Obesity and Pulmonary Function in African Americans

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Abstract

Background

Obesity prevalence in United States (US) adults exceeds 30% with highest prevalence being among blacks. Obesity is known to have significant effects on respiratory function and obese patients commonly report respiratory complaints requiring pulmonary function tests (PFTs). However, there is no large study showing the relationship between body mass index (BMI) and PFTs in healthy African Americans (AA).

Objective

To determine the effect of BMI on PFTs in AA patients who did not have evidence of underlying diseases of the respiratory system.

Methods

We reviewed PFTs of 339 individuals sent for lung function testing who had normal spirometry and lung diffusion capacity for carbon monoxide (DLCO) with wide range of BMI.

Results

Functional residual capacity (FRC) and expiratory reserve volume (ERV) decreased exponentially with increasing BMI, such that morbid obesity resulted in patients breathing near their residual volume (RV). However, the effects on the extremes of lung volumes, at total lung capacity (TLC) and residual volume (RV) were modest. There was a significant linear inverse relationship between BMI and DLCO, but the group means values remained within the normal ranges even for morbidly obese patients.

Conclusions

We showed that BMI has significant effects on lung function in AA adults and the greatest effects were on FRC and ERV, which occurred at BMI values < 30 kg/m2. These physiological effects of weight gain should be considered when interpreting PFTs and their effects on

respiratory symptoms even in the absence of disease and may also exaggerate existing lung diseases.

Introduction

Obesity is associated with increased morbidity, and mortality. The prevalence of obesity [as indicated by a body mass index (BMI) of ≥ 30 kg m^2] has increased in the US during the last several decades. It has increased from 15% in 1976–80, to 23% in 1988–94, to 32% in 2003–04 [1,2]. More than one-third (age-adjusted 34.9%) of US adults are now obese [3,4] and is projected to rise to over 50% by the year 2030 [5]. While the overall prevalence of obesity has increased, significant racial/ethnic disparities continue to exist; with highest prevalence among non-Hispanic black (47.8%) than non-Hispanic white (32.6%) adults [3].

The mass loading effect of adiposity on the thoracic cage and abdomen can have an effect on respiratory mechanics leading to decreased chest wall and lung compliance, decreased pulmonary gas exchange [6], limitations in exercise capacity [7–9] and altered pulmonary physiology [9–11].

Although the impact of obesity on PFTs has been addressed in previous studies [10,12–14], many of the previous studies have been small; or they were conducted with the subjects in the supine position [10], some studies [15–17] reported only spirometry results or they included only two BMI groups [13,18] and the study which included a wide range of BMI was done in exclusively white patients [11]. However, a study looking at the association of full lung function with wide range of BMI in AA patients is limited.

In our experience, we often encounter obese black patients reporting respiratory symptoms such as dyspnea and we hypothesized they will have abnormal lung function. Therefore, in this study we aim to determine the effects of obesity on PFTs in a large healthy African American subjects who exhibited a wide range of BMI.

Methods

The data used were collected from PFTs performed between 2008 and 2013. The most common indication for PFT was dyspnea. Participants performed spirometry, body plethysmography, and lung diffusion capacity for carbon monoxide (DLCO) according to American Thoracic Society/European Respiratory Society (ATS/ESR) standard protocols [19,20]. At the study visit weight was measured using a calibrated scale and height was measured with patients not wearing their shoes, using a calibrated stadiometer. The measurements of weight and height were used to calculate BMI and the BMI was categorized into 5 groups (see below) based on the established standard [21]. This study was conducted in accordance with amended Declaration of Helsinki. The institutional review board of Howard University approval was obtained and the requirement of informed consent was waived. All PFTs performed during the study period were reviewed. The PFTs not selected for this study were either having significant abnormality or patients had known cardiopulmonary disease. Patients comprising this study had the following characteristics: (1) age$\geq$18 years, (2) smoking history of < 10 pack-years, (3) BMI $\geq$ 20 kg/m^2 (4) black race (5) no known diagnosis of cardiopulmonary or chest wall disease, (6) expiratory volume in 1 second (FEV1) to vital capacity (FVC) ratio ($\geq$0.7), (7) DLCO $\geq$80% of predicted after adjusting for the patient's hemoglobin.

Spirometry was performed, to obtain FVC, FEV1, and FEV1/FVC ratio and values expressed as % predicted [22] except for the FEV1/FVC ratio where the actual measurement

was used. Lung volumes were measured using a body plethysmograph that was calibrated daily (Vmax version v21-2B; Yorba Linda, CA, USA) according to ATS/ERS Guidelines for lung volume testing [23]. Values derived were vital capacity (VC), functional residual capacity (FRC), total lung capacity (TLC), residual volume (RV), and expiratory reserve volume (ERV) and were reported as percentage of predicted values [24]. Predicted ERV was obtained by subtracting the predicted RV from the predicted FRC. TLC was determined by FRC plus inspiratory capacity, and RV was determined by TLC minus VC. DLCO was adjusted for hemoglobin concentration and expressed as percent of predicted.

