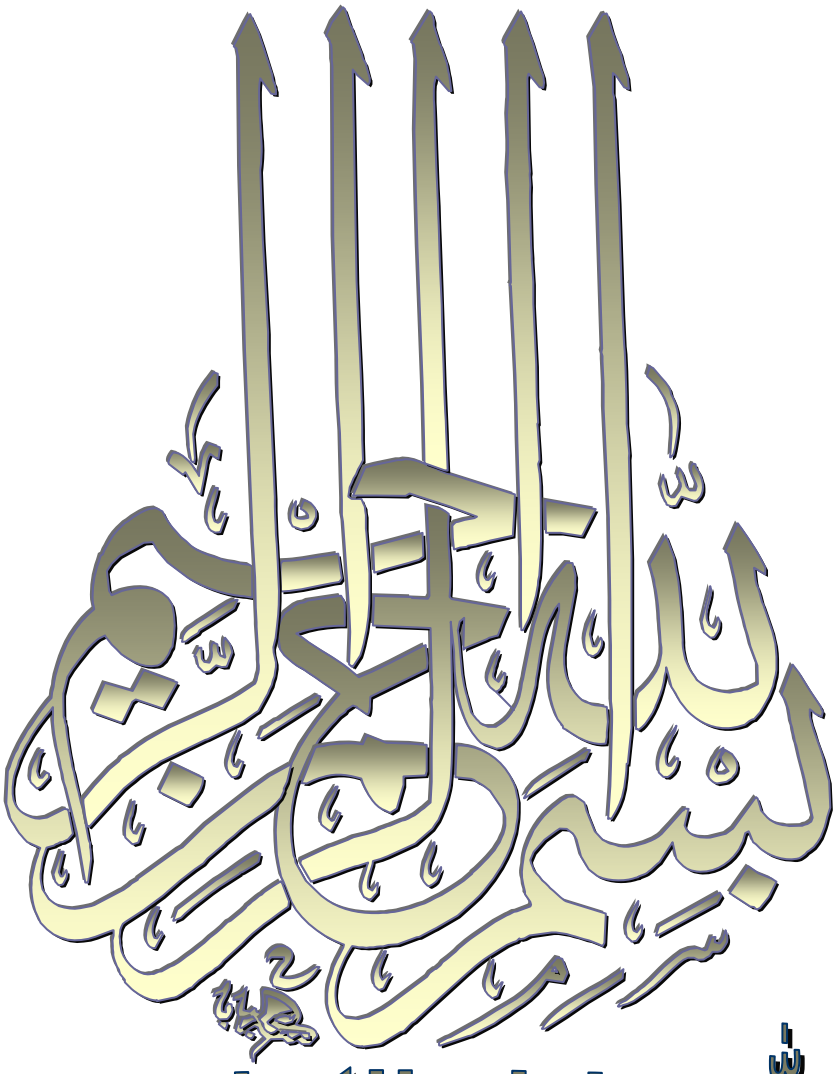

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EARLY DETECTION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AMONG HIGH RISK SMOKERS USING SPIROMETRIC SCREENING IN FAYOUM GOVERNORATE

Thesis

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بين المدخنين الأكثر عرضه للمرض
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بمحافظة الفيوم

رسالة مقدمة للحصول على درجة الماجستير
في الأمراض الصدرية و التدرن

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Abstract

Aim of the Work: is to evaluate the role of spirometry use for the early detection of airflow obstruction in a high-risk population.

Patients and Methods: spirometric screening of 200 male volunteer smokers who were not known to have COPD, and 30 apparently healthy male non smokers as control subjects.

Results:

- 80.5% of smokers had no airways obstruction and 19.5 % of smokers showed different degrees of irreversible airway obstruction.
- Severe COPD group showed the statistically significantly highest mean smoking index with no difference of statistical significance between other groups.
- 36.5% of subjects showed different degrees of small airways affection.
- There was a statistically significant negative (inverse) correlation between age and FEV_1 %(duration of smoking).
- There was no statistically significant correlation between ages, $FEV_{1\%}$ in the normal control.

