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SHORT REPORT

# Differences in the Measurement of Functional Residual Capacity Between Body Plethysmographs of Two Manufacturers

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**Abstract:** Body plethysmography is a fundamental method for the assessment of static lung volumes. Although equipment is provided by several manufacturers, there are no established cross-vendor tools for quality control. In the process of quality control and analysis of data on hyperinflation from the large COPD cohort COSYCONET, hints appeared that plethysmographs of different vendors might yield different values for static lung volumes. Functional residual capacity (FRC) differed about 0.67 litres between plethysmographs of the manufacturer Vyaire and Ganshorn. Absolute differences of residual lung volume (RV) and total lung capacity (TLC) were similar. It appears undeniable that differences of this magnitude have an impact on clinical interpretation. Thus, device harmonization seems to be required.

**Keywords:** lung function, body plethysmography, static lung volumes, functional residual capacity

## Introduction

Body plethysmography is a major tool in the inventory of lung function measurements and suited for the assessment of static lung volumes, especially functional residual capacity (FRC), residual volume (RV) and total lung capacity (TLC). Its physiological basis and practical implementation have been described in detail.[1] Equipment is provided by a number of manufacturers. There seem to be no independent devices for quality control to be used by all manufacturers. In view of the intricacies of the method, one has to consider the possibility that plethysmographs of different manufacturers show systematic differences in measured values.

In the multicenter COPD cohort COSYCONET (COPD and Systemic Consequences - Comorbidities Network), body plethysmography is part of assessments.[2] In the process of quality control and analysis, more and more hints appeared that plethysmographs of different manufacturers located at different participating study centers might yield different values for FRC and derived parameters.[3,4] This raised the question, whether suspected differences between devices could be verified, whether it reached relevant magnitude, and which factors might be responsible. If such differences should exist and exceed a certain magnitude, they might have consequences with regard to the applicability of reference values, irrespective of the use of ECSC (European community for coal and steel)[5] or more recent equations.[6,7]

## Methods

Data from COSYCONET were used. Anthropometric, clinical and functional data including spirometry (forced expiratory volume in 1 s, $FEV_1$; forced vital capacity, FVC) and body plethysmography (FRC, RV, TLC) were obtained following standardized protocols in 30 study centres throughout Germany.[2] The study protocol was approved by the

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Ethical Committees of all centres, and all participants gave their written informed consent. The study was performed in accordance with the declaration of Helsinki. ClinicalTrials.gov: NCT01245933.

The centres using a plethysmograph of the manufacturer Vyaire (CareFusion, Jaeger; Höchberg, Germany) provided data from 1988 COPD patients of GOLD grades 1–4[8] as described previously (38.1% female, mean (SD) age 65.1±8.4 years, GOLD grades 1/2/3/4: 9.4/42.6/38.5/9.5%).[4] Additionally, we included 156 patients (51.9% female, mean (SD) age 64.1±9.2 years, GOLD grades: 1/2/3/4: 8.3/46.8/33.3/11.5%) from one centre using a Ganshorn (Niederlauer, Germany) plethysmograph, applying the same criteria of data validity and completeness.[4] Thus, the present analysis included 2144 patients.

Analysis of baseline characteristics and comparison among both groups was performed (Table 1). As we did not measure the same patient in both plethysmographs, we than performed linear regression analyses of static lung volumes (FRC, RV, TLC), either as % predicted[9] or as absolute values in litres, as well as of RV/TLC %. As previously,[4] predictors were $FEV_1$ and FVC, both as % predicted,[10] sex, age, height and body mass index (BMI), and introducing an indicator variable for the type of plethysmograph. The magnitude of the respective regression coefficient would then indicate the difference between devices after adjustment for anthropometric and spirometric characteristics.

## Results

Analysis of the group of 156 patients showed that the relationship between predictors, especially $FEV_1$ and FVC, and RV/TLC % was the same as in the larger group,[4] thus patients did not appear to be qualitatively different and the pooled analysis was valid. Regarding RV/TLC %, it revealed a significantly ($p<0.001$ each) smaller average value in the 156 patients (Δ=−6.9; 95% CI: −7.9; −5.8). The same was true for % predicted values of FRC (Δ=−20.9; 95% CI: −25.4; −16.4), RV (Δ=−34.0; 95% CI: −40.5; −27.6), and TLC (Δ=−10.2; 95% CI: −12.7; −7.7), and for the absolute values in litres of FRC (Δ=−0.67; 95% CI: −0.82; −0.53; Figure 1), RV (Δ=−0.77; 95% CI: −0.92; −0.63), and TLC (Δ=−0.61; 95% CI: −0.77; −0.46). Details are shown in Table 2.

