

# Visceral adipose tissue level, as estimated by the bioimpedance analysis method, is associated with impaired lung function

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## ABSTRACT

**Aims/Introduction:** It has been reported that metabolic syndrome is associated with impaired lung function, and abdominal obesity is regarded as the most important determinant of this association. We evaluated the association between a component of metabolic syndrome, indices of body composition, including the total adipose tissue content, lean bodyweight and visceral adipose tissue content, as assessed by bioimpedance analysis, and lung function.

**Materials and Methods:** A total of 516 participants responded to our questionnaire to determine the smoking status and history of past diseases. Waist circumference, height, bodyweight, percent forced expiratory volume in 1 s (%FEV1) and percent forced vital capacity (%FVC) were measured. Fasting blood samples were obtained to determine the serum levels of high-density lipoprotein and triglyceride, and also the blood glucose. The body composition, including the total adipose tissue content and lean bodyweight, was measured, and the visceral adipose tissue content was estimated as the visceral adipose tissue level, by the bioimpedance analysis method.

**Results:** Waist circumference, estimated visceral adipose tissue level and blood pressure were significantly associated with the %FEV1, and the serum high-density lipoprotein cholesterol was significantly associated with the %FVC in men, after adjustment for age, smoking history, and past histories of bronchial asthma and ischemic heart disease. However, this association was not detected in women.

**Conclusions:** We found an association between the visceral adipose tissue level as estimated by the bioimpedance analysis method and lung function. (*J Diabetes Invest*, doi: 10.1111/j.2040-1124.2011.00189.x, 2012)

**KEY WORDS:** Abdominal obesity, Metabolic syndrome

## INTRODUCTION

There has been increasing interest in the association between metabolic syndrome and lung function<sup>1,2</sup>. Metabolic syndrome comprises a cluster of cardiovascular risk factors: abdominal obesity, hypertension, dyslipidemia and impaired glucose tolerance<sup>3</sup>. Furthermore, abdominal obesity has been reported as a key determinant of the association between metabolic syndrome and lung function<sup>4</sup>. Abdominal obesity is determined by the deposition of subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT). VAT is considered to be more strongly

related to inflammation and insulin resistance than SAT<sup>5,6</sup>. However, the association between VAT and lung function has not yet been fully elucidated.

The standard method used for the assessment of VAT is measurement of the VAT area on computed tomography (CT) images. However, this method is not cost-effective, and the associated exposure to radiation is problematic. The Tanita BC303 (Tanita Corp., Tokyo, Japan), a body composition analyzer, measures the total adipose tissue content (TAT) and lean bodyweight (LBW) by the bioimpedance analysis (BIA) method, based on the difference in electric resistance between fat and other tissues<sup>7</sup>. Furthermore, the VAT area is estimated as the VAT level, using a multiple regression equation including age, sex, anthropometry data and body composition<sup>8</sup>. The aim of the present study was to evaluate the association between lung function and VAT level measured using Tanita BC303 in both men and women.

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## METHODS

### Participants

We invited residents aged 45 years-of-age or older to participate in the study in Jimbo, a town of Toyama city with a population of 5007, and enrolled 2465 people aged 45 years or older. The study was carried out with the approval of the Ethics Committee of the University of Toyama (Ethics Committee, University of Toyama), and all the participants were assured that their personal health information would be kept confidential and secure.

### Questionnaire

We asked the participants to complete a questionnaire handed to them to determine their smoking status and history of bronchial asthma and ischemic heart disease. Bronchial asthma was defined as a positive answer to 'Have you had asthma?', and history of ischemic heart disease was assessed by the question 'Have you had angina pectoris or myocardial infarction?'

### Anthropometric and Bioimpedance Analysis

Waist circumference (WC) was measured by trained nurses at the level of the umbilicus at the end of normal expiration using a non-elastic measuring tape. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared ( $\text{kg}/\text{m}^2$ ). Blood pressure (BP) was measured with the participants in the seated position. The TAT, LBW and VAT level were measured by leg-to-leg impedance using TANITA BC303.

