25 (*Casanova et al., 2005*) = RV/TLC (*Nishimura et al., 2002*; *Budweiser et al.,*

229    *2014*) ≥0.4 (*Albuquerque et al., 2006; Shin et al., 2015*) or >0.35 plus an increased TLC (*Ruppel*

230    *1991*) or >0.3 plus RV% ≥120% (*Labbé et al., 2010*); air trapping = RV/TLC >0.35 plus a

231    normal TLC (*Ruppel 1991*) or RV% ≥120% *(Deesomchok et al., 2010).* To some extent, these

232 definitions overlap RV, IC and TLC and their derivatives. In addition, the relationship between

233 RV/TLC and TLC% is inconsistent in previous reports (*Deesomchok et al., 2010*; *Vaz Fragoso et*

234 *al., 2017*). Despite knowing that factor three involved lung volumes, we further evaluated the

235 relationships among all lung subdivisions with Pearson's or Spearman's correlation, and found

236 that RV%, FRC%, and TLC% were highly correlated ($r^2$=0.59-0.74), and that RV/TLC,

237 FRC/TLC and IC/TLC were also highly correlated ($r^2$=0.37-0.98). In contrast, the correlations of

238 RV/TLC, FRC/TLC and IC/TLC with TLC% were only $r^2$=0.08, 0.18, and 0.20, respectively.

239      RV, FRC, and TLC in %predicted are all related to static lung volume *(Gagnon et al., 2014*;

240 *Vaz Fragoso et al., 2017*). RV% is mainly composed of FRC%,(*Dykstra et al., 1999*) and FRC%

241 is mainly composed of TLC% in COPD. This is consistent with a previous report in which RV%

242 was highly correlated with FRC% (r=0.9) *(Deesomchok et al., 2010)*. Therefore, we recommend

243 that RV%, FRC%, and TLC% can be used as biomarkers for hyperinflation, and that RV/TLC

244 and IC/TLC (reciprocal FRC/TLC) can be used as biomarkers for air trapping, even though these

245 two types of biomarkers are closely related. It makes sense that the IC/TLC triad is more

246 sensitive than RV% (*Albuquerque et al., 2006*; *Zhang et al., 2013*) and $FEV_1$% in relation to

247 exercise capacity, as the IC/TLC triad, RV% and $FEV_1$% belong to different factors, denoting

248 that air trapping plays a more important role in exercise capacity than hyperinflation and airflow

249 obstruction *(Zhang et al., 2013)*.

250   *Spirometry and lung volume subdivisions.* The need for simultaneous measurements of lung

251   volume and spirometry is controversial. $FEV_1/FVC$, a biomarker of airway obstruction, was

252   significantly correlated with the biomarkers for air trapping and hyperinflation in this study

253   (Table 4). Airway obstruction can easily be assessed using spirometry. Therefore, additional

254   measurements of static lung volume add little to the clinical interpretation. This is consistent

255   with the study by Dykstra et al., in which 87% of 1,872 patients with reduced vital capacity had a

256   high RV/TLC, and only 10% had a low TLC% (*Dykstra et al., 1999*). This concept was further

257   confirmed in their report as $FEV_1$% was reported to predict RV%, RV/TLC, and TLC% (r=-0.76,

258   -0.66 and -0.33, respectively, all p<0.0001) *(Dykstra et al., 1999)*. Another study reported that a

259   low FVC% with a low $FEV_1/FVC$ ratio could be used as a marker of obstructive ventilation with

260   "pseudo-restriction" (*Aaron et al., 1999*). However, 10% of the patients in Dykstra's study had a

261   low TLC%, suggesting the coexistence of a mixed type (obstructive-restrictive impairment)

262   *(Dykstra et al., 1999)*. In addition, another study reported that 8% of asthmatics had restricted

263   ventilation (*Miller et al., 2007*). Gardner et al. reported that restriction of the lung may interfere

264   with classifying the severity of obstruction in patients with mixed obstructive-restrictive lung

265   disease according to $FEV_1$% adjusted for TLC%. This adjustment resulted in the downgrading of

266   83% of their patients to a lesser degree of obstruction *(Gardner et al., 2011)*. Aaron et al.

267   reported that a reduced FVC could only predict a reduced TLC by 40-50% *(Aaron et al., 1999)*.

268    Moreover, regarding the effect of bronchodilators on COPD, measurements of lung volume

269    response may be superior to those of flow response *(Deesomchok et al., 2010; McCartney et al.,*

270    *2016)*. Hence, we disagree with the notion that lung volume measurements are not necessary for

271    patients with reduced VC,*(Dykstra et al., 1999)* as FVC% and $FEV_1$% were modestly or not

272    correlated with TLC% in the present ($r^2$=0.04 and 0.01, Table 4), and previous studies (*Dykstra*

273    *et al., 1999*; *McCartney et al., 2016*) and were not correlated with expandable lung volumes

274    (Table 4, IC%, IRV%, ERV%, and IRV/TLC and ERV/TLC). The smaller the $FEV_1$%, the larger

275    the RV% and RV/TLC, even though TLC% had probably yet to change *(Vaz Fragoso et al.,*

276    *2017)*.