We subdivided the patients characteristics and PFT results into BMI categories of 20 to 24.9 kg/m^2 (normal weight or category 1), 25 to 29.9 kg/m^2 (over weight or category 2), 30 to 34.9kg/m^2 (mild obesity or category 3), 35 to 39.9 kg/m^2 (moderate obesity or category 4), $\geq$40kg/m^2 (morbid obesity or category 5) [21].

Descriptive statistics were computed to assess patient baseline demographics and PFTs for the different BMI categories. Analysis of variance (ANOVA) was performed to assess significant differences in means among the BMI categories with a Benferroni *post Hoc* analysis. The results were analyzed using multiple linear and polynomial regressions to assess the effects of BMI on lung volumes. Significance was taken as p value < 0.05 for all tests. Data analysis was conducted using the Statistical Analysis System software 9.3 (SAS Institute, Cary, NC) and Statistical Analysis and Graphics (NCSS 9.0.7, Kaysville, UT).

Results

Patient characteristics and mean values for FEV1/ FVC ratio, lung volumes and DLCO for the different BMI categories are summarized in Table 1 and S1 Fig. Age ranged from 18 to 87 years (median 47years) and BMI ranged from 20.05–64.38 kg/m^2 (median 28.15kg/m^2). The

Table 1. Demographics and Pulmonary Function Results for the Different BMI Groups (Kg/m^2).

	Normal Weight	Over Weight	Mild Obesity	Moderate Obesity	Morbid Obesity
	BMI = 20–24.9	BMI = 25–29.9	BMI = 30–34.9	BMI = 35–39.9	BMI $\geq$ 40
Variables					
Age (yr.)	44.88 (17.41)	47.43 (14.99)	49.16 (13.33)	49.80 (12.89)	40.54 (10.96)
BMI-kg/m^2	22.71 (1.29)	27.30 (1.37)	32.27 (1.39)	36.73 (1.14)	47.02 (5.90)
Gender					
Female	50	46	31	24	30
Male	51	54	33	11	9
FEV1/FVC	81.84 (7.41)	81.74 (5.28)	83.47 (4.60)	83.26 (4.62)	85.31¥ (4.11)
VC %	92.53 (12.13)	93.05 (11.89)	93.84 (13.04)	89.17 (9.12)	95.03 (12.29)
TLC%	93.99 (13.19)	95.05 (10.64)	96.53 (14.10)	91.63 (9.40)	93.77 (13.57)
RV%	96.36 (34.11)	98.42 (24.92)	101.63 (30.43)	96.33 (18.70)	90.78 (26.00)
FRC%	86.69 (16.38)	82.31 (15.10)	78.96 (19.46)	72.35 (11.44)	67.10 (15.09)
ERV%	73.64 (32.55)	58.74 (27.89)	44.87 (20.30)	35.28 (15.89)	33.42 (18.13)
DLCO%	92.69 (12.07)	90.02 (9.65)	93.61 (12.31)	87.49 (9.60)	82.85 (3.77)
RV/TLC	0.38 (0.17)	0.42 (0.33)	0.38 (0.13)	0.38 (0.10)	0.34 (0.10)
FRC/TLC	0.60 (0.20)	0.60 (0.41)	0.50 (0.16)	0.47 (0.13)	0.44 (0.12) ¥

* Values are expressed as No. or mean percentage of predicted (SD), RV/TLC and FRC/TLC are expressed as absolute ratios. Comparisons between BMI groups for ERV, FRC, and DLCO are shown in S1 Fig.

¥For FRC/TLC and FEV$_1$/FVC, P<0.05 compared to BMI groups 20–24.9 and 25–29.9kg/m^2

BMI = body mass index

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different BMI categories were well matched for gender except for the two highest BMI categories (moderate and morbid obesity); however, there were no significant differences in the best-fit regression lines between men and women for the effects of BMI (kg/m^2) on TLC%, VC%, RV%, FRC%, ERV%, or DLCO%. Therefore, the data from men and women have been grouped together. The lung function values were expressed as mean percentages of predicted values with FEV1/FVC, RV/TLC and FRC/TLC expressed as absolute ratios.

