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

Andrew Fretzayas, Maria Moustaki, Ioanna Loukou, Konstantinos Douros

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

© The Author(s) 2018. Published by Baishideng Publishing Group Inc. All rights reserved.

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 ≥ 95th percentile for age has been defined as obesity whereas BMI ≥ 85th and < 95th 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 ≥ 35 kg/m², or a BMI equivalent to at least 30 kg/m² 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
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\(^9\).

### 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 (FEV\(_1\)), forced vital capacity (FVC), FV\(_1\)/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 > 95\(^{th}\) 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\(^{14}\) 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 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 et al\(^9\), 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 et al\(^9\), 2012 | 112, 8.5-18.9 | Children diagnosed as asthmatics | BMI, WC | TLC, ERV |
| 3   | Davidson et al\(^{11}\), 2014 | 327, 6-17 | Children diagnosed as asthmatics | BMI | TLC, RV, FRC, ERV, VC |
| 4   | Rastogi et al\(^{14}\), 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 et al\(^{10}\), 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.
| No. | Ref. | Obesity indices | Study population | Main findings |
|-----|------|-----------------|------------------|--------------|
| 1   | Lazarus et al<sup>[16]</sup>, 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 FEV<sub>1</sub> after adjusting for height and weight |
| 2   | Li et al<sup>[18]</sup>, 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 et al<sup>[18]</sup>, 2006 | Trunk body fat | A cross-sectional study of 6784 students 6-20 yo | In children < 11 yr FEV<sub>1</sub> and FVC increased with BMI. In subjects > 12 yr lung function increased with BMI, reached a plateau (at a BMI Z score of ISD) and then decreased among those with highest BMI |
| 4   | Nageswari et al<sup>[19]</sup>, 2007 | % body mass | Twenty obese/overweight children and 20 normal-weight (controls), 12-16 yo | FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC were significantly lower in the obese group compared to the controls |
| 5   | Chen et al<sup>[20]</sup>, 2009 | Subtotal body fat (total-head) | A cross-sectional study of 718 children 6-17 yo | WC, but not BMI was positively associated with FEV<sub>1</sub> and FVC, and negatively associated with FEV<sub>1</sub>/FVC |
| 6   | Spathopoulos et al<sup>[21]</sup>, 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<sup>th</sup> centile was a significant independent predictor of reduced spirometric parameters after controlling for confounders |
| 7   | Cibella et al<sup>[22]</sup>, 2011 | BMI | Cross-sectional study carried out in a sample of 708 children 10-16 yo | FEV<sub>1</sub> and FVC were lower in children with BMI > 85<sup>th</sup> centile compared to those with normal BMI. No difference was found for FEV<sub>1</sub>/FVC, FVC |
| 8   | Feng et al<sup>[23]</sup>, 2012 | BMI | A cross-sectional performed on 1572 healthy children 9-18 yo. Children with asthma were excluded | WC was inversely associated with FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC. BMI was positively related with FEV<sub>1</sub> and FVC and negatively associated with FEV<sub>1</sub>/FVC |
| 9   | van de Griendt et al<sup>[24]</sup>, 2012 | BMI | One hundred twelve obese children 8.5-18.9 yo, taking part in a multidisciplinary treatment programme. | FEV<sub>1</sub> 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<sub>50</sub> |
| 10  | Paralikar et al<sup>[25]</sup>, 2012 | WC | Thirty obese boys 12-17 yo and 30 age-matched normal-weight boys | FEV<sub>1</sub>, FEV<sub>1</sub>/FVC and MVV were significantly decreased in the obese group |
| 11  | Bekkers et al<sup>[26]</sup>, 2013 | BMI, WC | Children from a birth cohort (n = 1,058) examined at the age of 8 yo | Large WC in girls was associated with lower FEV<sub>1</sub> /FVC ratio |
| 12  | Davidson et al<sup>[27]</sup>, 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 FEV<sub>1</sub>/FVC |
| 13  | Han et al<sup>[28]</sup>, 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 FEV<sub>1</sub> and FVC, and lower FEV<sub>1</sub>/FVC |
| 14  | Khan et al<sup>[29]</sup>, 2014 | BMI, WC, WHR, skinfold measurements | A sample of 1,583 children, < 18 yo. No data on asthma diagnosis was provided | Overweight/obese boys, had WC and WHR inversely associated with residual FVC, FEV<sub>0.75</sub>, and FEV<sub>1</sub>/FVC |
| 15  | Rastogi et al<sup>[30]</sup>, 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 FEV<sub>1</sub>/FVC, and MEF |
| 16  | Torun et al<sup>[31]</sup>, 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 | MEF and FEV<sub>25-75</sub> were significantly reduced in the overweight, obese and morbidly obese children |
and significantly associated with FEV1, FVC, and FEF25−75%, 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\(^\text{14}\) 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\(^\text{16}\) 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\(^\text{17}\) 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\(^\text{18,19}\) 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\(^\text{20}\), 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\(^\text{21}\) 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;
there was not available information on the duration of the overweight/obesity, a variable that may also have an impact on lung function. 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.

