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Work of Breathing in Obesity Assessed with Body Plethysmography Comparison with Emphysematic COPD and Pulmonary Fibrosis

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Abstract

Objectives: Body plethysmography is a lung function testing method usually applied for determination of thoracic gas volume and airways resistance, but option to measure work of breathing is available in most models. Although the method has been known over fifty years, assessment of work of breathing with it has not yet systematically studied in obesity. The aim of the study was to evaluate the relevance of work of breathing measured by body plethysmography in obese subjects and to compare the results with those of healthy controls and patients with pulmonary diseases of different pulmonary mechanics.

Methods: Altogether sixty-two adults were studied prospectively: healthy non-smoking obese subjects (BMI > 30, N = 15), patients with interstitial lung disease (ILD) (N =15), emphysematic COPD (emphysema) (N = 16) and healthy non-smoking controls (controls) (N = 16). Inspiratory, expiratory and total work of breathing (WOBin, WOBex and WOB) and specific work of breathing (sWOBin, sWOBex and sWOB) were measured.

Results: In obese subjects, WOB, WOBin ($p < 0.001$) and WOBex ($p = 0.002$) were elevated in comparison to controls. Also in ILD, WOB was significantly higher than in controls ($p < 0.006$). sWOBin, sWOBex and SWOB were significantly higher in emphysema than in the controls ($p < 0.001$).

Conclusions: In obesity and ILD WOB whereas in emphysematic COPD sWOB differed significantly from controls, which is caused by differences in lung mechanics and lung volumes. The results concerning COPD correspond earlier study, but the present results suggest that body plethysmography is suitable for the assessment of work of breathing also in obesity.

Keywords: Body plethysmography; Obesity; Work of breathing; Interstitial lung disease; COPD; Emphysema

Introduction

Work of breathing is usually determined by measurement of oesophageal pressure when an oesophageal balloon is intubated and volume of breathing at mouth is measured via changes in oesophageal pressure. This technique is invasive and usually applied during local anesthesia or in intubated subjects [1-5]. Without anesthesia, the measurement is uncomfortable for the patient. However, the assessment of work of breathing can give valuable diagnostic information about disturbances of respiratory mechanics in patients with dyspnoea.

Usually airways resistance and thoracic gas volume are measured with a constant volume (variable pressure) mode [6,7] when the patient is sitting inside a tight box. Pressure changes during breathing maneouvers are measured by a sensor on the wall of the plethysmograph. The estimate of specific work of breathing can be measured by plotting breathing volume measured at mouth (derived from integration of breathing flow) against box shift volume, which is measured from the change of pressure within the body plethysmograph due to compression and decompression of thoracic gas during breathing [6,8,9]. Previously some preliminarily data on specific work of breathing measured with plethysmography in cystic fibrosis [10] and COPD [11] have been reported. As far as we know, clinical studies of work of breathing in obesity measured with body plethysmography have not been published yet. Obesity has become interesting due to the epidemic of obesity in many civilized countries [12] e.g., expressed by symptoms of exercise induced dyspnoea.

Recently we applied flow plethysmography (variable volume or constant pressure plethysmography, when the patient is sitting in a box and breathing through a pneumotachograph outside the box and the volume changes inside the box are measured by a spirometer on the wall of the box) [7] to demonstrate, how alveolar gas compression distorts the forced expiratory flow-volume-curve in patients with different pulmonary mechanics at least at the middle fraction of forced expiratory flow. Different profiles of gas compression in stiff lungs, in patients with decreased elastic recoil in emphysema and in obesity were found [13]. In the present study, the same patients were explored in constant volume mode, exploring the relevance of calculated work of breathing indices.

Work of breathing was investigated in four groups of subjects with different pulmonary mechanics: healthy non-smoking subjects (controls), healthy non-smoking obese subjects (obese), patients with

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interstitial lung disease (ILD) and smoking or ex-smoking patients with COPD with emphysema (named here as emphysema) [13]. The differences in work of breathing in these groups were evaluated. In addition, correlations of work of breathing with some spirometric variables, diffusing capacity for carbon monoxide and trapped air were calculated.

