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Airflow obstruction and the metabolic syndrome: The Guangzhou Biobank Cohort Study

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Abstract

There is some evidence that chronic obstructive pulmonary disease (COPD) and the metabolic syndrome may be related, perhaps through systemic inflammation which is common to both. However, the association between the two conditions has not yet been clearly shown.

The present study involved 7,358 adults aged ≥50 years from a population-based survey, who undertook spirometry, a structured interview and had fasting metabolic markers measured.

Airflow obstruction (forced expiratory volume in one second/forced vital capacity ratio less than the lower limit of normal) was present in 6.7%, and the International Diabetes Federation metabolic syndrome criteria were met by 20.0%. The risk of metabolic syndrome was higher in those with airflow obstruction compared to those without (OR = 1.47, 95% CI 1.12-1.92), after controlling for potential confounders. Of the five components of the metabolic syndrome, only central obesity was significantly associated with airflow obstruction (OR = 1.43, 1.09-1.88) after adjusting for body mass index. Similar association was observed in both never and current smokers.

In this Chinese sample, airflow obstruction was associated with the metabolic syndrome, and in particular, its central obesity component. This may help explain the increased risk of cardiovascular diseases in COPD and so could guide future clinical practice.

Keywords: chronic obstructive pulmonary disease; comorbidity; central obesity; China; general population

Introduction

The term “chronic systemic inflammatory syndrome” has been proposed to take account of the inflammatory nature common to chronic obstructive pulmonary disease (COPD) and its comorbidities [1, 2]. One of these possible comorbidities is the metabolic syndrome, an aggregate of interrelated cardiometabolic risk factors, comprising glucose intolerance, abdominal obesity, dyslipidaemia, and hypertension, which are associated with an increased risk of cardiovascular disease and type 2 diabetes [3, 4].

Such proposition was built on the increasing body of evidence that systemic inflammation is related to the pathogenesis of both COPD [5] and the metabolic syndrome [3]. This was further supported by the finding that the metabolic syndrome was more common among people with advanced COPD, compared with age and sex matched controls [6]. However, an association between airflow obstruction, a hallmark of COPD, and the metabolic syndrome was not observed in three recent cross-sectional studies; two population samples from Taiwan [7] and Japan [8], and the other in Italy with healthy attendants of a day care centre and a home for the aged [9].

The current controversy limits our understanding of the joint aetiology and prognosis of COPD and the metabolic syndrome. The aim of this study was to examine the relationship between the two conditions, considering also each of the components of metabolic syndrome, in a large population-based sample in China.

Methods

Participants

The Guangzhou Biobank Cohort Study, a collaboration between the Guangzhou Number 12 People's Hospital and the Universities of Birmingham and Hong Kong, has been described in detail previously [10]. Participants were recruited from "The Guangzhou Health and Happiness Association for the Respectable Elders" (GHHARE), a community social and welfare association unofficially aligned with the municipal government where membership is open to older persons for a nominal monthly fee of 4 Yuan (US $0.5). About 7% of permanent Guangzhou residents aged 50 years and over are members of GHHARE, of whom 11% (about 10,000 participants) were randomly selected to take part in each of the two time periods (2003-04 and 2005-06). Participants were included if they were capable of consenting, ambulatory, and not receiving treatment modalities for life threatening conditions. Of those eligible, 90% of the men and 99% of the women participated. Ethical approval was received from the Medical Ethics Committee of the Guangzhou Medical Association. Written informed consent was obtained from all participants.

Measurements

Each enrolled participant underwent a physical examination and a detailed medical interview [10]. Relevant to this study, blood pressure was recorded as the average of the last two of three measurements taken using a digital sphygmomanometer (Omron 705CP, Kyoto, Japan). Waist circumference was measured horizontally through the narrowest part of the torso, between the lowest rib and the iliac crest. Levels of fasting glucose, triglyceride, and high-density lipoprotein (HDL)-cholesterol were determined by an automated clinical chemical analyzer (Shimadzu CL-8000, Kyoto, Japan). Body mass index (BMI), calculated by weight divided by height squared, was grouped in accordance with the World Health Organization recommendations for Asian populations [11].

A detailed smoking history was obtained and used to define individuals as never, former or current smokers. Pack years were calculated to quantify the exposure, where one pack year is equivalent to smoking an average of 20 cigarettes per day for one year. Level of physical activity (inactive, minimally active, and active) was quantified using the short version of the International Physical Activity Questionnaire (IPAQ) [12]. Educational level (primary or below, junior middle, senior middle or above) was used as proxy for socio-economic status.