### Blood Samples

Fasting blood samples were obtained from each of the participants to measure the serum levels of high-density lipoprotein (HDL) cholesterol and triglyceride, and also the blood glucose.

### Lung Function Test

Spirometry was completed as recommended by the American Thoracic Society/European Respiratory Society<sup>9</sup>. All participants repeated the required maneuvers three times while wearing nose clips. The highest of three measured forced expiratory volume in 1 s (FEV1) values was used for the analysis.

### Statistical Analysis

Data are presented as mean  $\pm$  SD, unless indicated otherwise. Analyses were carried out using a statistical software package (JMP, version 7.0.2; SAS Institute, Cary, NC, USA). A multiple linear regression analysis was used to assess the relationship between the lung function parameters and the variables under examination after adjustment for age, smoking history, history of bronchial asthma and history of ischemic heart disease, separately in men and women. In addition, the participants were divided into two groups based on the WC <90 cm and  $\geq$ 90 cm in men, and <80 cm and  $\geq$ 80 cm in women, in accordance with the statement of International Diabetes Federation<sup>3</sup> and the median VAT level, in order to assess the relationship to lung function by two-way ANOVA. *P*-values of <0.05 were considered to show statistical significance.

## RESULTS

Table 1 shows the characteristics of the participants. The survey examination was completed by 516 participants. Men showed a higher VAT level, a higher LBW and a lower percentage of TAT than women. However, there was no significant difference in the BMI or WC between the men and women.

Table 2 shows the association between lung function and the individual components of metabolic syndrome and body composition indices. The WC, systolic BP, diastolic BP and VAT

**Table 1** | Characteristics of the participants

<i>n</i>	Total 516	Men 214	Women 302	<i>P</i> -value
Age (years)	65.0 $\pm$ 9.5	65.2 $\pm$ 9.0	64.9 $\pm$ 9.9	0.66
%FEV1	96.4 $\pm$ 21.8	92.4 $\pm$ 18.1	99.2 $\pm$ 23.8	0.0005
%FVC	106.6 $\pm$ 17.7	105.6 $\pm$ 17.3	107.4 $\pm$ 18.0	0.27
BMI	23.3 $\pm$ 2.7	23.3 $\pm$ 2.5	23.2 $\pm$ 2.8	0.75
WC	83.6 $\pm$ 8.4	83.2 $\pm$ 7.3	83.8 $\pm$ 9.0	0.37
Systolic BP	134.3 $\pm$ 20.9	135.6 $\pm$ 20.5	133.5 $\pm$ 21.1	0.26
Diastolic BP	74.8 $\pm$ 11.7	76.9 $\pm$ 12.1	73.4 $\pm$ 11.3	0.0007
HDL	58.7 $\pm$ 13.4	55.8 $\pm$ 13.1	60.7 $\pm$ 13.2	<0.0001
Triglyceride	95.5 (70.3–133)	103 (75–140.3)	93 (69–129)	0.023
Fasting blood glucose	96.0 (90–103)	98 (92–108)	94.5 (89–100.3)	<0.0001
VAT level	9.4 $\pm$ 3.8	12.8 $\pm$ 3.1	6.9 $\pm$ 1.9	<0.0001
TAT	28.0 $\pm$ 7.2	21.8 $\pm$ 4.9	32.4 $\pm$ 5.0	<0.0001
LBW	3888.9 $\pm$ 765.4	4635.8 $\pm$ 503.3	3359.6 $\pm$ 381.4	<0.0001
Smoking history	148 (28.7%)	116 (54.2%)	32.0 (10.6%)	<0.0001
Bronchial asthma	30 (5.8%)	15 (7.0%)	15 (5.0%)	0.35
Ischemic heart disease	19 (3.7%)	10 (4.7%)	9 (3.0%)	0.35

BMI, body mass index; BP, blood pressure; %FEV1, percent forced expiratory volume in 1 s; %FVC, percent forced vital capacity; HDL, serum high-density lipoprotein; LBW, lean body weight; TAT, percentage of the total adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.