## Discussion

In the present analysis we addressed the question, whether body plethysmographs of two manufacturers showed systematic differences in the measured values of static lung volumes. Indeed, there were such differences. In direct comparison, the Ganshorn device yielded lower and the Vyaire devices higher values of static lung volumes, especially functional residual capacity (FRC). These findings were obtained via regression analysis, adjusting for patient characteristics known to affect lung volumes.[3] Notably, they were consistent regarding both absolute values and values in % predicted. The absolute differences of FRC, RV and TLC between plethysmographs were similar, with large overlap of confidence intervals, indicating that the 0.67 L difference in FRC translated into parallel differences in RV and TLC. As usual, these parameters were derived from FRC via consecutive breathing maneuvers involving the expiratory reserve volume (ERV) and the inspiratory vital capacity (VCin). It is clear that % predicted values differed as they depended on the volumes used for reference; they reached average values of about 21% for FRC, 34% for RV and 10% for TLC. It seems difficult to deny that differences of this magnitude are relevant, both as absolute values and as % predicted. Apart from the variability arising from the choice of reference equations, such differences are likely to affect the interpretation of plethysmographic results, potentially leading to marked over- or underestimation of hyperinflation depending on the device used.

**Table 1** Baseline Characteristics

| | Jaeger n = 1988 | Ganshorn n = 156 | p value |
|---|---|---|---|
| **GOLD grades 1/2/3/4** | 187/847/766/188 (9.4/42.6/38.5/9.5%) | 13/73/52/18 (8.3/46.8/33.3/11.5%) | 0.485 |
| **Age [years]** | 65.1 ± 8.4 | 64.1 ± 9.2 | 0.184 |
| **Height [cm]** | 171 ± 9 | 171 ± 10 | 0.840 |
| **BMI [kg/m$^2$]** | 26.6 ± 5.2 | 26.5 ± 4.9 | 0.791 |
| **Sex [male/female]** | 1231 (61.9%)/757 (38.1%) | 75 (48.1%)/81 (51.9%) | <0.001 |

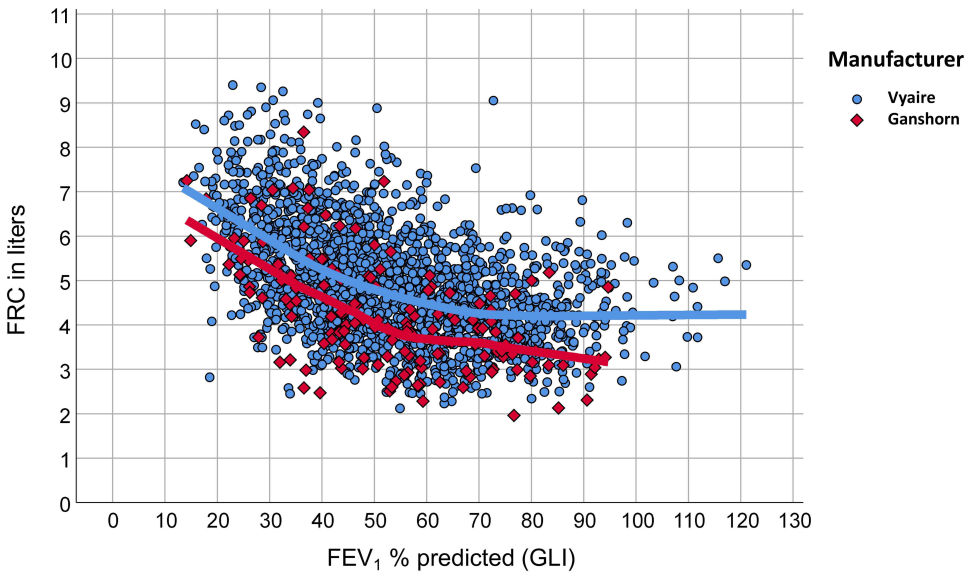


**Figure 1** Difference in FRC between body plethysmographs. The horizontal axis shows $FEV_1$ % predicted (GLI), the vertical axis FRC in litres measured by either the Vyaire (blue circles, n=1988) or the Ganshorn (red diamonds, n=156) plethysmograph. Additionally, LOESS fit lines are shown for both groups in the respective colors, indicating a difference of more than 0.5 litres between FRC values at a given value of $FEV_1$ % predicted. When residual terms after adjustment for $FEV_1$, FVC, sex, age, height and BMI were used, essentially the same picture was obtained, with the difference that the dependence on $FEV_1$ disappeared. This demonstrated that the difference shown in the graph was not due to residual confounding but a robust result even in unadjusted data.

It is unlikely that the observed differences are confined to the equipment of just the two manufacturers chosen. Their occurrence and magnitude could depend on factors involving hardware, software and the manner the shutter manoeuvre is performed. There are no obligatory calibration devices to be used by all manufacturers. We consider differences in software to be more likely and better amenable to future standardization. The shutter manoeuvre is usually performed at the end of normal tidal expiration, or shortly thereafter, with correction for the inspired volume. To our knowledge, in most plethysmographs, FRC is taken as that volume, while in others half of the tidal volume is added. While this might be adequate regarding the computation of airway resistance (Raw) from specific airway resistance (sRaw) as a value averaged over the breathing cycle, it implies a difference in FRC, and consequently in the computed Raw.[1] According to our experience, actual tidal volume may be as large as 1.0 or 1.5 L, despite the fact that more shallow breathing is recommended, thus a numerical difference of 0.67 L may easily be introduced. We also were informed by manufacturers on differences in the advice given to patients prior to the shutter manoeuvre which could affect FRC by promoting changes in lung volumes. In the present analysis, we cannot resolve these issues but the fact of large differences in FRC and derived volumes is not affected. It also has to be noted that the measurements in all study centers were performed did not involve any unusual procedures and were performed in accordance with both guidelines and what we know from clinical routine procedures. Thus, they have impact for clinical practice not just the cohort study from which the data used in this analysis were taken.