Lung function status

Details of spirometry have been described elsewhere [13]. At least three manoeuvres, without the use of bronchodilator, were performed and the best measure of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC was recorded. The quality of the results was assured by first passing a numerical check algorithm, then by visual inspection of flow-volume and volume-time loops. The equations derived from a Chinese population [14] were used to determine the predicted values and the lower limit of normal (LLN) for lung function parameters.

Airflow obstruction was defined by FEV_1/FVC <LLN in those who did not report physician-diagnosed asthma and bronchiectasis. The severity of obstruction was categorised based on FEV_1 % predicted, modelling the staging of COPD recommended by the Global Initiative for Obstructive Lung Disease (GOLD) [15]. Mild, moderate and severe obstruction were defined as FEV_1 % predicted >80%, 50%-80%, and <50%, respectively. Because of evidence that restrictive lung function abnormality is also associated with the metabolic syndrome [7-9], participants with restrictive abnormality, defined as FEV_1/FVC ≥LLN and FVC <LLN [16] were removed from the main analyses so that the comparison was between those with airflow

obstruction and those with normal lung function. However, we also briefly explored the relationship between restrictive abnormality and the metabolic syndrome.

Metabolic syndrome

We classified the metabolic syndrome according to the International Diabetes Federation (IDF) [4], which required having central obesity (defined as waist circumference ≥90 cm in men and ≥80 cm in women), plus any two of the following four criteria: (a) raised blood pressure (≥130/85 mm Hg); (b) raised fasting glucose (≥5.6 mmol/L); (c) raised triglycerides (≥1.7 mmol/L); and (d) reduced HDL-cholesterol: (<1.03 mmol/L in men or <1.29 mmol/L in women). Receiving specific treatment for a criterion was regarded as fulfilling the criterion.

Statistical analysis

Difference in characteristics by lung function status was evaluated using χ^2 test. Analysis of covariance was used to obtain age-adjusted means of metabolic markers. Glucose and triglyceride levels were logarithmically transformed and their geometric means are presented. Logistic regression models were built to assess the relationship between airflow obstruction and the metabolic syndrome or its components. We present three models: Model 1 adjusted for age, sex, education, smoking, and physical activity; Model 2 additionally adjusted for BMI; and Model 3, which was used specifically in the assessment of the components of metabolic syndrome, where the other four components were also included. We also examined whether any relationships were modified by sex, using interaction terms in the models, and by repeating all analyses in men and women separately. We tested the robustness of our findings to a different definition of airflow obstruction, with FEV_1/FVC <0.70 (compatible with the GOLD definition [15] and consistent with previous studies). All analyses were performed with Stata (version 10.1, Stata Corp., College Station, TX, USA).

Results

Of the 20,431 participants, 8,701 had available information and valid spirometry data. The age, sex and metabolic profile of these participants were similar to those without valid data. Among them, 1,343 (15.4%) were excluded because they reported to have physician-diagnosed asthma or bronchiectasis, or displayed a restrictive abnormality on spirometry. The remaining 7,358 participants comprised 2,008 men (27.3%) and 5,350 women (72.7%), with an overall mean age of 61.6 years (SD 6.7). The prevalence of airflow obstruction was similar in men (6.4%) and women (6.9%). Compared to the participants with normal lung function, those with airflow obstruction were older, less highly educated and had greater smoking exposure. BMI was also lower in this group, with a significantly higher proportion (9.9%) being in the underweight (<18.5 kg/m^2) category, compared to those with normal lung function (3.9%). The trend was consistent in both sexes (Table 1). There were no differences in blood pressure, fasting glucose and HDL-cholesterol levels across lung function status. However, in men but not in women, those with airflow obstruction had significantly smaller waist circumference (79.3 cm *vs*. 81.9 cm, $P = 0.001$) and lower triglyceride level (1.23 mmol/L *vs*. 1.38 mmol/L, $P = 0.021$). In both sexes, the proportions of participants receiving pharmacological treatment for hypertension, diabetes, and dyslipidaemia were similar in those with normal and reduced lung function (Table 1).