277        $FEV_1$% was also linearly related to IC (*Deesomchok et al., 2010*) and VC% (*Nishimura et*

278    *al., 2002*; *Deesomchok et al., 2010*) in this study, as $FEV_1$ was 0.76±0.26 of IC and IC was

279    0.71±0.20 of FVC. FVC%, SVC%, and $FEV_1$% were highly correlated in this study but not with

280    $FEV_1$/FVC, which may be because a reduction in FVC may result in a normal or mildly reduced

281    $FEV_1$/FVC due to pseudo-restriction *(Saint-Pierre et al., 2019 (in press))*.

282        In summary, TLC% cannot be replaced by FVC% and RV/TLC is most frequently and most

283    strongly correlated with other lung function variables and consistent with $FEV_1$/FVC. $FEV_1$% is

284    a marker of the severity of COPD. $D_L CO$% alone represented factor 5. Although these four

285    variables could be used to represent all 26 full lung function variables, we do not conclude that

286  the additional variables should not be collected/examined/included in models.

287

288  **Study limitations**

289  Diagnostic instability of COPD diagnosis has been reported in approximately 20% and 10% of

290  individuals with mild and moderate airflow obstruction, respectively, after 4-5 years of follow-up

291  (*Aaron et al., 2017*). However, most (92%) of our participants had moderate to very severe

292  airflow obstruction; therefore, we estimated that 6.7% of our participants probably had

293  diagnostic instability. Selecting an appropriate reference value is important, e.g. TLC or FVC has

294  been reported to be 12% lower in African Americans than in Caucasians (*Lapp et al., 1974*). In

295  this study, we arbitrarily reduced the reference values in the literature by 10-15%, as surveillance

296  reports on reference values were unavailable and to consistently follow our previous reports

297  (*Chuang et al., 2001*). Lung size has been reported to be different between Chinese participants

298  from southern China and northern China, however it is difficult to trace the study participants in

299  Taiwan, as some ancestors came from both northern and southern China. Nevertheless, the use of

300  correlation analysis may have reduced this potential bias. In Guangzhou, China, the estimated

301  prevalence rates of GOLD stage 2 or higher COPD in females and males are approximately 5%

302  and 10%, respectively (*Mannino et al., 2007*). Although we did not have prevalence data of

303  COPD in Taiwan, 96% of our cohort with COPD were male and only 4% were female (*Huang et*

304    *al., 2018*). The data from China are quite different from ours, which may be related to the

305    biomass fuel smoke exposure in the Chinese female population (*Mannino et al., 2007*). Although

306    our study population was small compared to previous reports (*Aaron et al., 1999*; *Dykstra et al.,*

307    *1999*), our patients had COPD alone, whereas previous studies have enrolled COPD patients

308    with various other lung diseases. This may raise concerns that the relationships between lung

309    volumes and their ratios to TLC among the study participants of previous studies may be

310    different from those in our study (*Ruppel 2012*). In addition, our data were all obtained before

311    bronchodilator inhalation, as pharmacological interventions may alter the relationship between

312    volume and capacity. Hence, the findings of this study should be interpreted with caution when

313    extrapolating to patients after bronchodilator inhalation. Furthermore, only two participants did

314    use ultra-long-acting beta agonists in this study, so that the duration of bronchodilator

315    withdrawal for most of the participants might be appropriate. The relationships among lung

316    function variables in the current study may also have been different if the lung volume and

317    capacity were expressed in a way other than % predicted. For example, a previous study reported

318    lung volume and capacity were standardized with cubed height or adjusted with multiple linear

319    regression analysis with adjustments for least square mean and adjustments of spirometry with z-

320    scores (*Vaz Fragoso et al., 2017*). However, these adjustments have not yet been widely used in

321    clinical practice, and further studies are needed to clarify this issue. In the present study,

322     %predicted and ratio of lung volume or capacity and TLC or FVC were used instead of using

323     absolute value in liters or mL/min/mmHg. This may have reduced confounding caused by body

324     height, sex, and age. In addition, anemia is a factor that should be considered for adjustment

325     when predicting $D_L CO$ (*Macintyre et al., 2005*). However, this may be a minor issue, as the

326     hemoglobin level was 14.4±1.7g/dL and 83.2% of our participants had normal hemoglobin levels

327     (≥13 g/dL) and the adjusted coefficient for predicted $D_L CO$ was 0.99 ±0.05 (5th percentile-95th

328     percentile: 0.89-1.06). Lastly, COPD has many phenotypes, however we did not specify these

329     phenotypes in this study.