Methods

The anthropometric and smoking data are summarised in Table 1. The details of the controls and patients studied prospectively are presented more thoroughly in an earlier publication [13]. Healthy obese non-smoking subjects (N=15) (BMI > 30), non-smoking patients with interstitial lung disease, mostly with moderate or severe degree (ILD) (N=15) (BMI < 30) and patients with severe or moderate emphysematic COPD assessed with reduction in pulmonary diffusing capacity for carbon monoxide [14] (emphysema) (N=16) (BMI < 30, FEV1/FVC < 0.7) were included in the study. However, patients with a significant bronchodilator response (∆ FEV1 ≥ 12% and > 200 mL) in spirometry were excluded. Also healthy non-smoking subjects (N=16) (BMI < 30) of similar gender and age as the patients were studied. The study has been approved by the ethical committee of Helsinki University Central hospital and the participants have given informed consent to the study.

The methods of spirometry, single-breath diffusing capacity as well as body plethysmography have been presented earlier [13]. Reference values of Viljanen [15] were used. The results of spirometry, diffusing capacity for carbon monoxide (DLCO), specific diffusing capacity (DLCO/VA) and trapped air, which was calculated as the difference between total lung capacity measured by body plethysmograpy and helium dilution methods have been reportedly earlier (15).

Body plethysmograph MasterScreen body Version 4.3., Würzburg, Germany was used and the measurement of the resistance of airways, specific conductance were presented earlier [13]. The measurements of breathing work were performed with a tidal breathing frequency of 30 breaths per minute at Functional Residual Capacity (FRC) level. For the measurement of resistive work for sWOB the whole resistance loop was measured continuously in real-time and effective airways resistence (sReff) was measured by integration of the ratio between the volume displacement tidal flow and the tidal-volume loop. sWOB was obtained from sReff computing, sReff being integral of the tidal flow volume / sWOB. According to the manufacturer, the estimate of specific work of breathing was determined as follows:

$$sWOB = \int dVbox \cdot dV \cdot (P_{amb} - P_{H2O}) \cdot F$$

sWOB = specific work of breathing, *Vbox* = shift volume recorded in the box chamber, *dV* = changes in breath volume measured at the mouth opening, *F*= system- and calibration specific constant.

$$WOB = \frac{sWOB}{FRCpleth + VT / 2}$$

WOB = work of breathing, *FRCpleth* = functional residual capacity, *VT* = tidal volume.

Total specific work of breathing (sWOB) and work of breathing (WOB) were evaluated. Inspiratory and expiratory sWOB and WOB were also evaluated. Specific work is related only to airways resistance, WOBs include also lung volume.

Graphical examples of measurements of sWOB can be found in Figure 1 in one healthy subject, one patient with ILD, one with emphysema and one healthy obese subject. With increasing sWOB the area under the curve increases.

Statistical methods

Some of the breathing work parameters were not normally distributed. Because of age and gender differed between the groups, the Wald Chi-Square test with adjustment for age and gender was used to compare the patients with ILD, emphysema and obesity with the control group.

Results from spirometry, diffusing capacity and body plethysmography are calculated as percent of predicted value which for spirometry and diffusing capacity were determinated by age, gender and height, the reference values for specific diffusing capacity by age, gender, height and weight.

The parameters of work of breathing for the whole patient material (N = 62) were not normally distributed and therefore the Spearman correlations were calculated.

Results

Results on comparison of parameters of work of breathing between patients and controls are shown in Table 2 and the mean values of WOB and sWOB of groups schematically in Figure 2. In obese subjects, WOBin, WOBex and WOB exceeded the values of the controls, but the values of specific work of breathing were only suggestively higher than those of the controls. In ILD, only WOB was significantly greater than in controls. In emphysema, sWOBin, sWOBex and sWOB were significantly increased compared to controls. Also WOBin was significantly higher in emphysema compared to controls. sWOBex and sWOBin emphysema were significantly higher than ILD, but compared to obese subjects the differences were not significant.

In all subjects and patients, inspiratory, expiratory and total sWOB were inversely correlated with DLCO, DLCO/VA, FEV1/FVC ratio and MEF50 (Table 3) and positively with trapped air ($p < 0.05$). sWOBex and sWOB were correlated with RV and RV/TLC ($p < 0.05$). WOBin, WOBex and WOB correlated inversely with ERV (Figure 3). Correlations between sWOB or WOB and TLC or VC became nonsignificant when the lung volumes were calculated as percent of predicted value.