The mean values for VC% predicted, TLC% predicted, RV% predicted remained within the normal range for the different BMI categories. The RV/TLC ratio did not change significantly between any of the BMI categories, but the FRC/TLC ratio and FRC decreased significantly between categories indicating that FRC is affected by BMI. The preservation of TLC in the presence of decreasing FRC with increases of BMI can be explained due to increase in inspiratory capacity. The slow VC was also remained unchanged with increases of BMI, however we noticed the FVC was lower than the slow VC and this could be due to airway compression during the forced maneuver. For FEV1/FVC ratio, although the mean of the BMI groups remained within the normal limits, the morbidly obese category had significantly higher FEV1/FVC ratio when compared to those with normal (p = 0.014) and overweight (p = 0.011) showing the obese group having lower mean FVC% predicted. The mean values of DLCO was within normal limits even in the morbidly obese category but showed a significant decrease with the increases of BMI. The morbidly obese category had a significantly lower mean DLCO when compared to those with normal BMI, over weight and mild obesity BMI categories (p<0.001, p = 0.004, and p<0.001 respectively).

Fig 1 shows the linear regressions for DLCO, VC, TLC, and RV. In all cases but DLCO, there was no significant linear relationship with BMI. The p-value of the linear regression for DLCO was < .0001. The lower prediction limit (LPL) and the upper prediction limit (UPL) of the regression line were plotted with some patients having values outside the prediction limits. The slopes of the linear regression for percentage of predicted values and BMI were -0.166 (DLCO), 0.005 (VC), -0.026 (TLC), and -0.016 (RV).

Multiple linear regression analysis showed a dramatic decrease in ERV as BMI increased. When compared to those with a normal BMI, ERV decreased by 14.08%, 27.4%, 38.61% and 43.7% in the overweight, mild obesity, moderate obesity and morbid obesity respectively (Table 2). An equally consistent negative correlation between BMI and FRC was also observed, although the changes are less dramatic. When compared to those with a normal BMI, FRC reduced by 4.7%, 8.8%, 16.2% and 20% in the overweight, mild obesity, moderate obesity and morbid obesity respectively (Table 2). The best-fit polynomial regressions for FRC and ERV were highly significant (Fig 2) with p<0.0001. The second order polynomial regression equations were: FRC = 0.0143*(BMI)^2–1.8448*(BMI) + 121.88 and ERV = 0.0742*(BMI)^2–7.0384*(BMI) + 195.29. The r^2 values for FRC and ERV were 0.151 and 0.269 respectively. The results indicate that both FRC and ERV decrease sharply with increase in BMI values.

Discussion

The result of this study confirms as well as reports new findings on the effects of obesity on lung function in AA adults. Among the variables, FRC and ERV had the most expressive values, decreasing with the increases of BMI as shown in previous studies [10–14]. However, our study shows the effects of BMI on lung volumes in blacks, information which has never being reported from any of the previous studies [10–12,14,18] that included small number and limited BMI groups or the largest study with wide range of BMI included only white patients [11].

