A new approach for the detection of obesity-related airway obstruction in lung-healthy individuals

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PII: S0954-6111(22)00290-6
DOI: https://doi.org/10.1016/j.rmed.2022.107025
Reference: YRMED 107025

To appear in: *Respiratory Medicine*

Received Date: 31 July 2022
Revised Date: 16 October 2022
Accepted Date: 19 October 2022


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Credit author statement

RJ Conceptualization, methodology, formal analysis, data curation, writing original draft, visualization, supervision.

NS Conceptualization, data curation, formal analysis, writing original draft, patient recruitment

HD Conceptualization, methodology, writing review and editing

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UO Conceptualization, writing review and editing, visualization

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ABSTRACT

Background

Subjects with obesity show an increased prevalence of airway obstruction but it is not clear in each case whether this reflects genuine lung disease. Via intentional increase in end-expiratory lung volume we studied the detection of obesity-induced airway obstruction in lung-healthy obese subjects.

Methods

The primary study population comprised 66 lung-healthy obese subjects and 23 normal weight subjects. Measurements were performed in a body plethysmograph allowing for recording and quantification of breathing loops in terms of specific airway resistance at both normal and intentionally elevated end-expiratory lung volume. The change in volume was documented by a shutter maneuver.

Results

The voluntary increase of lung volume led to a significant reduction of expiratory airway resistance in 11 of the 66 obese subjects. This reduction could be quantified by a change of total expiratory resistance (sRtEX) of >1 kPa*s but was also clearly visible in the breathing loops. sRtEX showed the largest change among all resistance parameters. The loops of normal weight subjects remained virtually unaffected by the change in lung volume. Moreover, those of 5 obese patients with COPD who were measured for comparison partially showed a reduction of resistance but airway obstruction remained.

Conclusion
The proposed breathing maneuver was simple to perform and allowed for a quantitative and qualitative detection of obesity-induced airway obstruction. This might help in reducing the likelihood of misdiagnosis and overtreatment of obese patients.

**Word count: 229 words**

**Highlights:**

- This work shows how obesity-related airway obstruction can be diagnosed and differentiated from genuine airway disease using a simple breathing maneuver in body plethysmography.

- Thus, the work is of high clinical relevance, as it avoids misdiagnosis and overtreatment.
INTRODUCTION

Obstructive lung diseases such as asthma or chronic obstructive pulmonary disease (COPD) are common worldwide and demand significant treatment resources (1, 2). Corresponding symptoms such as breathlessness and dyspnea as well as functional impairments also occur with obesity in lung-healthy individuals (3), and in patients with asthma obesity can act as an aggravating factor (4). Obesity can affect the lung through immunological and mechanical pathways. Adipose tissue produces cytokines such as TNF-alpha, IL-1β and IL-6, as well as adipokines that also have pro-inflammatory effects (3, 5). In addition, however, purely mechanically induced deteriorations may occur (3, 6-8). Thus, in diagnostic procedures it is a challenge to differentiate between such alterations and genuine respiratory disease.

The mechanical effects seem to be linked to a reduction of end-expiratory lung volume in resting ventilation (functional residual capacity, FRC), due to upwards displacement of the diaphragm by the additional body mass (9). As a consequence, the volume FRC is closer to residual volume (RV) than normal. This favours airway closure and inhomogeneous ventilation, manifesting as airway obstruction at the end of normal expiration when approaching residual volume. Obese subjects also tend to show airway hyperresponsiveness based on a reduction of airway lumen (10-12). These observations have led to the notion of less or not eosinophilic asthma in T2-low patients (13, 14), but the adequacy of this category including the diagnosis of asthma is questioned in current debates (15).

Obviously, the distinction between genuine airway disease and airway obstruction imposed by obesity is of clinical relevance and has consequences for treatment. Moreover, it might help to understand the fact that obese patients with asthma often show a reduced response to respiratory medication (16, 17). To avoid unnecessary, potentially harmful treatment of an
alleged respiratory disorder, an easy method for the identification of obesity-induced airway obstruction would be helpful.

