Prediction of air trapping or pulmonary hyperinflation by forced spirometry in COPD patients: Results from COSYCONET

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Supplementary methods

Postbronchodilator spirometry and body plethysmography were performed as recommended by the American Thoracic Society (ATS)/European Respiratory Society (ERS) [1] and Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP) [2, 3]; details on all assessments can be found elsewhere [4].

In COSYCONET, different body plethysmographs of several manufacturers were used. As influences of the device type on the measured values are possible, we included only data obtained by MasterScreen devices (Viasys, Jaeger) that were used in 29 of 31 study centers and provided the vast majority of examinations. The analysis of potential methodological differences between body plethysmographs provided by different vendors would require a separate study.

Supplementary statistical analysis

For continuous variables, mean values and standard deviations (SD) are given, and for categorical data the numbers (percentages) of patients. In the regression analyses, for each of the dependent variables, the analyses were performed either for the total group of patients, or males and females separately. We first entered each of the three spirometric predictors separately in combination with the covariates into the regression analyses. Subsequently, we assessed FEV_1 %pred combined with FVC %pred as well as FEV_1 %pred, FVC %pred and IVC %pred in triple combination. This approach was chosen instead of automatic stepwise search, as we were interested in the comparison of the single parameters with the combinations, particularly to identify the potential additional usefulness of IVC. For analysis of pooled data from visits 1–5, a mixed linear model was used to handle correlated data from repeated visits. For all computations, IBM SPSS Statistics Version 26 (Armonk, NY, USA) was employed. Figures were created using SigmaPlot 14 (Systat Software, San Jose, CA, USA). Statistical significance was assumed for $p<0.05$.

Supplementary discussion

Lung hyperinflation is closely related to the occurrence of air trapping and airway collapse, while airway collapse may depend on the respiratory effort and the magnitude of intrapleural pressure alterations [5]. This is the reason to expect that IVC should be larger than FVC and that the difference should reflect the differential airway collapse during slow versus fast expiration, and thus air trapping as a correlate of lung hyperinflation. Contrary to our expectations, we found IVC virtually useless for this purpose in the present COPD cohort. The most likely explanation is that the inspiratory slow maneuver shows high variability and is not well controlled. Moreover, influences of the BMI appear likely [6]. The measurement of IVC has been proposed in only few countries, including Germany [2], whereas most countries solely rely on FVC. There is also variability in the determination of RV, arising from variation in the measurement of FRC and ERV; these two measures were used to determine RV in the present study. Errors in the determination of RV and IVC are translated into errors in the determination of TLC. In any case, RV and TLC are affected in the same direction by errors originating in the measurement of FRC, and this might be the reason why RV/TLC showed better fits in the predictive equations than, e.g., RV %pred or FRC %pred. Our findings suggest that, provided FVC is known, IVC is not informative in COPD, at least regarding the estimation of RV/TLC. Additional analyses in healthy subjects and subjects with controlled asthma and normal or near-to-normal lung function [7] indicated that the expected difference is present in these patients, in whom it has, however, no obvious diagnostic value (data not shown).