There was an exponential relationship between BMI, ERV and FRC with a reduction in FRC and ERV detectable even in overweight individuals. In a regression analyses, for a person
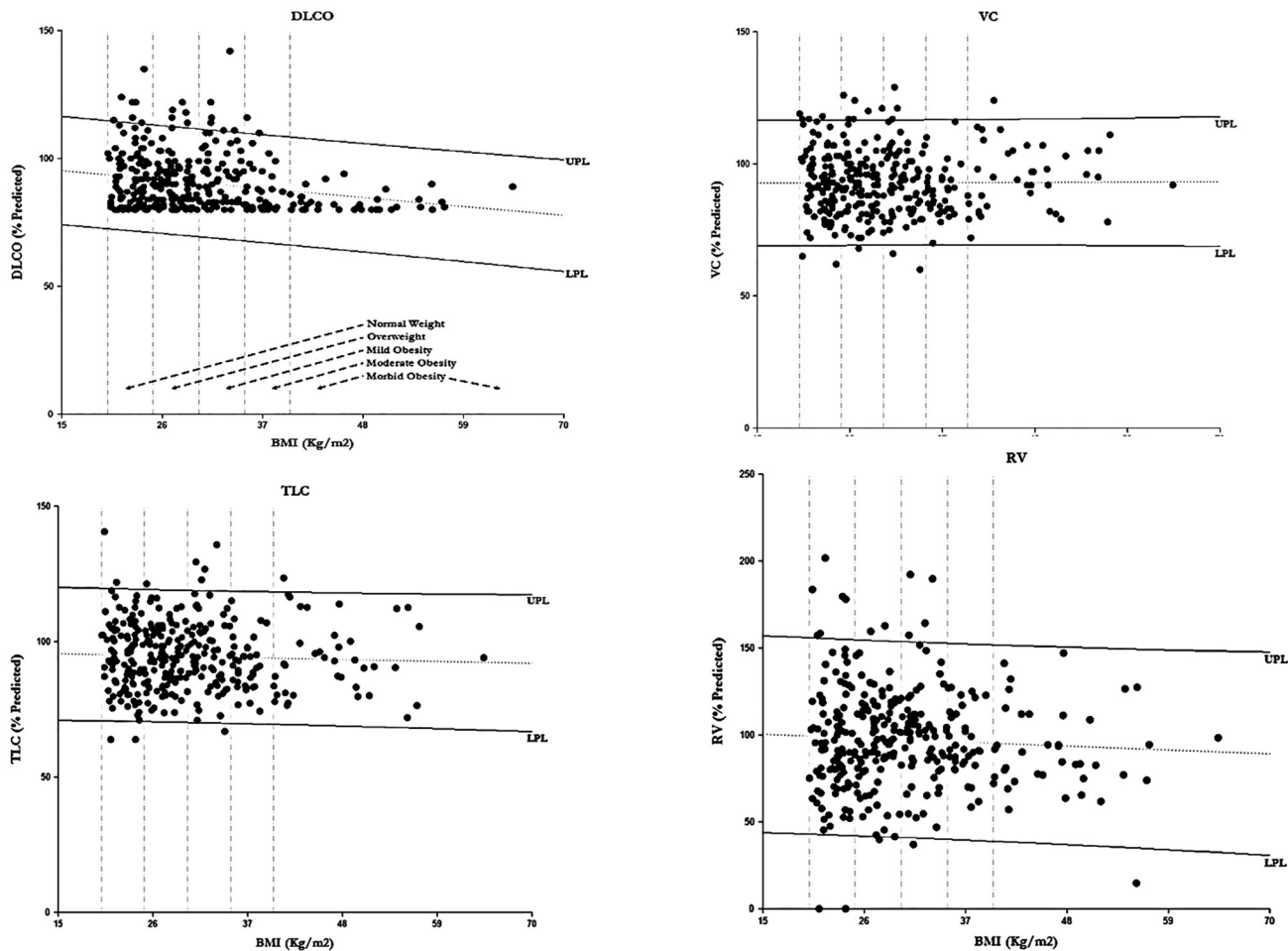
Fig 1. The linear regression between BMI and DlCO (top left), VC (top right), TLC (bottom left), and RV (bottom right). Linear regression between BMI and DLCO (P < .0001), VC (P = 0.895), TLC (P = 0.459) and RV (P = 0.301). The intervals represent the lower prediction limit (LPL) and the upper prediction limit (UPL) of the regression line. The vertical dash lines are the cut-points separating the BMI categories defined in the DLCO graph. The slopes of the linear regression for percentage of predicted values and BMI were -0.166 (DLCO), 0.005 (VC), -0.026 (TLC), and -0.016 (RV).

with BMI of 20Kg/m2, FRC and ERV were 90.70% and 84.20% respectively. While for a person with BMI 30Kg/m2, FRC and ERV are 79.41% and 50.92% respectively. Therefore, the FRC of a person with a BMI of 30 Kg/m^2 is only 88%; and ERV is only 60% of the values for a person with a BMI of 20Kg/m2. So, we see a drastic fall in FRC and ERV even when a person is at the borderline between overweight and mild obesity. The exponential decrease in FRC and ERV is similar to the findings of Jones et al. [11], however the absolute effect of BMI on FRC and ERV in their study was greater than in our patients. Similarly the absolute effect of BMI on FRC shown by Pelosi and colleagues [10] was much higher than Jones et al and our patients. However, Pelosi et al performed their studies on supine and anesthetized and Jones et al studied only white and ours are all black patients.

Some of the differences between the Jones and ours can be due to the race ethinicity difference in both studies. It is well known AAs have relatively longer lower extremities than did white subjects that in turn might influence BMI-fatness relations. Studies have shown, the same BMI categories are associated with lower levels of body fat in non-Hispanic blacks than in other race-ethnic groups [25–27] and health risks associated with a given BMI level may be

Table 2. Multiple Linear Regressions Modeling for the Association of BMI (kg/m²) and Lung Function.

Variables	Normal BMI = 20–24.9	Over Weight BMI = 25–29.9		Mild Obesity BMI = 30–34.9		Moderate Obesity BMI = 35–39.9		Severe Obesity BMI> 40	
		β (SE)	P value*	β (SE)	P value*	β (SE)	P value*	β (SE)	P value*
FEV₁/FVC	Ref	0.15 (0.77)	0.850	1.99 (0.88)	0.030	1.36 (1.09)	0.210	2.46 (1.05)	0.020
VC%	Ref	1.09 (1.54)	0.480	1.95 (1.76)	0.270	-4.44 (2.18)	0.040	-0.53 (2.09)	0.800
TLC%	Ref	1.20 (1.73)	0.490	2.30 (1.97)	0.240	-3.55 (2.43)	0.150	-1.55 (2.34)	0.510
RV%	Ref	1.35 (3.96)	0.730	3.28 (4.50)	0.470	-1.07 (5.57)	0.850	-3.26 (5.37)	0.550
FRC	Ref	-4.66 (2.23)	0.040	-8.79 (2.54)	<0.001	-16.24 (3.14)	<0.001	-19.76 (3.03)	<0.001
ERV	Ref	-14.09 (3.62)	<0.001	-27.4 (4.12)	<0.001	-38.61(5.09)	<0.001	-43.66 (4.91)	<0.001
DLCO	Ref	-2.68 (1.47)	0.070	1.05 (1.68)	0.530	-4.37 (2.08)	0.040	-9.18 (2.00)	<0.001
RV/TLC	Ref	0.02 (0.03)	0.390	-0.02 (0.03)	0.650	-0.01 (0.04)	0.940	0 .01 (.038)	0.900

Model: Lung Function = BMI + Age + Gender

Abbreviations: BMI = Body Mass Index; SE = Standard Error.

