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SPIROMETRIC PARAMETERS IN MALNOURISHED GIRLS WITH ANOREXIA NERVOSA

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Repercussions of obesity on the lung function have been widely studied. The effect of serious malnutrition is less well known. The aim of study was to determine spirometric parameters in 102 malnourished girls with anorexia nervosa. Among these patients, only 71 aged 12-18 years (mean 15.6), mean BMI 15.8 kg/m^2, met the ATS/ERS forced expiratory maneuver criteria for spirometry. The most frequently observed abnormalities were: decreased IC seen in 33 (46%) girls and decreased PEF in 45 (63%) patients. Maximum voluntary ventilation was within the normal range in all but 2 subjects. Diminished values of FEV_1, FVC, FEV_1/FVC, MEF_{50} were observed in 10 (14%), 13 (18%), 3 (4%), and 3 (4%) patients, respectively. We found strong positive correlations between weight and absolute values of the examined parameters. We assume that spirometric abnormalities in anorexia are probably a result of respiratory muscle weakness and body mass loss.

Key words: *anorexia nervosa, malnutrition, pulmonary function, spirometry*

INTRODUCTION

Morbid obesity and severe malnutrition are the two extremes in the spectrum of eating disorders. The repercussions of extreme obesity on the respiratory system have been widely studied, including obesity-hypoventilation syndrome, reduced forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), diminished expiratory reserve volume (ERV), functional residual capacity (FRC), maximum expiratory flows (MEFs), decreased diffusion capacity for carbon monoxide (DLCO), decreased maximum voluntary ventilation, and sleep-related breathing disturbances (1).

However, the effect of serious malnutrition on the respiratory system is less well known. Studies in rats show that severe caloric restriction decreases production of surfactant, the amount of elastic fibers in the alveolar septa, the number of alveoli, which causes a corresponding increase in the alveolar volume and a decrease in the surface area. Although these findings are suggestive of emphysema, they do not identify tissue destruction and are usually considered "emphysema-like" lung structure abnormalities (2-4).

Anorexia nervosa is frequent and is the purest form of human malnutrition in that it is independent of other diseases or environmental causes. It affects mainly young women (0.2-0.5%) and usually begins in adolescence or young adulthood (5). So far a few studies evaluating pulmonary function tests in anorexia have been performed, in relatively small and selected groups of patients, revealing conflicting results (6-11).

The aim of our study was to estimate spirometric disturbances in a large group of anorexic girls referred to the Department of Pediatrics and Endocrinology before refeeding treatment.

MATERIAL AND METHODS

The study was performed according to the standards set by the Helsinki Declaration from 1975 regarding the Human Research. The study protocol was approved by a local Ethics Committee at the Medical University of Silesia in Zabrze, Poland, and all subjects gave informed consent.

A hundred and two girls with newly detected anorexia nervosa admitted between January 2004 and January 2008 to the Department of Pediatrics and Endocrinology of the Silesian University of Medicine in Zabrze, Poland were initially enrolled in this study. All patients fulfilled the diagnostic criteria of anorexia nervosa (5). Patients with known recurrent respiratory symptoms or respiratory infection in the preceding 3 months and smokers were excluded from the study.

All maximum expiratory flow/volume (MEFV) measurements were performed before refeeding therapy, using a LUNGTEST 1000 pneumotachometer system (MES, Krakow, Poland). The calibration of equipment conformed to the European Community for Steel and Coal guidelines (12). Measurements were performed with the child sitting straight and wearing a nose clip. The children were encouraged, and performed, after full inspiration, a maximally forced and prolonged expiration. All children performed at least three technician-accepted curves, and for each child the two curves with the highest sum of forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were used for the final analysis. MEFV maneuvers were acceptable when the flow/volume curves showed a rapid rise to peak flow and a full prolonged expiratory curve, and met the ATS criteria for acceptability and reproducibility (13). The backward extrapolated volume (Vbe) for the start of the test evaluation was <0.15 l (as an absolute value) and as a percentage of FVC it was <5%. The forced expiratory time (FET) was accepted according to Arets *et al* (14) as ≥2 sec. Reproducibility was evaluated by the absolute and percentage difference between FVCs (ΔFVC <200ml or ΔFVC% <5%) and the absolute and percentage difference between FEV_1 (ΔFEV_1 <200 ml or ΔFEV_1 <5%) (12). The time to peak expiratory flow (tPEF) as the start-of-test criterion, which was not accepted in the ATS consensus report (13), was not analyzed. Results were expressed in absolute values and as a percentage of predicted values by comparing with reference values for gender, age, and height (12).

All patients were also instructed on the performance of the inspiratory capacity (IC) maneuver. The IC was determined by having the patients inhale while seated. After four to six consistent end-expiratory levels (FRC position), the patient was instructed to inspire slowly to TLC and then to return to normal breathing. The two largest IC measurements from at least three acceptable trials had to agree within 5% or 60 ml. For IC, predicted values were calculated as a difference between predicted total lung capacity (TLC) and predicted functional residual capacity (FRC).

