Arch Bronconeumol. 2009;**45(8)**:376-382

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Original Article

Relation Between Atherosclerotic Calcifications Detected in Chest Computed Tomography and Lung Function

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ARTICLE INFO

Article history:
Received October 27, 2008
Accepted December 22, 2008
Online April 25, 2009

Keywords:
Atherosclerosis
Respiratory function tests
Tomography spiral computed

ABSTRACT

Background and objectives: A few recent epidemiological findings indicate a link between atherosclerosis and some lung functions. We studied further the relation between calcified chest atherosclerosis as seen in computed tomography (CT) and several lung functional parameters.
Patients and methods: Male construction workers originally screened for occupational lung cancer with CT had their chest atherosclerosis (aorta, the origins of its cervical branches, the coronary arteries and heart valves) visually classified. The relation between the atherosclerotic calcification scores and lung function (total lung capacity [TLC], forced expiratory volume in one second [FEV_1%], forced vital capacity [FVC%], maximal expiratory flow when 50% of FVC remains to be exhaled, total and specific diffusing capacities; all above expressed as percent of predicted value, and the FEV_1/FVC% ratio) were studied with the general linear model adjusted for smoking, exposure years for asbestos, and body mass index (n = 432).
Results: All lung functions except TLC showed significant negative associations with calcifications in aorta and in its branches. TLC showed such association only with atherosclerosis in the ascending aorta.
Conclusions: Aortic atherosclerosis seems to be related with poor lung function. This may be due to deteriorated bronchial circulation, but other mechanisms can also be involved. Lung function poorer than would be expected due to pulmonary reasons may indicate aortic atherosclerosis.

Relación entre las calcificaciones ateroscleróticas en el tórax detectadas mediante tomografía computarizada y la función pulmonar

Palabras clave:
Aterosclerosis
Pruebas de función respiratoria
Tomografía computarizada helicoidal

RESUMEN

Introducción: Varios hallazgos epidemiológicos recientes indican que hay una conexión entre la aterosclerosis y algunas funciones pulmonares. Examinamos en más detalle la relación entre la aterosclerosis calcificada de tórax, según se visualiza en la tomografía computarizada (TAC), y varios parámetros de función pulmonar.
Pacientes y métodos: En obreros de la construcción masculinos a quienes inicialmente se realizó una TAC para la detección precoz de cáncer de pulmón ocupacional, se efectuó también una clasificación visual de la aterosclerosis en la zona torácica (aorta, origen de arterias del cayado aórtico, arterias coronarias y válvulas cardíacas). Se evaluó la relación entre las puntuaciones de la calcificación aterosclerótica y los parámetros de función pulmonar —capacidad pulmonar total (TLC), volumen espiratorio forzado en el primer segundo (FEV_1%), capacidad vital forzada (FVC%), flujo espiratorio máximo cuando queda un 50% de la FVC por espirar y capacidades de difusión total y específica (todos ellos expresados como porcentajes del valor predicho), así como el cociente FEV_1/FVC%— con un modelo lineal general ajustado para tabaquismo, años de exposición al asbesto e índice de masa corporal (n = 432).
Resultados: Todos los parámetros de la función pulmonar, salvo la TLC, mostraron asociaciones negativas y significativas con la calcificación de la aorta y de sus ramas. La TLC sólo mostró tal asociación con la aterosclerosis en la aorta ascendente.

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0300-2896/$ - see front matter

Conclusiones: La aterosclerosis aórtica parece estar relacionada con una función pulmonar deficiente. Esto puede deberse al deterioro de la circulación bronquial, pero también pueden intervenir otros mecanismos. Una función pulmonar más deficiente de lo esperado según las condiciones pulmonares puede indicar aterosclerosis aórtica.

Introduction

Some recent epidemiological findings indicate a link between atherosclerosis and lung function. Reduced pulmonary function — forced expiratory volume in one second (FEV_1%) and forced vital capacity (FVC)— was independently associated with aortic stiffness evaluated from the carotid-femoral pulse-wave velocity in men.[1] An association was also found between reduced lung function (FEV_1 and FVC) and coronary heart disease. This relation may be stronger in women than in men[2]. Among white subjects, participants with impaired lung function had a modestly increased risk of ischemic stroke even if they had never smoked nor had respiratory symptoms[3]. Reduced lung function predicted increased fatality in cardiac events in a population sample of apparently healthy men[4]. On the other hand, in another study there was no association between abnormal lung function (FEV_1% and FVC%) and aortic pulse wave velocity[5]. The nature of association and especially the mechanism between atherosclerosis and lung function therefore remain unspecified.