Coefficients are expressed as change in percent predicted lung function per unit BMI (kg/m²)

*P value less than 0.001 were deemed significant, after the Bonferroni adjustment

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lower for blacks than for whites [28–31], however, if this holds true for lung function merits further study using more accurate measures of body composition.

We found the effects of obesity on the extremes of lung volumes, at total lung capacity (TLC) and RV to be modest and none significant and VC was unaffected with increasing BMI. Many other studies report an association between increasing body weight and decreasing TLC [11,16,32], however, the changes are small, and TLC is usually maintained above the lower limit of normal, even in severe obesity [11,12,16,33,34]. Similarly the RV and the RV-to-TLC
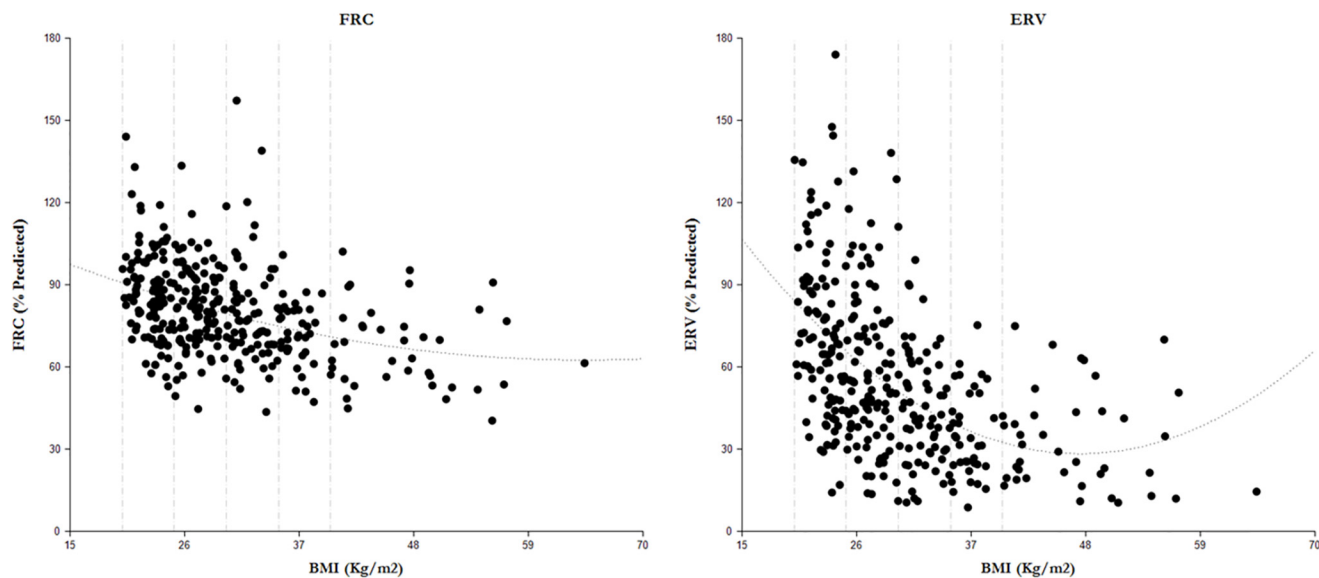

Fig 2. The polynomial regressions for FRC (left) and ERV (right). The r^2 values for FRC and ERV were 0.151 and 0.269, and the second order polynomial regression equations were as follows: FRC = 0.0143*(BMI)² –1.8448*(BMI) + 121.88 and ERV = 0.0742*(BMI)² –7.0384*(BMI) + 195.29 with p < 0.0001. The BMI classifications are the same as those in Fig 1.

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ratio remained normal as reported by others [16,35–37]. In the presence of well-preserved RV, the reduction in FRC can be explained by marked decrease in the ERV[11]. ERV can decline further in the supine position as the diaphragm assumes a higher position in the chest [38].