	Healthy N=16	Obese. N = 15	ILD N= 15	Emphysema N =16
	Mean (SD) (Range)			
Men/Women	10 / 6	4 / 11	7 / 8	10 / 6
Weight (kg)	70.94 (9.54) (51 – 88)	95.01(16.8) (78 – 134)	71.65 (9.1) (52-85)	58.4 (13.7)(35-83)
Height (cm)	170.69 (6.05) (161 – 179)	163.1 (9.2) (148 – 181)	169.0 (9.6) (150 – 185)	168.9 (9.1)(155-183)
BMI (kg/m2)	24.18 (2.30) (19.7 – 27.5)	35.5 (3.1)(30.8 – 41.8)	25.0 (1.83)(20.8 – 28.4)	20.3 (3.81)(12.7 – 27.1)
Age (years)	65.06 (11.19) (35 – 79)	63.4 (9.2)(44 – 78)	60.1 (11.1) (40 – 77)	62.7 (7.36) (44 – 74)
Smokers /exsmokers	0/0	0/0	0/1	11/5
Smoking (pack years)	0	0	20	41.4 (8.0)

Table 1: Anthropometric and smoking data on the subjects and patients [13].

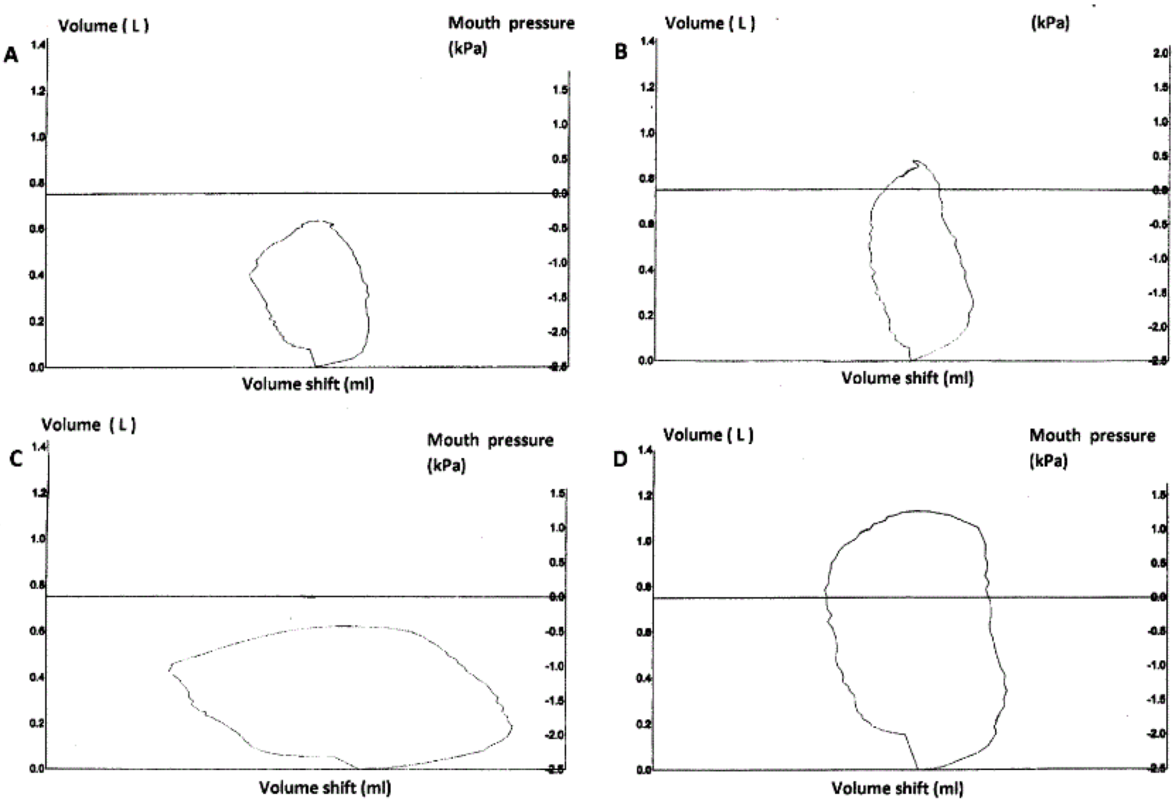

Figure 1: One example on the sWOB-results, e.g., mouth volume versus box shift volume recordings for subjects or patients on the study groups is presented. The sWOB is the surface area of the loops.
A. A non-smoking healthy 75-year-old man. His FEV1 is 2.44 l, 78% of predicted, FEV1/FVC ratio 78%, 95% of predicted value, FEV1/FVC ratio 37%, 46% of predicted. Diffusing capacity is 87% and specific diffusing capacity 107% of predicted value.
B. A 62-year-old woman with nonspecific interstitial pneumonia (NSIP) with moderate restrictive ventilatory impairment in spirometry, FEV1 1.48 l, 59% of predicted, FVC 1.71 l, 55% of pred., FEV1/FVC ratio 0.87%, 108% of predicted value.
C. A 56-year-old woman with emphysematic COPD whose FEV1 is 0.95 l, 34% of predicted, FVC 2.56 l, 74% of predicted, her diffusing capacity is 23% and specific diffusing capacity 24% of predicted value.
D. A 54-year-old obese woman with BMI of 35.1, with FEV1 3.35 l, 115% of pred., FVC 4.17 l, 116% of pred., FEV1/FVC 80.2%, 99% of pred. Diffusing capacity is 95% and specific diffusing capacity 88% of predicted value.

	Controls N=16	Obese subjects N=15	Patients with ILD N=15	Patients with emphysema N=17	Obese vs. controls	ILD vs. contr.	Emph. vs contr.	Obese vs. Emph.	Obese vs. ILD	Emph. vs. ILD
