Clinical Nutrition 29 (2010) 756–760

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original Article

Abdominal fat mass contributes to the systemic inflammation in chronic obstructive pulmonary disease☆

Erica P.A. Rutten [a,b,*], Marie K. Breyer [a], Martijn A. Spruit [a], Trineke Hofstra [a], Paula P.M.J. van Melick [a], Annemie M.W.J. Schols [a], Emiel F.M. Wouters [a,b]

[a] Program Development Center, Center of expertise for chronic organ failure (Ciro), Horn, The Netherlands
[b] Department of Respiratory Medicine, University Hospital Maastricht, Maastricht, The Netherlands

ARTICLE INFO

Article history:
Received 25 January 2010
Accepted 28 April 2010

Keywords:
Adipose tissue
Abdominal
Pulmonary disease
Chronic obstructive
Inflammation

SUMMARY

Back ground & aims: Altered body composition in chronic obstructive pulmonary disease (COPD) is often reflected by muscle wasting, while only few studies have focused on abdominal fat mass. The contribution of abdominal fat mass to the systemic inflammation often present in COPD has not been examined yet. The aim of the present study was to investigate if abdominal fat mass contributes to the systemic inflammation in patients with moderate to severe COPD.
Methods: Muscle wasting (fat free mass index $<$17.1 kg/m^2 for men and 14.6 kg/m^2 for women) and abdominal fat mass (android/gynoid %fat mass $>$1.0 for men and $>$0.8 for women) were assessed by dual-energy X-ray absorptiometry in 295 patients with moderate to severe COPD (175 men). Plasma C-reactive protein (CRP) concentration was analysed by high sensitive (HS)-ELISA.
Results: Diffusion capacity was higher in patients with abdominal obesity. In addition, fat mass index was a significant determinant for plasma CRP concentration. In a subgroup of patients with CRP$<$5 mg/l ($n = 168$), CRP was positively associated with abdominal fat mass. In addition, a significant proportion of abdominal obese patients had muscle wasting, and CRP levels were higher in these patients compared to the patients without abdominal obesity.
Conclusion: Abdominal fat mass contributes to the systemic inflammation in COPD. This study provides further evidence for systemic phenotyping of patients with COPD incorporating besides markers of muscle mass also markers of abdominal obesity.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is traditionally characterized by partially irreversible airflow limitation, but nowadays, COPD is accepted as a systemic disorder reflected in a variety of extra-pulmonary features.[1] As one of these features, muscle wasting is often shown[2] predominantly in the patients with emphysema.[3] Identifying causes and treatment of skeletal muscle wasting received a lot of attention[4] as it is negatively associated with exercise capacity,[5] quality of life[6] and survival.[7] In contrast, the contribution of fat mass (FM) and its distribution in the systemic pathology of COPD have reached only just some attention. Available data indicate a prevalence of obesity (defined by BMI $>$30 kg/m^2) in mild-to-moderate COPD patients of about 20%.[8] In addition, about 40% of male and 20% of female patients with COPD entering a cardiopulmonary rehabilitation in Canada were obese.[9] Remarkably, in the same manuscript, about 70% of the men and 45% of the women showed abdominal obesity (defined by waist circumference $>$102 cm for men, $>$88 cm for women). These data indicate that there is a subgroup of patients with normal weight but abdominal obesity. However, the systemic consequences of abdominal obesity in patients with COPD are not investigated yet.

As another extra-pulmonary consequence, COPD is characterized by low grade systemic inflammation, which is often reflected by increased plasma levels of C-reactive protein (CRP).[10] Moreover, in a review it was stated that the co-presence of COPD and cardiovascular co-morbidity is high in a susceptible subgroup of elderly people[11] and the Third National Health and Nutrition Examination Survey concluded that the presence of elevated plasma CRP levels in subjects with COPD are associated with an increased risk for the development of cardiovascular co-morbidity.[12] The underlying causes of increased plasma CRP concentration in COPD are not clear yet. Studies investigating an

☆ This work was presented at the American Thoracic Society congress in 2008.