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. 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. 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, a syndrome that may further contribute to hypoventilation in obesity. 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. 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. 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. 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. 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. 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. 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). Forno et al. 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.

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.

REFERENCES

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide
trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128 9 million children, adolescents, and adults. Lancet 2017; 389: 2627-2642 [PMID: 29029897 DOI: 10.1016/S0140-6736(17)31239-9]

2 Ng M, Fleming T, Robinson M, Thompson B, Graetz N, Margono C, Mullany EC, Biryukov S, Abbafati C, Abers SA, Abraham PF, Abu-Rmeileh NM, Acho T, Al-Buhairan FS, Alemu ZA, Alifonno R, Ali MK, Ali R, Guzman NA, Anwar M, Anwar P, Banerjee A, Barquera S, Basu S, Bennett DA, Bhutta Z, Blore J, Cabral N, Nonato IC, Chang JC, Chowdhury R, Courville KJ, Criqui MH, Cundiff DK, Dabhdadar KC, Dandona L, Davis A, Dayama A, Dharmaratne SD, Ding EL, Durrani AM, Esteghamati A, Farzadfar F, Fay DF, Feigin VL, Flaxman A, Forouzanfar MH, Goto A, Green MA, Gupta R, Hafezi-Nejad N, Hankey GJ, Harelwood HC, Hawmoeller R, Hay S, Hernandez L, Hussein A, Idrisov BT, Ikeda N, Ishami F, Jahanpour J, Jassal SK, Jee SH, Jeffreys M, Jonas JB, Kabagambe EK, Khalifa SE, Kengne AP, Khader YS, Khang YH, Kim D, Kimknoti RW, King JM, Koko Y, Kosen S, Kwan G, Lai T, Leinsalu M, Li Y, Liang X, Liu S, Logroscino G, Lotufo PA, Lu Y, Ma J, Mannoo NK, Mensah GA, Merriman TR, Mokdad AH, Moschsandraus J, Naghavi M, Naheed A, Nand D, Narayam KM, Nelson EL, Neuhouser ML, Nisar MI, Ohkubo Y, Oto SI, Pedroza A, Prabhakaran D, Roy N, Sampson U, Seo H, Seplanou SG, Shibuya K, Shiri R, Shiuie I, Singh GM, Singh JA, Skirbekk V, Stapelberg NJ, Sturua L, Sykes BL, Tobias M, Tran BX, Trasande L, Toyoshima H, van de Vijver S, Vasankari TJ, Veerman JL, Velasquex-Melenes G, Vlassov VV, Vollset SE, Von T, Wang C, Wang X, Weiderpass E, Werdecker A, Wright J, Yang YC, Yatsuri H, Youn J, Youn SI, Zhao Y, Zhou M, Zhu S, Lopez AD, Murray CJL. Health Effects of Overweight and Obesity in 195 Countries over 25 Years. N Engl J Med 2017; 377: 13-27 [PMID: 28604169 DOI: 10.1056/NEJMoa1614362]