Computed tomography (CT) makes it possible to locate chest calcified atherosclerosis unlike indirect methods such as recordings of pulse wave velocity. We used data from a previous CT screening study of lung cancer[6] to work out more exactly the relation between calcified chest atherosclerosis and several measures of lung function.

Materials and Methods

Study Subjects

642 asbestos exposed workers were invited and 602 participated in a CT screening study for lung cancer with lung function measurement, clinical examination and health questionnaire[6]. All had either asbestosis irrespective of smoking (n = 85) or bilateral pleural plaques with a smoking history at least for 10 years. Due to a major sex discrepancy women were excluded from this analysis. All men with images available (n = 505) were later classified for chest atherosclerotic changes.

The sample mean age was 63 years (range 38-81), body mass index (27.3, range 16.7-40.4 kg/m^2), smoked pack-years 23 (0-81, one cigarette pack containing 20 cigarettes) and asbestos exposure years 26 (2-48). 16 persons had never smoked, 360 were ex-smokers (had stopped regular smoking more than 6 months before questioning), 127 were current smokers and for 2 persons the smoking data was missing. Patients had their erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) analyzed by using standard laboratory methods. Patient files were searched for previously diagnosed cardiovascular diseases related to atherosclerosis. 180 workers had one or more such diseases: 114 had hypertension, 75 coronary heart disease, 7 obliterative arteriosclerosis and 35 diabetes mellitus. 325 workers did not have any of these diagnoses. The patients gave their written informed consent and the study protocol was accepted at the local ethical committee.

Functional and radiological methods

The lung function studies were performed within 0-3 days after the CT scan examination. Flow-volume spirometry was performed with a rolling-seal spirometer (Mijnhardt BV; Bunnik, Holland) connected to a microcomputer (Medikro MR-3; Medikro, Kuopio, Finland). The flow-volume curve was formed with the envelope method from curves obtained from at least 3 successive forced expiratory breathing maneuvers, by using the standards of the European Respiratory Society[7]. The following parameters were measured: FVC, FEV_1, the FEV_1/FVC ratio, and forced expiratory flow at the level when 50% of the FVC remains exhaled ($MEF_{50\%}$). The single breath diffusing capacity for carbon monoxide (DLCO), specific diffusing capacity (DLCO related to alveolar volume, DLCO/VA), and the total lung capacity (TLC) with the helium single-breath dilution method were measured by using a Masterlab Transfer or a Compact Lab Transfer device (Erich Jaeger, Würzburg, Germany); the mean values from at least two successive measurements were recorded[8] and the values were corrected for haemoglobin[9]. The spirometric and diffusing capacity results were compared with the reference values[10]. Thus, the parameters are called FEV_1%, FVC%, $MEF_{50\%}$, DLCO% and DLCO/VA%.

The subjects were examined with single-slice unenhanced spiral CT (Picker PQ 2000 scanner/ Picker International, Highland Heights, Ohio, USA: 125 mA, 140 kV, collimation 10 mm, pitch 1.5, exposure time 1.5 sec) supine, in full inspiration from the apical lungs to the costophrenic angle. Hard copies were inspected at lighted view boxes. The method for visual scoring of atherosclerotic changes has been described in detail[11]. A single observer classified blinded the following vascular calcifications each by using reference images and a visual scale (0 = no calcified atherosclerosis, 1 = some calcification, 2 = moderate calcification and 3 = extensive calcification):

- Coronary arteries: left anterior descendens (LAD), left circumflex, and right coronary artery.
- Aorta: ascending, arch, descending.
- Origin of arteries leaving the aortic arch: brachiocephalic, left carotid, left subclavian.
- Heart valves: aortic, mitral (no calcifications existed in pulmonary or tricuspid valves).

The sum scores in the above categories were also calculated. There was a great variation in the occurrence of calcifications, but only 17 individuals out of 505 (3.4%) were free of any (total calcification sum score = 0) above mentioned calcifications[11].

