

World Journal of *Clinical Pediatrics*

World J Clin Pediatr 2018 May 8; 7(2): 67-74





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- 67 Is obesity related to the lung function of non-asthmatic children?

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NAME OF JOURNAL
World Journal of Clinical Pediatrics

ISSN
ISSN 2219-2808 (online)

LAUNCH DATE
June 8, 2012

FREQUENCY
Quarterly

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PUBLICATION DATE
May 8, 2018

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Is obesity related to the lung function of non-asthmatic children?

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Author contributions: All authors contributed equally to this paper.

Conflict-of-interest statement: Dr. Moustaki has nothing to disclose.

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Manuscript source: Invited manuscript

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Received: February 12, 2018

Peer-review started: February 12, 2018

First decision: March 2, 2018

Revised: March 12, 2018

Accepted: April 11, 2018

Article in press: April 11, 2018

Published online: May 8, 2018

Abstract

Overweight and obesity are highly prevalent in developed and developing countries among children and adolescents. During the last two decades, it became evident that excess weight is adversely related to respiratory health in childhood and adolescence mainly in terms of asthma occurrence. Additionally, there is a mounting body of evidence that overweight/obesity may also affect lung function in non-asthmatic subjects. The aim of this review was to present and discuss the studies that investigated this issue in non-asthmatic children and adolescents. Only a few studies have evaluated the impact of excess weight on static volumes and their results point towards an inverse relationship between overweight/obesity and functional residual capacity. More studies have been conducted on the impact of excess weight on dynamic lung volumes with inconsistent, however, results. Nevertheless, a relatively consistent finding was that the ratio of forced expiratory volume in 1 s/forced vital capacity was significantly lower among overweight/obese children compared to their counterparts with normal weight. The underlying mechanisms of these observations have not been adequately elucidated but it is believed to result from complex interaction of mechanical, developmental, and metabolic causes. There is a need for more well-designed studies in order to clarify the impact of excess weight on lung function in non-asthmatic subjects, as well as to explore the contribution of factors such as duration and degree of obesity, and fat distribution. Despite the absence of conclusive data, there are still

convincing evidence to be communicated to the children and their families as part of the arguments to encourage them to adopt a healthier lifestyle.

Key words: Obesity; Lung function; Spirometry; Lung volumes; Plethysmography

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Core tip: We herein present an overview of the existing studies regarding the influence of excess weight on static and dynamic volumes of lung function in otherwise healthy children and adolescents. Although the existing data, are to some extent, conflicting, it seems that in this age group, obesity is correlated to a significant, though not necessarily clinically important, decrease of forced expiratory volume in 1 s/forced vital capacity ratio and a reduction of functional residual capacity. These observations are of clinical relevance, as they may be the origin of respiratory problems in adulthood, especially if obesity persists till then.

Fretzayas A, Moustaki M, Loukou I, Douros K. Is obesity related to the lung function of non-asthmatic children? *World J Clin Pediatr* 2018; 7(2): 67-74 Available from: URL: <http://www.wjgnet.com/2219-2808/full/v7/i2/67.htm> DOI: <http://dx.doi.org/10.5409/wjcp.v7.i2.67>

INTRODUCTION

There is sufficient data indicating that the prevalence of overweight and obesity among children and adolescents is substantial, particularly in industrialized countries. In a recent global pooled analysis, it was found that the mean body mass index (BMI) and the prevalence of obesity have increased worldwide in children and adolescents over the last four decades^[1]. This rising trend has attenuated or even plateaued-albeit at high levels-in high income countries, since the end of the previous century. On the contrary, the rising still continues in middle and low income countries^[2]. The high prevalence of overweight and obesity is of utmost importance for public health; the increased BMI in childhood and adolescence enhances substantially the likelihood of overweight or obesity persistence in adulthood^[3] and so, the adverse health effects are not restricted to children. The most extensively studied health effects of overweight and obesity in adulthood involve cardiovascular diseases and cancer^[4]. However, it has become more than obvious that obesity is also associated with respiratory health through various pathophysiologic pathways^[5] and can affect lung function even in otherwise healthy subjects^[5].

The aim of this review is to present the existing data on the impact of obesity in plethysmographic and spirometric indices of pulmonary function of otherwise

healthy children. The implications of the relevant observations would also be discussed.