The observed reduction of FRC and ERV with increasing BMI has clinical implications. There is consistent evidence that, because the FRC is so low in obesity, closing capacity exceeds the FRC, and airway closure can occur within the tidal breaths [39–44] leading to maldistribution of ventilation and impaired gas exchange and hypoxemia [39,40]. In obese individuals, distribution of normal regional ventilation may be reversed [45–47]. Holley et al.[46] found that, in obese subjects with marked reductions of ERV to <20% predicted, ventilation was preferentially distributed to the upper zones of the lung, leaving the lower, dependent zones relatively under ventilated. The reduction in FRC and ERV in obesity is also associated tidal expiratory flow limitation (EFL), especially in the supine [44,48]. The presence of tidal EFL and/or airway closure can be a risk of peripheral airway injury [42] and this may be one of the potential mechanisms explaining the observed link between obesity and bronchial asthma [42,43,49] and the complaints of dyspnea that we often encounter in our obese patients in clinical practice.

The DLCO in this study remained with in normal limits even in the morbidly obese but decreased as BMI increased. The effect of obesity on the DLCO in many studies was reported to be normal, [11,14,50,51] even in morbid obesity [35]. However, some studies suggest it may be increased in extremely obese subjects [11,14,18] probably as a result of the increase in blood volume [11,14,35,52]. Even though the mean predicted values of subjects grouped by degree of obesity were within the normal limits the DLCO decreased as BMI increased. However the decrease was minimal and was seen in the extremes of obesity. The reductions in DLCO with extremes of obesity in this study can be due the effects of reduced FRC and ERV leading to a ventilation perfusion (V/Q) mismatch and micro atelectasis that occur as BMI increases but can also be due other undiagnosed cardiorespiratory illnesses such as pulmonary embolism and pulmonary hypertension which commonly occur in obesity and are known to reduce DLCO.

In summary in this study we confirm the most consistent finding s of the effects of obesity on lung volumes which is the reductions in FRC and ERV in black patients. We also report for the first time the absolute effects of increasing BMI on FRC and ERV is much lower in blacks when compared to the reported data in whites [11]. Contrary to the findings of any other study we also report a decreasing in DLCO with increases of BMI. However our study is not without limitations. First BMI is used as a proxy of obesity but BMI measurements lack the ability to differentiate between lean, fat mass and the distribution of fat which might have a deferential effect on lung volumes. Consequently, a higher BMI may not predict the physiological changes on the lung function universally. Studies have shown that dual energy X-ray absorptiometry (DEXA) had significantly better correlation with lung function impairment than anthropometric measurements [50]. In NHANES, however, BMI was found to be highly correlated with percentage body fat as measured by DEXA [27]. USA and international definitions of overweight and obesity for adults are also based on BMI. Standard BMI categories are well established and widely used and most studies that have examined the effects of obesity on lung function have used BMI. Moreover, this was a cross-sectional study and a cause and effect relationship between obesity and decreased lung function could not be inferred. Another limitation is that our entire patient population was black, and the findings may not translate to other ethnic groups.

Conclusion

With the epidemic of obesity, health care providers will often encounter obese patients to report greater respiratory symptoms requiring PFTs. Physiologically, increasing weight gain is associated with lung volume reduction even in the absence of specific respiratory disease, and may also exaggerate the effects of existing lung disease. Therefore it is important to consider the physiological changes associated with obesity when interpreting PFTs.

Supporting Information

S1 Dataset.
(XLSX)

S1 Fig. Effects of BMI on FEV1/FVC (top left), DLCO (top right), ERV (bottom left) and FRC (bottom right). The horizontal solid lines are significant differences between-group comparisons from ANOVA and post hoc test.
(TIF)

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Author Contributions

Conceived and designed the experiments: AM AVT. Performed the experiments: VP ANT WD ODP SH AVT. Analyzed the data: JN RS. Contributed reagents/materials/analysis tools: JN RS. Wrote the paper: AM SA. Critically reviewed the manuscript: AM SA JN RS ANT VP WD ODP SH AVT.

References

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL (2002) Prevalence and trends in obesity among US adults, 1999–2000. JAMA 288: 1723–1727. PMID: 12365955

2. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM (2006) Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 295: 1549–1555. PMID: 16595758

3. Ogden CL CM, Kit BK, Flegal KM (2013) Prevalence of obesity among adults: United States, 2011–2012. National Center for Health Statistics NCHS data brief. PMID: 24152742

4. Ogden CL, Carroll MD, Kit BK, Flegal KM (2012) Prevalence of obesity in the United States, 2009–2010. NCHS Data Brief 82: 1–8. PMID: 22617494

5. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M (2011) Health and economic burden of the projected obesity trends in the USA and the UK. Lancet 378: 815–825. doi: 10.1016/S0140-6736(11)60814-3 PMID: 21872750

6. Yap JC, Watson RA, Gilbey S, Pride NB (1995) Effects of posture on respiratory mechanics in obesity. J Appl Physiol (1985) 79: 1199–1205.