Data were expressed as means ±SD. Commercially available Statistica software (StatSoft, Krakow, Poland) was used for all data elaboration. Pearson's correlation was used to assess the relationship between body weight, height or BMI and spirometric parameters. $P<0.05$ was taken as indicative of significant differences in all comparisons. Values expressed as a percent of predicted values were compared with reference values.

RESULTS

Of the 102 anorexic girls, aged 12-18 years, only 71 (69.6%) met the ATS/ERS forced expiratory maneuver criteria for spirometry. Flow-volume loops obtained from these patients were given further statistical evaluation. The demographic data of these girls are summarized in *Table 1*.

Table 2 shows the mean values of abnormal examined spirometric parameters in the 71 anorexic girls with acceptable flow-volume loops. The most frequently observed abnormalities were: decreased inspiratory capacity (IC) seen in 33

Table 1. Demographic data of anorexic girls with acceptable spirometry.

Number	Age	Height (cm)	Body weight (kg)	BMI kg/m^2
71	15.6 ±1.7 (12–18)	162.1 ±6.5 (144–176)	42.0 ±6.5 (27–56)	15.81±1.9 (10.9–24.1)

Values are means ±SD and range in parenthesis.

Table 2. Mean values and number of abnormal spirometric parameters in 71 anorexic girls with acceptable flow-volume loops.

	Absolute values	% of predicted	Number and (%) of cases below lower limit
FEV_1 (l)	2.71 ±0.53 (1.26–3.62)	95.1 ±16 (49–144)	10 (14.1%)
FVC (l)	3.04 ±0.54 (2.00–4.16)	89.8 ±13.1 (51–123)	13 (18.3%)
FEV_1/FVC	88.9 ±8.5 (52.9–100)	101.9 ±9.6 (61–114)	3 (4.2%)
PEF (l/s)	4.75 ±1.17 (1.96–7.76)	74.1 ±16.7 (39–124)	45 (63.3%)
MEF_{50} (l/s)	3.71 ±0.93 (1.68–5.79)	94.0 ±22.1 (53–156)	3 (4.2%)
MEF_{25} (l/s)	2.48 ±0.59 (1.25–3.83)	120.8 ±28.5 (59–201)	2 (2.8%)
IC (l)	1.74 ±0.34 (0.88–2.54)	77.5 ±15.0 (40–120)	33 (46.5%)
MVV (l/min)	73.7 ±16.8 (45.8–120.4)	117.1 ±26.9 (69–208)	2 (2.8%)

Values are means ± SD.

Table 3. Relationships between spirometric parameters and height, weight, and BMI in anorexic girls.

		FVC	FEV_1	PEF	MEF_{50}	MEF_{25}	IC	MVV	ERV
Height	r	0.58	0.54	0.40	0.35	0.30	0.28	0.27	0.38
	P	0.0005	0.0002	0.001	0.004	0.012	0.037	0.045	0.004
Weight	r	0.65	0.55	0.46	0.30	0.17	0.40	0.28	0.42
	P	0.0001	0.0001	0.001	0.04	0.16	0.003	0.034	0.001
BMI	r	0.50	0.40	0.37	0.20	0.05	0.30	0.19	0.27
	P	0.001	0.001	0.002	0.11	0.67	0.019	0.165	0.045

r-Pearson's correlation coefficient

(46%) girls and decreased PEF observed in 45 (63%) of them. However, maximum voluntary ventilation was within the normal range in all but 2 (2.8%) subjects. Diminished values below the lower limit of FEV_1, FVC, FEV_1/FVC, MEF_{50} were observed in 10 (14%), 13 (18%), 3 (4%), and 3 (4%) patients, respectively. In 10 patients, the simultaneously diminished FEV_1 and FVC suggested a restrictive defect of ventilation, but obstructive disturbances were found (FEV_1/FVC below lower limit) in only 3 patients (*Table 2*).

We found statistically significant positive correlations between the body weight and the absolute values of the most examined spirometric parameters. These relationships were stronger than those between the height or BMI and the spirometric parameters (*Table 3*).

DISCUSSION

To our knowledge we examined the largest cohort of anorexic girls so far. However, we only performed spirometric procedures without body plethysmography. Our results show that only 70% of the examined girls met the acceptability and reproducibility criteria for spirometry postulated by the ATS and ERS (12, 13). It should be underlined that no girl achieved an FET >6 s during the flow/volume maneuver, so we decided according to Arets *et al* (14) to decrease the acceptable FET to >2 s. Arets *et al* (14) showed that when children reached an FET of >2 s, this confirmed a maximum expiratory effort in >90% of children.