5 Peters U, Suratt BT, Bates JHT, Dixon AE. Beyond BMI: Obesity and Lung Disease. Chest 2018; 153: 702-709 [PMID: 28728934 DOI: 10.1016/j.chest.2017.07.010]

6 Krebs NF, Himes JH, Jacobson D, Nicklas TA, Guilday P, Styne D. Assessment of child and adolescent overweight and obesity. Pediatrics 2007; 120 Suppl 4: S193-S228 [PMID: 18055652 DOI: 10.1542/peds.2007-2329D]

7 Ogden CL, Flegal KM. Changes in terminology for childhood overweight and obesity. Nutr Health Stat Report 2010, (25): 1-5 [PMID: 20939253]

8 van de Grietd EJ, van der Baan-Sloutweg OH, van Essen-Zandvliet EE, van der Palen J, Tammiona-Smeulders CL, Benninga MA, van Aalderen WM. Gain in lung function after weight reduction in severely obese children. Arch Dis Child 2012; 97: 1039-1042 [PMID: 23076338 DOI: 10.1136/archdischild-2011-301304]

9 Li AM, Chan D, Wong E, Yin J, Nelson EA, Fok TF. The effects of obesity on pulmonary function. Arch Dis Child 2003; 88: 361-363 [PMID: 12651773 DOI: 10.1136/adc.8.4361]

10 Kongkaiattlekul T, Sritipayanaw S, Chomtho S, Deerojawanong J, Prapphal N. Relationship between Obesity Indices and Pulmonary Function Parameters in Obese Thai Children and Adolescents. Indian J Pediatr 2015; 82: 1112-1116 [PMID: 25947270 DOI: 10.1007/s12095-015-1777-4]

11 Rastogi D, Bhalani K, Hall CB, Isasi CR. Association of pulmonary function with adiposity and metabolic abnormalities in urban minority adolescents. Ann Am Thorac Soc: 2014; 11: 744-752 [PMID: 24785169 DOI: 10.1513/AnnalsATS.201311-403OC]

12 Davidson WJ, Mackenzie-Rife KA, Wittman MB, Montgomery MD, Ball GD, Egbogah S, Eves ND. Obesity negatively impacts lung function in children and adolescents. Pediatr Pulmonol 2014; 49: 1003-1010 [PMID: 24167154 DOI: 10.1002/ppul.222915]

13 Liyanage G, Jayamnane B D, Aqiff M, Siwardhana D. Effect of body mass index on pulmonary function in children Ceylon Med J 2016; 61: 163-166 [PMID: 28076945 DOI: 10.4038/jm. v61.4.3832]

14 Cibelfa F, Bruno A, Cuitetta G, Buccheri S, Melis MR, De Cantis L, Grutta S, Viegi G. An elevated body mass index increases lung volume but reduces airflow in Italian schoolchildren. PLoS One 2015; 10: e0127154 [PMID: 25970463 DOI: 10.1371/journal. pone.0127154]

15 Yao TC, Tsai HJ, Chang SW, Chung RH, Hsu JY, Tsai MH, Liao SL, Hua MC, Li SH, Chen LC, Yeh KW, Tseng YL, Lin WC, Chang SC, Huang JL. Prediction of Allergies in Taiwanese Children (PATCH) Study Group. Obesity disproportionately impacts lung volumes, airflow and exhaled nitric oxide in children. PLoS One 2017; 12: e0174691 [PMID: 28376119 DOI: 10.1371/ journal.pone.0174691]

16 Cibelfa F, Cuitetta G, La Grutta S, Melis MR, Buccheri S, Viegi G. A cross-sectional study assessing the relationship between BMI, asthma, atopy, and eNO among schoolchildren. Ann Allergy Asthma Immunol 2011; 107: 330-336 [PMID: 21962093 DOI: 10.1016/j.anai.2011.08.001]

17 Han YY, Forno E, Celedón JC. Adiposity, fractional exhaled nitric oxide, and asthma in U.S. children. Am J Respir Crit Care Med 2014; 190: 32-39 [PMID: 24922361 DOI: 10.1164/rccm.201403-0565OC]