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p-value	p-value	p-value	p-value	p-value	p-value
WOB in (kPa * L)	0.16 (0.11)	0.30 (0.15)	0.28 (0.14)	0.23 (0.11)	<0.001	0.053	0.003	0.172	0.220	0.379
WOB ex (kPa * L)	0.16 (0.11)	0.31 (0.18)	0.26 (0.16)	0.27 (0.13)	0.002	0.022	0.025	0.501	0.220	0.984
WOB (kPa * L)	0.31 (0.21)	0.62 (0.32)	0.54 (0.30)	0.50 (0.22)	< 0.001	0.006	0.026	0.243	0.220	0.654
sWOBin (kPa*L*L)	0.64 (0.41)	0.88 (0.51)	0.85 (0.38)	1.24 (0.61)	0.039	0.107	<0.001	0.149	0.703	0.045
SWOBex (kPa*L*L)	0.65 (0.43)	0.88 (0.52)	0.80 (0.42)	1.41 (0.63)	0.062	0.214	<0.001	0.040	0.452	0.003
sWOB (kPa*L*L)	1.28 (0.82)	1.77 (1.01)	1.67 (0.79)	2.66 (1.19)	0.034	0.118	<0.001	0.072	0.472	0.007

Note: The p-values of Wald Chi-Square test are given, adjustments for age and gender have been performed. Because of several simultaneous comparisons, the limit of significance is $p < 0.01$. Emph.= Emphysema, Contr. = Controls.

Table 2: Work of breathing in different patient groups.

In the subgroups these correlations were minor or missing possibly based on the restricted number of patients and rather homogenous groups (data not shown).

Discussion

Total WOB was increased in obesity and ILD compared to controls, and so were also expiratory and inspiratory WOB in obesity. On contrary to that, in emphysema, inspiratory, expiratory and total sWOB were increased compared to controls.

Conventional constant volume body plethysmography can measure specific work of breathing (sWOB) by utilizing the volume changes of breathing air measured at the mouth combining the data with box shift volume, which reflects the degree of compression or decompression in the alveolar space. Work of breathing (WOB) is specific work of breathing divided by the mean lung volume at tidal breathing which is FRCpleth + VT/2, when a strong resistance oriented component is left. Body plethysmography shows only the restive work of breathing and is not able to show elastic properties of the work of breathing.