If the airway obstruction is primarily due to a reduction of end-expiratory lung volume, it should disappear when this volume is increased to normal. This could be achieved by voluntarily raising FRC in resting ventilation, and the effect on airway resistance could be directly observed via body plethysmography. The present work aimed to determine the feasibility of this approach and its usefulness in the detection of obesity-induced airway obstruction. For this purpose, lung-healthy obese subjects and lung-healthy subjects with normal weight were studied.

**MATERIALS AND METHODS**

**Study design and recruitment process**

In this cross-sectional study, obese patients served as case group and normal weight patients as control group. For the case group, the inclusion criteria comprised a current BMI of ≥ 30 kg/m², age ≥ 18 years, without the diagnosis of pulmonary disease such as asthma or COPD, absence of infection, and physical fitness sufficient to travel to the lung function laboratory.

For the control group, the inclusion criteria were BMI < 25 kg/m², age ≥ 18 years and absence of infection; in this group, subjects were excluded if diagnosed with pulmonary disease. Subjects who turned out to be unable to adequately perform the pulmonary function measurements were also excluded; this was the case in one participant with obesity. For comparison we included 5 patients with the physician-based diagnosis of chronic obstructive pulmonary disease (COPD) and FEV₁/FVC <0.7 ((18)).

To recruit subjects with obesity, general medical teaching practices of the LMU were contacted, as well as obesity self-help groups in the Munich area, with presentations at their...
meetings. Furthermore, advertisements were placed in the hospital intranet magazine. After contact by potential participants and preliminary verification of inclusion criteria, an appointment was made.

All examinations were performed at one study visit. First, a medical history was taken ensuring that patients did not have a physician-based diagnosis of obstructive airway disease. Second, body height, weight, neck, waist and hip circumference were determined. Then baseline body plethysmography and spirometry were performed. Finally, the body plethysmography involving intentional changes of lung volume was done.

**Ethics approval and consent to participate**

The study was conducted in accordance with the Declaration of Helsinki and had been approved by the Ethics Committee of the Medical Faculty of the Ludwig-Maximilians-Universität (LMU) Munich (Reference AZ 17-735); all patients gave their written informed consent.

**Assessments**

**Baseline body plethysmography and spirometry**

After instructing the patients about the procedure of measurements, body plethysmography (Masterscreen Body, Jaeger, Höchberg, Germany) was performed as usual (19). This involved determination of the breathing loops corresponding to specific airway resistance (sRaw) during resting ventilation, the end-expiratory occlusion (shutter) maneuver to determine FRC, determination of the expiratory reserve volume (ERV) after opening to determine residual volume (RV), and maximal inspiration to determine total lung capacity (TLC). It was followed by forced maximal expiration to determine FEV₁ and FVC. This sequence of maneuvers was performed at least twice. Moreover, spirometry was repeated separately in order to avoid
potential exhaustion from the previous measurements. All assessments were performed in accordance with the current recommendations (19-21). Specific airway resistance was evaluated either as total resistance (sRt) involving the maximum excursions of box pressure or shift volume, respectively, or as effective resistance (sReff) involving a method of averaging over the loop; for details see the Supplemental Figure S1 and the overview by Criée et al. (19).

Moreover, the inspiratory (sRtIN, sReffIN) and expiratory (sRtEX, sReffEX) parts of specific airway resistance were determined. Predicted values for spirometric parameters are computed according to GLI (22), those of plethysmographic volumes according to ECSS (23).

*Intentional changes of lung volume*

In the next step, recordings of breathing loops at voluntarily altered end-expiratory lung volume were obtained; for the underlying hypothesis and expected changes see Figure 1. If breathing loops indicated airway obstruction at normal FRC, their normalization was taken as indicator of obesity-induced obstruction. The increase in volume was achieved by asking the participants to perform a deep inspiration and not to return to FRC, but to remain at a self-determined, higher, but still feasible level for a few breathing cycles. An occlusion maneuver was initiated when, according to the volume tracings at the screen, the elevated position had stabilized, but as early as possible to avoid discomfort for the subject. This sequence was sufficient to record breathing loops at elevated volume and to determine this volume.

The maneuvers were monitored on the screen of the body plethysmograph in such a way that the patients' breathing could be corrected if necessary. If the measurements were qualitatively insufficient, the examination was repeated. The respiratory loops and measured values were considered sufficient if they were free from artefacts and the volume change
measured in the occlusion maneuver and that visible from the recording on the screen were similar.