The prevalence of the metabolic syndrome in this sample was 20.0% (95% confidence interval [CI] 19.1%-20.9%). Although the prevalence was higher in women (22.9%) than in men (12.4%), there was no evidence from the heterogeneity of effect across strata that the association of lung function status and the metabolic syndrome varied with sex (data not shown). Results are therefore presented for men and women together. Table 2 shows the

relationship between lung function status and the metabolic syndrome and its components. While the metabolic syndrome (22.6% *vs*. 19.8%), central obesity (34.1% *vs*. 33.1%), and raised blood pressure (56.7% *vs*. 53.4%) were more common in individuals with airflow obstruction compared to those with normal lung function, the opposite was seen for raised fasting glucose (34.3% *vs*. 36.9%), raised triglycerides (29.6% *vs*. 33.4%), and reduced HDL-cholesterol (15.9% *vs.* 16.6%). Nevertheless, none of these differences were statistically significant in univariate analyses. Adjusting for age, sex, education, smoking, and physical activity (Model 1) did not alter the lack of association, although the risk estimates changed slightly. However, the metabolic syndrome was significantly associated with the presence of airflow obstruction when BMI was additionally adjusted for (Model 2), with the odds ratio (OR) being 1.47 (95% CI 1.12-1.92). Among the five components of metabolic syndrome examined, only central obesity was significantly associated with airflow obstruction (OR = 1.43; 95% CI 1.09-1.88).

There was no evidence that the relation of airflow obstruction and the metabolic syndrome varied by smoking. The presence of airflow obstruction was associated with a higher prevalence of metabolic syndrome in lifelong never smokers (adjusted OR = 1.47; 95% CI 1.09-2.00) and in current smokers (adjusted OR = 3.46; 1.28-9.36).

The association between airflow obstruction and metabolic syndrome remained when those with self-reported physician-diagnosed asthma or bronchiectasis were included (adjusted OR = 1.39; 95% CI 1.08-1.80). Replacing the definition of airflow obstruction with FEV_1/FVC <0.70 did not alter the pattern of the relationships, though the magnitude of the OR estimate was slightly lower for the metabolic syndrome (adjusted OR = 1.34; 1.04-1.71), and essentially the same for central obesity (adjusted OR = 1.41; 1.10-1.81).

Table 3 shows the relationship between airflow obstruction and metabolic syndrome or its central obesity component, according to the severity of obstruction. There was a significant linear trend of increasing odds for the metabolic syndrome with decreasing FEV_1 % predicted before and after adjustment for confounders, although the association was significant only in those having severe obstruction (FEV_1 % predicted <50%) (adjusted OR = 2.34; 95% CI 1.39-3.95). Similar trend was also observed in the association between airflow obstruction and central obesity.

Although the main aim of our study was to examine the potential relationship between airflow obstruction and the metabolic syndrome, we also examined the association of the latter with restrictive abnormality. The prevalence of restrictive abnormality was 13.8% (n = 1,178). The OR for the metabolic syndrome among this group, compared to those with normal lung function was 1.87 (95% CI 1.59-2.20), for central obesity was 1.67 (1.40-1.99), and for hypertension was 1.19 (1.03-1.36). There were no statistical significant associations between restrictive abnormality and the other components.

Discussion

The results of the current analysis suggest that a higher prevalence of metabolic syndrome, and essentially its central obesity component, is associated with airflow obstruction once BMI has been adjusted for, in a sample of older adults in Guangzhou. To the best of our knowledge, the present study sample represents one of the largest studies addressing the relationship.

Our finding of the association between airflow obstruction and the metabolic syndrome is consistent with the results of a small case-control study [6]. The magnitude of excess risk was lower in our study, but the previous study was based on COPD patients attending cardiopulmonary rehabilitation, where participants had more severe airflow obstruction, and the reported results were not adjusted for potential confounders.