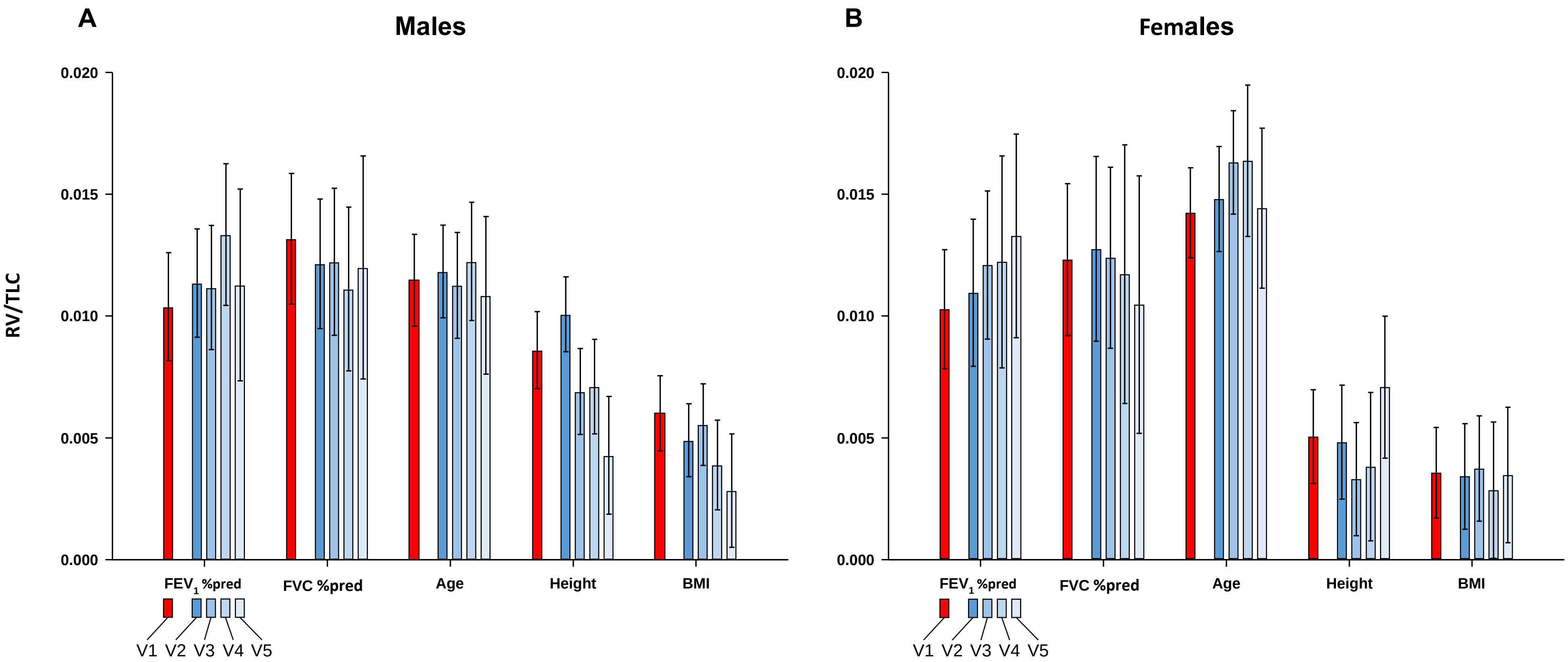
We restricted the analysis to data obtained with a single type of body plethysmograph that has a wide distribution worldwide. While spirometers on the market have to satisfy stringent criteria that ensure their comparability, no such internationally established standards exist for body plethysmography. A study comparing devices from different manufacturers in the same patients would be helpful to clarify the issue of comparability. If different populations are used, the influence of differences in populations cannot be excluded.