**Table 2** | Standardized partial regression coefficient between lung function and each variable after adjustment for age, smoking history and past history

	%FEV1		%FVC	
	Men	Women	Men	Women
WC	-0.18**	-0.02	-0.12	0.08
Systolic BP	-0.18**	-0.06	-0.18**	-0.11
Diastolic BP	-0.14*	0.04	-0.09	0.04
HDL	0.12	-0.01	0.15*	-0.01
Triglyceride	-0.001	0.07	-0.07	0.08
Fasting blood glucose	-0.04	-0.09	-0.08	-0.07
VAT level	-0.15*	0.07	-0.11	0.10
TAT	-0.11	-0.04	-0.09	0.03
LBW	-0.10	0.07	-0.02	0.23**

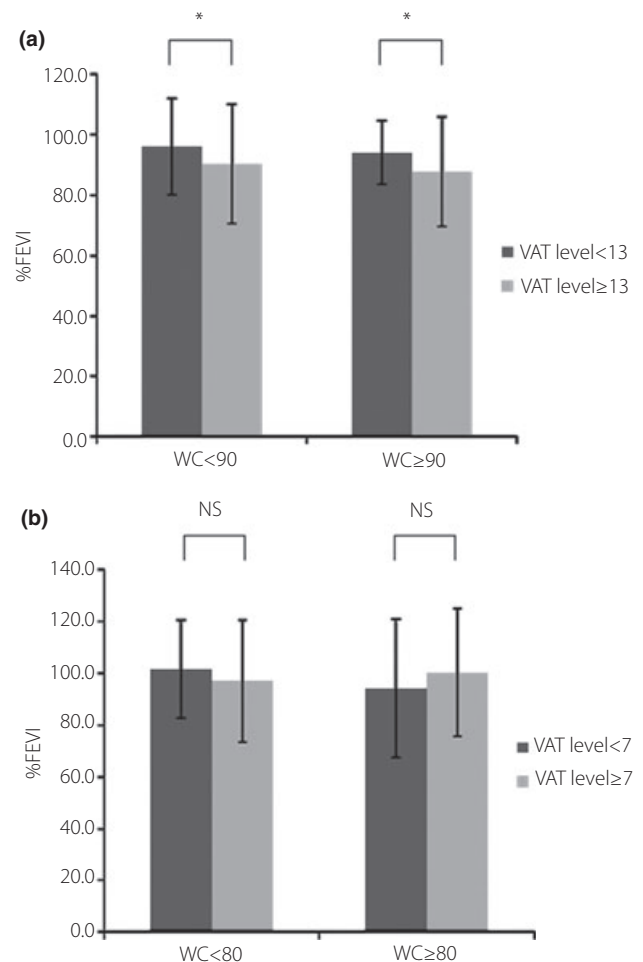
\* $P < 0.05$ , \*\* $P < 0.01$ . BP, blood pressure; %FEV1, percent forced expiratory volume in 1 s; %FVC, percent forced vital capacity; HDL, serum high-density lipoprotein; LBW, lean body weight; TAT, percentage of the total adipose tissue; VAT, visceral adipose tissue; WC, waist circumference.

level were identified as being associated with the %FEV1, and the serum HDL was identified as being associated with the %FVC, although only in men. However, neither the LBW nor the TAT was associated with lung function. In women, no significant association was detected between lung function and the components of metabolic syndrome, TAT or the VAT level. However, the LBW was associated with the %FVC. We analyzed the association between lung function and VAT level after excluding subjects who had a positive smoking history and a history of bronchial asthma using Pearson's correlation coefficient. In men ( $n = 90$ ), VAT level was significantly associated with %FEV1 ( $r = -0.24$ ,  $P = 0.021$ ) and %FVC ( $r = -0.33$ ,  $P = 0.0016$ ). In women ( $n = 257$ ), VAT level was not associated with %FEV1 ( $r = 0.08$ ,  $P = 0.21$ ) and %FVC ( $r = -0.002$ ,  $P = 0.97$ ).