- There was a statistically significant negative (inverse) correlation between smoking index and FEV_1%.
- There was a statistically significant negative (inverse) correlation between smoking index and FEF_{25-75} %.

Conclusion:

The present study may represent a potentially useful model to use the spirometry in high-risk groups as an effective and easy method for the early detection of COPD.

Key words:

Role of spirometry in COPD.

Discussion

In 1990, COPD ranked sixth among the most common causes of death and is predicted to rank third by the year 2020.
(Mannino DM, 2005).

As we enter the new millennium, it seems that the only available method to prevent the development of severe forms of COPD is early diagnosis of the disease followed by persistent concerted actions to persuade newly diagnosed patients to stop smoking ***(GOLD, 2007).***

Cigarette smoking is the major risk factor for COPD, inducing inflammatory changes in the airway and an protease/ antiprotease imbalance as well as an oxidant/antioxidant imbalance, leading to irreversible damage to the most peripheral structures of the lung (emphysema) ***(MacNeeW, 2005).***

Approximately 15 to 20% of smokers develop COPD ***(Burrows, et al., 1977)***.

As smoking is a behavior that can be changed, a key issue in avoiding the development of severe forms of COPD would be to identify susceptible smokers at an early stage of the disease and to persuade them to stop smoking.

So our study is aiming to evaluate the role of spirometry use for the early detection of airflow obstruction in a high-risk population.

The present study was conducted in El Fayoum Hospital, chest department, by spirometric screening of 200 male volunteer smokers who were not known to have COPD, and thirty apparently healthy male non smokers as control subjects.

All subjects were from El Fayoum Governorate in the period between October 2008 and April 2009.

The age of the smoker group ranged between 40 to 72 years with (mean 49.97 ± 7.2) which matched with the age of the normal control which ranged between 41 to 65 years (mean 48.57 ± 5.6) and the age distribution between the two groups showed no statistically significant difference, patients who had included a history of respiratory disease or respiratory tract infection during the last 4 weeks before the study were excluded.

The group selected was a high risk population so the smoking index was high ranged between 400-2250 with mean (755.4 ± 363.2), Patients of (60 – 69) years old had the highest mean smoking index but there was no statistically significant difference between other age groups.

Spirometric screening was done for all subjects (smokers & non smokers) and the flow-volume loop was performed and the percentage of predicted values of FVC, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$ were recorded.

Ventilatory function pre and post bronchodilator were performed for all subjects to detect the degree of reversibility ***(GOLD, 2007).***

In the present study 39 smokers out of 200 smokers with percentage of 19.5% were found to have irreversible airways obstruction (COPD) according to **GOLD 2007** and 161 smokers (80.5%) had no airways obstruction.

Beside, the smoker group showed statistically significant lower value for all spirometric parameters recorded than normal control group.

In smoker group mild airway obstruction was found in 3%, moderate airway obstruction was found in 9% and severe airway obstruction was found in 7.5% according to ***(GOLD, 2007).***

The absence of complaint inspite of presence of severe cases return to the fact that all subjects were from rural areas in addition to that they

were hard manual workers who never seek medical advice except when they had severe alarming symptoms.

Previous study performed in the United States and Canada for the Lung Health Study (LHS) showed slightly higher percentage of subjects with airway obstruction, results varied from 21.8 to 35.7% (mean, 25%). Additionally, 5% had severe airway obstruction which is close to the present study.

The difference with the present study results may be related to our inclusion criteria for smokers who had no history of respiratory symptoms.

They performed their screening study on 73,000 smokers aged 35 to 60 years who were recruited in 10 centers ***(Connett et al., 1993)***.

The present study is in agreement with another large screening study which was performed in pulmonary outpatient clinics in 12 large cities of Poland, 11,027 subjects were screened their age was (51.8 ± 12.5) years , 80% were current smokers or ex-smokers with a smoking history of 26.1 ± 16.8 pack-years. Spirometric signs of airway obstruction were found in 24.3% of screened subjects, signs of mild obstruction were found in 9.5% of all subjects, moderate obstruction was found in 9.6%, and severe obstruction was found in 5.2%, the obstructive pattern of ventilatory impairment was classified according to the European Respiratory Society Guideline**,** they explained the high prevalence of airways obstruction in their study to be in part by the quality of cigarettes and another factor which could play a role was the high level of environmental air pollution**(Zieliñski et al., 2006).**

Regarding the smoking index the group of severe airway obstruction in our study showed the statistically significantly highest mean smoking index with no difference of statistical significance between other groups.