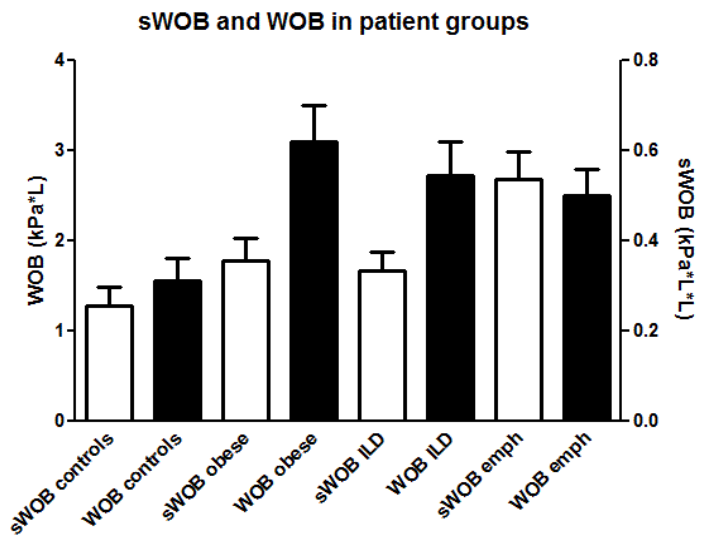

Figure 2: Schematic presentation of the mean values of sWOB and WOB in the patient groups, mean and SEM are presented. Emph.= Emphysematic COPD. White columns represent sWOB and black columns WOB.

Parameter	N	sWOBin	sWOBex	sWOB	WOBin	WOBex	WOB
DLCOc (%)	62	-0.281 (0.027)	-0.323 (0.011)	-0.297 (0.019)	-0.147 (0.253)	-0.188 (0.144)	-0.168 (0.192)
DLCOc/VA (%)	62	-0.297 (0.019)	-0.346 (0.006)	-0.322 (0.011)	-0.098 (0.448)	-0.155 (0.229)	-0.127 (0.324)
FEV1/FVC (%)	62	-0.265 (0.038)	-0.290 (0.022)	-0.293 (0.021)	0.107 (0.407)	0.056 (0.663)	0.085 (0.509)
MEF50 (%)	62	-0.276 (0.03)	-0.321 (0.011)	-0.324 (0.01)	-0.052 (0.688)	-0.010 (0.941)	-0.023 (0.861)
ERV (%)	62	-0.104 (0.423)	-0.123 (0.341)	-0.113 (0.383)	-0.350 (0.005)	-0.340 (0.005)	-0.352 (0.005)
RV (%)	62	0.239 (0.062)	0.319 (0.012)	0.301 (0.018)	0.061 (0.635)	0.010 (0.939)	0.026 (0.840)
RV/TLC (%)	62	0.214 (0.094)	0.282 (0.026)	0.263 (0.039)	0.005 (0.971)	0.069 (0.593)	0.041 (0.754)
Trapped air (l)	62	0.316 (0.012)	0.371 (0.003)	0.350 (0.005)	0.048 (0.712)	0.110 (0.394)	0.68 (0.599)

Note: The lung function parameters are dealt with as percent of predicted values. The spearman correlation coefficients and the p-values (in parentheses) are indicated. Significant correlations are printed in bold letters. RV= Residual Volume, ERV = Expiratory Reserve Volume, TLC= Total lung capacity, MEF50= Maximal expiratory flow at the level when 50% of FVC remains exhaled.

Table 3: Spearman correlations of breathing work and spirometric and diffusing capacity results in all subjects (N=62).

In ILD, WOB and in obesity also WOBin and WOBex were increased compared to controls. However sWOB in obesity or ILD was not increased compared to controls, the explanation of which is that lung volume is incorporated in the formula of WOB but not in the formula of sWOB. The same explanation might in emphysema explain the opposite finding - sWOB being significantly different from controls, and WOB differing nonsignificantly from the controls. Anyway, the present results indicate that both sWOB and WOB are needed in assessment of work of breathing depending on the characteristics of the disease studied. Also in previous literature, increased work of breathing in obesity has been found [3,16,17]. Compliance of the lungs and the respiratory system are low because of fat accumulations in thorax and abdomen. Pleural pressure is increased and the dimensions of peripheral airways are diminished. Obese patients are breathing against increased intra-abdominal mass, requiring increased pressure-volume work. Especially inspiratory work of breathing is increased which causes strain to the diaphragm [2,4,5,18,19]. Furthermore, the ventilatory drive may be decreased in obesity [20]. In a consequence, in obesity the increase of peripheral resistance leads to an increase of air compression and finally work of breathing is increased.