Our results appear to contradict three recent reports, which suggested that restrictive abnormality but not airflow obstruction was associated with the metabolic syndrome [7-9]. Closer scrutiny, however, shows that the population sample in the study by Lin *et al*. [7] was younger, with mean age of 37 years, whereas chronic airflow obstruction is relatively uncommon before the fifth decade of life [17]. It is possible that the prevalence of obstructive lung disease was low in their sample, resulting in insufficient power to detect any association. Although the univariate and multivariate analyses presented by Fimognari and colleagues [9] suggested that obstructive abnormality was unlikely to be related to the metabolic syndrome, confounders such as smoking and physical activity were not controlled for. Despite having a large sample size (N = 2,396) with a similar prevalence of obstruction (7.6%) compared with our study, Nakajima and associates [8] detected no association between obstructive abnormality and the metabolic syndrome. When fitting our data in a similar model to that described by Nakajima *et al*. [8], which included sex, age, height, and smoking status (yes/no) but not BMI, the OR for the metabolic syndrome was 1.05 (95% CI 0.84-1.31), which is more comparable to their finding (OR = 0.88; 95% CI 0.57-1.37). It may be that adjustment for BMI might have altered their results. However, in agreement with these studies, we also observed an association between restrictive abnormality and the metabolic syndrome. The adjusted OR (1.87) was similar to that reported in the Japanese study using similar LLN criteria and IDF definition (1.75) [8], but less comparable with the Taiwanese

(1.33) [7] and the Italian study (3.23) [9], where different definitions of restrictive abnormality (based on fixed ratio) and metabolic syndrome were employed.

Current available evidence has suggested that obesity (BMI ≥30 kg/m^2) is more commonly found in patients with COPD than in the general population [18]. In this analysis, we found that among the components of the metabolic syndrome, central obesity was the main single factor linked with airflow obstruction. This resonates with reports of previous studies from various settings, which suggested an inverse association between lung function parameters (FEV_1 and FVC) and central obesity (as measured by waist circumference or waist/hip ratio) [19-25]. However, the relationship between FEV_1/FVC ratio (as a continuous variable) and central obesity is not clear, with some [20-22], but not other studies [23-25] reporting such an association. Until recently, no previous study had demonstrated the link between the presence of airflow obstruction and central obesity. Similar to our findings, a recent cross-sectional study from France also demonstrated that the central obesity component of the metabolic syndrome was significantly associated with both obstructive and restrictive lung function impairment [26]. It is important to note that our finding that central obesity is more common in those who had airflow obstruction compared to those with normal lung function initially appears to be contradictory to the observation of lower mean waist circumference in the former group. However, it is explained by the fact that underweight (BMI <18.5 kg/m^2) was more prevalent among those with airflow obstruction compared to those without. Taking aside the underweight group, for any given BMI, central obesity (waist circumference ≥90 cm in men or ≥80 cm in women) was more common in those with airflow obstruction, compared to those with normal lung function (data not shown).

On the other hand, we did not find associations between airflow obstruction and other components of the metabolic syndrome. Similar results were reported in the case-control study by Marquis and colleagues [6] except that they also found that high blood pressure was more common in COPD compared with controls. Our results are in contrast with the findings of a recent analysis of the combined data from two large cohort studies (N = 20,296) showing that COPD was associated with a higher risk of diabetes (OR = 1.4) and hypertension (OR = 1.4). The risks were higher in those with more advanced (GOLD stage 3 or 4) COPD (OR = 1.5 and 1.6, respectively) [27].

Smoking, a major risk factor for COPD, has been attributed as one of the main causes of increased systemic inflammation [5], possibly explaining any link between COPD and other chronic conditions such as the metabolic syndrome. Nevertheless, our results showed that the association between the metabolic syndrome and airflow obstruction was also found in never smokers. It is possible that risk factors for airflow obstruction, such as passive smoking [13] may be driving the inflammatory response. In our never smoking subgroup, airflow obstruction was associated with metabolic syndrome in those who had been exposed to passive smoking or occupational dust but not in those without such exposures (data not shown). The inflammatory response in the metabolic syndrome is particularly related to central obesity, as demonstrated by elevated levels of C-reactive protein in those with higher waist circumference [28]. Nevertheless, whether it remains to be clarified how systemic inflammation associated with COPD and that associated with central obesity (and hence metabolic syndrome) might interact.

There are several potential limitations that deserve mention. Although recruited from an association whose membership is open to anyone for a low fee that is affordable by most, our