Lokke et al., (2006) concluded that the primary risk factor for COPD is chronic tobacco smoking, 80 to 90% of cases of COPD are due to smoking. Exposure to cigarette smoke is measured in pack-year, the average number of packages of cigarette smoked daily multiplied by the number of years of smoking. Not all smokers will develop COPD, but continuous smokers have at least a 25 % risk after 25 years. The likelihood of developing COPD increase with increasing age as cumulative smoke exposure increases.

In this study there was also a statistically significant negative (inverse) correlation between smoking index and FEV_1% i.e. an increase in smoking index is associated with a decrease in FEV_1%.

It is known that the severity of COPD is related to the degree of smoking i.e. with increase smoking index there are decrease of FEV_1**%(Anthonisen et al., 2002).**

The Lung Health Study (LHS) clearly demonstrated that smoking cessation at an early stage of COPD resulted in an improvement of FEV_1 during the first year after smoking cessation followed by a plateau and a very slow decline. At the end of the fifth year of follow-up, FEV_1 in sustained nonsmokers (22% of those who stopped smoking at entry) was only 73 mL lower than at entry. Thus, the rate of decline of FEV_1 after successful smoking cessation was 15 mL/year, which is similar to that seen in healthy nonsmoking populations ***(Anthonisen et al., 2002)***.

Also, ***(Xu et al, 1992)*** in a longitudinal study of 8,000 COPD patients, found that those who stopped smoking ceased to lose pulmonary function at an accelerated rate**.**

Historically, **Fletcher and Peto** were the first to report beneficial effects of smoking cessation on the rate of FEV_1 decline in patients with COPD.

We presume from that the only confirmed method to slow down the FEV_1% decline in COPD patients is smoking cessation.

In this study there was a statistically significant negative (inverse) correlation between age and FEV_1% i.e. an increase in age is associated with a decrease in FEV_1% (increase in the duration of smoking).

These results are in agreement with **ATS, 2002 which mentioned** that the loss of FEV_1 in excess of the normal decline with aging is 9 ml per year for each pack-year of smoking.

The present study showed spirometric signs of small airway affection about 37.5 % that varied from mild group about 21.5 % to moderate group 7.5 % to severe affection about 7.5 % of all smokers group which mean that there is early affection of the small airways in healthy smokers.

Hogg et al., 2004 mentioned that one of the earliest histological abnormalities that can be detected in cigarette smokers is the presence of macrophages in the lumen of the respiratory bronchioles. However, an inflammatory infiltrate can also be identified within the walls of both membranous and respiratory bronchioles in subjects with COPD this lead to early small airway affection so similar to the large airways affection there is alteration of the all of the small airway wall compartments in patients with COPD.

The present study showed that there was a statistically significant negative (inverse) correlation between smoking index and FEF_{25-75}% i.e. an increase in smoking index is associated with a decrease in FEF_{25-75}%.

These results are in agreement with ***Anthonisen*** **et al., 2002** who mentioned that the man who has smoked one pack daily for 30 years will have an FEF_{25-75}% less than it would have been had if he not smoked.

But these results are in disagreement with ***James et al., 2006*** who study a total of 5,938 adult never-smokers and 3,570 current smokers from NHANES III using FEF_{25-75}% to evaluate their utility in measuring the effect of smoking on airflow limitation with spirometric data meeting **American Thoracic Society standards**, he proved that FEF_{25-75}% measurements can be misleading and can cause an unacceptably large number of probable false-negative results and probable false-positive results & he explained that by that the lower limit of normal for FEF_{25-75}%is an absolute rather than a relative value in all predicting equations is a factor in the high incidence of probable false-negative results.