Statistical Methods

The relation between the atherosclerotic calcification score at a certain site (e.g. at LAD) and site specific sum scores (e.g. coronary sum score) and each lung function measurement was studied with the general linear model/multiple regression (SPSS 14.0; SPSS Inc., Ill, U.S.A.). Analyses were primarily adjusted for pack-years of

Table 1
Association Between FEV_1% and Calcified Atherosclerosis (Multiple Regression). Adjusted for Pack-Years of Smoking, Exposure Years for Asbestos and Body Mass Index

Vessel	B (Coefficient)	B: 95% Lower	B: 95% Upper	*P*-Value
Coronary: LAD	−2.366	−4.523	−0.208	0.032[a]
Coronary: LCX	−0.988	−3.323	1.346	0.406
Coronary: Rt	−1.614	−3.815	0.587	0.150
Coronary sum	−0.717	−1.554	0.121	0.093
Aorta: ascending	−6.041	−8.530	−3.553	0.000[b]
Aorta: arch	−7.430	−9.760	−5.099	0.000[b]
Aorta: descending	−5.262	−7.593	−2.930	0.000[b]
Aortic sum	−3.050	−3.998	−2.102	0.000[b]
Aortic origin: brachiocephalic	−7.593	−10.348	−4.839	0.000[b]
Aortic origin: left carotid	−8.208	−11.687	−4.729	0.000[b]
Aortic origin: left subclavian	−6.289	−8.642	−3.937	0.000[b]
Aortic origin sum	−3.642	−4.762	−2.522	0.000[b]
Valve: aortic	−1.912	−4.329	0.505	0.121
Valve: mitral	−2.599	−8.255	3.058	0.367
Valve sum	−1.720	−3.770	0.331	0.100

LAD: left anterior descendens; LCX: left circumflex; Rt: right coronary artery.
B = regression coefficient, indicates change in FEV_1%/calcification score.
[a] $P < 0.05$.
[b] $P < 0.001$.

Table 2
Association Between FVC% and Calcified Atherosclerosis (Multiple Regression). Adjusted for Pack-Years of Smoking, Exposure Years for Asbestos and Body Mass Index

Vessel	B (Coefficient)	B: 95% Lower	B: 95% Upper	*P*-Value
Coronary: LAD	−1.125	−3.124	0.873	0.269
Coronary: LCX	−0.162	−2.318	1.993	0.882
Coronary: Rt	−1.631	−3.661	0.399	0.115
Coronary sum	−0.426	−1.200	0.348	0.280
Aorta: ascending	−4.135	−6.459	−1.812	0.001[a]
Aorta: arch	−3.446	−5.669	−1.223	0.002[a]
Aorta: descending	−3.033	−5.214	−0.852	0.007[a]
Aortic sum	−1.718	−2.618	−0.818	0.000[b]
Aortic origin: brachiocephalic	−3.813	−6.415	−1.211	0.004[a]
Aortic origin: left carotid	−5.265	−8.517	−2.013	0.002[a]
Aortic origin: left subclavian	−4.067	−6.273	−1.860	0.000[b]
Aortic origin sum	−2.164	−3.226	−1.102	0.000[b]
Valve: aortic	−0.317	−2.553	1.920	0.781
Valve: mitral	−2.116	−7.336	3.105	0.426
Valve sum	−0.507	−2.405	1.390	0.600

LAD: left anterior descendens; LCX: left circumflex; Rt: right coronary artery.
B = regression coefficient, indicates change in FEV_1%/calcification score.
[a] $P < 0.01$.
[b] $P < 0.001$.

Table 3
Association Between FEV_1/FVC% and Calcified Atherosclerosis (Multiple Regression). Adjusted for Age, Pack-Years of Smoking, Exposure Years for Asbestos and Body Mass Index

Vessel	B (Coefficient)	B: 95% Lower	B: 95% Upper	*P*-Value
Coronary: LAD	−0.064	−1.321	1.193	0.920
Coronary: LCX	0.110	−1.224	1.443	0.872
Coronary: Rt	0.776	−0.449	2.00	0.214
Coronary sum	0.128	−0.360	0.617	0.607
Aorta: ascending	−0.802	−2.180	0.577	0.254
Aorta: arch	−2.633	−4.021	−1.245	0.000[c]
Aorta: descending	−1.192	−2.623	0.238	0.102
Aortic sum	−0.806	−1.390	−0.222	0.007[b]
Aortic origin: brachiocephalic	−2.925	−4.466	−1.383	0.000[c]
Aortic origin: left carotid	−2.131	−4.089	−0.173	0.033[a]
Aortic origin: left subclavian	−2.155	−3.519	−0.790	0.002[b]
Aortic origin sum	−1.287	−1.945	−0.629	0.000[c]
Valve: aortic	−0.410	−1.755	0.936	0.550
Valve: mitral	0.493	−2.570	3.557	0.752
Valve sum	−0.229	−1.379	0.920	0.695