* Corresponding author. Dept of Respiratory Medicine, University Maastricht, P.O. Box 616, 6200 MD Maastricht, The Netherlands. Tel.: +31 475587651; fax: +31 475587592.
E-mail address: ericarutten@ciro-horn.nl (E.P.A. Rutten).

0261-5614/$ – see front matter
doi:10.1016/j.clnu.2010.04.007

association between plasma CRP concentration and markers of pulmonary inflammation in COPD are inconsistent.[13] In healthy obese subjects, abdominal fat mass is recognized as a source for low grade systemic inflammation defined by plasma CRP concentration (in the range of 0–3 mg/L).[14] In addition, it has been shown that the ratio of the android to the gynoid % FM is a determinant for cardiovascular risk in healthy women.[15] Referring to the higher prevalence of cardiovascular co-morbidity in COPD, it is relevant to investigate if the abdominal fat mass is also linked to the systemic inflammation in patients with COPD. In the present study, we hypothesized that abdominal fat mass in patients with COPD does significantly contribute to the low grade systemic inflammation measured by plasma CRP concentration.

2. Methods

Data were collected in 295 patients with COPD (175 men) who were screened for pulmonary rehabilitation at the Centre of expertise for chronic organ failure (ciro), the Netherlands[16] and retrospectively analysed. All subjects were clinically stable for at least 4 weeks prior participation. Lung function parameters (forced expiratory volume in the first second, FEV1; forced vital capacity, FVC) were collected using standardized spirometry (Masterlab®, Viasys, Germany). Diffusion capacity of carbon monoxide (DLCO) was assessed by using single-breath method (Masterlab®, Jaeger, Germany). All values obtained were compared with a reference value and expressed as percentages of the predicted value.[17] Arterial oxygen pressure (P_aO_2) was determined in an arterial blood sample obtained by puncture of the artery radial while breathing room air and in the sitting position. The degree of co-morbidities was measured using the modified Charlson co-morbidity index.[18]

A total body scan was performed by dual-energy x-ray absorptiometry (DEXA) using a Lunar Prodigy® system (GE Healthcare, Madison, WI, USA). From the total body scan, body composition was assessed: BMI, fat free mass index (FFMI) = fat free mass (lean mass + bone mineral content)/length^2 and fat mass index (FMI) = FM/length^2. The location of the android and gynoid region was situated as described previously by Eis et al.[15] The ratio of the percentage FM in the android region to the percentage FM in the gynoid region (A/G FM) is used to indicate abdominal obesity. In addition, a post-absorptive venous blood sample was collected from the patients to analyse CRP as a biomarker of systemic inflammation. CRP was assessed in duplicate by high-sensitivity particle-enhanced immunoassay (COBAS Mira®, Radiometer, Copenhagen).

3. Statistical analysis

Data are described as mean ± SD and checked for normality. CRP was not normally divided and thus log transformed for analyses. The study group was post-stratified for abdominal obesity defined as A/G FM >1.0 for men and >0.8 for women.[19] To define muscle wasting, we used the criteria of Vestbo et al (FFMI <17.1 kg/m^2 for men and 14.6 kg/m^2 for women)[20] Additional analyses were performed in a subgroup of subjects with only clinically normal CRP levels (<5 mg/L, $n = 168$,[21]) in order to prevent that the contribution of the abdominal FM to the systemic inflammation in COPD was covered by other disease relating factors. CRP levels were compared in the subgroup after stratification into 4 groups based on abdominal obesity and muscle wasting: abdominal obese subjects, subjects with muscle wasting, subjects with both abdominal obesity and muscle wasting and subjects with neither abdominal obesity nor muscle wasting. Comparison between groups was done by the analysis of variance test and the post hoc LSD test for normal divided variables and the Tukey Cramer test for CRP. Pearson's correlation coefficient was calculated to determine significant covariates of abdominal fat mass and CRP levels. Subsequently, multivariate stepwise regression analyses was performed to investigate a relationship between log(CRP) levels and marker for body composition. Analyses were performed using Statistical Package for the Social Sciences (SPSS) version 15.01 for Windows®. A p-value <5% was considered statistically significant.