participants are unlikely to be totally representative of the older population in China. Nevertheless, bias would only be introduced if we had systematically missed those who had a specific relation between lung function status and metabolic profile – for example, those who had normal lung function and had metabolic syndrome, which is unlikely. In addition, the prevalence rates of airflow obstruction [29], and relevant cardiovascular morbidities, such as hypertension [30] and diabetes [31], were similar to those in recent surveys using national samples of Chinese, suggesting it is less likely that we have over-estimated the association. While it could be inappropriate to infer our findings to other populations, especially those in the developed world, given the large proportion of never smokers in our sample, our findings are relevant and important to China and other developing countries, where the majority of the women do not smoke, yet the burden of COPD in the female population is growing. As in other large scale prevalence surveys [29, 32], airflow obstruction was defined based on spirometric measurement. However, the use of the LLN criteria reduced the risk of over-diagnosis in our older sample [33] and a comprehensive and stringent quality check ensured only those data which were valid and reliable were included. While we could not exclude the possibility of having misclassified some asthmatic subjects as having chronic airflow obstruction because post-bronchodilator spirometry was not performed, the prevalence of self-reported physician-diagnosed asthma (1.7%) was comparable to that reported in a population survey (1.8% in those >45 years) [34]. Dyspnoea, which is a feature of chronic lung disease, could limit the level of physical activity and potentially confound the association between central obesity and airflow obstruction [35]. However, inclusion of dyspnoea (based on self-report using the Medical Research Council [MRC] respiratory questionnaire) in the regression models did not alter the magnitude of the ORs (1.49 [95% CI 1.13-1.95] for the metabolic syndrome, and 1.41 [1.07-1.85] for central obesity). We acknowledge that with a cross-sectional design temporal relationship and thus causality

cannot be established. Nevertheless, our message that the metabolic syndrome is associated with airflow obstruction has important clinical implications, which might raise the attention of clinicians to the coexistence of the two conditions, even in the absence of smoking. Future research using a prospective study design is warranted to confirm the direction of the observed association and to explain the underlying mechanism.

In summary our study suggests that the presence of airflow obstruction is related to the metabolic syndrome; the risk escalating with increasing severity of obstruction. This association is limited to the central obesity component of the metabolic syndrome. This finding may partly explain the elevated risk of cardiovascular disease among those with COPD. As a result of increased life expectancy, the concomitant occurrence of two or more chronic conditions (multimorbidity) is becoming increasingly common [36]. At present most chronic conditions are managed according to clinical guidelines that were designed to cater for the specific needs of individual diseases with little reference to multimorbidity [1, 2]. Our findings give evidence to suggest that future guidelines should evolve and develop a holistic approach to treating chronic diseases to meet the challenge of an ageing society.

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References

1. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? *Lancet*. 2007; 370: 797-9.
2. Fabbri LM, Luppi F, Beghé B, Rabe KF. Complex chronic comorbidities of COPD. *Eur Respir J*. 2008; 31: 204-12.
3. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005; 365: 1415-28.
4. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. www.idf.org/webdata/docs/IDF_Meta_def_final.pdf. Date last accessed: January 22 2009.
5. MacNee W. Pulmonary and systemic oxidant/antioxidant imbalance in chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 2005; 2: 50-60.
6. Marquis K, Maltais F, Duguay V, Bezeau AM, LeBlanc P, Jobin J, Poirier P. The metabolic syndrome in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil*. 2005; 25: 226-32.
7. Lin WY, Yao CA, Wang HC, Huang KC. Impaired lung function is associated with obesity and metabolic syndrome in adults. *Obesity (Silver Spring)*. 2006; 14: 1654-61.
8. Nakajima K, Kubouchi Y, Muneyuki T, Ebata M, Eguchi S, Munakata H. A possible association between suspected restrictive pattern as assessed by ordinary pulmonary function test and the metabolic syndrome. *Chest*. 2008; 134: 712-8.
9. Fimognari FL, Pasqualetti P, Moro L, Franco A, Piccirillo G, Pastorelli R, Rossini PM, Incalzi RA. The association between metabolic syndrome and restrictive

ventilatory dysfunction in older persons. *J Gerontol A Biol Sci Med Sci*. 2007; 62: 760-5.

