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Metabolic syndrome and risk of pulmonary involvement

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Summary
Metabolic syndrome (MS) is a complex disorder recognized clinically by the findings of abdominal obesity, elevated triglycerides, atherogenic dyslipidaemia, elevated blood pressure, high blood glucose and/or insulin resistance. It is associated with a pro-thrombotic and a pro-inflammatory state. A growing body of evidence suggests that individuals in the community with moderate airflow limitation may have co-existing systemic inflammation with this background. Therefore, we examined a population of 237 patients with metabolic disorder for the concomitant presence of functional pulmonary involvement, as assessed by FEV_1 and FVC impairment. Criteria for the identification of the MS included 3 or more of the following: waist circumference: (>102 cm in men, >88 cm in women), triglycerides levels (≥150 mg/dl), high-density lipoprotein cholesterol levels (<40 mg/dl in men, <50 mg/dl in women), blood pressure (≥135/≥85 mm Hg), and fasting glucose levels (>100 mg/dl). 119 subjects were diagnosed MS. Non-smokers patients suffering from MS presented lower spirometric values, with a trend to ventilatory restrictive more than obstructive pattern. Also in smokers patients with MS there was a trend to harmonic decrease in FEV_1 and FVC but not in FEV_1/FVC ratio, although the changes did not reach statistical significance. Mainly abdominal circumference, and also insulin resistance were retained as independent predictors of both FEV_1 and FVC changes. However, HDL-C was the strongest predictor of FEV_1 and FVC changes, with an inverse association.

Introduction

Metabolic syndrome (MS) is a cluster of risk factors that increase the probability to develop type 2 diabetes (T2D) and cardiovascular disease. The features of MS (abdominal obesity, atherogenic dyslipidaemia, mild elevated blood pressure, increased blood glucose concentrations and/or insulin resistance) are also associated with a pro-thrombotic and a pro-inflammatory state.[1] A growing body of evidence suggests that individuals in the community with moderate airflow limitation may have co-existing systemic inflammation.[2] In particular, systemic inflammation is

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Table 1 Demographic and metabolic characteristics of the population included in the study.

Age	60.11 ± 11.60
Sex	132 M and 105 F
Smoking history	27.82 ± 18.65
Waist circumference (cm)	101.46 ± 11.80
Triglycerides (mg/dl)	159.75 ± 141.40
HDL-C (mg/dl)	48.53 ± 14.11
Fasting glucose (mg/dl)	102.38 ± 18.81
Hypertension (yes/no)	168/70
Insulin resistance (yes/no)	117/121

present also in chronic obstructive pulmonary disease (COPD), a complex disorder characterized local pulmonary inflammation in response to inhalation of noxious particles or toxic gases, especially cigarette smoke.[3] Currently there is growing recognition that the inflammatory response extends beyond the lung.[4] In fact, it is likely that the inflammation in the lung 'spills over' into the systemic circulation to produce systemic effects such as muscle wasting, cachexia, atherosclerosis, and cardiac disease have been associated with COPD.[5] Comorbidities are common in COPD and may become harder to manage when COPD is present, either because COPD adds to the total level of disability or because COPD therapy adversely affects the comorbid disorder.[3]

It is now accepted that patients with COPD often have one or more component of the MS, with a slightly lower frequency in severe COPD.[6] However, we still do not know if individual with MS have an higher risk and incidence to develop COPD, although it has been reported that diabetes is independently associated with reduced lung function, and obesity in T2 diabetic patients could further worsen the severity of COPD.[7]

With this background, we investigated a population of patients with metabolic disorder for the concomitant presence of pulmonary involvement assessed by ordinary pulmonary function tests (PFTs).

Methods

Patients

We included in this study 237 subjects (132 males, 105 females) who were consecutively admitted in four months to the metabolic disorders outpatient office of our university hospital because of suspected MS. All patients denied suffering from COPD or other identified pulmonary diseases. The NCEP ATP-III criteria that we used for the identification of the MS is the association of 3 or more of the following: waist circumference (>102 cm in men, >88 cm in women), triglycerides levels (≥150 mg/dl), high-density lipoprotein cholesterol (HDL-C) levels (<40 mg/dl in men, <50 mg/dl in women), blood pressure ≥130/≥85 mm Hg), and fasting glucose levels (>100 mg/dl).[8] Insulin resistance was measured with the homeostasis model assessment for insulin resistance or HOMA-IR (HOMA-IR = insulin [μU/mL] × glucose [mmol/L]/22.5.[9] All patients included in the present study were in a stable state at distance (minimum 8 weeks) from pulmonary infection or acute bronchitis. All subjects denied that they have suffered from an episode of right-heart failure (with peripheral oedema) or acute respiratory failure. None of them was suffering from muscular weakness.

Table 2 Comparison of PFTs between non-smokers with MS (54 subjects) and non-smokers without MS (58 subjects).

Pulmonary Function Test	MET-SYN	No MET-SYN	*p* value
FEV_1 (l)	2.42 ± 0.73	2.90 ± 0.93	0.0051
FEV_1 (% pred)	99.92 ± 16.42	107.26 ± 14.88	0.0174
FVC (l)	2.86 ± 0.87	3.44 ± 16.20	0.0037
FVC (% pred)	96.20 ± 15.46	104.43 ± 16.20	0.0082
FEV_1/FVC	0.845 ± 0.061	0.844 ± 0.069	0.892

Table 3 Comparison of PFTs between smokers with MS (65 subjects) and smokers without MS (60 subjects).

Pulmonary Function Test	MET-SYN	No MET-SYN	*p* value
FEV_1 (l)	2.62 ± 0.84	2.81 ± 0.80	0.218
FEV_1 (% pred)	94.92 ± 18.29	98.02 ± 19.80	0.176
FVC (l)	3.19 ± 0.95	3.45 ± 0.93	0.166
FVC (% pred)	93.35 ± 15.87	97.79 ± 16.98	0.169
FEV_1/FVC	0.813 ± 0.065	0.808 ± 0.065	0.411

Conventional spirometry

FVC and FEV_1 were measured with standard spirometric techniques (Masterlab, Jaeger, Wurzburg, Germany). All values obtained were related to age and gender and expressed as percentage of their predicted value.

Statistical analysis

Subjects' characteristics were summarized as mean and S.D. for continuous variables and frequency and percentage for categorical variables. Spearman rank correlation coefficients were estimated between the study variables and potential confounders including BMI, waist circumference, triglycerides levels, HDL-C levels, blood pressure, and fasting glucose levels. Multiple linear regression models were used to examine the association between waist circumference, triglycerides levels, HDL-C levels, blood pressure, and fasting glucose levels (as indicators of MS) and ventilatory function. Separate regression models with FVC, FEV_1 and FEV_1/FVC as the outcome variables, with waist circumference, triglycerides levels, HDL-C levels, blood pressure, and fasting glucose levels as predictor variables, were examined in turn. To exclude the possibility of confounding by smoking-induced respiratory disease, all multivariate models were repeated in the subgroup of non-smokers. All statistical analyses were performed using the SPSS statistical software version 12.0 (SPSS, Inc., Chicago, IL, USA).