Recently, ***Buffels et al., (2004)*** demonstrated that spirometry is an effective screening tool in the detection of COPD in general practice, especially in its early stages, even in patients who underestimate and do not report any relative symptoms**.**

The diagnosis of COPD at an early stage and awareness of the health consequences of COPD should be strong motivations for smoking cessation as the only confirmed effective method for prevention of COPD is smoking cessation and short antismoking advice reinforced by nicotine replacement therapy yields a 20 to 30% long term success rate the preliminary results of combination therapy with the antidepressant drug bupropion and nicotine replacement therapy are even more promising ***(Jorenby DE, et al.,1999).***

Contents

List of Abbreviations

α_1AT	Alpha-1 anti-trypsin.
α_1PI	Alpha-1 proteinase inhibitor.
ADL	Activity of daily living.
ANP	Atrial natriuretic peptide.
ATS	American Thoracic Society.
AVP	Arginin vasopressin.
BAL	Bronchoalveolar lavage.
BMD	Bone mineral density.
BMI	Body mass index.
BODE	Body mass index, obstruction, dyspnea and exercise.
BTS	British Thoracic Society.
CD	Cell differentiated
COPD	Chronic obstructive pulmonary disease.
CRP	C-reactive protein.
CT	Computed tomography
CysLT	Cysteinyl leukotriene receptor.
DLCO	Diffusion capacity of the lung to carbon monoxide.
DPIs	Dry powder inhalers.
ECP	Eosinophil cationic protein.
EPO	Eosinophil peroxidase.
ERS	European respiratory society.
ET-1	Endothelin-1.
F/V loop	Flow volume loop.
FEF_{25-75}	Forced expiratory flow 25 to 75% of forced vital capacity.
FEV_1	Forced expiratory volume in the first second.

FFM	Fat free mass.
FRC	Functional residual capacity.
FVC	Forced vital capacity.
GM-CSF	Granylocyte macrophage colony stimulating factor.
GOLD	Global Initiative for Chronic Obstructive Lung Disease.
H_2O_2	Hydrogen peroxide.
HS-CRP	High sensitive C-reactive protein.
IC	Inspiratory capacity.
ICS	Inhaled corticosteroids.
IL-1	Interleukin-1.
IL-6	Interleukin-6.
IL-8	Interleukin-8
INO_2	Inducible nitric oxide synthase.
Kco	Diffusion coefient of carbon monoxide.
LABA	Long acting B_2 agonist.
LDL	Low density lipoprotein.
LHS	Lung health study.
LTB_4	Leukotrienes B_4.
MBL	Mannose binding lectin.
MBP	Mannose binding protein.
MCP-1	Macrophage chemotactic protein-1.
MDI	Metered-dose inhaler.
$MEPHX_1$	Microsomal epoxide hydrolase-1.
MIP-1$^{\alpha}$	Macrophage inflammatory protein-1α.
MIP-1β	Macrophage inflammatory protein-1β.
MMPs	Matrix metalloproteinases.

MPO	Myeloperoxidase.
NF-kβ	Nuclear factor-kβ.
NK cells	Natural killer cells.
NO_2	Nitrogen dioxide.
O_3	Ozone.
$PaCO_2$	Partial pressure of carbon monoxide in arterial blood.
PaO_2	Partial pressure of oxygen in arterial blood.
PDGF	Platelet derived growth factor.
RAAS	Renin-angiotensin-aldosterone system.
REE	Resting energy expenditure.
RV	Residual volume.
SABA	Short acting B_2 agonist.
SAP	Serum amyloid P component.
SHBG	Sex hormone binding globulin.
SI	Smoking index.
SLP_1	Secretory leukoproteinases inhibitor.
SNS	Sympathetic nervous system.
SO_2	Sulphur doxide.
TGF-β_1	Transforming growth factor beta-1.
TLC	Total lung capacity.
TLR	Toll like receptor.
TNF-α	Tumor necrosis factor alpha.
VA/Q	Ventilation/perfusion ratio.
VIP	Vasoactive intestinal peptide.
VLDL	Very low density lipoprotein.
6MW	Six minute walking distance.