DEFINITION OF OBESITY

Different expert committees have advocated the use of BMI as a convenient tool with acceptable reliability for the screening of obesity in children aged 2-18 years^[6]. In particular, BMI $\geq 95^{\text{th}}$ percentile for age has been defined as obesity whereas BMI $\geq 85^{\text{th}}$ and $< 95^{\text{th}}$ percentile for age as overweight^[7]. The majority of studies that investigated the association of obesity with lung function in childhood and adolescence used BMI as an indicator of obesity. However, in some studies researchers preferred to use waist circumference percentiles (WCP) because this index is believed to reflect more accurately the amount of visceral adipose tissue^[6]. The results of all relevant studies will be presented here, irrespective of the tool that was used for the definition of obesity.

IMPACT OF OVERWEIGHT-OBESITY ON PLETHYSMOGRAPHIC INDICES OF LUNG FUNCTION (STATIC LUNG VOLUMES)

PubMed was searched from January 1997 till the end of October 2017. Only articles in English language were eligible. Five studies were identified that had investigated the impact of overweight/obesity on the plethysmographic indices of lung function in children and adolescents. A summary of these studies is presented in Table 1, in chronological order. The relationship of BMI with total lung capacity (TLC) was investigated by all researchers without finding any significant association. The only exception was the study of van de Griendt *et al*^[8] who did not simply assessed the relationship of BMI with TLC but rather tried to explore the effect of BMI reduction on lung volumes after an intervention program of weight reduction. The % predicted TLC increased by 2.27% (0.86%-3.86%) after weight loss and this increase was statistically significant. Nevertheless, the population of this study was consisted of extremely obese children with either a BMI equivalent $\geq 35 \text{ kg/m}^2$, or a BMI equivalent to at least 30 kg/m^2 plus a comorbidity related to obesity; as a consequence, it is questionable whether generalization of the study findings is proper or not. Quite similarly, however, in the study of Li *et al*^[9], and despite the absence of any association between BMI and TLC, there was a significant inverse correlation between trunk and subtotal body fat with TLC. Kongkiattikul *et al*^[10], who also explored the association of trunk or body fat percentage with lung volumes, presented only data regarding functional residual capacity (FRC), and no information was given for TLC.

Four studies presented data for FRC and showed either significantly lower FRC levels in subjects with

Table 1 Summary of studies that investigated the impact of overweight/obesity on the plethysmographic indices of lung function

| No. | Ref. | No. of children, age range (yr) | Exclusion criteria for the study population | Obesity indices | Plethysmographic variables |
|-----|---|---------------------------------|---|---|--|
| 1 | Li <i>et al</i> ^[9] , 2003 | 64, 7-18 | Children with chronic cardiorespiratory problems | BMI, Trunk Body Fat, and Subtotal Body Fat (total-head). The last 2 indices were calculated as a percentage of body mass | TLC, RV, FRC |
| 2 | van de Griendt <i>et al</i> ^[8] , 2012 | 112, 8.5-18.9 | Children diagnosed as asthmatics | BMI, WC | TLC, ERV |
| 3 | Davidson <i>et al</i> ^[12] , 2014 | 327, 6-17 | Children diagnosed as asthmatics | BMI | TLC, RV, FRC, ERV, VC |
| 4 | Rastogi <i>et al</i> ^[11] , 2014 | 168, 13-18 | History of smoking or chronic inflammatory conditions | BMI, WC, Waist-hip ratio | TLC, RV, FRC, RV/TLC, ERV, IC |
| 5 | Kongkiattikul <i>et al</i> ^[10] , 2015 | 45, 8.6-17.3 | Children with an underlying pulmonary disease | BMI, WC, WHR Hip circumference Body fat percentage Truncal fat percentage Fat mass index Fat free mass index | TLC, RV, FRC, RV/TLC (only results for FRC were presented) |

BMI: Body mass index; TLC: Total lung capacity; RV: Residual volume; FRC: Functional residual capacity; IC: Inspiratory capacity; WC: Waist circumference; WHR: Waist-hip ratio; ERV: Expiratory reserve volume.

adiposity or, similarly, a statistically significant inverse association between FRC and adiposity. BMI was the index of adiposity in three of these studies whereas Li *et al*^[9] found an inverse association between FRC and trunk or subtotal body fat but not with BMI. From the studies that presented data for expiratory reserve volume (ERV) and residual volume (RV)^[11,12], it seems that both ERV and RV decreased with increased adiposity. ERV also increased on an average of 15% in severely obese individuals who lost weight following an intervention program^[8].