330     **CONCLUSIONS**

331     This study identified several collinear relationships among individual lung function variables

332     Selecting multiple variables with close relationships for correlation studies should be performed

333     with caution. This study also differentiated variables for air trapping and lung hyperinflation.

334     Lung volume measurements are necessary even when spirometry data are available. We

335     identified four of 26 lung function variables from individual latent factors that could be used to

336     concisely represent lung function.

337

338    **Appendix 1:** The 26 lung function variables with their units.

1    TLC, L
2    TLC% predicted, %
3    FRC, L
4    FRC% predicted, %
5    FRC/TLC
6    RV, L
7    RV% predicted, %
8    RV/TLC
9    Expiratory reserve volume, L
10   Expiratory reserve volume, ERV% predicted, %
11   ERV/TLC
12   IC, L
13   IC% predicted, %
14   IC/TLC
15   Inspiratory reserve volume, L
16   Inspiratory reserve volume, IRV% predicted, %
17   IRV/TLC
18   Diffusion capacity for cabon monoxide, $D_L CO$, mL/min/mmHg
19   $D_L CO$% predicted, %
20   Forced vital capacity, FVC, L
21   FVC% predicted, %
22   Forced expiratory volume in one second, $FEV_1$, L
23   $FEV_1$% predicted, %
24   $FEV_1$/FVC
25   Slow vital capacity, SVC, L
26   SVC% predicted, %

339

340    **Appendix 2**

341    TLC was defined as IC plus FRC.*(Wanger et al., 2005)* Thoracic gas volume was measured by

342    panting at a rate of 1 Hz when the flow was occluded at the end of stable expiration. FRC was

343    calculated from thoracic gas volume after adjusting for stable tidal volume. IC was measured

344    from the end of stable expiration to the top of TLC as far as possible after panting. $V_T$ was

345    averaged from several stable breaths at rest, and IRV was measured from IC minus the averaged

346    $V_T$. ERV was measured as SVC minus IC, and RV was measured as FRC minus ERV. Predicted

347    IC was calculated as predicted TLC minus predicted FRC, and predicted ERV was calculated as

348    predicted FRC minus predicted RV.(Deesomchok *et al.,* 2010)

349

350    **Figure Legends**

351

352    Figure 1. Flow diagram. A total of 104 participants with chronic obstructive pulmonary disease
353    were screened. 94 patients were enrolled and analyzed after excluding 10 participants. Of the 94
354    participants, two participants missed the lung volume measurements, and six participants missed
355    diffusing capacity for carbon monoxide. The differences in demographic data and spirometry
356    between the six and 88 participants were not statistically significant except body weight and
357    body mass index (54.5±3.0 kg versus 61.7±9.7 kg, p <0.001 and 20.9±1.3 kg/m$^2$ versus 22.7±3.2
358    kg/m$^2$ p <0.05, respectively).

360 **References**

361 Aaron, SA, RE Dales, P Cardinal. 1999. How accurate is spirometry at predicting restrictive
362     pulmonary impairment? *Chest* **115**: 869-873

363 Aaron, SD, WC Tan, J Bourbeau, DD Sin, RH Loves, J MacNeil, GA Whitmore, CRR Network.
364     2017. Diagnostic Instability and Reversals of Chronic Obstructive Pulmonary Disease
365     Diagnosis in Individuals with Mild to Moderate Airflow Obstruction. *Am J Respir Crit*
366     *Care Med* **196**: 306-314. DOI 10.1164/rccm.201612-2531OC.

367 Albuquerque, AL, LE Nery, DS Villaça, TY Machado, CC Oliveira, AT Paes, N J.A. 2006.
368     Inspiratory fraction and exercise impairment in COPD patients GOLD stages II-III. *Eur*
369     *Respir J* **28**: 939-944. DOI 10.1183/09031936.06.00040506.

370 ATS/ERS, S. 2002. ATS/ERS Statement on respiratory muscle testing. *Am J Respir Crit Care*
371     *Med* **166**: 518-624 DOI 10.1164/rccm.166.4.518.

372 Budweiser, S, M Harlacher, M Pfeifer, RA Jörres. 2014. Co-morbidities and hyperinflation are
373     independent risk factors of all-cause mortality in very severe COPD. *COPD* **11**: 388-400.
374     DOI 10.3109/15412555.2013.836174.

375 Calverley, PMA, NG Koulouris. 2005. Flow limitation and dynamic hyperinflation: key concepts
376     in modern respiratory physiology. *Eur Respir J* **25**: 186-199. DOI
377     10.1183/09031936.04.00113204.