10. Jiang C, Thomas GN, Lam TH, Schooling CM, Zhang W, Lao X, Adab P, Liu B, Leung GM, Cheng KK. Cohort profile: The Guangzhou Biobank Cohort Study, a Guangzhou-Hong Kong-Birmingham collaboration. *Int J Epidemiol*. 2006; 35: 844-52.
11. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004; 363: 157-63.
12. Deng HB, Macfarlane DJ, Thomas GN, Lao XQ, Jiang CQ, Cheng KK, Lam TH. Reliability and validity of the IPAQ-Chinese: the Guangzhou Biobank Cohort study. *Med Sci Sports Exerc*. 2008; 40: 303-7.
13. Yin P, Jiang CQ, Cheng KK, Lam TH, Lam KH, Miller MR, Zhang WS, Thomas GN, Adab P. Passive smoking exposure and risk of COPD among adults in China: the Guangzhou Biobank Cohort Study. *Lancet*. 2007; 370: 751-7.
14. Ip MS, Ko FW, Lau AC, Yu WC, Tang KS, Choo K, Chan-Yeung MM; Hong Kong Thoracic Society; American College of Chest Physicians (Hong Kong and Macau Chapter). Updated spirometric reference values for adult Chinese in Hong Kong and implications on clinical utilization. *Chest*. 2006; 129: 384-92.
15. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, Fukuchi Y, Jenkins C, Rodriguez-Roisin R, van Weel C, Zielinski J; Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2007; 176: 532-55.
16. Venkateshiah SB, Ioachimescu OC, McCarthy K, Stoller JK. The utility of spirometry in diagnosing pulmonary restriction. *Lung*. 2008; 186: 19-25.

17. Mannino DM, Gagnon RC, Petty TL, Lydick E. Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med*. 2000; 160: 1683-9.
18. Eisner MD, Blanc PD, Sidney S, Yelin EH, Lathon PV, Katz PP, Tolstykh I, Ackerson L, Iribarren C. *Respir Res*. 2007; 8:7.
19. Lazarus R, Gore CJ, Booth M, Owen N. Effects of body composition and fat distribution on ventilatory function in adults. *Am J Clin Nutr*. 1998; 68: 35-41.
20. Chen R, Tunstall-Pedoe H, Bolton-Smith C, Hannah MK, Morrison C. Association of dietary antioxidants and waist circumference with pulmonary function and airway obstruction. *Am J Epidemiol*. 2001; 153: 157-63.
21. Canoy D, Luben R, Welch A, Bingham S, Wareham N, Day N, Khaw KT. Abdominal obesity and respiratory function in men and women in the EPIC-Norfolk Study, United Kingdom. *Am J Epidemiol*. 2004; 159: 1140-9.
22. Ochs-Balcom HM, Grant BJ, Muti P, Sempos CT, Freudenheim JL, Trevisan M, Cassano PA, Iacoviello L, Schünemann HJ. Pulmonary function and abdominal adiposity in the general population. *Chest*. 2006; 129: 853-62.
23. Santana H, Zoico E, Turcato E, Tosoni P, Bissoli L, Olivieri M, Bosello O, Zamboni M. Relation between body composition, fat distribution, and lung function in elderly men. *Am J Clin Nutr*. 2001; 73: 827-31.
24. 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.
25. Chen Y, Rennie D, Cormier YF, Dosman J. Waist circumference is associated with pulmonary function in normal-weight, overweight, and obese subjects. *Am J Clin Nutr*. 2007; 85: 35-9.

26. Leone N, Courbon D, Thomas F, Bean K, Jégo B, Leynaert B, Guize L, Zureik M. Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. *Am J Respir Crit Care Med*. 2009; 179:509-16.

27. Mannino DM, Thorn D, Swensen A, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J*. 2008; 32: 962-9.

28. Santos AC, Lopes C, Guimarães JT, Barros H. Central obesity as a major determinant of increased high-sensitivity C-reactive protein in metabolic syndrome. *Int J Obes (Lond)*. 2005; 29: 1452-6.

29. Zhong N, Wang C, Yao W, Chen P, Kang J, Huang S, Chen B, Wang C, Ni D, Zhou Y, Liu S, Wang X, Wang D, Lu J, Zheng J, Ran P. Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. *Am J Respir Crit Care Med*. 2007; 176: 753-60.

30. Reynolds K, Gu D, Muntner P, Wu X, Chen J, Huang G, Duan X, Whelton PK, He J; InterASIA Collaborative Group. Geographic variations in the prevalence, awareness, treatment and control of hypertension in China. *J Hypertens*. 2003; 21: 1273-81.

31. Gu D, Reynolds K, Duan X, Xin X, Chen J, Wu X, Mo J, Whelton PK, He J; InterASIA Collaborative Group. Prevalence of diabetes and impaired fasting glucose in the Chinese adult population: International Collaborative Study of Cardiovascular Disease in Asia (InterASIA). *Diabetologia*. 2003; 46: 1190-8.

32. Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet*. 2007; 370: 741-50.