In the whole patient material, a negative correlation between inspiratory, expiratory and total WOB and ERV percent of predicted value was found. ERV was negatively correlated also with BMI (-0.296; rho=0.019) suggesting that obesity would be involved in this association between ERV and WOB, as would also be expected [21]. In obesity, the adipose masses in thorax and abdomen reduce the function of diaphragm which all decreases FRC. As a consequence, ERV declines because FRC is reduced and the residual volume (RV) is not. Within the obesity group, the association between ERV and WOB did not reach significance most probably explained by the small number in the rather homogenous group. Also ILD is characterized by small ERV as outcome of the restrictive pulmonary disease, whereas controls and emphysematic COPD patients typically showed large ERV, giving sufficient variation for correlation calculations within the whole material of patients and subjects.

In COPD with emphysema, inspiratory, expiratory and total sWOB and WOBin were significantly increased compared to controls. In COPD with emphysema this finding might be explained for the most by the obstructive component of COPD evoking resistive breathing work, because the elastic component of breathing work of emphysematic lung is probably not measured with the used method as easily as the resistive work caused by the obstructive component. This is also in line with earlier study [11]. In addition, significant inverse correlation of diffusing capacity and specific diffusing capacity, and positive one with

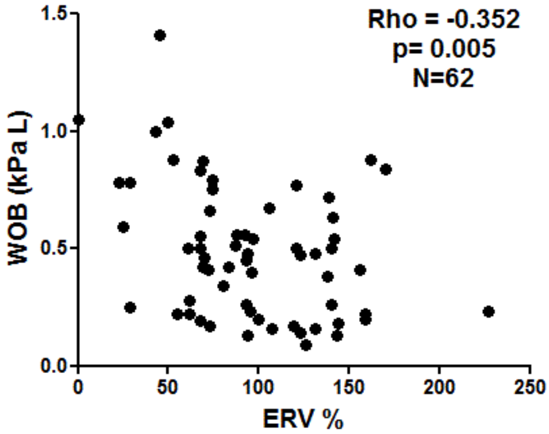

Figure 3: Correlation of WOB with ERV percent of predicted value in all subjects and patients.

air trapping and RV with sWOB was found through the whole patient material.

One restriction of the present study was that the patient groups were not very large, but this comes from the difficulties to find suitable patients during the study period. However, there were significant differences between the patient groups and control subjects. In addition, significant correlations between parameters of work of breathing and several conventional lung function parameters were found in the whole patient material.

Another restriction of the present study was that, oesophageal pressure measurements [4,5] were not available for comparison. However, the present examination measures resistive work of breathing, the oesophageal pressure method the whole work of breathing of the respiratory system. In addition, the present results on increased sWOB in COPD are similar as in earlier study [11] giving more force on the present results. Comparisons with oesophageal measurements should, however, be subject of further investigations.

Nowadays the dyspnoea index is usually determined utilizing different questionnaires [22], which however, is a rather subjective approach. Body plethysmography offers an objective non-invasive method to assess work of breathing, as a reason of dyspnoea. The method appears to be useful in measurements of obese subjects. In obesity, there is still a need for this kind of comfortable, easy and non-invasive test; e.g., to differential diagnosis of dyspnoea or simply to demonstrate the increased work of breathing as motivation for reduction of weight.

sWOB can be determined with every conventional plethysmograph, representing the integral of breathing volume at mouth (dV) and box shift volume (dVbox). Therefore sWOB and WOB are available on any body plethysmography equipment as soon as these parameters are determined and provided. The present results encourage applying these methods in assessment of respiratory symptoms in obesity.

As a conclusion, body plethysmography is available nearly in all well-equipped laboratories performing lung function tests. The results indicate that this non-invasive method might be helpful to assess a surrogate of work of breathing in obese subjects in order to assess the reasons for their dyspnoea.

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