378 Casanova, C, C Cote, JP de Torres, A Aguirre-Jaime, JM Marin, V Pinto-Plata, BR Celli. 2005.
379     Inspiratory-to-total lung capacity ratio predicts mortality in patients with chronic
380     obstructive pulmonary disease. *Am J Respir Crit Care Med* **171**: 591-597. DOI
381     10.1164/rccm.200407-867OC.

382 Chuang, ML, SF Huang, CH Su. 2015. Cardiovascular and respiratory dysfunction in chronic
383     obstructive pulmonary disease complicated by impaired peripheral oxygenation. *Int J*
384     *Chron Obstruct Pulmon Dis* **10**: 329-337 DOI 10.2147/COPD.S7620.

385 Chuang, ML, IF Lin, K Wasserman. 2001. The body weight-walking distance product as related
386     to lung function, anaerobic threshold and peak $VO_2$ in COPD patients. *Respir Med* **95**:
387     618-626 DOI 10.1053/rmed.2001.1115.

388 Cohen, Z (2017). Pulmonary function testing. Egan's fundamentals of respiratory care. R. M.
389     Kacmarek, J. K. Stoller and A. J. Heuer. St. Louis, Elsevier**:** 400-427.

390 de Winter, JD, D Dodou, PA Wieringa. 2009. Exploratory Factor Analysis With Small Sample
391     Sizes. *Multivariate Behavioral Research* **44**: 147-181. DOI 10.1080/00273170902794206.

392 Deesomchok, A, KA Webb, L Forkert, YM Lam, D Ofir, D Jensen, DE O'Donnell. 2010. Lung
393     hyperinflation and its reversibility in patients with airway obstruction of varying severity.
394     *COPD* **7**: 428-437 DOI 10.3109/15412555.2010.528087.

395 Dykstra, BJ, PD Scanlon, MM Kester, KC Beck, PL Enright. 1999. Lung volumes in 4,774
396       patients with obstructive lung disease. *Chest* **115**: 68-74

397 Gagnon, P, JA Guenette, D Langer, L Laviolette, V Mainguy, F Maltais, F Ribeiro, D Saey.
398       2014. Pathogenesis of hyperinflation in chronic obstructive pulmonary disease. *Int J Chron*
399       *Obstruct Pulmon Dis* **9**: 187-201 DOI 10.2147/COPD.S38934.

400 Gardner, ZS, GL Ruppel, DA Kaminsky. 2011. Grading the severity of obstruction in mixed
401       obstructive-restrictive lung disease. *Chest* **140**: 598-603. DOI 10.1378/chest.10-2860.

402 GINA Committees. 2017. Global Initiative for Asthma (UPDATED 2017) *Disclosure forms for*
403       *GINA Committees are posted on the GINA Website,* www.ginasthma.org, : 1-156

404 GOLD Committees. 2017. Global Strategy for the Diagnosis, Management, and Prevention of
405       Chronic Obstructive Pulmonary Disease (revised 2015). *Disclosure forms for GOLD*
406       *Committees are posted on the GOLD Website,* www.goldcopd.org

407 Hogarty, KY, CV Hines, JD Kromrey, JM Ferron, KR Mumford. 2005. The quality of factor
408       solutions in exploratory factor analysis: the influence of sample size, communality, and
409       overdetermination. *Educational and Psychological Measurement* **65**: 202-226. DOI
410       10.1177/0013164404267287.

411 Huang, TH, TR Hsiue, SH Lin, XM Liao, PL Su, CZ Chen. 2018. Comparison of different
412       staging methods for chronic obstructive pulmonary disease in predicting outcomes. *Eur*
413       *Respir J* **51**: 1700577. DOI 10.1183/13993003.00577-2017.

414 Johns, DP, JA Walters, EH Walters. 2014. Diagnosis and early detection of COPD using
415       spirometry. *J Thorac Dis* **6**: 1557-1569. DOI 10.3978/j.issn.2072-1439.2014.08.18.

416 Labbé, G, E Merlin, C Kauffman, JL Fauquert, MC Héraud, A Labbé. 2010. [The role of lung
417       volume measurements by plethysmography in the follow-up of asthma in children]. *Rev*
418       *Mal Respir.* **27**: 42-48. DOI 10.1016/j.rmr.2009.11.002.

419 Lapp, NL, HE Amandus, R Hall, WKC Morgan. 1974. Lung volumes and flow rates in black
420       and white subjects. *Thorax* **29**: 185–188

421 Macintyre, N, RO Crapo, G Viegi, DC Johnson, CP van der Grinten, V Brusasco, F Burgos, R
422       Casaburi, A Coates, P Enright, P Gustafsson, J Hankinson, R Jensen, R McKay, MR Miller,
423       D Navajas, OF Pedersen, R Pellegrino, J Wanger. 2005. Standardisation of the single-
424       breath determination of carbon monoxide uptake in the lung. *Eur Respir J* **26**: 720-735
425       DOI 10.1183/09031936.05.00034905.