Statistical analysis

Mean values and standard deviations, or frequencies and percentages were calculated for data description, depending on the type of data. Unpaired t-tests were used to compare groups, and paired t-test to compare values between different conditions. Spirometric data were analyzed by logistic regression analysis. To define subjects with obesity-induced airway obstruction, each of the six parameters of specific airway resistance was tested separately, with the expectation that specifically the expiratory part of the breathing loops should change (see Figures 2A and 2B). For this purpose, the baseline value of each resistance parameter during breathing at normal end-expiratory lung volume was plotted against its change after elevation of end-expiratory lung volume. Statistical analyses were performed with SPSS (Version 26.0.0.1, IBM). The level of statistical significance was set at p-value <0.05.

RESULTS

Baseline characteristics of the study groups

Overall, n=66 lung-healthy obese individuals and n=23 lung-healthy, normal-weight subjects (Group NW) were included. The lung-healthy obese subjects were further divided into those without (Group ObnoAO) and those with (Group ObAO) obesity-induced airway obstruction, following the procedure described below; for baseline characteristics see Table 1. There were significant differences between ObnoAO and ObAO regarding age, waist circumference and most volumetric lung function measures.

Obese lung-healthy subjects
Figure 2 illustrates the qualitative changes in breathing loops in elevated versus normal breathing position that occurred in a subject with obesity-induced obstruction versus a subject without. If resistance values obtained at elevated breathing position were plotted against those obtained at normal breathing position, it was apparent that a number of subjects showed markedly lower values. Among all parameters, sRtEX showed the clearest subdivision into subjects, in whom the respective parameter was increased in normal and decreased during elevated breathing position, versus subjects with low baseline value and virtually no change. This subdivision provided the basis for our definition of obesity-induced airway obstruction in lung-healthy subjects as shown in Figure 3. The group with obstruction (ObAO) showed a reduction of sRtEX by ≥ 1 kPa*s, while the group without obstruction (ObnoAO) showed changes < 1 kPa*s, with no overlap between groups.

Pattern of resistance parameters with normal breathing at FRC

To further illustrate the results, we plotted median values of the resistance parameters. In normal end-expiratory position (Figure 4), the obese subjects without obstruction (ObnoAO) showed a pattern similar to that of NW subjects, without significant differences between groups (p>0.05 each) and with all parameters being within the normal range. In contrast, obese subjects with obstruction (ObAO) were clearly different from the others, showing the largest deviation for sRtEX, i.e., the parameter chosen for definition. Inspiratory resistances and those averaged over the breathing loop were less different, underlining the need for a separate analysis of the expiratory part.

Figure 5 illustrates the median values at voluntarily elevated end-expiratory volume. While for the ObnoAO and NW groups the results were virtually identical to those shown in Figure 4, the subjects with obesity-induced obstruction (ObAO) showed values within or close to the
normal range. This included sRtEX. Numerical data on the changes in resistance parameters by elevating lung volume are shown in Table 2. In all groups, this was accompanied by statistically significant changes but only those in the ObAO group for sRtEX was a large and distinctive reduction. All other changes were minor, and the slight elevations observed in the groups ObnoAO and NW were probably due to artifacts from the efforts to keep the elevated lung volume. If these artifacts occurred in ObAO, they were much smaller than the effect of the shift in volume and did not compensate this. It was also apparent that the averaging over the breathing loop in terms of effective specific resistance was much less sensitive that the total specific resistance especially in expiration.

According to the occlusion manoeuvre, groups ObAO, ObnaoAO and NW elevated their volume (mean ± SD) by 1.40 ± 0.47 L, 1.50 ± 0.48 L and 1.50 ± 0.32 L, respectively. There were no significant differences between groups, and in correlation analyses the magnitude of the change in volume was not related to that of the change in sRtEX in any of the groups.