LAD: left anterior descendens; LCX: left circumflex; Rt: right coronary artery.
B = regression coefficient, indicates change in FEV_1/FVC %/calcification score.
[a] $P < 0.05$.
[b] $P < 0.01$.
[c] $P < 0.001$

Table 4
Association Between $MEF_{50\%}$ and Calcified Atherosclerosis (Multiple Regression). Adjusted for Pack-Years of Smoking, Exposure Years for Asbestos and Body Mass Index

Vessel	B (Coefficient)	B: 95% Lower	B: 95% Upper	*P*-Value
Coronary: LAD	−5.106	−8.380	−1.833	0.002[b]
Coronary: LCX	−3.049	−6.601	0.503	0.092
Coronary: Rt	−3.589	−6.938	−0.240	0.036[a]
Coronary sum	−1.680	−2.952	−0.409	0.010[a]
Aorta: ascending	−7.648	−11.476	−3.820	0.000[c]
Aorta: arch	−10.723	−14.296	−7.151	0.000[c]
Aorta: descending	−8.332	−11.883	−4.782	0.000[c]
Aortic sum	−4.368	−5.822	−2.914	0.000[c]
Aortic origin: brachiocephalic	−11.493	−15.697	−7.289	0.000[c]
Aortic origin: left carotid	−11.081	−16.418	−5.745	0.000[c]
Aortic origin: left subclavian	−9.206	−12.805	−5.608	0.000[c]
Aortic origin sum	−5.294	−7.011	−3.578	0.000[c]
Valve: aortic	−3.639	−7.321	0.043	0.053
Valve: mitral	−5.044	−13.669	3.580	0.251
Valve sum	−3.286	6.409	−0.164	0.039[a]

LAD: left anterior descendens; LCX: left circumflex; Rt: right coronary artery.
B = regression coefficient, indicates change in $MEF_{50\%}$/calcification score.
[a] $P < 0.05$.
[b] $P < 0.01$.
[c] $P < 0.001$.

Table 5
Association Between Total Diffusing Capacity (DLCO%) and Calcified Atherosclerosis (Multiple Regression). Adjusted for Pack-Years of Smoking, Exposure Years for Asbestos and Body Mass Index

Vessel	B (Coefficient)	B: 95% Lower	B: 95% Upper	*P*-Value
Coronary: LAD	−0.683	−2.893	1.526	0.544
Coronary: LCX	−0.633	−3.012	1.747	0.601
Coronary: Rt	−0.139	−2.387	2.109	0.903
Coronary sum	−0.204	−1.060	0.651	0.639
Aorta: ascending	−4.031	−6.605	−1.456	0.002[b]
Aorta: arch	−5.422	−7.849	−2.995	0.000[c]
Aorta: descending	−2.927	−5.341	−0.514	0.018[a]
Aortic sum	−2.011	−3.003	−1.019	0.000[c]
Aortic origin: brachiocephalic	−5.223	−8.081	−2.364	0.000[c]
Aortic origin: left carotid	−3.864	−7.479	−0.249	0.036[a]
Aortic origin: left subclavian	−4.879	−7.309	−2.450	0.000[c]
Aortic origin sum	−2.442	−3.613	−1.270	0.000[c]
Valve: aortic	−1.02	−3.493	1.443	0.415
Valve: mitral	1.428	−4.340	7.195	0.627
Valve sum	−0.550	−2.645	1.545	0.606

LAD: left anterior descendens; LCX: left circumflex; Rt: right coronary artery.
B = regression coefficient, indicates change in total DLCO%/calcification score.
[a] $P < 0.05$.
[b] $P < 0.01$.
[c] $P < 0.001$.