Figure 1 shows the association among the %FEV1, WC and the VAT level. Participants were divided into two groups according to WC, and each group was again subdivided based on the median VAT level (median VAT 13 in men and seven in women). Differences in the WC and VAT levels were analyzed by two-way ANOVA. In men, higher VAT levels were significantly associated with lower %FEV1 values in each of the groups divided by the WC. No effect of WC or interaction was detected. In women, there was no significant effect of the VAT level or WC, and no interaction.

## DISCUSSION

The present study showed a significant association between the %FEV1 and WC and VAT level in men using the BIA method. It has been reported that deposition of adipose tissue or visceral adipose tissue measured by CT scan is associated with impaired lung function<sup>10–13</sup>. In view of non-invasiveness and simplicity, the BIA method is favorable, and the VAT level estimated by



**Figure 1** | Percent forced expiratory volume in 1 s (%FEV1) for different waist circumference (WC) and visceral adipose tissue (VAT) levels was analyzed by two-way ANOVA. \* $P < 0.05$ , difference due to VAT level, two-way ANOVA.

the BIA method could be a surrogate marker of VAT area measured by CT or magnetic resonance imaging in clinical settings or a population survey. Furthermore, higher VAT levels were associated with lower %FEV1 values in both groups divided by the WC ( $\geq 90$  cm and  $< 90$  cm). However, neither the WC nor the VAT level was associated with the lung function in women.

Body mass index, adipose tissue and abdominal height have been reported to be associated with impaired lung function<sup>10–16</sup>. It has been suggested that abdominal obesity mechanically influences the lung volume, peripheral airway size and respiratory muscle weakness<sup>10–15</sup>. However, adipose tissue has been shown to act as an endocrine organ and influences systemic inflammation<sup>6,17</sup>. Furthermore, systemic inflammation has been shown to be associated with a decline of lung function<sup>14,18</sup>. It has been suggested that systemic inflammation associated with deposition of adipose tissue might influence lung function. A previous study investigated participants with greater BMI, and showed the association between deposition of adipose tissue and

restrictive or mixed dysfunction<sup>10–13</sup>. In the present study, VAT level of participants was shown to be associated with %FEV1, but not with %FVC. This discrepancy might be attributed to the difference of BMI. Indeed, participants in the present study had a relatively lower BMI and WC than participants in the previous study. We speculate that there was a relatively minor effect of mechanical oppression of the chest wall and diaphragm as a result of the lower BMI of participants.

Although both VAT and SAT are associated with increased concentrations of inflammatory cytokines, the results of multivariate analyses have shown that VAT is more important<sup>6</sup>. We evaluated the association between the VAT level and the %FEV1 in two subgroups divided by the WC. A negative relationship was noted in each subgroup between the VAT level and the %FEV1, suggesting that VAT might be the key determinant of the association between abdominal obesity and lung function.

The association between HDL cholesterol level and lung function has been reported<sup>1,2,19</sup>, which is consistent with the present findings. However, the mechanism remains unclear. Heresi *et al.* investigated the effect of HDL cholesterol level on outcome in patients with pulmonary arterial hypertension and showed that HDL cholesterol was a prognostic factor for better survival. The authors hypothesized that the anti-oxidant and anti-inflammatory property of HDL cholesterol was involved<sup>20</sup>. These effects of HDL cholesterol are possibly associated with lung function.

Lean bodyweight, evaluated by BIA or dual energy X-ray absorptiometry, has been reported to be associated with lung function<sup>10,11,13</sup>, which was consistent with the present findings. Santana *et al.*<sup>10</sup> suggested that LBW was associated with respiratory muscle strength and affected lung function.