426 Mannino, DM, AS Buist. 2007. Global burden of COPD: risk factors, prevalence, and future
427       trends. *Lancet* **370**: 765-773. DOI 10.1016/S0140-6736(07)61380-4.

428 McCartney, CT, MN Weis, GL Ruppel, RP Nayak. 2016. Residual Volume and Total Lung
429       Capacity to Assess Reversibility in Obstructive Lung Disease. *Respir care* **61**: 1505-1512.
430       DOI 10.4187/respcare.04323.

431 Miller, A, A Palecki. 2007. Restrictive impairment in patients with asthma. *Respir Med* **101**:
432      272-276 DOI 10.1016/j.rmed.2006.05.008.

433 Miller, MR, R Crapo, J Hankinson, V Brusasco, F Burgos, R Casaburi, A Coates, P Enright, CP
434      van der Grinten, P Gustafsson, R Jensen, DC Johnson, N MacIntyre, R McKay, D Navajas,
435      OF Pedersen, R Pellegrino, G Viegi, J Wanger. 2005. General considerations for lung
436      function testing. *Eur Respir J* **26**: 153-161 DOI 10.1183/09031936.05.00034505.

437 Miller, MR, J Hankinson, V Brusasco, F Burgos, R Casaburi, A Coates, R Crapo, P Enright, CP
438      van der Grinten, P Gustafsson, R Jensen, DC Johnson, N MacIntyre, R McKay, D Navajas,
439      OF Pedersen, R Pellegrino, G Viegi, J Wanger. 2005. Standardisation of spirometry. *Eur
440      Respir J* **26**: 319-338 DOI 10.1183/09031936.05.00034805.

441 Nishimura, K, T Izumi, M Tsukino, T Oga. 2002. Dyspnea is a better predictor of 5-year survival
442      than airway obstruction in patients with COPD. *Chest* **121**: 1434-1440. PMID: 12006425.

443 O'Donnell, DE, SM Revill, KA Webb. 2001. Dynamic hyperinflation and exercise intolerance in
444      chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* **164**: 770-777 DOI
445      10.1164/ajrccm.164.5.2012122.

446 Rencher, AC, WF Christensen (2012). Methods of multivariate analysis. , A John Wiley & Sons,
447      Inc., Publication.

448 Ruppel, GL (1991). Lung volume tests. Manual of pulmonary function testing. G. L. Ruppel. St.
449      Louis, Mosby Year Book**: 1-22.

450 Ruppel, GL. 2012. What is the clinical value of lung volumes? *Respir Care* **57**: 26-35 DOI
451      10.4187/respcare.01374.

452 Saint-Pierre, M, J Ladha, DC Berton, G Reimaoa, G Castellia, M Marillier, A Bernard, DE
453      O'Donnell, JA Neder. 2019 (in press). Is the Slow Vital Capacity Clinically Useful to
454      Uncover Airflow Limitation in Subjects With Preserved $FEV_1$/FVC Ratio? *Chest* pii:
455      S0012-3692(19)30143-6 DOI 10.1016/j.chest.2019.02.001.

456 Shin, TR, YM Oh, JH Park, KS Lee, S Oh, DR Kang, S Sheen, JB Seo, KH Yoo, JH Lee, TH
457      Kim, SY Lim, HI Yoon, CK Rhee, KH Choe, JS Lee, SD Lee. 2015. The Prognostic Value
458      of Residual Volume/Total Lung Capacity in Patients with Chronic Obstructive Pulmonary
459      Disease. *J Korean Med Soc* **30**: 1459-1465. DOI 10.3346/jkms.2015.30.10.1459.

460 Tantucci, C, P Donati, F Nicosia, E Bertella, S Redolfi, M De Vecchi, L Corda, V Grassi, R Zulli.
461      2008. Inspiratory capacity predicts mortality in patients with chronic obstructive
462      pulmonary disease. *Respir Med* **102**: 613-619. DOI 10.1016/j.rmed.2007.11.004.