IMPACT OF OVERWEIGHT-OBESITY ON SPIROMETRIC INDICES OF LUNG FUNCTION

Table 2 depicts the summary of the studies that investigated the relationship of overweight/obesity in children and/or adolescents with the spirometric variables of lung function. Twenty-three relevant studies were identified by searching PubMed from January 1997 till October 2017. Only articles in English language were eligible.

As a general remark, the findings of these 23 studies are, to some extent, inconsistent. In 3 of the studies^[9], which are discussed in the rest of the present paragraph, no difference was found in forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), FV1/FVC and FEF_{25%-75%} between obese and/or overweight and normal-weight children. Li *et al* did not find an association between BMI and other adiposity indices with spirometric variables within a group of obese subjects. The study, however, did not include either overweight or normal weight individuals to serve as controls. Taking, therefore,

into consideration the small sample size and the limited variation of BMI, as all subjects had BMI > 95th centile, it is likely that this study may have not had the power to detect significant associations between BMI and spirometric parameters. Liyanage *et al*^[13] also did not find any difference when they compared overweight and obese with normal weight children. However, because the former two categories constituted one group the effect of more severe obesity on dynamic lung volumes may have been missed. Similarly, Rastogi *et al*^[11] did not find any association between BMI or waist circumference and spirometric variables. However, asthma was neither an exclusion criterion for participants recruitment nor was taken into account in the final analysis. Accordingly, definitive conclusions cannot be drawn from this study for non-asthmatic adolescents. Kongkiattikul *et al*^[10], who measured static as well as dynamic volumes, mentioned only the statistical significance that observed for FRC. It could therefore be hypothesized that no difference of spirometric variables was identified among the studied subjects in relation to the degree of their adiposity.

Twenty out of 23 studies revealed statistical association between the degree of adiposity and at least one of the spirometric variables. In general, the results depict a trend of significantly decreased spirometric values in the individuals at higher BMI centiles. Interestingly, however, a number of these studies revealed results that were not so clear-cut and implied a more complex association between obesity and lung function; these particular studies are discussed in some details in the following lines^[14,15]. Yao *et al*^[15] recruited obese children irrespective of asthma status. Nevertheless, in their analysis they controlled for physician-diagnosed asthma and found that excess weight was positively

Table 2 Summary of studies that investigated the impact of overweight/obesity on spirometric indices of lung function