4. Results

The study group was characterized by moderate to severe COPD, and in general normal BMI and FFMI (Table 1). In both sexes, the patients with abdominal obesity had higher values of BMI, FFMI, FMI, FEV1/FVC and DLCO. In addition, the women with abdominal obesity were older compared to those without abdominal obesity. The Charlson co-morbidity index was not different between the patients with abdominal obesity and those without abdominal obesity. Plasma CRP concentration was higher in the women with abdominal obesity compared their counterparts without abdominal obesity (Fig. 1). There was a significant correlation between plasma CRP concentration and gender, age, BMI, FFMI, FMI, A/G FM but not with PaO_2 (data not shown). The multivariate stepwise regression analysis with log(CRP) as dependent variable and the significant covariates as independent variables, showed that gender, age and FMI were significant determinants in the way that men are more prone to have higher CRP levels (Table 2). The coefficient of determination of the regression model was however low (14%).

In a subgroup of COPD patients with CRP < 5 mg/L ($n = 168$), CRP significantly correlated with gender, age, BMI, FFMI, FMI and A/G FM. Performing a stepwise multiple regression analysis with log(CRP) as dependent variable in the subgroup of patients, the

Table 1
Characteristics of the study group stratified for sex and abdominal obesity.

	Men		Women	
	Abdominal obese	Not abdominal obese	Abdominal obese	Not abdominal obese
Number of patients, *n*	126	49	73	47
Age, *y*	66.6 ± 9.3	65.4 ± 9.8	61.7 ± 9.3	57.0 ± 9.1**
Body composition				
BMI, kg/m^2	26.1 ± 4.2	20.8 ± 3.7**	25.7 ± 4.8	19.6 ± 2.4**
FFMI, kg/m^2	18.5 ± 2.0	16.9 ± 1.8**	15.9 ± 1.7	14.6 ± 1.3**
FMI, kg/m^2	7.6 ± 2.8	3.5 ± 2.3**	9.7 ± 3.7	5.0 ± 1.9**
Muscle wasting, %	26.2	51.0**	30.4	48.9**
Lung function parameters				
FEV1, l	1.31 ± 0.53	1.16 ± 0.42	1.00 ± 0.46	0.89 ± 0.40
FEV1, %pred	44.5 ± 15.5	40.9 ± 15.0	44.6 ± 17.7	38.2 ± 16.9
FVC, l	3.19 ± 0.89	3.23 ± 0.85	2.43 ± 0.70	2.36 ± 0.86
FVC, %pred	83.6 ± 19.6	87.9 ± 21.2	88.0 ± 24.9	88.4 ± 24.6
FEV1/FVC, % pred	40.5 ± 11.5	36.1 ± 9.6*	41.1 ± 11.6	35.5 ± 9.7**
DLCO, %pred	56.9 ± 19.3	44.9 ± 14.6**	53.1 ± 16.5	38.6 ± 14.2**
PaO_2, KPa	9.2 ± 1.2	9.1 ± 1.3	9.3 ± 1.4	9.1 ± 1.4
Charlson co-morbidity index				
1	55	24	34	23
2	32	8	9	9
3	12	7	9	3
>3	5	3	5	1

Data are mean ± SD.
Abbreviations: FEV1: forced expiratory volume expressed in 1 s; FVC: functional volume capacity; FEV1/FVC: tiffeneau index; DLCO: diffusing capacity for carbon monoxide; PaO_2: arterial oxygen pressure; BMI: body mass index; FFMI: fat free mass index; FMI: fat mass index. Symbols indicate significant differences with abdominal obesity: *$p < 0.05$, **$p < 0.01$.