The association of two different measures of body habitus with lung function: A population-based study

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Summary
Background: The relation between obesity and respiratory function is complex and may be confounded by other components of body habitus such as lean muscle mass. The present study aimed to explore the association between two different measures of body habitus (Body Mass Index — BMI, and lean muscle mass) with lung function.
Methods: We used data from 2663 adults who participated in a community-based survey and provided measures of lung function, BMI and 24-h urinary creatinine excretion to quantify lean muscle mass.
Results: There was a positive linear association between 24-h urinary creatinine excretion and lung function as measured by both Forced Expiratory Volume in 1 s (FEV1) and Forced Vital Capacity. A one standard deviation increment in 24-h urinary creatinine excretion was associated with a 45 ml increase in FEV1 (95% confidence intervals CI: +16 to +73). There was no linear association between body mass index and lung function although those in the extreme categories of BMI had lower measures of lung function compared to a reference group with a BMI of 20–24.9 kg/m². For FEV1, BMI less than 20 kg/m² was 122 ml lower (95% CI: −234 to −10); BMI greater than 30 kg/m² was 85 ml lower (95% CI: −160 to −9).
Conclusions: Lean muscle mass and BMI have very different associations with lung function that have implications for understanding the relationship between body habitus and lung function.

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Body mass index and lung function 1897

Introduction

Obesity is an increasingly important public health challenge which impacts on a variety of respiratory diseases. A commonly used epidemiological measure of obesity is body mass index (BMI) which is easily measured in large populations. However, the cross-sectional evidence on the association between obesity as measured by BMI and lung function is complex, probably partly as a consequence of the observation of data from heterogeneous populations. A review stated that there is an inverse relationship between body mass index and FEV1, and other investigators have reported an inverted U shaped relation between these variables using population-based data. A recent study reported that in individuals with a BMI less than 25 kg/m², FEV1 is positively associated with BMI and the authors speculated that this may be a consequence of confounding by muscle mass, a variable that may account for the differing associations reported between BMI and lung function in other study populations. Bone-free lean muscle mass is positively associated with lung function and Forced Vital Capacity (FVC) is positively associated with fat free mass as measured by skinfold thickness measurements and also with measures of muscular strength. To date there have been no population-based studies of measures of total lean muscle mass and lung function.

Using 24-h urinary creatinine excretion, a simple validated biochemical marker of total skeletal muscle mass, we have investigated the relation between total body muscle mass and lung function using data from a randomly selected population and compared this with the associations between BMI and lung function.

Patients and methods

The participants are drawn from a previously reported randomly selected community-based population of 2633 adults aged 18-70 living in Nottingham first studied in 1991 that had a participation rate of 48–59% eligible individuals. The study was approved by the Nottingham City Hospital Ethics Committee.

In 1991 participants were asked to abstain from inhaled bronchodilators for 4 h and from oral bronchodilators for 8 h before their study visit. Subjects completed a computer-administered lifestyle questionnaire that included a semi-quantitative dietary questionnaire (DietQ, Tinuviel Software, Warrington, Cheshire, UK). Forced Expiratory Volume in 1 s (FEV1) and Forced Vital Capacity (FVC) were then measured using a dry bellows spirometer (Vitalograph, Buckingham, UK), taking the best of three technically satisfactory manoeuvres with the subject seated. Data were collected on a variety of anthropometric measures including height and weight, and a blood sample and 24-h urine collections obtained from those who consented to provide specimens. Written instructions were provided to optimise the accuracy of the 24-h urine collection, and the self-report of the participant used to verify the accuracy of 24-h urine collection. If the self-report indicated that the urine sample was sub-optimal, then the times of urine collection were used to generate a corrected measure of 24-h urinary creatinine collection. After venesection, serum samples were separated by centrifugation, within 15 min and stored at –80° centigrade. The 24-h urinary creatinine excretion was calculated by weighing returned specimens to estimate volume, and an aliquot was separated and sent for estimation of creatinine concentrations using a reaction rate assay on an Olympus AU5000 analyser. Serum CRP was measured in 2005 using a highly sensitive automated immunoturbidimetric assay on an Olympus AU5400 analyser.