Table 6
Association Between Specific Diffusing Capacity (DLCO/VA%) and Calcified Atherosclerosis (Multiple Regression). Adjusted for Pack-Years of Smoking, Exposure Years for Asbestos and body mass index

Vessel	B (Coefficient)	B: 95% Lower	B: 95% Upper	*P*-Value
Coronary: LAD	−0.531	−2.680	1.617	0.627
Coronary: LCX	−1.020	−3.333	1.293	0.386
Coronary: Rt	0.490	−1.696	2.676	00.660
Coronary sum	−0.141	−0.973	0.692	0.740
Aorta: ascending	−2.018	−4.541	0.506	0.117
Aorta: arch	−4.581	−6.954	−2.207	0.000[c]
Aorta: descending	−2.366	−4.718	−0.014	0.049[a]
Aortic sum	−1.472	−2.444	−0.500	0.003[b]
Aortic origin: brachiocephalic	−4.068	−6.863	−1.273	0.004[b]
Aortic origin: left carotid	−1.805	−5.334	1.724	0.315
Aortic origin: left subclavian	−4.576	−6.941	−2.210	0.000[c]
Aortic origin sum	−1.952	−3.099	−0.806	0.001[b]
Valve: aortic	−2.188	−4.580	0.205	0.073
Valve: mitral	2.648	−2.956	8.253	0.354
Valve sum	−1.226	−3.261	0.809	0.237

LAD: left anterior descendens; LCX: left circumflex; Rt: right coronary artery.
B = regression coefficient, indicates change in total DLCO%/calcification score.
[a] $P < 0.05$.
[b] $P < 0.01$.
[c] $P < 0.001$.

smoking, exposure years for asbestos, and body mass index. Age was adjusted only for the FEV_1/FVC% ratio, because other lung functions were presented as percentages for age-specific reference values. Other covariate patterns were also studied. Multivariate analyses were carried out with 432 patients due to missing data in several variables. *P*-values < 0.05 were regarded as significant.

Results

FEV_1% was inversely related to atherosclerosis in the aorta and the origins of its cervical branches (Table 1). The weak inverse association between FEV_1% and LAD disappeared when stronger predictors, such as the aortic sum score, were added into the model (data not shown). This was due to the mutual correlation between LAD and atherosclerosis at other sites.

The results concerning FVC% (Table 2), FEV_1/FVC% (Table 3), $MEF_{50\%}$ (Table 4), DLCO% (Table 5) and DLCO/VA% (Table 6) were similar, showing significant associations between the lung functions and calcifications in aorta and in its branches. The TLC% showed an inverse association only with atherosclerosis in the ascending aorta (B= –2.229, *P*= 0.017). When the inflammatory markers (ESR and CRP) were added into the models the estimates for the relation between lung functions and atherosclerosis weakened somewhat but mainly remained significant (data not shown). Restricting analyses to previously disease-free workers only or adding cardiovascular disease and diabetes into the models as extra covariates (as well as eliminating all covariates) did not influence the results noteworthy.

Discussion

We found a clear inverse relationship between calcified atherosclerosis and lung function as based on several measures of function. The associations were significant not only concerning FEV_1% and FVC% as previously noted but also concerning their ratio FEV_1/FVC%, $MEF_{50\%}$ and the diffusing capacity of lung tissue. The most important sites of atherosclerosis with this respect were the aorta as well as the origins of the great arteries leaving the aortic arch.

The study subjects were middle-aged or elderly blue-collar male workers, and atherosclerotic changes were common among them as judged from the CT images and disease reports in the files. Our visual classification system of atherosclerotic changes has shown good to excellent intra- and interobserver agreement, except for the left carotid inter-observer rating[11]. In the analyses, we adjusted for factors that might affect both lung function and atherosclerosis (body mass index, smoked pack-years). Due to the nature of the study group we also adjusted for the duration of asbestos exposure, although this is not known to have an effect on atherosclerosis. Generalization of the results to normal population should be done with care. Lacking hard copies of images, missing covariate information (especially the recording of patient weight) or failure to conduct the lung function studies for any reason restricted the number of patients in our analyses. This has most likely minor effect of the overall results, which were little affected by changes in the used covariant pattern. The study used a single slice CT device with thicker cuts than most equipment today. This should not induce any bias in results but may dilute the results to some extent.

Pulmonary vascular abnormalities are frequently present in patients with respiratory disorders, including chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, sarcoidosis, neuromuscular or chest wall disorders, and disorders of ventilatory control including sleep apnoea syndromes and obesity hypoventilation syndrome[12]. Due to the cross-sectional nature of our study it is not possible to conclude whether vascular disease precedes lung functional deterioration or vice versa. Both mechanisms may co-act.