33. Hardie JA, Buist AS, Vollmer WM, Ellingsen I, Bakke PS, Mørkve O. Risk of over-diagnosis of COPD in asymptomatic elderly never-smokers. *Eur Respir J*. 2002; 20: 1117-22.

34. Tang T, Ding Y, Zhen J. Epidemiological survey and analysis on bronchial asthma in Guangdong Province. *Zhonghua Jie He He Hu Xi Za Zhi*. 2000; 23: 730-3.

35. Sin DD, Jones RL, Man SF. Obesity is a risk factor for dyspnea but not for airflow obstruction. *Arch Intern Med*. 2002; 162: 1477-81.

36. van den Akker M, Buntinx F, Metsemakers JF, Roos S, Knottnerus JA. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol*. 1998; 51: 367-75.

Table 1 Characteristics and age-adjusted metabolic profile of 7,358 Chinese adults aged ≥50 years according to sex and lung function status, Guangzhou Biobank Cohort Study, 2003-2006

	Men			Women		
	Normal lung function	Airflow obstruction	*P*-value	Normal lung function	Airflow obstruction	*P*-value
n (%)	1,880 (93.6)	128 (6.4)		4,982 (93.1)	368 (6.9)	
Age (years); mean±SD	63.5±6.2	67.1±5.6	<0.001	60.7±6.7	62.7±6.7	<0.001
Education; n (%)						
≤Primary	502 (26.7)	53 (41.4)		2,367 (47.5)	215 (58.4)	
Junior middle	555 (29.5)	33 (25.8)		1,293 (26.0)	82 (22.3)	
≥Senior middle	823 (43.8)	42 (32.8)	0.001	1,322 (26.5)	71 (19.3)	<0.001
Smoking history; n (%)						
Never	551 (29.3)	18 (14.1)		4,723 (94.8)	324 (88.0)	
Former	690 (36.7)	60 (46.9)		144 (2.9)	23 (6.3)	
Current	639 (34.0)	50 (39.1)	0.001	115 (2.3)	21 (5.7)	<0.001
Smoking exposure (pack years); mean±SD	18.8±24.0	30.4±26.5	<0.001	0.6±4.4	2.1±9.1	<0.001
Physical activity; n (%)						
Inactive	169 (9.0)	7 (5.5)		480 (9.6)	24 (6.5)	
Minimally active	954 (50.7)	60 (46.9)		2,430 (48.8)	180 (48.9)	
Active[#]	757 (40.3)	61 (47.7)	0.16	2,072 (41.6)	164 (44.6)	0.12
Body mass index, n (%)						
<18.5 kg/m^2 (Underweight)	80 (4.3)	16 (12.5)		188 (3.8)	33 (9.0)	
18.5-22.9 kg/m^2 (Normal)	711 (37.8)	65 (50.8)		1,870 (37.5)	146 (39.7)	
23.0-24.9 kg/m^2	521 (27.7)	27 (21.1)		1,255 (25.2)	87 (23.6)	
≥25.0 kg/m^2 (Overweight)	568 (30.2)	20 (15.6)	<0.001	1,669 (33.5)	102 (27.7)	<0.001
Waist circumference (cm); mean (95% CI)	81.9 (81.4-82.2)	79.3 (77.8-80.8)	0.001	77.5 (77.2-77.7)	76.7 (75.9-77.6)	0.09
Systolic blood pressure (mmHg); mean (95% CI)	132.9 (131.9-133.8)	134.8 (131.1-138.5)	0.32	129.1 (128.5-129.7)	128.8 (126.6-131.0)	0.80
Diastolic blood pressure (mmHg); mean (95% CI)	76.3 (75.8-76.8)	76.2 (74.2-78.2)	0.92	72.6 (72.3-72.9)	71.9 (70.8-73.0)	0.23
Fasting glucose (mmol/L); mean[¶] (95% CI)	5.56 (5.51-5.61)	5.39 (5.19-5.59)	0.12	5.52 (5.49-5.55)	5.44 (5.32-5.56)	0.22
Triglyceride (mmol/L); mean[¶] (95% CI)	1.38 (1.35-1.41)	1.23 (1.12-1.35)	0.02	1.44 (1.42-1.46)	1.43 (1.35-1.51)	0.84
HDL-cholesterol (mmol/L); mean (95% CI)	1.54 (1.52-1.55)	1.58 (1.51-1.64)	0.28	1.74 (1.73-1.75)	1.76 (1.72-1.80)	0.44
Treatment for hypertension; n (%)	503 (26.8)	37 (28.9)	0.60	1,354 (27.2)	98 (26.6)	0.82
Treatment for diabetes; n (%)	138 (7.3)	8 (6.3)	0.65	383 (7.7)	29 (7.9)	0.89
Treatment for dyslipidaemia; n (%)	328 (6.6)	28 (7.6)	0.45	119 (6.3)	6 (4.7)	0.46

[#]: Vigorous activity at least 3 days a week achieving at least 1500 metabolic equivalent-minutes per week or activity on 7 days of the week achieving at least 3000 metabolic equivalent-minutes per week.