In the present study, we found differences in the association between lung function and VAT level, WC, HDL cholesterol, and LBW between men and women. The sex difference in the relationship between components of metabolic syndrome (including glucose level, blood pressure and HDL cholesterol level) and lung function have been reported<sup>19</sup>. There are morphological differences in the lungs between the two sexes, including the lung size, airway diameter and diffusion surface. Furthermore, sex hormones, including estrogen and progesterone, can influence ventilation and other pulmonary functions<sup>21</sup>. It would be difficult to exclude the possibility that these factors might have affected the results in the present study. In addition to these factors, the difference in VAT level, HDL cholesterol level and LBW between the sexes, or the issue of statistical power might be involved. It has been shown that women have a different pattern of fat distribution and a smaller VAT volume<sup>22</sup>. In the present study, women showed a smaller VAT level. If it were considered that the deposition of VAT influences pulmonary function, the absence of any association between the WC or VAT level with pulmonary function in women might be explained by the lower deposition of VAT in women.

The present study showed an increase in systolic blood pressure was associated with a decline of %FEV and %FVC in men.

These findings are in line with previous observations, although the mechanism is still unclear. Schnabel *et al.*<sup>23</sup> reported an association between both high blood pressure and the use of beta-blockers with impaired lung function. We did not investigate the use of antihypertensive agents, and cannot precisely explain the mechanism underlying the association between the systolic blood pressure and lung function in men. However, the influence of beta-blockers on lung function cannot be excluded.

The present study had several limitations. First, we could not individually assess the influence of VAT and SAT on lung function, because we did not quantify SAT.

Second, there is a problem with the validity of the BIA method in assessing VAT. Several types of body composition analyzers using the BIA method have been developed, and the reported correlation coefficients between the estimated VAT by the BIA method and the VAT area measured by CT ranged from 0.6 to 0.9<sup>24–27</sup>. However, the VAT level estimated by the Tanita BC303 is reported to be correlated to the VAT area measured by CT (correlation coefficient 0.83)<sup>8</sup>, and we consider it worthwhile that the deposition of adipose tissue, which is associated more strongly with impairment of lung function than WC, can be detected by the BIA method, a non-invasive and cost-effective measurement tool.

In conclusion, we found an association between the VAT level, as estimated by the BIA method, and lung function. However, this association was not seen in women, probably as a result of the lower VAT in women.

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## REFERENCES

1. Nakajima K, Kubouchi Y, Muneyuki T, *et al.* A possible association between suspected restrictive pattern as assessed by ordinary pulmonary function test and the metabolic syndrome. *Chest* 2008; 134: 712–718.
2. Lin WY, Yao CA, Wang HC, *et al.* Impaired lung function is associated with obesity and metabolic syndrome in adults. *Obesity* 2006; 14: 1654–1661.
3. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the international diabetes federation. *Diabet Med* 2006; 23: 469–480.
4. Leone N, Courbon D, Thomas F, *et al.* Lung function impairment and metabolic syndrome. The critical role of abdominal obesity. *Am J Respir Crit Care Med* 2009; 179: 509–516.
5. Usui C, Asaka M, Kawano H, *et al.* Visceral fat is a strong predictor of insulin resistance regardless of cardiorespiratory fitness in non-diabetic people. *J Nutr Sci Vitaminol* 2010; 56: 109–116.
6. Pou KM, Massaro JM, Hoffmann U, *et al.* Visceral and subcutaneous adipose tissue volumes are cross-sectionally