Smoking status was defined in three categories; current smoker (those who had smoked within one month of the study in 1991), ex-smoker and never smokers. The number of pack-years smoked was estimated for subjects from their reported age at starting smoking, and the usual amount smoked during this period.

We analysed the cross-sectional association between both 24-h urinary creatinine excretion and BMI with lung function using multiple linear regression with adjustment for a priori confounding factors of age, sex, height, smoking status and cigarette pack-years smoked. Linearity of the data was tested using the likelihood ratio test; if the association was linear, the final model presented the exposure as a continuous variable and if the association was non-linear a categorical variable was used in analyses. As the associations between BMI and lung function were non-linear, BMI was coded as a categorical variable (BMI <20 kg/m², 20–24.9 kg/m², 25–29.9 kg/m² and ≥30 kg/m²). Potential confounding factors including vitamin C, magnesium, protein intake and serum C-reactive protein were investigated by adding them to the a priori model and if the size of effect changed by 10% or more they were considered to be a potential confounding factor and retained in the model. Similarly, the impact of adding age as a categorical variable and higher order variables such as age squared and height squared on the relationships observed were also explored and retained if the size of effect changed by 10% or more. As the association with lung function was linear, the 24-h urinary creatinine excretion data are presented in terms of change in lung function per standard deviation increase in 24-h urinary creatinine excretion. We used the same model established for 24-h creatinine excretion to explore the association of BMI with both FEV1 and FVC independently, modelling BMI as a categorical variable. The association of both 24-h urinary creatinine excretion and BMI with lung function is presented with and without adjustment for the alternative measure of body habitus. Effect modification by gender as defined by an interactive term with a p-value of 0.10 or less was explored and absent, so the data are presented for the complete study population. The analyses were carried out using STATA version 11 (Stata Corporation, College Station, Texas).

Results

Of the 2633 individuals who participated in the study, 2614 (99%) provided data on BMI, and 1702 (65%) provided 24-h urinary samples. The mean age of those who participated was 44.4 years (standard deviation sd, 13.6), 50% were male and 23% were current smokers (Table 1). The mean 24-h urine volume was 2.13 L (sd 0.76) and the mean uncorrected 24-h urinary creatinine excretion was 13.52 mmol/day (sd 4.25) and the mean corrected 24-h urinary creatinine excretion was 13.88 mmol/day (sd 4.48). Those who
provided 24-h urinary samples were older and had a lower prevalence of current cigarette smoking than those who did not provide a urinary sample (Table 1).

There was a linear association between FEV₁ and uncorrected 24-h urinary creatinine excretion, with a standard deviation increment in 24-h urinary creatinine excretion being associated with an increase of 45 ml (95% confidence intervals CI: 16 to 73) after adjusting for sex, age, height, smoking status and smoking pack-years. Similar associations were also seen between Forced Vital Capacity and 24-h urinary excretion, with a standard deviation increment in 24-h urinary creatinine excretion being associated with an increase of 39 ml (95% confidence intervals CI: 4 to 75) after adjusting for the same covariates. The size of association observed increased after adjustment for BMI as a covariate (Table 2). Repeating analyses using the 24-h urinary creatinine data corrected for sample collection irregularities made no appreciable difference to these associations. No association was observed between 24-h urinary creatinine excretion and the FEV₁:FVC ratio.

The associations between FEV₁ and FVC and BMI were non-linear and are presented in categories in Table 2 for the total study population and also stratified by gender as the association between body mass index and FEV₁ (p = 0.08) and FVC (p < 0.01) did demonstrate some evidence of an interaction with gender. Using a BMI of 20 up to 24.9 kg/m² as a reference group, those with a BMI of less than 20 kg/m² had a lower lung function with values of 169 ml (95% CI: 266 to 72) and 224 ml (95% CI: 336 to 114) for FEV₁ and FVC respectively. Those with a BMI of equal to or greater than 30 kg/m² had a significantly reduced FVC compared to the reference category (130 ml, 95% CI: 206 to 54), but no significant decrease in FEV₁ (48 ml, 95% CI: 114 to 19). These associations were appreciably altered after adjustment for 24-h urinary creatinine excretion with a decreased size of association with lung function for those with a BMI less than 20 kg/m² and an increased size of association for those with a BMI greater than 25 kg/m² (Table 2). There was a linear association between BMI and the FEV₁:FVC ratio, with a one unit increase in BMI being associated with a decrease of 0.16% (95% CI: 0.09 to 0.24).