| No. | Ref. | Obesity indices | Study population | Main findings |
|-----|---|--|---|---|
| 1 | Lazarus <i>et al</i> ^[34] , 1997 | Total body fat calculated from equations based on skinfold thickness | Representative sample of 2464 Australian school children aged 9, 12, and 15 yo | Total body fat was inversely associated with FVC and FEV1 after adjusting for height and weight |
| 2 | Li <i>et al</i> ^[9] , 2003 | Trunk and subtotal (total-head) body fat mass | Sixty-four obese children, 7-18 yo without cardiorespiratory problems. | No significant associations between the obesity and the spirometric indices |
| 3 | Perez-Padilla <i>et al</i> ^[35] , 2006 | Trunk body fat | A cross-sectional study of 6784 students 6-20 yo | In children < 11 yr FEV1 and FVC increased with BMI. In subjects > 12 yr lung function increased with BMI, reached a plateau (at a BMI Z score of 1SD) and then decreased among those with highest BMI |
| 4 | Nageswari <i>et al</i> ^[36] , 2007 | % body mass | Twenty obese/overweight children and 20 normal-weight (controls), 12-16 yo | FEV1, FVC, FEF _{25%-75%} were significantly lower in the obese group compared to the controls |
| 5 | Chen <i>et al</i> ^[18] , 2009 | Subtotal body fat (total-head) | A cross-sectional study of 718 children 6-17 yo | WC, but not BMI, was positively associated with FEV1 and FVC, and negatively associated with FEV1/FVC |
| 6 | Spathopoulos <i>et al</i> ^[37] , 2009 | % body mass | Three hundred fifty-seven overweight, 300 obese, and 196 normal-weight children. Not well-controlled asthma cases were excluded | All spirometric parameters were significantly different across the three groups. BMI > 85 th centile was a significant independent predictor of reduced spirometric parameters after controlling for confounders |
| 7 | Cibella <i>et al</i> ^[16] , 2011 | BMI | Cross-sectional study carried out in a sample of 708 children 10-16 yo | FEV1 and FVC were lower in children with BMI > 85 th centile compared to those with normal BMI. No difference was found for FEF _{25%-75%} , FEV1/FVC |
| 8 | Feng <i>et al</i> ^[19] , 2012 | BMI | A cross-sectional performed on 1572 healthy children 9-18 yo. Children with asthma were excluded | WC was inversely associated with FEV1, FVC and FEV1/FVC. BMI was positively related with FEV1 and FVC and negatively associated with FEV1/FVC |
| 9 | van de Griendt <i>et al</i> ^[8] , 2012 | BMI | One hundred twelve obese children 8.5-18.9 yo, taking part in a multidisciplinary treatment programme. | FEV1 and FVC increased by 2.91% and 3.08% after weight reduction following a 6 mo intervention program and this increase was significant. No significant change was observed in MEF ₅₀ |
| 10 | Paralikar <i>et al</i> ^[38] , 2012 | WC | Thirty obese boys 12-17 yo and 30 age-matched normal-weight boys | FEV1, FEV1/FVC and MVV were significantly decreased in the obese group |
| 11 | Bekkers <i>et al</i> ^[20] , 2013 | BMI, WC | Children from a birth cohort (<i>n</i> = 1058) examined at the age of 8 yo | Large WC in girls was associated with lower FEV1 /FVC ratio |
| 12 | Davidson <i>et al</i> ^[12] , 2013 | BMI | Three hundred twenty-seven children 6-17 yo referred for lung testing due to various respiratory problems. Individuals with cardiopulmonary, chest wall disease, or asthma, were excluded | Positive relationship between BMI z-score and percent predicted FVC, and VC. Negative relationship between BMI z-score and FRC, ERV, RV, and FEV1/FVC |
| 13 | Han <i>et al</i> ^[17] , 2014 | BMI, PBF, WC | Cross-sectional study in 2681 children 6-17 yo | Among children without asthma, BMI, PBF, and WC were associated with higher FEV1 and FVC, and lower FEV1/FVC |
| 14 | Khan <i>et al</i> ^[39] , 2014 | BMI, WC, WHR, skinfold measurements | A sample of 1583 children, < 18 yo. No data on asthma diagnosis was provided | Overweight/obese boys, had WC and WHR inversely associated with residual FVC, FEV _{0.75} , and FEV1 |
| 15 | Rastogi <i>et al</i> ^[11] , 2014 | BMI | A sample of 168 adolescents, 13-18 yo, irrespective of asthma status | Obese adolescents had lower RV, RV/TLC ratio, ERV, and FRC, and higher IC adolescents; the 2 groups did not differ in measures of lower airway obstruction, namely FEV1/FVC, and MEF |
| 16 | Torun <i>et al</i> ^[40] , 2014 | BMI | A cross-sectional study of 30 overweight, 34 obese and 64 morbidly obese children, 9-17 yo, referred to a paediatric endocrinology dept. Asthmatic patients were excluded from the study | PEF and FEV ₂₅₋₇₅ were significantly reduced in in the overweight, obese and morbidly obese children |