18 Chen Y, Rennie D, Cormier Y, Dosman JA. Waist circumference associated with pulmonary function in Canadian children. Pediatr Pulmonol 2009; 44: 216-221 [PMID: 19205050 DOI: 10.1002/ppul.20854]

19 Feng K, Chen L, Han SM, Zhu GJ. Ratio of waist circumference to chest circumference is inversely associated with lung function in Chinese children and adolescents. Respiracy 2012; 17: 1114-1118 [PMID: 22758916 DOI: 10.1111/j.1440-1843.2012.02219.x]

20 Bekkers MM, Wijga AH, de Jongste JC, Kerkhof M, Postma D, Gehring U, Smit HA, Brumekreek B. Waist circumference, BMI, and lung function in 8-year-old children: the PLAAM birth cohort study. Pediatr Pulmonol 2013; 48: 674-682 [PMID: 23143885]
Fretzayas A et al. Obesity and lung function

DOI: 10.1002/pupl.22722

21 Forino E, Han YY, Mullen J, Celedón JC. Overweight, Obesity, and Lung Function in Children and Adults–A Meta-analysis. *J Allergy Clin Immunol Pract* 2018; 6: 570-581.e10 [PMID: 28967546 DOI: 10.1016/j.jaip.2017.07.010]

22 Santamaria F, Montella S, Greco L, Valerio G, Franzese A, Maniscalco M, Fiorentino G, Peroni D, Pietrobelli A, De Stefano S, Sperli F, Boner AL. Obesity duration is associated to pulmonary function impairment in obese subjects. *Obesity* (Silver Spring) 2011; 19: 1623-1628 [PMID: 23115108 DOI: 10.1038/oby.2011.1]

23 Lear SA, Humphries KJ, Kohli S, Chockalingam A, Frohlich ST. Effects of body fat on ventilatory function in children and adolescents: cross-sectional findings from a random population sample of school children. *Pediatr Pulmonol* 1997; 24: 187-194 [PMID: 9330415 DOI: 10.1002/slc.4280970243; 13: 236-240 [PMID: 22919162 DOI: 10.1089/ped.2014.0349]

24 Robinson PD. Obesity and its impact on the respiratory system. *Paediatr Respir Rev* 2014; 15: 219-226 [PMID: 23092493 DOI: 10.1016/j.prrv.2014.06.003]

25 Parameswaran K, Todd DC, Sot M. Altered respiratory physiology in obesity. *Can Respir J* 2006; 13: 203-210 [PMID: 16779465 DOI: 10.1155/2006/834786]

26 Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. *Am J Respir Crit Care Med* 1999; 159: 1527-1532 [PMID: 10228121 DOI: 10.1164/ajrccm.159.5.9809079]

27 Arens R, Mazumdar H. Childhood obesity and obstructive sleep apnea syndrome. *J Appl Physiol* (1985) 2010; 108: 436-444 [PMID: 19875714 DOI: 10.1152/japplphysiol.00689.2009]

28 Lecube A, Sampol G, Muñoz X, Lloberes P, Hernández C, Simó R. Insulin resistance is related to impaired lung function in morbidly obese women: a case-control study. *Diabetes Metab Res Rev* 2010; 26: 639-645 [PMID: 20882512 DOI: 10.1002/dmrr.1131]

29 Mann JP, Valenti L, Scorletti E, Byrne CD, Nobili V. Nonalcoholic Fatty Liver Disease in Children. *Semin Liver Dis* 2018; 38: 1-13 [PMID: 29471561 DOI: 10.1055/s-0038-1627456]

30 Forno E, Weiner DJ, Mullen J, Sawicki G, Kurland G, Han YY, Cloutier MM, Canino G, Weiss ST, Litonjua AA, Celedón JC. The effect of obesity on pulmonary lung function of school aged children in Greece. *Pediatr Pulmonol* 2009; 44: 273-280 [PMID: 19208374 DOI: 10.1002/ppul.20995]

31 Parikh SR, Kathriotis RG, Pathak NR, Jani MB. Assessment of pulmonary functions in obese adolescent boys. *Lung India* 2012; 29: 236-240 [PMID: 22919162 DOI: 10.4103/0970-2113.99106]

