

ABSTRACT

Chronic Obstructive Lung Disease (COPD) is a common complex multisystem disease with multiple comorbidities that contribute to symptoms, exacerbations and mortality; the most common cardiovascular comorbidity is the ischemic heart disease. These two diseases share certain risk factors, the most frequent is smoking cigarettes. Currently, there is evidence that other novel mechanistic risk factors can contribute to the pathogenesis of cardiovascular disease, including endothelial dysfunction, which is the earliest stage of atherosclerosis and affects the progression and onset of cardiovascular event. For its measurement a standardized and validated technique is used: the flow mediated dilation (FMD). FMD is defined as the maximum percent increase in arterial diameter by a reactive hyperaemia after a transient ischemia period. In literature, few papers demonstrated that COPD has a reduced FMD in comparison to healthy subjects and it is related both to the degree of bronchial obstruction and to the habitual level of physical activity.

Regarding physical activity several studies reported an improvement of FMD after an exercise training program in patients with different chronic conditions. On the contrary in COPD, the exercise-mediated improvement in endothelial function has been shown only in retrospective studies, while the only prospective study showed no changes.

Based on these assumptions we hypothesized:

1. COPD patients have a reduced FMD compared to healthy subjects but higher than ischemic heart disease (CAD) patients.
2. A walking training program improved FMD in COPD patients.

STUDY 1.

Subjects: 106 subjects (M, ages 60-80) were recruited: 30 healthy, 30 COPD, 30 CAD and 16 COPD+CAD.

Methods: Each subject performed a spirometry, physical activity monitoring for one week and the endothelial function test.

Results: There were no differences between groups for age and BMI. With the onset of the disease, in particular the cardiovascular disease, we observed a reduction of FMD: healthy $7.6 \pm 2.2\%$, COPD $5.0 \pm 1.6\%$, CAD $3.6 \pm 1.4\%$ and BPCO + CAD $3.5 \pm 0.7\%$ (ANOVA, $p < 0.001$); therefore COPD had a lower FMD than healthy but better than CAD ($p = 0.001$) and BPCO+CAD ($p < 0.001$). The only factors independently associated with FMD were the presence of the disease and the number of daily steps ($r^2 = 0.55$, $p = 0.02$).

STUDY 2.

Subjects: 16 COPD (11 M) were recruited: 8 attended to the training program (exercise group, Ex) while 8 refused (control group, C).

Methods: At baseline, each subject performed: a spirometry, physical activity monitoring for one week, the 6 minute walk test and the endothelial function test. Only Ex group performed a maximum cardiopulmonary test at cycloergometer. The Ex group followed a supervised training program on treadmill (45 min, 2 times a week for 8 weeks). After 8 weeks, the same tests were performed.

Results: There were no significant differences in age, BMI, respiratory function, basal artery diameter, FMD and exercise capacity between the two groups. However, the C group is more active than Ex (N° of steps, C: 7462 ± 2111 vs Ex: 4265 ± 2996 , $p=0.02$). After 8 weeks FMD improved in the Ex group (+ 2.98%, $p=0.006$) but not in the C group (-0.27%, $p=0.22$).

Conclusions: These findings confirm the hypothesis that COPD patients have a reduced FMD compared to healthy subjects but higher than ischemic heart disease (CAD) patients. Moreover, the onset of cardiovascular disease decreased FMD even in COPD patients. Furthermore, an 8 week supervised training program improves FMD in COPD patients; this improvement can be considered another positive effect of rehabilitation. Both studies emphasized the importance of an active lifestyle.