**Obese patients with COPD**

In order to test whether in obese patients with COPD the elevation of end-expiratory volume would lead to disappearance of airway obstruction, we additionally included 5 patients with COPD of spirometric GOLD grad 2 (5 females, age 66.8 ± 8.6 years, BMI 36.5 ± 5.5 kg/m², range 31.6-45.1 kg/m²). All of them had elevated values of sRtEX (>1.2 kPa*s) at normal breathing position (3.98 ± 2.71 kPa*s) and still showed elevated values after increasing the end-expiratory lung volume (2.58 ± 1.42 kPa*s). Two examples of typical breathing loops are shown in the Supplemental Figure 3.
The present investigation proposes an approach to identify patients with obesity-induced airway obstruction. Our population of lung-healthy obese patients, i.e., those without the diagnosis of asthma or COPD, showed a prevalence of about 17% for this disorder. They were identified using an easy-to-perform breathing maneuver in the body plethysmograph. This indicates that the airway obstruction in the OBAO as reflected in breathing loops and specific airway resistance disappeared when the end-expiratory volume of resting ventilation was voluntarily increased. We took that as proof that the obstruction was due to the reduction in lung volume but not to genuine obstructive airway disease. Lung-healthy subjects with normal weight always showed normal values of resistance. We propose this novel approach of intentional increase of lung volume and its assessment by body plethysmography as a simple, easy-to-perform tool for the identification of obesity-induced airway obstruction. It does not require special equipment, provides a unique application of plethysmography if this is available and might help to avoid misdiagnosis and overtreatment in these patients.

With worldwide increasing prevalence of obesity (24, 25), the clinical relevance of obesity-induced airway obstruction is obvious. The situation is complicated by the fact that an association between obesity and the diagnosis of asthma is known (9, 26). Obese subjects with asthma have been described as phenotypes with peculiar characteristics (13, 14, 27), e.g., high symptom burden, lack or low expression of TH2 markers including eosinophilic inflammation, and low response to asthma therapy. The weaker response to inhalation therapy is well known (16, 17), in line with improvements after bariatric surgery (28). Often the link between asthma and obesity is attributed to immunological factors, including modulation of allergen responses by leptin and adiponectin (29-31), but mechanical factors have also been considered (6, 9). To identify the contribution of such factors acting externally on a healthy lung is relevant, to
exclude misdiagnosis and unnecessary inhalation therapy, potentially with corticosteroids implying higher costs (32, 33) and avoidable side effects (34, 35).

The airway obstruction in obese patients is probably linked to a reduction in end-expiratory lung volume (26, 36) resulting from an elevated position of the diaphragm at the end of the normal expiration (8). This leads to end-expiratory volumes (FRC) being closer to residual volume, near which airway closure and inhomogeneous ventilation occur even in the healthy lung, as known from classical physiology (37, 38). If the reduction linked to obesity causes obstruction in this manner, it is natural to ask whether restoration of volume leads to normalization of airway resistance and homogeneous ventilation. The effects of intentional elevation of end-expiratory lung volume can easily be investigated in the body plethysmograph. In our study, a few breathing cycles turned out to be sufficient, as the visual changes of the breathing loops (see Figures 1A and 1B) already allowed the detection of obesity-induced airway obstruction. This could be best quantified via the total expiratory specific airway resistance (sRtEX) but quantification was not essential. It might also be that smoking exaggerates the effect as it is linked to dysfunction of the small airways. The two groups of obese subjects with and without airway obstruction showed about the same percentages of smokers, ex-smokers and never-smokers, but numbers were too small to address this additional question.

From a clinical point of view, a concern of our approach could be that the voluntary elevation of end-expiratory lung volume would lead to apparently normal breathing loops in obese subjects with a diagnosis of obstructive airway disease. For this purpose we applied the approach in 14 obese patients with asthma, however all of them showed normal breathing loops and therefore no sign of obesity-induced obstruction. In order to find subjects with obstruction at baseline we included further 5 obese patients with moderate COPD. Three of
these patients showed a marked reduction of sRtEX at higher end-expiratory volume but all of them were still above 1.2 kPa*s as cut-off value for the presence of airway obstruction (see Supplemental Figure S3, (19)). These observations suggest that the proposed approach does not lead to misdiagnosis of these patients as lung-healthy. However, future studies should evaluate the usefulness of the proposed technique in obese patients with obstructive airway disease. This could be of particular interest as the part of airway dysfunction due to obesity would need a different treatment due to genuine lung disease. It might also be relevant for future studies, that data obtained by the forced oscillation technique have suggested that in lung-healthy subjects and subjects with asthma the effects on airway function related to obesity were not fully explained by the reduction in FRC (39, 40).