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| 17 | Bekkers <i>et al</i> ^[41] , 2015 | BMI, WC | Children from a birth cohort examined at the ages of 8 yo (<i>n</i> = 1090) and 12 yo (<i>n</i> = 1288) | At 8 yo, large WC was associated with lower FEV1/FVC after adjusting for BMI (only in girls) |
| 18 | Kongkiattikul <i>et al</i> ^[10] , 2015 | BMI, FMI, body fat percentage, truncal fat percentage, mean fat free mass index | Forty-five obese children, 8-18 yo | Negative correlation between FRC and almost all obesity indices |
| 19 | Cibella <i>et al</i> ^[14] , 2015 | BMI | A cross-sectional study of 2393 healthy children 10-17 yo. Children with asthma were excluded | FVC and FEV1 were positively but disproportionately correlated to weight. FEV1/FVC and FEF _{25-75%} /FVC ratios were negatively correlated to weight |
| 20 | Costa Junior <i>et al</i> ^[42] , 2016 | BMI, WC, body composition (tetrapolar bioimpedance) | A cross-sectional study of 40 obese and 35 normal-weight children, 6-10 yo. Children with respiratory problems were excluded | Obese children had lower FEV1 and FEV1/FVC |
| 21 | Liyanage <i>et al</i> ^[13] , 2016 | BMI | A cross-sectional study of 55 obese and 220 normal-weight children, 9-15 yo. Children with asthma were excluded | No significant difference in spirometric values |
| 22 | Akin <i>et al</i> ^[43] , 2017 | BMI, WC, neck circumference | A cross-sectional study of 178 children, 5 to 15 yo. Children with asthma were excluded | Negative correlation between FEV1, FEV1/FVC, and obesity indices |
| 23 | Yao <i>et al</i> ^[15] , 2017 | BMI | 1717 children, 5 to 18 yo, irrespective of asthma status | BMI is associated positively with FVC, FEV1, and PEF, and FEF _{25-75%} , but negatively with FEV1/FVC |

yo: Years old; PBF: Percent body fat; WHR: Waist-to-hip ratio; MVV: Maximum voluntary ventilation; BMI: Body mass index; WC: Waist circumference; WHR: Waist-hip ratio; FEV1: Forced expiratory volume in 1 s; FVC: Forced vital capacity.

and significantly associated with FEV1, FVC, and FEF_{25%-75%}, but negatively and significantly associated with FEV1/FVC. In order to interpret these findings they commented that the lower FEV1/FVC ratio in relation to higher FEV1 and FVC indicated that the lung volumes were larger in obese subjects but the airways size has not grown proportionately. Quite similar results were found in another recent study by Cibella *et al*^[14] who also analyzed their data after controlling for age, and showed that the effect of excess weight on spirometric values was independent of age. It is worth mentioning that the results of a precedent study from the same research group in 2011^[16] did not point to the same direction. However, the results of these two studies are not comparable since the population of the 2011 study included both asthmatic and non-asthmatic subjects without taking into account for asthma status. The study that first described this distinct trend of associations between adiposity indices and spirometric variables was that of Han *et al*^[17] in 2014 which was, however, designed to explore the association of obesity indices and asthma. It is very interesting that the finding of significantly lower FEV1/FVC ratio in obese/overweight subjects has not been exclusively observed in the aforementioned studies; it is almost universally present among the rest of the presented studies.

The results quite often varied in studies^[18,19] that used different surrogates of obesity (BMI or WC). This discrepancy indicates that adiposity markers are not necessarily interchangeable at least as far it concerns studies exploring the variations of lung function variables. Furthermore, it seems that the population age span may have affected the results of the studies to

some extent. As it was shown in the PIAMA birth cohort study^[20], significantly lower FEV1/FVC was observed in the whole study population, regardless of gender, at the age of 12 years but not at the age of 8 years. Therefore cross sectional studies that included children between 6-18 years may have resulted in different findings depending on the number of subjects in each specific age sub-group.

DISCUSSION

The above presented findings, despite a degree of inconsistency, indicate that the excess weight in childhood and adolescence has an adverse influence on the lung function of otherwise healthy subjects. A recent meta-analysis^[21] that evaluated the effects of overweight/obesity in both children and adults found that lung function is detrimentally affected but its pattern differs between adults and children. Based on the data of the included studies, authors showed that the FEV1/FVC ratio was lower in obese/overweight children with a decrement of 2.4%. They did not find a significant difference for FEV1 or FVC. However, these conclusions were reached through a pooled analysis in asthmatic and non-asthmatic children and without having controlled for asthma status within the childhood population.