Our findings reveal a source of variation in body plethysmographic results that should ameliorated by harmonization between manufacturers. Variations of the observed magnitude hamper the usefulness of body plethysmography, and we believe that clinicians and researchers should be aware of this in order to exploit the full potential of this powerful lung function tool.

## Take Home Message

Body plethysmographs of two manufacturers showed marked differences in the measured values of static lung volumes that likely to have an impact on clinical interpretation. Some harmonization seems needed.

## COSYCONET Study Group

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**Table 2** Results from Multivariate Regression Analyses of the Dependent Variables Given in the Top Row and the Predictors Given Below

| Predictors | RV/TLC [%] | FRC %Predicted | RV %Predicted | TLC %Predicted | FRC [l] | RV [l] | TLC [l] |
|---|---|---|---|---|---|---|---|
| **$FEV_1$ %pred** | −0.2 [−0.2; −0.2] | −1.4 [−1.5; −1.3] | −1.5 [−1.7; −1.4] | −0.6 [−0.6; −0.5] | −0.05 [−0.05; −0.04] | −0.04 [−0.04; −0.03] | −0.04 [−0.04; −0.03] |
| **FVC %pred** | −0.2 [−0.3; −0.2] | 0.5 [0.4; 0.6] | −0.1 [−0.2; 0.1] | 0.5 [0.5; 0.6] | 0.02 [0.02; 0.02] | 0.00 [0.00; 0.00] | 0.03 [0.03; 0.04] |
| **Age [years]** | 0.3 [0.2; 0.3] | −0.1 [−0.3; 0.0] | −1.0 [−1.2; −0.8] | −0.2 [−0.3; −0.2] | 0.00 [0.00; 0.01] | 0.01 [0.01; 0.02] | −0.02 [−0.02; −0.01] |
| **Height [cm]** | −0.1 [−0.2; −0.1] | 0.3 [0.1; 0.5] | 0.2 [−0.1; 0.4] | −0.2 [−0.3; −0.1] | 0.04 [0.04; 0.05] | 0.03 [0.02; 0.04] | 0.07 [0.07; 0.08] |
| **BMI [$kg/m^2$]** | −0.2 [−0.2; −0.1] | −1.4 [−1.7; −1.2] | −1.3 [−1.6; −1] | −0.4 [−0.6; −0.3] | −0.05 [−0.05; −0.04] | −0.03 [−0.04; −0.02] | −0.03 [−0.03; −0.02] |
| **Sex [female vs male]** | 3.1 [2.3; 3.8] | 15.2 [11.9; 18.5] | 14.2 [9.4; 18.9] | 7.8 [5.9; 9.7] | −0.43 [−0.53; −0.32] | −0.24 [−0.35; −0.13] | −0.81 [−0.93; −0.70] |
| **Plethysmograph [Ganshorn vs Jaeger]** | −6.9 [−7.9; −5.8] | −20.9 [−25.4; −16.4] | −34.0 [−40.5; −27.6] | −10.2 [−12.7; −7.7] | −0.67 [−0.82; −0.53] | −0.77 [−0.92; −0.63] | −0.61 [−0.77; −0.46] |

**Notes**: Non-standardized regression coefficients and their 95% confidence intervals are given. % predicted refers to GLI reference values. Please note that the differences between plethysmographs regarding the absolute volumes are of similar magnitude and that their confidence intervals overlap, indicating that the difference regarding FRC is that which determined those regarding RV and TLC as derived parameters.
**Abbreviations**: FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity.

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## Data Sharing Statement

The basic data are part of the German COPD cohort COSYCONET (www.asconet.net) and available upon request. The website of the network provides a detailed procedure for respective applications. The data can be obtained after submission of a proposal that is evaluated by the steering committee. Qualified requests should be addressed to: Mrs Inge Kokot, Competence Network Asthma and COPD, Philipps-University of Marburg, Email: kokot@asconet.net

All results to which the manuscript refers are documented appropriately in the text, figures or tables.

## Ethics Approval and Consent to Participate

COSYCONET was approved by the ethical committees of all study centres and all patients gave written informed consent. The study was performed in accordance with the declaration of Helsinki.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

Peter Alter declares no relevant competing interests. Jan Orszag declares no relevant competing interests. Emiel F. M. Wouters declares no relevant competing interests. Claus F. Vogelmeier declares grants or contracts to his institution from the German Ministry of Education and Science (BMBF), AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Grifols, and Novartis, consulting fees from AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GlaxoSmithKline, Menarini, Novartis, and Nuvaira, MedUpdate, payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Aerogen, AstraZeneca, Boehringer Ingelheim, CSL Behring, Chiesi, GlaxoSmithKline, Menarini, and Novartis, all of which are outside the scope of the submitted work. Rudolf A. Jörres declares no relevant competing interests.

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