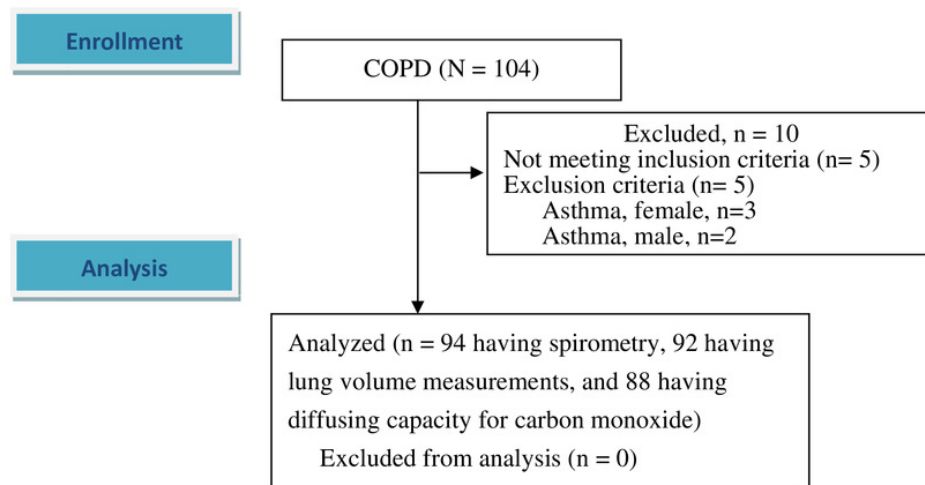
463 Vassaux, C, L Torre-Bouscoulet, S Zeineldine, F Cortopassi, H Paz-Diaz, BR Celli, VM Pinto-
464      Plata. 2008. Effects of hyperinflation on the oxygen pulse as a marker of cardiac
465      performance in COPD. *Eur Respir J* **32**: 1275-1282 DOI 10.1183/09031936.00151707.

466 Vaz Fragoso, CA, HC Cain, R Casaburi, PJ Lee, L Iannone, LS Leo-Summers, PH Van Ness.

467        2017. Spirometry, Static Lung Volumes, and Diffusing Capacity. *Respir Care* **62**: 1137-
468        1147. DOI 10.4187/respcare.05515.
469  Wanger, J, JL Clausen, A Coates, OF Pedersen, V Brusasco, F Burgos, R Casaburi, R Crapo, P
470        Enright, CP van der Grinten, P Gustafsson, J Hankinson, R Jensen, D Johnson, N
471        Macintyre, R McKay, MR Miller, D Navajas, R Pellegrino, G Viegi. 2005. Standardisation
472        of the measurement of lung volumes. *Eur Respir J* **26**: 511-522 DOI
473        10.1183/09031936.05.00035005.
474  Zhang, Y, XG Sun, WL Yang, XY Tan, JM Liu. 2013. Inspiratory fraction correlates with
475        exercise capacity in patients with stable moderate to severe COPD. *Respir Care* **58**: 1923-
476        1930. DOI 10.4187/respcare.01927.
477

# Figure 1

Flow diagram.

A total of 104 participants with chronic obstructive pulmonary disease were screened. 94 patients were enrolled and analyzed after excluding 10 participants. Of the 94 participants, two participants missed the lung volume measurements, and six participants missed diffusing capacity for carbon monoxide. The differences in demographic data and spirometry between the six and 88 participants were not statistically significant except body weight and body mass index (54.5±3.0 kg versus 61.7±9.7 kg, p <0.001 and 20.9±1.3 kg/m$^2$ versus 22.7±3.2 kg/m$^2$ p <0.05, respectively)

Demographics and lung function in 94 participants with chronic obstructive pulmonary disease.

TLC: total lung capacity, L: liter, FRC: functional residual capacity, RV: residual volume, IC: inspiratory capacity, $D_L CO$: diffusing capacity for carbon monoxide, FVC: forced vital capacity, $FEV_1$: forced expired volume in one second, SVC: slow vital capacity. [†]n=92, [‡]n=88, [¶]n=91, * ( GOLD Committees 2017 ) , [#]median (25th-75th percentiles).

1     Table 1. Demographics and lung function in 94 participants with chronic obstructive pulmonary

2     disease.

| | mean | SD |
|---|---|---|
| Age, years | 68.1 | 7.2 |
| Height, cm | 164.5 | 5.8 |
| Weight, kg | 61.3 | 9.6 |
| Body mass index, kg/m$^2$ | 22.6 | 3.2 |
| Cigarette smoke[†], pack·year | 45 | 35.5-60[#] |
| TLC% predicted[†], % | 116 | 103-137[#] |
| FRC% predicted[†], % | 143 | 35 |
| FRC/TLC[†] | 0.71 | 0.08 |
| RV% predicted[†], % | 170 | 55 |
| RV/TLC[†] | 0.56 | 0.09 |
| Expiratory reserve volume, ERV% predicted[†], % | 82 | 55-121[#] |
| ERV/TLC[†] | 0.15 | 0.08 |
| IC% predicted[†], % | 87 | 26 |
| IC/TLC[†] | 0.29 | 0.08 |
| Inspiratory reserve volume, IRV% predicted[†], % | 78 | 47 |
| IRV/TLC[†] | 0.15 | 0.09 |
| $D_L$CO% predicted, %, unadjusted for Hemoglobin[‡] | 76 | 26 |
| FVC% predicted, % | 83 | 22 |
| $FEV_1$% predicted, % | 54 | 19 |
|      Mild, $FEV_1$%≥80%*, n, % | 8 (9) | |
|      Moderate, 50%≤ $FEV_1$%<80%*, n, % | 47 (50) | |
|      Severe, 30%≤ $FEV_1$%<50%*, n, % | 30 (32) | |
|      Very severe, $FEV_1$%<30%*, n, % | 9 (10) | |
| $FEV_1$/FVC | 0.51 | 0.12 |
| SVC% predicted[¶], % | 82 | 70-107[#] |