[¶]: Geometric mean

Table 2 Relationship between airflow obstruction and the metabolic syndrome or its components, Guangzhou Biobank Cohort Study, 2003-2006

	Metabolic syndrome	Central obesity[#]	Raised blood pressure[#]	Raised fasting glucose[#]	Raised triglycerides[#]	Reduced HDL-cholesterol[#]
Normal lung function[¶]	1,361 (19.8)	2,268 (33.1)	3,664 (53.4)	2,531 (36.9)	2,292 (33.4)	1,139 (16.6)
Airflow obstruction	112 (22.6)	169 (34.1)	281 (56.7)	170 (34.3)	147 (29.6)	79 (15.9)
Crude OR (95% CI)	1.18 (0.95-1.47)	1.05 (0.86-1.27)	1.14 (0.95-1.37)	0.89 (0.74-1.08)	0.84 (0.69-1.02)	0.95 (0.74-1.22)
Adjusted OR (95% CI)						
Model 1[+]	1.01 (0.81-1.27)	0.89 (0.73-1.09)	0.98 (0.81-1.18)	0.80 (0.66-0.97)	0.82 (0.67-1.00)	0.95 (0.74-1.22)
Model 2	1.47 (1.12-1.92)	1.43 (1.09-1.87)	1.10 (0.91-1.34)	0.87 (0.71-1.06)	0.94 (0.76-1.16)	1.03 (0.80-1.33)
Model 3	-	1.43 (1.09-1.88)	1.10 (0.90-1.34)	0.83 (0.68-1.02)	0.91 (0.74-1.13)	1.03 (0.79-1.34)

[#]: Central obesity: waist circumference ≥90 cm in men or ≥80 cm in women; raised blood pressure: ≥130/85 mm Hg, or receiving treatment for hypertension; raised fasting glucose: ≥5.6 mmol/L, or a previous diagnosis of type 2 diabetes; raised triglycerides: ≥1.7 mmol/L; reduced HDL-cholesterol: <1.03 mmol/L in men or <1.29 mmol/L in women, or treatment for dyslipidaemia

[¶]: Referent category

[+]: Model 1: adjustment for age, sex, education, smoking, physical activity; Model 2: Model 1 plus body mass index; Model 3: Model 2 plus waist circumference, systolic blood pressure, glucose, HDL-cholesterol, and triglyceride, where appropriate

Table 3 Adjusted[#] odds ratios for the metabolic syndrome and central obesity according to severity of airflow obstruction, Guangzhou Biobank Cohort Study, 2003-2006

	Normal lung function	Airflow obstruction			
		Mild (FEV_1 % predicted ≥80%)	Moderate (FEV_1 % predicted ≥50% and <80%)	Severe (FEV_1 % predicted <50%)	*P*-value for linear trend
n	6,862	127	250	119	
n (%) with metabolic syndrome	1,361 (19.8)	24 (18.9)	55 (22.0)	33 (27.7)	
Crude OR (95% CI)	1.00	0.94 (0.60-1.47)	1.14 (0.84-1.55)	1.55 (1.03-2.33)	0.05
Adjusted OR (95% CI)	1.00	1.23 (0.72-2.10)	1.30 (0.90-1.87)	2.34 (1.39-3.95)	0.001
n (%) with central obesity	2,268 (33.1)	35 (27.6)	90 (36.0)	44 (37.0)	
Crude OR (95% CI)	1.00	0.77 (0.52-1.14)	1.14 (0.88-1.48)	1.19 (0.82-1.73)	0.32
Adjusted OR (95% CI)	1.00	0.94 (0.55-1.61)	1.50 (1.04-2.16)	2.03 (1.18-3.48)	0.002

[#]: Adjustment for age, sex, education, smoking, physical activity and body mass index