There are several factors that could have attributed to the relatively diverse findings of the studies we included in the present systematic review. The sample size employed was small in some of them; in others, the age range of the recruited participants was fairly wide and no age groups for sub-analysis were specified; not all studies excluded children with asthma diagnosis;

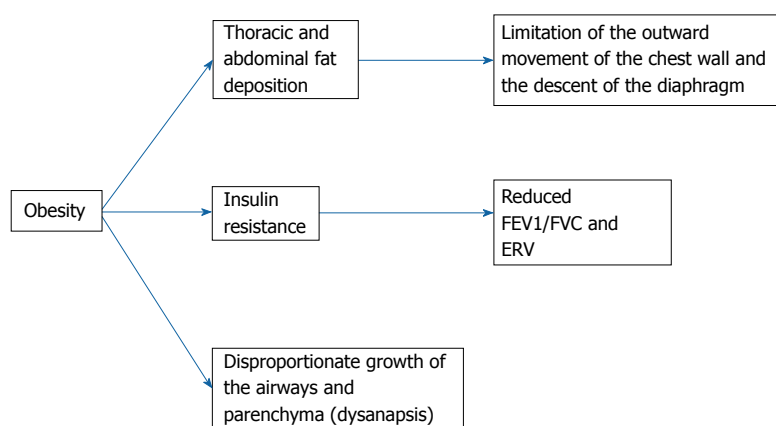


Figure 1 Mechanisms underlying reduced lung function in obese children. ERV: Expiratory reserve volume; FEV1: Forced expiratory volume in 1 s; FVC: Forced vital capacity.

there was not available information on the duration of the overweight/obesity, a variable that may also have an impact on lung function^[22]. The variation of obesity prevalence among the different populations, as well as the type of fat deposition which was not taken into account in the majority of the studies, may also have contributed to the observed discordance of the results among some of the studies. A factor not to be overlooked is that studied populations were of different ethnicity, and it is known that the amount of visceral adiposity tissue is dependent on ethnic origin^[23]. Lastly, data for maturity stage (Tanner stage) were not provided in any of the studies and therefore no adjustment was made for this parameter.

The physiologic mechanisms that underlie the impact of obesity on lung function are not entirely understood. It seems that the thoracic and abdominal fat deposition limit the outward movement of the chest wall and the descent of the diaphragm^[24]. Additionally, obesity is associated with reduced compliance of the respiratory system although it is not clarified whether both lung and chest wall compliance are reduced or not^[24,25]. It is also of note that obesity may coexist with obstructive sleep apnea syndrome (OSAS). Obese children have a 4.5 fold increased risk for OSAS^[26] a syndrome that may further contribute to hypoventilation in obesity^[27]. More recent studies suggest that the adverse effects of obesity on lung function are due not only to mechanical reasons but also to the metabolic abnormalities encountered in obesity. Rastogi *et al.*^[11] found that insulin resistance was a significant determinant of FEV1/FVC ratio and ERV in adolescents, even after adjusting for general and truncal adiposity. The above are supported from the results of a recent study conducted in obese women^[28]. Additionally hepatic steatosis is more prevalent in obese children and as it was recently shown in adult population hepatic steatosis was associated with poor pulmonary function^[29]. The main proposed mechanisms underlying reduced lung function in obese children are depicted in Figure 1.

Another interesting aspect on this issue was proposed by Forno *et al.*^[30] who have shown in a recent study that obesity was related to dysanapsis. The notion of dysanaptic growth of the lung was first introduced by Green *et al.*^[31] in 1974 and it indicates a normal but disproportionate growth of the airways and parenchyma so as large lungs to be accompanied by airways with incommensurate small proportions^[31,32]. In spirometry airway dysanapsis is indicated by normal FEV1 (above the 5th centile), normal high FVC (above the 75th centile), and low FEV1/FVC ratio (< 0.8)^[38]. Forno *et al.*^[30] used the data of six different cohorts and analyzed them cross-sectionally - or longitudinally if that was feasible - and found that obesity was associated with dysanapsis in childhood and adolescence.

In the majority of studies the lung function values of overweight/obese children were within normal limits, and so, it could be argued that the impairment of lung function is of no clinical relevance. This may seem plausible while the subjects are at rest but it would not be likely in the case of exercise tolerance. It should be kept in mind that obesity is not only a consequence of sedentary life style but also that the physical performance of obese subjects may be lower. The latter may be due in part to the altered lung function that leads to a vicious cycle of inadequate physical activity and obesity persistence. Additionally, the persistence of overweight/obesity to adulthood may also adversely affect their lung function as adults^[22,33].

As obesity is a worldwide public health problem, its adverse impact on lung function of non-asthmatic children and adolescents is of utmost importance since it may contribute to the increased morbidity of obese subjects. The physicians should be aware of this aspect of obesity and communicate this information to children and their families.

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P- Reviewer: Arslan N, Tarantino G **S- Editor:** Ji FF

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