3     TLC: total lung capacity, L: liter, FRC: functional residual capacity, RV: residual volume, IC:

4     inspiratory capacity, $D_L$CO: diffusing capacity for carbon monoxide, FVC: forced vital capacity,

5     $FEV_1$: forced expired volume in one second, SVC: slow vital capacity. [†]n=92, [‡]n=88, [¶]n=91,

6     *(GOLD Committees 2017), [#]median (25th-75th percentiles).

Factor analysis showing rotated component matrix[a]

For all abbreviations, please refer to Table 1. Extraction method: Principal component analysis. Rotation method: Varimax with Kaiser normalization. [a]Rotation converged in 5 iterations. Bolded number indicating the important variables (arbitrarily defined as value >0.85) in that factor, Italic number indicating the variables with moderate importance (arbitrarily defined as value >0.5) in that factor.

Table 2. Factor analysis showing rotated component matrix[a]

| | Factors | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| TLC%p | 0.27 | **0.93** | 0.17 | -0.1 | -0.1 |
| FRC%p | -0.2 | **0.94** | 0.11 | -0.13 | -0.08 |
| FRC/TLC | *-0.68* | *0.65* | 0.1 | -0.21 | -0.07 |
| RV%p | -0.07 | **0.89** | -0.32 | -0.13 | -0.16 |
| RV/TLC | -0.39 | *0.53* | *-0.67* | -0.16 | -0.14 |
| IC%p | **0.96** | .011 | 0.08 | 0.09 | -0.03 |
| IC/TLC | *0.67* | *-0.66* | -0.1 | 0.21 | 0.04 |
| IRV%p | **0.94** | 0.07 | 0.1 | 0.01 | -0.03 |
| IRV/TLC | **0.86** | -0.19 | 0.03 | -0.01 | 0.13 |
| ERV%p | -0.18 | 0.22 | **0.91** | -0.04 | 0.14 |
| ERV/TLC | -0.24 | 0.02 | **0.91** | -0.03 | 0.09 |
| $D_L CO$%p | 0.07 | -0.25 | 0.19 | 0.18 | **0.92** |
| FVC%p | 0.48 | -0.09 | *0.76* | 0.12 | -0.04 |
| $FEV_1$%p | 0.37 | -0.26 | *0.54* | *0.65* | 0.06 |
| $FEV_1$/FVC | -0.00 | -0.22 | -0.04 | **0.94** | 0.15 |
| SVC%p | *0.57* | 0.06 | *0.77* | 0.08 | 0.04 |

1   For all abbreviations, please refer to Table 1. Extraction method: Principal component analysis.

2   Rotation method: Varimax with Kaiser normalization. [a]Rotation converged in 5 iterations. Bolded

3   number indicating the important variables (arbitrarily defined as value >0.85) in that factor, Italic

4   number indicating the variables with moderate importance (arbitrarily defined as value >0.5) in

5   that factor.

Pearson Correlations (r) Pair-Wise Deletion between lung volumes in 92* participants with obstructive airway disease.

TLC: total lung capacity, FRC: functional residual capacity, RV: residual volume, ERV: expiratory reserve volume, IC: inspiratory capacity, IRV: inspiratory reserve volume, $D_L CO$: diffusing capacity for carbon monoxide. %: % predicted. [#]Spearman correlation coefficient, [§]p <0.0001, [†]p <0.001, [**]p <0.01, and [*]p <0.05. NS= non-significant. *Two of 94 participants missed lung volume measurements.

Table 3. Pearson Correlations (r) Pair-Wise Deletion between lung volumes in 92* participants with obstructive airway disease.