7. Faintuch J, Souza SAF, Valezi AC, Sant'Anna AF, Gama-Rodrigues JJ (2004) Pulmonary function and aerobic capacity in asymptomatic bariatric candidates with very severe morbid obesity. Revista do Hospital das Clínicas 59: 181–186. PMID: 15361982

8. Sebastian JC (2013) Respiratory physiology and pulmonary complications in obesity. Best Practice & Research Clinical Endocrinology & Metabolism 27: 157–161. doi: 10.1016/j.beem.2013.04.014 PMID: 23731878

9. Littleton SW (2012) Impact of obesity on respiratory function. Respirology 17: 43–49. doi: 10.1111/j.1440-1843.2011.02096.x PMID: 22040049

10. Pelosi P, Croci M, Ravagnan I, Tredici S, Pedoto A, Lissoni A, et al. (1998) The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. Anesth Analg 87: 654–660. PMID: 9728848

11. Jones RL, Nzekwu M-MU (2006) THe effects of body mass index on lung volumes*. CHEST Journal 130: 827–833.

12. Watson RA, Pride NB (2005) Postural changes in lung volumes and respiratory resistance in subjects with obesity. Journal of Applied Physiology 98: 512–517. PMID: 15475605

13. Sahebjami H, Gartside PS (1996) PUlmonary function in obese subjects with a normal fev1/fvc ratio. Chest 110: 1425–1429. PMID: 8989055

14. Ray CS, Sue DY, Bray G, Hansen JE, Wasserman K (1983) Effects of obesity on respiratory function. Am Rev Respir Dis 128: 501–506. PMID: 6614644

15. Schachter LM, Salome CM, Peat JK, Woolcock AJ (2001) Obesity is a risk for asthma and wheeze but not airway hyperresponsiveness. Thorax 56: 4–8. PMID: 11120896

16. Collins LC, Hoberty PD, Walker JF, Fletcher EC, Peiris AN (1995) The effect of body fat distribution on pulmonary function tests. Chest 107: 1298–1302. PMID: 7750322

17. Lazarus R, Sparrow D, Weiss ST (1997) Effects of obesity and fat distribution on ventilatory function: the normative aging study. Chest 111: 891–898. PMID: 9106566

18. Rubinstein I, Zamel N, DuBarry L, Hoffstein V (1990) Airflow limitation in morbidly obese, nonsmoking men. Annals of Internal Medicine 112: 828–832. PMID: 2378649

19. American Thoracic Society. (1995) Single-breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique—1995 update. Am J Respir Crit Care Med 152: 2185–2198. PMID: 8520796

20. American Thoracic Society. (1995) Standardization of Spirometry, 1994 Update. Am J Respir Crit Care Med 152: 1107–1136. PMID: 7663792

21. Expert Panel on the Identification, Evaluation, and Treatment of Overweight in Adults. (1998) Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: executive summary. Am J Clin Nutr 68: 899–917. PMID: 9771869

22. Hankinson JL, Odencrantz JR, Fedan KB (1999) Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 159: 179–187. PMID: 9872837

23. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. (2005) Standardisation of the measurement of lung volumes. Eur Respir J 26: 511–522. PMID: 16135736

24. Crapo RO, Morris AH, Clayton PD, Nixon CR (1982) Lung volumes in healthy nonsmoking adults. Bull Eur Physiopathol Respir 18: 419–425. PMID: 7074238

25. Aloia JF, Vaswani A, Ma R, Flaster E (1996) Body composition in normal black women: the four-compartment model. J Clin Endocrinol Metab 81: 2363–2369. PMID: 8964878

26. Evans EM, Rowe DA, Racette SB, Ross KM, McAuley E (2006) Is the current BMI obesity classification appropriate for black and white postmenopausal women? Int J Obes 30: 837–843.

27. Flegal KM, Shepherd JA, Looker AC, Graubard BI, Borrud LG, Ogden CL, et al. (2009) Comparisons of percentage body fat, body mass index, waist circumference, and waist-stature ratio in adults. The American Journal of Clinical Nutrition 89: 500–508. doi: 10.3945/ajcn.2008.26847 PMID: 19116329

28. Aloia JF, Vaswani A, Mikhail M, Flaster ER (1999) Body composition by dual-energy X-ray absorptiometry in black compared with white women. Osteoporos Int 10: 114–119. PMID: 10501790

29. Stevens J, Plankey MW, Williamson DF, Thun MJ, Rust PF, Palesch Y, et al. (1998) The body mass index-mortality relationship in white and African American women. Obes Res 6: 268–277. PMID: 9688103

30. Abell JE, Egan BM, Wilson PW, Lipsitz S, Woolson RF, Lackland DT (2007) Age and race impact the association between BMI and CVD mortality in women. Public Health Rep 122: 507–512. PMID: 17639654

31. Abell JE, Egan BM, Wilson PW, Lipsitz S, Woolson RF, Lackland DT (2008) Differences in cardiovascular disease mortality associated with body mass between Black and White persons. Am J Public Health 98: 63–66. PMID: 18048799

