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Brief Report

Pulmonary capillary permeability and pulmonary microangiopathy in diabetes mellitus

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ABSTRACT

Significant increase in permeability surface (PS) in patients with diabetes confirms pulmonary microcirculation damage in these patients.

1. Introduction

The lungs exhibit a complex microcirculation network whose structure and function can be altered in diabetes (pulmonary microangiopathy) [1–3]. Unfortunately, clinical assessments, including pulmonary function test and lung diffusing capacity for carbon monoxide (DLCO) measurement, are insufficient for a precise diagnosis [4–6]. Perfusion chest computed tomography (pCT) is a non-invasive, sensitive technique that images hemodynamics on the basis of tissue density changes during the flow of contrast agent through the vascular bed of tested structures [7,8].

Recently, we had demonstrated a significant increase of CT perfusion parameters in the course of diabetes mellitus (DM), which seemed to confirm pulmonary microangiopathy [9]. Our

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Abbreviations: DLCO, lung diffusion capacity for carbon monoxide; DLCO/VA, lung diffusing capacity for carbon monoxide/alveolar volume; FEV1, forced expiratory volume in one second; pCT, perfusion chest computed tomography; MTT, mean transit time; PS, permeability surface; ROI, regions of interest; TLC, total lung capacity; VC, vital capacity; PFT, pulmonary function test.

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present goal was to assess which pCT parameters play a significant role in the diagnosis of pulmonary microangiopathy associated with DM.

2. Materials and methods

Thirty never-smoking subjects (15 diabetic patients and 15 healthy controls) were enrolled in the study. No participants had been diagnosed with any acute or chronic respiratory diseases affecting pulmonary function. Standard morphological, biochemical and PFT tests were performed.

PFTs were performed in accordance with ATS/ERS guidelines [10,11]. pCT tests were performed according to an axial protocol with the use of a 64-row CT scanner (GE-Light Speed VCT, USA). Perfusion was evaluated in a 4 cm in diameter part of the lung situated 2 cm below the carina. During the test, 40 ml of non-iodinated contrast medium was administered intravenously at the rate of 4 ml/s and with a delay of 12 s. In order to minimize breathing artifacts, the test was performed during suspended inspiration and with temporal resolution of 1 s (40 pictures in 40 s). For each 5-mm slice of lung, 40 scans were obtained. Eighteen elliptical regions of interest (ROIs) were chosen (from 3 to 20), for which perfusion measurements were performed. The perfusion between the anterior and posterior part of lungs was assessed (Fig. 1).

Reference ROI 1 was located in the pulmonary artery, while ROIs 3–20 were positioned in a similar location in both lungs and classified as front, medial or back. ROI 2 situated in the aorta was not necessarily evaluated during data analysis.

The following parameters of local perfusion were determined (CT Perfusion 4, GE Healthcare USA):

1) Blood volume (BV) – the volume of a vascular bed supplied with blood (ml/100 g lung tissue).
2) Blood flow (BF) – the volume of blood flowing through a defined region in 1 min (ml/100 g/min).
3) Permeability surface (PS) – the vascular permeability for contrast medium penetrating from intravascular to extravascular space (ml/100 g/min).
4) Mean transit time (MTT) – the mean time needed for blood to pass vascular bed (s).

The study protocol had been approved by a bioethics committee (No. NKEBN/14/2006).

In statistical analysis, the χ^2-test, *t*-test and the analysis of variance (ANOVA) were applied. Statistical significance was determined at $p < 0.05$. Data analysis was carried out using Statistica *Data Miner + QC* software.

3. Results

In the DM group 7 patients were diagnosed with type 1 DM and 8 patients with type 2 DM. The mean time since the diagnosis of DM was 16 years (±13.2). Macroangiopathy was found in 11 patients: hypertension in 10, cardiac infarction in 1, and diabetic foot in 1. Diabetic microangiopathy was found in 12 patients: nephropathy in 7, retinopathy in 9, and polyneuropathy in 7.

There were significant differences in the DM and control subjects in VC ($p = 0.05$), TLC ($p = 0.05$), and biochemical markers (fibrinogen $p = 0.05$, HbA1c $p = 0.001$, CRP $p = 0.05$) (Table 1). Mean HbA1c in DM was 9.4% (80 mmol/mol) indicating poor glycemia control. In pCT, in ROIs 3–20, no statistically significant differences were revealed in the mean area of ROIs, in BF, BV, and MTT. Similarly, no differences were found between front and back lung parenchyma either in the DM or in the CG. However, significant differences were found for PS in ROIs 3–20 as well as between the front and back ROIs. PS value was significantly higher in the DM compared with the CG (Table 1).

4. Discussion

The current study demonstrates evidence of a relationship between PS and damage to lung parenchyma. PS was significantly higher in DM patients compared to the CG. The values were higher in all ROIs 3–20 and the front and back ROIs of the assessed lung parenchyma. In particular the permeability of contrast medium in the back ROIs of lungs was significantly higher.

It is impossible to determine absolutely whether the increased PS indicates only structural damage to the vessels or altered functionality as well. PS allows quantifying the flow dynamics for capillaries in pulmonary microcirculation and simultaneously (indirectly) reflects structural changes in these vessels. These changes result in increased permeability of capillaries for contrast medium from intravascular to extravascular space. Hence, PS provides information on the

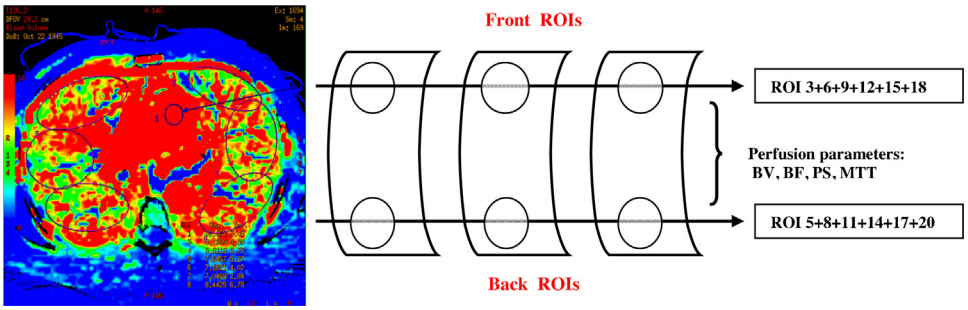

Fig. 1 – Diagram of determining and summing ROIs in pulmonary perfusion assessment.