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A possible link between increased metabolic activity of fat tissue and aortic wall inflammation in subjects with COPD. A retrospective ^{18}F-FDG-PET/CT pilot study

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Summary
Background: Fat tissue, and particularly visceral fat, is known to play a role in low grade systemic inflammation in COPD, and is likely to contribute to the excess cardiovascular comorbidity in COPD. Therefore, we aimed to study ^{18}FDG-PET-assessed inflammation of the aorta and the (visceral) fat, and evaluate its interrelations and differences in subjects with and without COPD.
Methods: We retrospectively identified 42 patients (71% male, 48% current smokers, mean age 66.6 ± 8.3 years, mean BMI 25.1 ± 4.3 kg/m^2), who underwent ^{18}F-FDG-PET/CT for suspected early stage bronchus carcinoma. COPD-diagnosis was based on spirometry and defined as $FEV_1/FVC <$ lower limit of normal. Inflammatory status of aortic and fat regions was defined as the average of obtained maximum target-to-background ratios ($_{mean}TBR_{max}$). The TBR is the standardized uptake value (SUV) normalized to ^{18}F-FDG blood pool activity.

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Results: Compared to controls, patients with COPD ($n = 19$; 45%) had increased $_{mean}TBR_{max}$ of both the abdominal aorta (1.31 ± 0.14 vs. 1.49 ± 0.31; $p = 0.02$) and the abdominal visceral fat (0.28 ± 0.09 vs. 0.38 ± 0.18; $p = 0.047$), while inflammatory activity of the abdominal subcutaneous fat failed to show statistically significant differences (0.21 ± 0.09 vs. 0.24 ± 0.09; $p = 0.345$). In all patients, $_{mean}TBR_{max}$ of abdominal visceral fat was correlated with $_{mean}TBR_{max}$ of the abdominal aorta, independently of age and BMI ($\beta = 0.590$, $p = 0.002$).
Conclusion: Metabolic activity of the abdominal aorta and visceral fat is increased in COPD patients compared to peers. The degree of visceral fat metabolic activity is associated with aortic inflammation. More prospective research is warranted concerning the role of visceral fat in the development of vascular comorbidity in COPD.

Introduction

Although defined by the presence of chronic airflow limitation, chronic obstructive pulmonary disease (COPD) is nowadays considered a complex, heterogeneous and multicomponent condition [1,2]. It is increasingly recognized that cardiovascular disease has an increased incidence in subjects with COPD even when controlled for shared risk factors as smoking [3,4]. In subjects with mild to moderate COPD, the main cause of death is cardiac [5].

COPD is associated with low-grade systemic inflammation, which has been suggested to originate from the pulmonary compartment and then again stimulate the atherosclerotic process [6]. However, the COPD-specificity of this low-grade systemic inflammation is still unclear and a matter of debate [6,7]. Adipose tissue is known as a metabolic active organ and important source of inflammatory markers [8] and its role as a cardiovascular risk factor has been well determined [9]. Also in COPD patients, increased levels of systemic inflammation have been particularly reported in obese subjects [7,10—12]. In addition, an independent cluster of COPD patients has been recognized, characterized by a high proportion of obesity, cardiovascular disorders, diabetes and systemic inflammation [13,14].

Moreover, the inflammatory capacity of abdominal visceral fat is considerably greater in comparison with other fat depots [15,16]. Interestingly, recently, increased visceral fat mass has been reported in non-obese COPD compared to a well matched control group [17].

Positron emission tomography with ^{18}F-fluorodeoxyglucose (FDG-PET) has emerged as a novel and sensitive imaging technique to identify both atherosclerotic disease activity [18,19] and metabolic activity of the visceral fat [20]. Increased aortic inflammation as measured by FDG-PET has already been seen in COPD patients compared to non-COPD ex-smokers [21].

We hypothesized that subjects with COPD had increased metabolic activity of the visceral fat compared to controls and that this might be associated with increased atherosclerotic activity. Therefore, using FDG-PET, we aimed to study: 1) whether or not the metabolic activity of the visceral fat, the subcutaneous fat and the aorta is increased in patients with COPD compared to matched controls; 2) Whether or not the metabolic activity of the visceral or subcutaneous fat is associated with aortic inflammatory activity.

Methods

Study population

From January 2006 to August 2008, 43 consecutive subjects who underwent non-contrast FDG/PET-CT scanning for suspected bronchus carcinoma without evidence for lymphatic or distant metastasis were retrospectively identified. One patient was excluded because of lacking spirometry. A total of 42 patients were included for analysis. These retrospective analyses are IRB exempt due to the use of de-identified, pre-existing data.

Recorded demographics

Smoking status, patients' cardiovascular medical history and pharmacological cardiovascular treatment (listed in Table 2) were registered in the digitalized hospital charts. "Any cardiovascular comorbidity" was defined as at least one of the listed cardiovascular comorbidities in the history of an individual patient.

FDG/PET-CT

Image analysis of the vessels

Image analysis was performed on a dedicated commercially available workstation (Extended Brilliance Workspace V4.0.0.3206; Philips Medical Systems Inc.; Cleveland, Ohio). One experienced reader (A. v. M.) analyzed all scans (example in Fig. 1). Methodology for analysis and reproducibility of the measurements has been previously reported [22].

The FDG-uptake in different aortic regions was quantified as the maximum arterial standardized uptake value (SUV) (highest pixel activity within the region of interest). The SUV is the decay-corrected tissue concentration of FDG in kBq/ml, adjusted for the injected FDG dose and the body weight of the patient. By averaging the maximum SUV values of all arterial slices of the different vascular territories analyzed a $_{mean}SUV_{max}$ value was derived for all arteries.

The arterial target-to-background ratio (TBR) was calculated by normalizing the arterial SUV for blood pool activity by dividing the SUV values in the arteries by the average blood mean SUV estimated from the superior vena