The advice given to the subjects was to remain “blown-up” upon end-expiration and breathe “somehow under the ceiling”, and with this advice the maneuver could be performed by nearly all subjects recruited. It is probably not necessary to perform a shutter measurement, when the volume tracing is monitored to verify the change. We performed the additional shutter closure only in order to quantify the change in volume. Importantly, the proposed maneuver does not require additional equipment or re-programming of the body plethysmograph.

We defined obesity-induced airway obstruction using body plethysmography, as this offered the possibility to measure at different lung volumes. Whether other methods such as forced oscillation are also suitable for this has to be assesses in future studies. We additionally evaluated the results of slow and forced spirometry (see Supplement). The flow-volume curve of obese subjects is known to exhibit a mixture of restrictive and potentially obstructive changes (26), combined with a reduction of expiratory reserve volume (ERV). Only part of the subjects with obesity-induced obstruction according to body plethysmography could be
detected using spirometry. It turned out that the combination of FEV\textsubscript{1} with ERV was best for this purpose. However, as illustrated in the Supplemental Figure S2, for a range of values this only allowed the exclusion of obesity-induced obstruction with high certainty. In the range where obesity-induced obstruction was located, also many subjects without obstruction were found. This implies that in the presence of airway obstruction according to body plethysmography it cannot be decided whether the disorder is due to obesity.

Based on the data presented we propose to examine the approach which we developed as a tool that can be easily applied in clinical practice. Independent of the fact that at present the data base is limited and detailed data on the physiological mechanisms are not available, the approach seems at least valuable as a qualitative method for which even visual inspection of the breathing loops seems sufficient. Further studies should focus on revealing the prevalence of obesity induced airway obstruction in larger populations, the problem of detecting an additional contribution of obesity on obstruction in patients with airway disease and the use of methods to disentangle underlying mechanisms, such as forced oscillation techniques that allow to differentiate between central and peripheral resistances. It is reassuring that a similar approach of voluntarily elevating end-expiratory volume has already been used to demonstrate alterations in baseline values as well as changes in resistance parameters determined via impulse oscillometry (41). This work is fully in line with our results although the range of applicability may be wider for body plethysmography, since it is available in many places and the outcome is directly visualized.

**Limitations**

The study included 66 lung-healthy obese subjects, of whom 11 were identified as showing obesity-induced airway obstruction. In other populations, the percentage of subjects with
obstruction might differ. Regarding the absence of obstructive airway disease we relied on the reports of patients not to be diagnosed with such disease previously. None of the patients did have respiratory medication and the values of FeNO were in the normal range. In the following work, the lung function measurements were repeated twice, which deviates from the recommendations of the guidelines to repeat lung function measurements three times. However, the measurements were all performed by one person, as soon as there were indications that the breathing maneuvers were not performed correctly, the measurements were repeated.

Conclusions

Obese subjects are often diagnosed with obstructive airway disease but the causes of this obstruction are not clear in each patient. In the present work, we propose a method to identify subjects in whom airway obstruction is caused by obesity and does not reflect genuine airway disease. It relies on voluntary elevation of end-tidal breathing volume during resting ventilation in the body plethysmograph. If the signs of obstruction disappear, it is due to obesity-associated reduction of lung volume. The proposed method does not require additional equipment, is simple to perform and might be diagnostically useful in view of the worldwide increasing prevalence of obesity.

Data availability

All results to which the manuscript refers, are documented appropriately in the text, figures or tables. The data will be made available upon request, i.e. individual participant data that underlie the results reported in this article after de-identification, with investigators whose
proposed use of the data has been approved by an independent review committee. Proposal
may be submitted up to 9 months following this article publication. Proposals should be
directed to Kathrin.Kahnert@med.uni-muenchen.de.

Consent to publish

Not applicable

Authors contributions:

RJ was involved in the conception of the study, analyzing and interpreting the data,
statistical analysis, conceptualizing and drafting of the manuscript, approved the final
submitted version, and agreed to be accountable for all aspects of the work.

NS was involved in patient enrolment, analyzing and interpreting the data, statistical
analysis, conceptualizing and drafting of the manuscript, approved the final submitted
version, and agreed to be accountable for all aspects of the work.