| | TLC%[#] | FRC% | FRC/TLC | RV% | RV/TLC | ERV%[#] | ERV/TLC | IC% | IC/TLC | IRV% | IRV/TLC | $D_L$CO% |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TLC%[#] | | 0.86$^§$ | 0.44$^§$ | 0.77$^§$ | 0.26$^{**}$ | -0.27$^{**}$ | NS | 0.33$^{**}$ | -0.46$^§$ | 0.41$^§$ | NS | -0.28$^{**}$ |
| FRC% | | | 0.75$^§$ | 0.87$^§$ | 0.52$^§$ | 0.32$^{**}$ | NS | NS | -0.76$^§$ | NS | -0.28$^{**}$ | -0.34$^{**}$ |
| FRC/TLC | | | | 0.62$^§$ | 0.62$^§$ | 0.29$^{**}$ | 0.29$^{**}$ | -0.63$^§$ | -0.99$^§$ | -0.53$^§$ | -0.65$^§$ | -0.29$^{**}$ |
| RV% | | | | | 0.71$^§$ | NS | -0.23$^*$ | NS | -0.63$^§$ | NS | -0.22$^*$ | -0.47$^§$ |
| RV/TLC | | | | | | -0.45$^§$ | -0.57$^§$ | -0.44$^§$ | -0.61$^§$ | -0.38$^{⑤}$ | -0.51$^§$ | -0.43$^§$ |
| ERV%[#] | | | | | | | 0.92$^§$ | NS | -0.3$^{**}$ | NS | NS | NS |
| ERV/TLC | | | | | | | | NS | -0.27$^{**}$ | NS | NS | 0.21$^*$ |
| IC% | | | | | | | | | 0.62$^§$ | 0.95$^§$ | 0.77$^§$ | NS |
| IC/TLC | | | | | | | | | | 0.52$^§$ | 0.65$^§$ | 0.27$^*$ |
| IRV% | | | | | | | | | | | 0.77$^§$ | NS |
| IRV/TLC | | | | | | | | | | | | 0.21$^*$ |

1  TLC: total lung capacity, FRC: functional residual capacity, RV: residual volume, ERV: expiratory reserve volume, IC:

2  inspiratory capacity, IRV: inspiratory reserve volume, $D_L$CO: diffusing capacity for carbon monoxide. %: % predicted.

3  [#]Spearman correlation coefficient, $^§$p <0.0001, $^†$p <0.001, $^{**}$p <0.01, and $^*$p <0.05. NS= non-significant. *Two of 94

4  participants missed lung volume measurements.

Pearson Correlations (r) Pair-Wise Deletion between lung volumes and spirometry in participants with obstructive airway disease.

TLC: total lung capacity, FRC: functional residual capacity, RV: residual volume, ERV: expiratory reserve volume, IC: inspiratory capacity, IRV: inspiratory reserve volume, $D_LCO$: diffusing capacity for carbon monoxide, FVC: forced vital capacity, $FEV_1$: forced expired volume in one second, SVC: slow vital capacity. %: % predicted. #Spearman correlation coefficient, §p <0.0001, †p <0.001, **p <0.01, and *p <0.05. n = 94 having spirometry, 92 having lung volume measurements, and 88 having $D_LCO$.

1 Table 4. Pearson Correlations (r) Pair-Wise Deletion between lung volumes and spirometry in
2 participants with obstructive airway disease.

| | FVC% | FEV$_1$% | FEV$_1$/FVC | SVC%[#] |
|---|---|---|---|---|
| FVC% | | 0.77[§] | 0.04 | 0.86[§] |
| FEV$_1$% | | | 0.63[§] | 0.62[§] |
| FEV$_1$/FVC | | | | -0.03 |
| TLC%[#] | 0.20[*] | -0.11 | -0.32[**] | 0.39[†] |
| FRC% | -0.09 | -0.35[†] | -0.36[†] | 0.09 |
| FRC/TLC | -0.33[**] | -0.5[§] | -0.36[†] | -0.28[**] |
| RV% | -0.29[**] | -0.48[§] | -0.35[†] | -0.2 |
| RV/TLC | -0.65[§] | -0.67[§] | -0.28[**] | -0.67[§] |
| ERV%[#] | 0.43[§] | 0.27[**] | -0.07 | 0.58[§] |
| ERV/TLC | 0.45[§] | 0.29[**] | -0.03 | 0.5[§] |
| IC% | 0.51[§] | 0.44[§] | 0.08 | 0.62[§] |
| IC/TLC | 0.32[**] | 0.49[§] | 0.36[†] | 0.25[*] |
| IRV% | 0.5[§] | 0.37[†] | 0.01 | 0.63[§] |
| IRV/TLC | 0.32[**] | 0.29[**] | 0.06 | 0.51[§] |
| D$_L$CO% | 0.19 | 0.34[**] | 0.29[**] | 0.18 |

3  TLC: total lung capacity, FRC: functional residual capacity, RV: residual volume, ERV:

4  expiratory reserve volume, IC: inspiratory capacity, IRV: inspiratory reserve volume, D$_L$CO:

5  diffusing capacity for carbon monoxide, FVC: forced vital capacity, FEV$_1$: forced expired

6  volume in one second, SVC: slow vital capacity. %: % predicted. [#]Spearman correlation

7  coefficient, [§]p <0.0001, [†]p <0.001, [**]p <0.01, and [*]p <0.05. n = 94 having spirometry, 92 having

8  lung volume measurements, and 88 having D$_L$CO.