32. Ray CS, Sue DY, Bray G, Hansen JE, Wasserman K (1983) Effects of obesity on respiratory function. American Review of Respiratory Disease 128: 501–506. PMID: 6614644

33. Watson RA, Pride NB, Thomas EL, Fitzpatrick J, Durighel G, McCarthy J, et al. (2010) Reduction of total lung capacity in obese men: Comparison of total intrathoracic and gas volumes. Journal of Applied Physiology 108: 1605–1612. doi: 10.1152/japplphysiol.01267.2009 PMID: 20299612

34. Guenette JA, Jensen D, O'Donnell DE (2010) Respiratory function and the obesity paradox. Current Opinion in Clinical Nutrition and Metabolic Care 13: 618–624. doi: 10.1097/MCO.0b013e32833e3453 PMID: 20975350

35. Biring MS, Lewis MI, Liu JT, Mohsenifar Z (1999) Pulmonary physiologic changes of morbid obesity. Am J Med Sci 318: 293–297. PMID: 10555090

36. Sampson MG, Grassino AE (1983) Load compensation in obese patients during quiet tidal breathing. J Appl Physiol Respir Environ Exerc Physiol 55: 1269–1276. PMID: 6629961

37. Watson RA, Pride NB (1985) Postural changes in lung volumes and respiratory resistance in subjects with obesity. J Appl Physiol 98: 512–517.

38. Parameswaran K, Todd DC, Soth M (2006) Altered respiratory physiology in obesity. Canadian Respiratory Journal 13: 203–210. PMID: 16779465

39. Hedenstierna G, Santesson J, Norlander O (1976) Airway closure and distribution of inspired gas in the extremely obese, breathing spontaneously and during anaesthesia with intermittent positive pressure ventilation. Acta Anaesthesiol Scand 20: 334–342. PMID: 793285

40. Farebrother MJ, McHardy GJ, Munro JF (1974) Relation between pulmonary gas exchange and closing volume before and after substantial weight loss in obese subjects. Br Med J 3: 391–393. PMID: 4854081

41. Hakala K, Mustajoki P, Aittomaki J, Sovijarvi AR (1995) Effect of weight loss and body position on pulmonary function and gas exchange abnormalities in morbid obesity. Int J Obes Relat Metab Disord 19: 343–346. PMID: 7647827

42. Milic-Emili J, Torchio R, D'Angelo E (2007) Closing volume: a reappraisal (1967–2007). Eur J Appl Physiol 99: 567–583. PMID: 17237952

43. Mahadev S, Farah CS, King GG, Salome CM (2013) Obesity, expiratory flow limitation and asthma symptoms. Pulm Pharmacol Ther 26: 438–443. doi: 10.1016/j.pupt.2012.05.004 PMID: 22609068

44. Ferretti A, Giampiccolo P, Cavalli A, Milic-Emili J, Tantucci C (2001) Expiratory flow limitation and orthopnea in massively obese subjects. Chest 119: 1401–1408. PMID: 11348945

45. Demedts M (1980) Regional distribution of lung volumes and of gas inspired at residual volume: influence of age, body weight and posture. Bull Eur Physiopathol Respir 16: 271–285. PMID: 7397438

46. Holley HS, Milic-Emili J, Becklake MR, Bates DV (1967) Regional distribution of pulmonary ventilation and perfusion in obesity. J Clin Invest 46: 475–481. PMID: 6021200

47. Hurewitz AN, Susskind H, Harold WH (1985) Obesity alters regional ventilation in lateral decubitus position. J Appl Physiol (1985) 59: 774–783.

48. Pankow W, Podszus T, Gutheil T, Penzel T, Peter J, Von Wichert P (1998) Expiratory flow limitation and intrinsic positive end-expiratory pressure in obesity. J Appl Physiol (1985) 85: 1236–1243.

49. Beuther DA, Weiss ST, Sutherland ER (2006) Obesity and asthma. Am J Respir Crit Care Med 174: 112–119. PMID: 16627866

50. Sutherland TJ, Goulding A, Grant AM, Cowan JO, Williamson A,Williams SM, et al. (2008) The effect of adiposity measured by dual-energy X-ray absorptiometry on lung function. Eur Respir J 32: 85–91. doi: 10.1183/09031936.00112407 PMID: 18353855

51. Sharp JT, Henry JP, Sweany SK, Meadows WR, Pietras RJ (1964) THE TOTAL WORK OF BREATHING IN NORMAL AND OBESE MEN. The Journal of clinical investigation 43: 728–739. PMID: 14149924

52. Zavorsky GS, Hoffman SL (2008) Pulmonary gas exchange in the morbidly obese. Obesity Reviews 9: 326–339. doi: 10.1111/j.1467-789X.2008.00471.x PMID: 18331421