There was no confounding of these associations by intake of protein, vitamin C or magnesium or by serum C-reactive protein levels. There was no effect modification of the associations between lung function and 24-h urinary creatinine excretion by gender, but the association between body mass index and FEV₁ (p = 0.08) and FVC (p < 0.01) did demonstrate some evidence of an interaction with gender.

### Discussion

In this study, we report for the first time that 24-h urinary creatinine excretion is associated with higher FEV₁ and FVC cross-sectionally, in a randomly selected population after adjusting for confounding factors including BMI. This observation supports the hypothesis that total lean muscle mass is positively associated with lung function and is
BMI had lower FEV1 and FVC and those with a high BMI had a potential linear association with BMI, although those with a low BMI had lower FVC and those with a high BMI had a lower FVC compared to the reference group.

The population studied was a random sample from the electoral register of a Local Authority Area in Nottingham, and is thus likely to be a representative sample of the general population. The physiological measurements of lung function and the biological samples were collected in a standardised manner, and neither participants nor those involved in the data collection were aware of the hypothesis being tested. We were able to adjust for protein, vitamin C and magnesium intake and serum CRP as markers of nutritional depletion and systemic inflammation, both of which are considered possible causes of the skeletal muscle dysfunction observed in COPD.13 However, we are unable to exclude the possibility that the measurement error in the dietary measurements by food frequency questionnaires may have resulted in an incomplete adjustment for these dietary constituents.

There has been much interest in the association between body habitus and lung function as this provides an insight into the potential impact of developmental and environmental factors on lung function and hence may increase understanding of reversible factors amenable to interventions that...
aim to optimise lung function. The availability of data on urinary creatinine excretion provides an opportunity to assess the association between lean muscle mass and lung function in a large epidemiological study, and to compare this with BMI, which is regularly used as a measure of body habitus in population-based studies. Creatine in muscle gradually degrades to creatinine, which is then excreted in the urine, and the excretion rate of creatinine is considered to be proportional to total lean body mass. This measure has been validated against a variety of non-radiological measures of lean muscle mass with correlation coefficients that vary from 0.63 to 0.99. Other factors in addition to total creatinine excretion is thus probably one of the best available methods to rank total lean body mass in large epidemiological studies without exposing individuals to unnecessary radiation. In addition, 24-h urinary excretion has been reported to have good repeatability with a coefficient of variation of 9.3%. Other factors in addition to total body muscle mass may also influence 24-h urinary creatinine excretion, particularly age, gender, protein intake and renal function. Although we were able to adjust for the first three factors as part of the analysis, we are unable to exclude the possibility that renal function may be an unadjusted confounding factor in our analysis as we did not measure our study participants’ renal function. However, this seems unlikely as our population had a mean age of 46 years, and hence we would anticipate that impaired renal function would have a low prevalence that is probably no higher than 7% and hence unlikely to confound our observations.

Our cross-sectional data do not permit temporal relationships to be considered, and therefore it is possible that higher lung function may lead to an elevated total muscle mass possibly by increasing the ability to exercise. This is certainly plausible as both lung function and the body musculature both develop in parallel during childhood and adolescence. The biological mechanisms that underpin these observations that total muscle mass is positively associated with lung function are poorly understood. Possible candidate explanations include the role of intercostal muscles, or the diaphragm in developing and maintaining lung function, or early nutrition and growth which has consistently been associated with higher lung function. Chronic respiratory diseases and in particular COPD are associated with reduced muscle mass and strength when the primary insult is to the lungs and hence the reduced muscle bulk and function are likely to be a secondary phenomenon.

Our data are consistent with the observation that in individuals with a BMI less than 25 kg/m², FEV₁ is positively associated with BMI⁹ as this may be a consequence of confounding by muscle mass in adults who are not overweight.

In summary, we report the positive linear association between total lean muscle mass and lung function and non-linear associations between BMI and lung function in a population-based study of adults. These observations may be of relevance to further understanding the complex associations between measures of body habitus and lung function which represent the cumulative effects of multiple exposures over the course of a lifetime.

Conflict of interest
None.

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References