The most frequently observed abnormalities seen in our girls were decreased PEF and an IC below the lower limit. In ten girls restrictive changes were suspected. Obstructive changes were seen only in three subjects. Abnormalities in pulmonary function, including low to normal VC as well as a decrease in FEV_1, have previously been demonstrated in patients with anorexia nervosa (7, 8). During nutritional support, vital capacity and FEV_1 increased significantly by day 30 (8). Lands *et al* (15) reported normal spirometric values in nine anorexic adolescents whose physical fitness appeared to be lowered by diminished muscle mass or muscular dysfunction. Gonzalez-Moro *et al* (10) also observed normal values of FVC and FEV_1 in 12 anorexic young women.

Undernutrition negatively influences respiratory muscle function and structure both through a direct effect of loss of contractile elements, and also indirectly, by worsening or inducing muscle composition derangements (16, 17). Hence, diminished PImax (peak inspiratory pressure) and PEmax (peak expiratory pressure) were observed in anorexia nervosa (10, 16). Diaphragmatic contractility can be severely depressed, but it significantly increases with nutritional support (8).

It is well known that FVC and especially PEF are determined not only by the lung volume, dimensions of the large intra- and extra-thoracic airways, and lung elastic recoil, but also by the force generated by expiratory muscles and the speed at which the maximum alveolar pressure is reached, which depends on the force-velocity properties of the expiratory muscles (18).

Poor cooperation and poor effort may occur during maximum inhalation, exhalation, and during the prolonged exhalation phase of the M/F maneuver. It should be born in mind that submaximum inhalation falsely reduces the PEF, FEV_1, and FVC values (19). Poor inhalation effort is common, but is not objectively evident in any single spirometric record, being detectable only by invasive physiological measurements or possibly by subjective visual observation of the subject's performance (19). The type of inspiratory maneuver preceding forceful expiration could affect the magnitude of the PEF. The values of PEF are significantly higher if the FVC maneuver is preceded by fast inspiration without a postinspiratory pause than when it is preceded by slow inspiration with 4-6 seconds postinspiratory pause (20).

Our results (*i.e.*, low PEF, ERV, FEV_1, and FVC) may be explained by diminished respiratory muscle force, mainly in the diaphragm, due to weight loss. We found relatively strong correlations between spirometric parameters and body weight. Pieters *et al* (9) found that body mass index was significantly correlated with vital capacity, and the duration of anorexia was inversely correlated with total lung capacity.

Undernutrition prolongs the activity of inspiratory muscles during expiration, decreases the neuromuscular inspiratory drive, reduces tidal volume (VT) and minute ventilation (VE) and increases inspiratory and expiratory times in rats (4). The activity of inspiratory muscles during expiration opposes rapid emptying of the lungs. Dias *et al* (4) suggested a prolongation of the time required for inspiratory muscle relaxation during expiration. The relaxation of respiratory muscles is very important in the regulation of breathing. The diaphragm must return to its optimal muscle length between each inspiration. A study in humans with anorexia nervosa confirmed that VT, minute ventilation, and occlusion pressure is lower than in healthy persons, but that the time of inspiration (Tin) and Tin/Ttot does not differ between malnourished girls and controls (10). Unlike Arora *et al* (6), we found normal maximum voluntary minute ventilation in our patients. A study done by Biadi *et al* (21) confirmed that anorexic women have a lower maximum minute ventilation, working capacity, and oxygen uptake during exercise when compared with healthy controls.

Results obtained by Coxson *et al* (11) in 21 girls with anorexia nervosa show that long-term caloric malnutrition is associated with a loss of lung tissue, which is consistent with the presence of emphysema. As the BMI decreases in subjects who are anorexic, there is a decrease in the diffusion capacity, as well as an increase in both the mean volume of gas per weight of lung tissue and the percentage of the lung that is expanded beyond the normal range. Furthermore, there is a significant correlation between the body mass index and the CT measures of emphysema. Coxson's *et al* study (11) is in line with the postmortem studies of malnourished patients, who died in the Warsaw Ghetto during World War II, that show a surprisingly high percentage (13.5%) of the people below 40 years old who had pulmonary emphysema (22). However, Stanescu and Pieters (23) accepted Coxson's *et al* (11) results with caution, indicating that the histological description of emphysematous changes in autopsied people in Warsaw Ghetto were not precise. Gonzalez-Moro *et al* (10) and others (9) observed a significant elevation in RV, in RV/TLC ratio, and in FRC in anorexia nervosa patients compared with the control group. We found diminished inspiratory capacity values in 46% of our anorexic girls. Inspiratory capacity can be used to monitor exercise induced dynamic hyperinflation and, measured at rest, to predict improvements in dyspnea in patients with chronic obstructive pulmonary disease and emphysema (24). Low values of IC can indirectly reflect the elevation of FRC reported in anorexia (10), but FRC can be measured using body-plethysmography.

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