HD was involved in the interpretation of the data from this analysis, took part in the
discussion and critical revision of this manuscript, approved the final submitted version, and
agreed to be accountable for all aspects of the work.

D K.-G. was involved in the interpretation of the data from this analysis, took part in the
discussion and critical revision of this manuscript, approved the final submitted version, and
agreed to be accountable for all aspects of the work.

SK was involved in the interpretation of the data from this analysis and drafting of the
manuscript, approved the final submitted version, and agreed to be accountable for all
aspects of the work.
UO was involved in the interpretation of the data from this analysis and drafting of the manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

NK was involved in the interpretation of the data from this analysis and drafting of the manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

PA was involved in the interpretation of the data from this analysis, took part in the discussion and critical revision of this manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

HM was involved in the interpretation of the data from this analysis and drafting of the manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

JB was involved in the interpretation of the data from this analysis, took part in the discussion and critical revision of this manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

DN was involved in the interpretation of the data from this analysis, took part in the discussion and critical revision of this manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

KK was involved in the design and set-up of the study, as well as quality control, statistical analysis and conceptualizing and drafting of the manuscript, approved the final submitted version, and agreed to be accountable for all aspects of the work.

All authors have read and approved the manuscript.

**Competing interests**

The authors declare no competing interests.
Acknowledgements

Not applicable

Funding

The project required no external funding.
**Literature**

Figure Legends

Figure 1. Illustration of the breathing maneuver used to detect obesity-induced airway obstruction in the body plethysmograph.

The lung volumes are illustrated as a function of breathing position, in the upper part of the Figure as bar graphs, followed by the respective breathing loops. In addition, an information on the associated peripheral airway resistances, as well as information on the inhomogeneity of ventilation is given. Breathing loops are explained in the Supplemental Figure S1, and corresponding measured breathing loops can be seen in the Supplemental Figures 2A and 2B. The graphical depiction is inspired by Figure 2 in the publication by Beuther et al. (9).

Figure 2. Examples of breathing loops obtained in the body plethysmograph, with specific airway resistance being inversely proportional to the slope of the curves.

It can be evaluated by different approaches (see Supplemental Figure S1). Panel A: obese lung-healthy subject with obesity-induced airway obstruction. The left curve refers to normal breathing position the right to voluntary increase of the end-expiratory lung volume. This change in volume leads to the disappearance of the signs of airway obstruction and inhomogeneous ventilation und virtually normalizes the curve. Panel B: obese lung-healthy subject without obstruction. The left curve refers to normal breathing position, the right to voluntary increase of the end-expiratory lung volume. Both curves are normal and very similar.

Figure 3. sRtEX in normal breathing position versus difference of sRtEX between normal and elevated breathing position in lung-healthy subjects with obesity.

It can be seen that by means of a decrease of sRtEX by at least 1 kPa*s two groups can be defined. In ObnoAO, marked in blue, there were only changes whose magnitude scattered...
around zero. In contrast, ObAO, marked in red, showed a systematic decrease in specific airway resistance, which was at least one kPa*s in all cases. This numerical classification was consistent with that resulting from visual inspection of the respiratory loops (see Figures S2A and S2B).

**Figure 4.** Specific airway resistance in kPa*s of groups ObnoAO and ObAO (obese lung-healthy without or with airway obstruction) and group NW (lung-healthy normal weight) at normal breathing position.

Median values are shown, additionally the upper limit of normal of specific resistance (1.2 kPa*s). It can be seen that, at least for total resistances, the values of group ObAO were outside the normal range. Values of groups ObnoAO and NW were not significantly different from each other and within the normal range. For elevated breathing position see Figure 2B.

**Figure 5.** Specific airway resistances in kPa*s of groups ObnoAO and ObAO (obese lung-healthy without or with obstruction) and group NW (lung-healthy normal weight) at voluntarily elevated breathing position.