Some prospective studies point towards pulmonary changes being antecedent to cardiovascular effects. Lung function impairment was predictive of increased all-cause mortality during a long-term follow up[13,14]. Most deaths were due to cardiovascular disease, neoplasms being the second most common cause of death[13]. The mechanism by which lung disease could cause non-respiratory pathology remains unknown. It has been speculated, however, that autonomic dysfunction, chronic muscle wasting, or oxidative stress could be involved[14]. Increased systemic and pulmonary vascular resistance and increased vessel stiffness has been suggested as cause of altered pulmonary function in hypertension[15].

Several studies have suggested that systemic inflammation, that is present both in chronic obstructive lung disease and in atherosclerosis, would be an important link between these conditions[12,16-19]. Systemic inflammation may hasten the progression of atherosclerosis and promote cardiovascular morbidity and mortality in COPD [12]. Including ESR and CRP in our models diluted somewhat the relations between lung functions and atherosclerosis indicating a limited role of these inflammatory markers as mediators between the two conditions. More delicate inflammatory markers (such as high-sensitive CRP) could be studied to analyse the matter further.

Also, atherosclerosis may affect more directly the lungs via compromised perfusion of the pulmonary structures. Bronchial arteries are small vessels originating from the descending aorta and 10 different anatomical patterns were angiographically recognized[20]. It is not possible to visualize small bronchial arteries with unenhanced CT, but CT angiography dedicated for that purpose may be performed with a multi-detector device and thin slices[21]. Little seems to be known about bronchial artery atherosclerosis. Such atherosclerosis is most likely correlated to that in aorta and in its branches. Systemic bronchial circulation was important for the normal lung function in an animal experiment[22]. Bronchial arterial devascularisation with transsection caused significant physiologic and morphologic changes in pig lungs[23]. Reduced FEV_1 and FVC values have been noted in diabetic patients[24] and bronchial atherosclerosis has been suspected as a mechanism[25]. It is likely that atherosclerosis in aorta deteriorates bronchial circulation thus perturbing lung function. Coronary or valve sclerosis did not exert equally strong influence on lung function in our material.

FEV_1, FVC, $MEF_{50\%}$ and FEV_1/FVC are dynamic lung function parameters measured in forced expiration. TLC, on the other hand, represents static lung volume. It is measured in slow maximal inspiration and expiration and it includes also the residual volume, which cannot be measured in dynamic spirometry. TLC is the volume of gas in the lungs and intrathoracic airways and it is dependent on the properties of lung parenchyma, surface tension, the force of respiratory muscles and the properties of the airways[7]. Although the dynamic functions also depend on these determinants, the most important are the muscles in the airways walls. Thus, it is understandable that the dynamic functions are more influenced by vascular processes involving the bronchial arteries than the TLC-value is.

FEV_1/FVC% especially indicates airways obstruction[26]. Zureik et al[1] reported a finding corresponding to ours: FEV_1/FVC% ratio was negatively related to arterial pulse wave velocity, but less than FEV_1% and FVC%. The decrease of the elastic recoil of lungs caused by ageing can emphasize the associations between FEV_1/FVC% ratio and atherosclerotic findings. However, the association between FEV_1/FVC% ratio and atherosclerosis may also be related to obstruction in COPD[1,27]. When bronchial inflammation progresses into a systemic inflammation in COPD atherosclerotic findings could be increased.

$MEF_{50\%}$ is a lung function parameter indicating peripheral airways obstruction. It is less specific for obstruction than the FEV_1/FVC% ratio, and it may be reduced also in restrictive stages[26,27]. As far as we

know there are not earlier reports on the association of $MEF_{50\%}$ with atherosclerotic findings.

Most previous studies on associations between cardiovascular pathology and lung function have used FVC or FEV_1[28,29]. In the present study, also the pulmonary parenchyma (as measured with the diffusing capacity values) was affected by atherosclerosis, which is a novel finding. Lungs are highly vascular, which explains why the impairment of perfusion, regardless of the possible mechanisms, easily affects their diffusing properties.

Our study supports and specifies the previous findings pointing to the relations between atherosclerosis and lung function. We were able to identify the site of atherosclerosis likely to be responsible for functional deterioration. The most evident reason for this is atherosclerosis in bronchial arteries or at their origins, which deteriorates bronchial circulation. Lung function poorer than would be expected due to pulmonary reasons may indicate aortic atherosclerosis.

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