32 Khan S, Little J, Chen Y. Relationship Between Adiposity and Pulmonary Function in School-Aged Canadian Children. *Pediatr Allergy Immunol Pulmonol* 2014; 27: 126-132 [PMID: 25276486 DOI: 10.1089/ped.2014.0349]

33 Suresh S, O’Callaghan M, Sly PD, Mamun AA. Impact of childhood anthropometry trends on adult lung function. *Chest* 2015; 147: 1118-1126 [PMID: 25340561 DOI: 10.1378/chest.14-0698]

34 Lazarus R, Colditz G, Berkey CS, Speizer FE. Effects of body fat on ventilatory function in children and adolescents: cross-sectional findings from a random population sample of school children. *Pediatr Pulmonol* 1997; 24: 187-194 [PMID: 9330415 DOI: 10.1002/slc.4280970243; 13: 236-240 [PMID: 22919162 DOI: 10.1089/ped.2014.0349]

35 Perez-Padilla R, Rojas R, Torres V, Borgia-Aburto V, Olaziz G, The Empece Working Group. Obesity among children residing in Mexico City and its impact on lung function: a comparison with Mexican-Americans. *Arch Med Res* 2006; 37: 165-171 [PMID: 16314204 DOI: 10.1016/j.arcm.2005.05.009]

36 Nageswari KS, Sharma R, Kohli DR. Assessment of respiratory and sympathetic cardiovascular parameters in obese school children. *Indian J Physiol Pharmacol* 2007; 51: 235-243 [PMID: 18341219]

37 Spapathopoulos D, Paraskakis E, Trypsianis G, Tsalkidis A, Arvanitidou V, Emпорiаduо M, Bournos D, Chatzimichael A. The effect of obesity on pulmonary lung function of school aged children in Greece. *Pediatr Pulmonol* 2009; 44: 273-280 [PMID: 19208374 DOI: 10.1002/ppul.20995]

38 Paralikar SJ, Kathriotis RG, Pathak NR, Jani MB. Assessment of pulmonary functions in obese adolescent boys. *Lung India* 2012; 29: 236-240 [PMID: 22919162 DOI: 10.4103/0970-2113.99106]

39 Khan S, Little J, Chen Y. Relationship Between Adiposity and Pulmonary Function in School-Aged Canadian Children. *Pediatr Allergy Immunol Pulmonol* 2014; 27: 126-132 [PMID: 25276486 DOI: 10.1089/ped.2014.0349]

40 Torun E, Cakir E, Ozgюk F, Ozgen IT. The effect of obesity degree on childhood pulmonary function tests. *Balkan Med J* 2014; 31: 235-238 [PMID: 25337419 DOI: 10.5152/balkanmedj.2014.13101]

41 Bekkers MB, Wijga AH, Gehrung U, Koppelman GH, de Jongste JC, Smit HA, Bruneekreef B. BMI, waist circumference at 8 and 12 years of age and FVC and FEV1 at 12 years of age; the PIAMA birth cohort study. *BMC Pulm Med* 2015; 15: 39 [PMID: 25986340 DOI: 10.1186/s12890-015-0032-0]

42 Costa Junior D, Peixoto-Souza FS, Araujo PN, Barbalho-Moulin MC, Alves VC, Gomes EL, Costa D. Influence of Body Composition on Lung Function and Respiratory Muscle Strength in Children With Obesity. *J Clin Med Res* 2016; 8: 105-110 [PMID: 26767078 DOI: 10.14740/jcmr2382w]

43 Akin O, Arslan M, Haymana C, Karabulut E, Hachiamdioglu B, Yavuz ST. Association of neck circumference and pulmonary function in children. *Ann Allergy Asthma Immunol* 2017; 119: 27-30 [PMID: 28527867 DOI: 10.1016/j.anai.2017.04.018]

P-Reviewer: Arslan N, Tarantino G S-Editor: Ji FF I-Editor: Filippolia E-Editor: Tan WW