Median values are shown, additionally the upper limit of normal of specific airway resistance (1.2 kPa*s). Compare with Figure 2A. At increased breathing position, the values of group ObAO were almost completely within the upper limit of normal, thereby demonstrating the disappearance of the airway obstruction, while the values of ObnoAO and NW were virtually unchanged and remained within the normal range.
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<tr>
<td>Smoker (yes)</td>
<td>22 (40.0%)</td>
<td>6 (54.5%)</td>
<td>6 (26.1%)</td>
</tr>
<tr>
<td>FeNO (ppb)</td>
<td>15.9 (2.0)</td>
<td>17.7 (2.6)</td>
<td>16.8 (2.3)</td>
</tr>
<tr>
<td>FEV₁(L)</td>
<td>3.00 ± 0.70</td>
<td>2.14 ± 0.40***</td>
<td>3.33 ± 0.70</td>
</tr>
<tr>
<td>FEV₁ (%predicted)</td>
<td>91.5 ± 14.1</td>
<td>77.1 ± 9.4**</td>
<td>93.7 ± 8.5</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.79 ± 0.82</td>
<td>2.84 ± 0.57***</td>
<td>4.08 ± 0.87</td>
</tr>
<tr>
<td>FVC (%predicted)</td>
<td>92.5 ± 11.7</td>
<td>79.8 ± 9.8**</td>
<td>94.7 ± 7.6</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.792 ± 0.058</td>
<td>0.754 ± 0.071</td>
<td>0.820 ± 0.057</td>
</tr>
<tr>
<td>ERV (L)</td>
<td>0.77 ± 0.5</td>
<td>0.28 ± 0.26**</td>
<td>1.31 ± 0.59</td>
</tr>
<tr>
<td>ERV (%predicted)</td>
<td>59.3 ± 31.2</td>
<td>25.0 ± 21.1***</td>
<td>92.4 ± 34.8</td>
</tr>
<tr>
<td>FRC (L)</td>
<td>2.77 ± 0.67</td>
<td>2.64 ± 0.73</td>
<td>3.33 ± 0.74</td>
</tr>
<tr>
<td>FRC (%predicted)</td>
<td>90.3 ± 18.7</td>
<td>87.2 ± 21.3</td>
<td>109.1 ± 18.5</td>
</tr>
<tr>
<td>RV (L)</td>
<td>1.99 ± 0.48</td>
<td>2.50 ± 0.83**</td>
<td>2.03 ± 0.45</td>
</tr>
<tr>
<td>RV (%predicted)</td>
<td>119.7 ± 22.9</td>
<td>135.0 ± 37.3</td>
<td>135.8 ± 21.1</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>5.93 ± 1.00</td>
<td>5.59 ± 1.24</td>
<td>6.17 ± 1.08</td>
</tr>
<tr>
<td>TLC (%predicted)</td>
<td>98.5 ± 11.3</td>
<td>98.8 ± 18.6</td>
<td>103.3 ± 7.5</td>
</tr>
</tbody>
</table>

**Table 1. Baseline characteristics of the study cohort.** Anthropometric data of the different groups. Mean values and standard deviations are given. Predicted values for spirometric parameters are computed according to GLI ¹⁹, those of plethysmographic volumes according to ECSS ²⁰. Lung function parameters refer to normal breathing position. FEV₁ = forced expiratory volume in 1 s, FVC = forced vital capacity, ERV = expiratory reserve volume, FRC = functional residual capacity, RV = residual volume, TLC = total lung capacity. FeNO = fractional concentration of exhaled nitric oxide, BMI = body mass index. *geometric mean (SD), SD to be understood as factor of variability. Statistical comparisons were performed between groups ObnoAO and ObAO using the unpaired t-test or chi-square statistics.

*p<0.05, **p<0.01, ***p<0.001.
Table 2. Specific airway resistance at normal FRC and with elevated end-expiratory volume. Mean values and standard deviations are given. P values refer to ANOVA comparing the baseline values (normal FRC) between the three groups. * p<0.05, **p<0.01, ***p<0.001 regarding the comparison of values at normal and elevated breathing position for each of the three groups using the paired t-test.
Lung volumes

Normal weight

Resting FRC

Obese

Resting FRC

Voluntarily elevated FRC

Breathing loops in plethysmography

Peripheral airway resistance

Inhomogeneity of ventilation

Figure 1.
Figure 2.
Figure 3.
Figure 4.
Figure 5.
Highlights:

• We propose a method to detect obesity-related airway obstruction via body plethysmography.

• This method is based on a simple breathing maneuver and directly visualizes the result.

• Applicability and usefulness are demonstrated in lung-healthy obese subjects.

• Our results are easily applicable and might help to avoid misdiagnosis and overtreatment.