Supplementary Table S1. Subject characteristics at visits 2 to 5

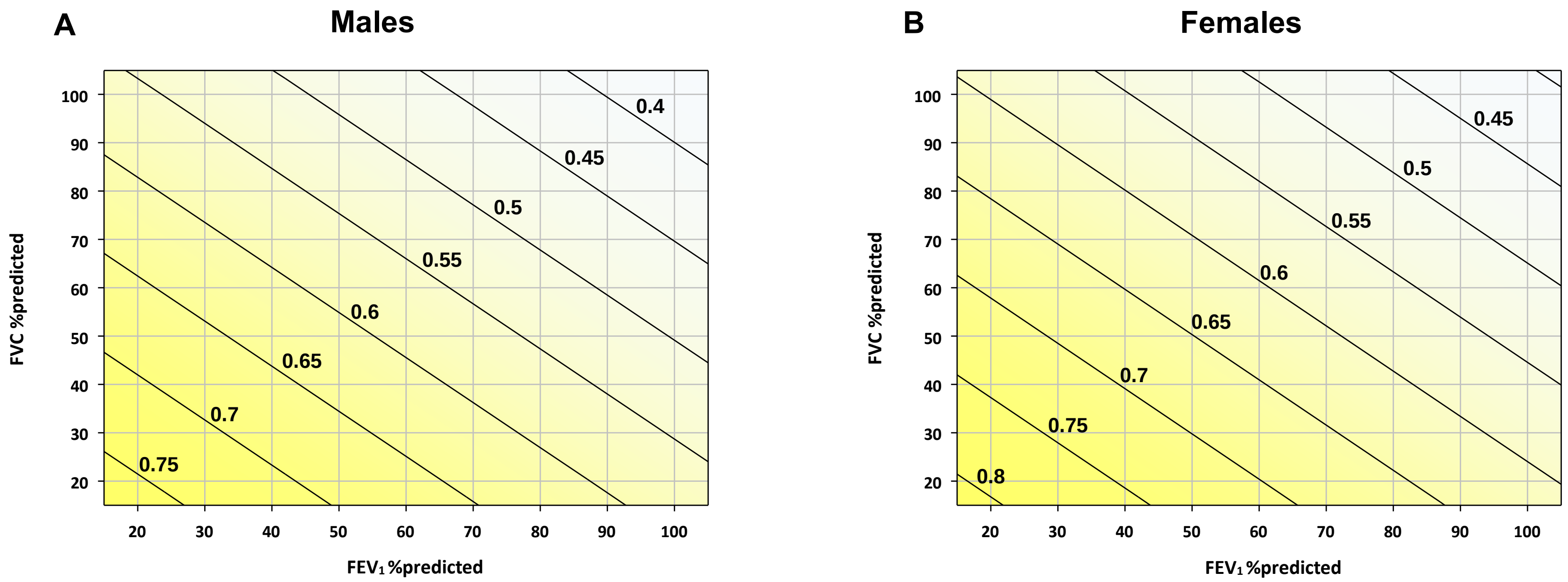
	Visit 2 **n = 1787**	**Visit 3** **n = 1545**	**Visit 4** **n = 1060**	**Visit 5** **n = 777**
Days after visit 1	197 ± 32	575 ± 50	1119 ± 70	1658 ± 72
Anthropometric data				
Sex [m/f]	1130/657	946/599	662/398	472/305
Age [y]	65.5 ± 8.3	66.2 ± 8.2	67.3 ± 8.1	68.4 ± 8.0
Height [cm]	171 ± 9	171 ± 9	172 ± 9	171 ± 9
BMI [kg/m²]	26.7 ± 5.2	26.6 ± 5.2	26.7 ± 5.2	26.4 ± 4.9
Lung function				
FEV_1 %pred	53.0 ± 18.4	52.5 ± 18.6	52.8 ± 18.6	53.7 ± 19.3
FVC %pred	79.0 ± 18.9	78.5 ± 19.4	78.8 ± 19.5	80.1 ± 19.8
RV/TLC	0.545 ± 0.107	0.552 ± 0.108	0.549 ± 0.110	0.551 ± 0.110

Data are mean±standard deviation, numbers or percentages. FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; RV = residual volume; TLC = total lung capacity.

Supplementary Figure S1



Supplementary Figure S2. RV/TLC predicted by FEV_1 + FVC + covariates



Supplementary figure legends

Figure S1. Effects to be expected on changes in the RV/TLC ratio based on the predictors FEV_1 %pred, FVC %pred, age, height and BMI as obtained from non-standardized regression coefficients by multivariable analyses in males (A) and females (B). Coefficients were multiplied by practically feasible factors, whereby a decrease of 5 %pred points in FEV_1 and FVC, an increase of 5 years of age, a decrease of 5 cm of body height and a decrease of 2.5 kg/m^2 in BMI was taken assumed. In addition, 95% confidence intervals are shown.

Figure S2. Nomograms in males (A) and females (B) enabling to estimate the RV/TLC ratio. These were obtained from a mixed model based on FEV_1 %pred and FVC %pred as predictors, including age, height and BMI as covariates. For the nomogram, an age of 65 years and a BMI of 25 kg/m^2 was assumed for both sexes, moreover a height of 175 cm for males and of 165 cm for females. Vertical bars show the standard deviation to be expected from the models. To account for individual anthropometric characteristics, the coefficients given in Table 2 can be used by multiplying the regression coefficients with the individual differences in anthropometric characteristics from the assumed values and adding the results to the estimate derived from the nomogram. An example of a regression equation is given in the legend of Table 2.

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