- related to markers of inflammation and oxidative stress: the Framingham Heart Study. *Circulation* 2007; 116: 1234–1241.
7. Pietrobelli A, Rubiano F, St-Onge MP, *et al.* New bioimpedance analysis system: improved phenotyping with whole-body analysis. *Eur J Clin Nutr* 2004; 58: 1479–1484.
  8. Nishizawa M, Sato H, Ikeda Y. The body composition analyzer by BIA as a self-healthy management tool. *Rinsho Byori* 2007; 138: 158–164.
  9. Pellegrino R, Viegi G, Brusasco V, *et al.* Interpretative strategies for lung function tests. *Eur Respir J* 2005; 26: 948–968.
  10. Santana H, Zoico E, Turcato E, *et al.* Relation between body composition, fat distribution, and lung function in elderly men. *Am J Clin Nutr* 2001; 73: 827–831.
  11. Wannamethee SG, Shaper AG, Whincup PH. Body fat distribution, body composition, and respiratory function in elderly men. *Am J Clin Nutr* 2005; 82: 996–1003.
  12. Babb TG, Wyrick BL, DeLorey DS, *et al.* Fat distribution and end-expiratory lung volume in lean and obese men and women. *Chest* 2008; 134: 704–711.
  13. Rossi AP, Watson NL, Newman AB, *et al.* Effects of body composition and adipose tissue distribution on respiratory function in elderly men and women: the health, aging, and body composition study. *J Gerontol A Biol Sci Med Sci* 2011; 66: 801–808.
  14. McClean KM, Kee F, Young IS, *et al.* Obesity and the lung: 1. Epidemiology. *Thorax* 2008; 63: 649–654.
  15. Ochs-Balcom HM, Grant BJ, Muti P, *et al.* Pulmonary function and abdominal adiposity in the general population. *Chest* 2006; 129: 853–862.
  16. Sutherland TJ, Goulding A, Grant AM, *et al.* The effect of adiposity measured by dual-energy X-ray absorptiometry on lung function. *Eur Respir J* 2008; 32: 85–91.
  17. Kahn SE, Zinman B, Haffner SM, *et al.* Obesity is a major determinant of the association of C-reactive protein levels and the metabolic syndrome in type 2 diabetes. *Diabetes* 2006; 55: 2357–2364.
  18. Shaaban R, Kony S, Driss F, *et al.* Change in C-reactive protein levels and FEV1 decline: a longitudinal population-based study. *Respir Med* 2006; 100: 2112–2120.
  19. Choi JH, Park S, Shin YH, *et al.* Sex differences in the relationship between metabolic syndrome and pulmonary function: the 2007 Korean National Health and Nutrition Examination Survey. *Endocr J* 2011; 58: 459–465.
  20. Heresi GA, Aytekin M, Newman J, *et al.* Plasma levels of high-density lipoprotein cholesterol and outcomes in pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2010; 182: 661–668.
  21. Harms CA. Does gender affect pulmonary function and exercise capacity? *Respir Physiol Neurobiol* 2006; 28: 124–131.
  22. Demerath EW, Sun SS, Rogers N, *et al.* Anatomical patterning of visceral adipose tissue: race, sex, and age variation. *Obesity* 2007; 15: 2984–2993.
  23. Schnabel E, Karrasch S, Schulz H, *et al.* High blood pressure, antihypertensive medication and lung function in a general adult population. *Respir Res* 2011; 12: 1–8.
  24. Nagai M, Komiya H, Mori Y, *et al.* Development of a new method for estimating visceral fat area with multi-frequency bioelectrical impedance. *Tohoku J Exp Med* 2008; 214: 105–112.
  25. Ryo M, Maeda K, Onda T, *et al.* A new simple method for the measurement of visceral fat accumulation by bioelectrical impedance. *Diabetes Care* 2005; 28: 451–453.
  26. Browning LM, Mugridge O, Dixon AK, *et al.* Measuring abdominal adipose tissue: comparison of simpler methods with MRI. *Obes Facts* 2011; 4: 9–15.
  27. Browning LM, Mugridge O, Chatfield MD, *et al.* Validity of a new abdominal bioelectrical impedance device to measure abdominal and visceral fat: comparison with MRI. *Obesity* 2010; 18: 2385–2391.