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Ventilatory function impairment and risk of cardiovascular death and of fatal or non-fatal myocardial infarction

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Ventilatory function impairment and risk of cardiovascular death and of fatal or non-fatal myocardial infarction. P. Lange, J. Nyboe, G. Jensen, P. Schnohr, M. Appleyard.

ABSTRACT: The relationship of ventilatory function to cardiovascular events was studied in 12,511 men and women, enrolled in 1976–1978 in a prospective population study. Until the end of 1983, 388 subjects died because of a cardiovascular disease, 133 died within 30 days of developing myocardial infarction (fatal myocardial infarction), while 238 had a non-fatal myocardial infarction.

Cox proportional hazards models were employed for the analysis. In the models including tobacco smoking, cholesterol level, blood pressure, diabetes mellitus and body-mass index as covariates, forced expiratory volume in one second in percentage of predicted (FEV_1%pred), forced vital capacity in percentage of predicted (FVC%pred), and the ratio between FEV_1 and FVC (FEV_1/FVC) were significantly related to the risk of cardiovascular death, *e.g.* compared with subjects with FEV_1%pred or FVC%pred ≥80 the risk of death from cardiovascular disease among subjects with FEV_1%pred or FVC%pred <60 was approximately twice as high. There was a nonsignificant trend towards an increased risk of fatal myocardial infarction with reduction of FVC%pred, but in general the regression models did not show consistent relationship between lung function impairment and risk of myocardial infarction.

In the regression models, which only included age and sex as covariates, reduced FVC%pred and FEV_1%pred were significantly related to both cardiovascular mortality and to fatal myocardial infarction, but not to the non-fatal infarction, whereas the FEV_1/FVC ratio was not related to fatal or to non-fatal myocardial infarction.

Our results suggest that although impaired ventilatory function is a significant predictor of death from myocardial infarction and other cardiovascular diseases, it should not be regarded as a genuine risk factor for ischaemic heart disease.

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In 1978, COHEN [1] proposed that impaired lung function might be a common denominator for the various health effects of cigarette smoking. In agreement with this hypothesis, impaired ventilatory function has been significantly related to both total [2–5] and cause specific mortality [4, 6–9] in many longitudinal studies. In addition, the relationship between poor lung function and increased risk of death has been observed even among lifetime nonsmokers [10, 11]. While it is apparent that a strong link should exist between impaired ventilatory function and mortality from lung disease, there is at present no satisfactory explanation for the association between lung function impairment and non-pulmonary mortality. One explanation for this association could be that pulmonary impairment, through some unknown mechanism, is causally related to the development of various malignant and non-malignant diseases [1, 12]. This explanation implies that poor lung function should be regarded as a risk factor for development of various diseases. However, another possibility could be that lung function is an indicator of general health status, "vitality", of an individual, which will influence the course of all types of chronic disease [13]. The latter notion indicates, that the association between reduced lung function and increased mortality might simply reflect the fact that subjects already weakened at the time of lung function measurement, have a higher risk of death than healthy subjects.

In the present study we investigated the association between ventilatory function and ischaemic heart disease (IHD) and cardiovascular mortality. We have chosen acute myocardial infarction (AMI-) as an early indicator of IHD. It was *a priori* expected that if lung function impairment was a genuine risk factor for IHD, it should be significantly related to both incidence of first time AMI and to cardiovascular mortality. On the other hand,

if impaired lung function is not a coronary risk factor, but merely reflects the presence of some chronic disease and/or poor health status, one might expect it to be related to cardiovascular mortality, but not necessarily to the incidence of non-fatal AMI. In the analysis we used data from The Copenhagen City Heart Study, a large prospective epidemiological study primarily designed to identify risk factors for IHD.

Subjects and methods

Population

The Copenhagen City Heart Study was initiated in 1976. The participants were selected among 90,000 persons living in a defined area around Rigshospitalet, the State University Hospital of Copenhagen. Details of the selection procedure of the study sample and of the examination procedures have previously been given elsewhere [14, 15].

The present analysis comprised subjects who participated in the initial examination, which took place from 1976–1978. The subjects younger than 30 yrs of age and those with AMI prior to the enrolment were excluded, together with the subjects with insufficient data for the analysis (table 1). This resulted in a population of 12,511 subjects, who were followed until the end of 1983 by means of the National Health Service Registries for deaths and hospital discharges. The average follow-up period was 6.5 yrs. During this period 1,098 of the subjects eligible for the analysis died. In subjects who died or were admitted to hospital, autopsy reports and hospital records were obtained.

Definition of end-points for the analysis

Three different end-points were analysed: a) non-fatal AMI; b) fatal AMI; and c) death caused by cardiovascular disease.

The diagnosis of AMI was made according to the World Health Organization (WHO) criteria, which demand fulfilment of two out of the following three criteria: 1) typical chest pain for more than 30 min; 2) typical electrocardiogram (ECG) changes; and 3) enzyme elevation. A fatal case of AMI was registered if the patients died within 30 days from the AMI diagnosis. Death from cardiovascular disease was registered if the main cause of death on the death certificate had a code number 400–450 according to the 8th revision of the International Classification of Diseases [16]. During the follow-up period, we observed 133 cases of fatal AMI, 238 cases of non-fatal AMI, and 388 deaths from cardiovascular disease (table 1).

Description of potential risk variables

The variables of main interest for the present analysis were forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and the ratio between these measurements (FEV_1/FVC). The ventilatory function variables were measured with an electronic spirometer (Monaghan N 403, Littleton, Colorado, USA), which was calibrated daily. As a criterion for the correct performance, at least two measurements differing less than 5% from each other had to be produced.

Table 1. – Study population for the analysis

Sample selected January 1st, 1976	19698
Died before planned visit	369
Alive at planned visit	19329
Responders	14223
Excluded	
Previous AMI	449
Younger than 30 yrs	962
Missing data	301
Population at risk	12511
End-points until 31 December, 1983	
Died from all causes	1098
Died from cardiovascular disease	388
New cases of non-fatal AMI	238
New cases of fatal AMI	133

AMI: acute myocardial infarction.

We used internal reference values, which were generated from the spirometric data from a subgroup of lifetime nonsmokers without diabetes mellitus, bronchial asthma, heart disease, pulmonary symptoms and with daily consumption of alcohol of less than five drinks. The estimated regressions of FEV_1 and FVC in ml (ambient temperature and pressure saturated (ATPS)) on age (yrs) and height (cm) with standard errors (SE) and the coefficients of determination (r^2) were as follows:

For women:

FEV_1 = 410 - 27.6×age + 21.2×height; SE=426; r^2=0.46

FVC = -217 - 28.4×age + 28.2×height; SE=503; r^2=0.43

For men:

FEV_1 = -469 - 35.2×age + 32.0×height; SE=628; r^2=0.51

FVC = -1921 - 35.4×age + 44.6×height; SE=760; r^2=0.48

For each participant the adjustment of the observed spirometric data to the prediction equations was done by calculating the observed FEV_1 and FVC as percentage of predicted (FEV_1%pred and FVC%pred). For the analyses we classified the participants into the following categories: subjects with normal FEV_1: FEV_1%pred ≥80; subjects with slightly reduced FEV_1: 60 ≤FEV_1%pred <80; and finally, subjects with moderately or severely reduced FEV_1: FEV_1%pred <60. The same limits were used to classify the subjects according to FVC%pred.

The classification according to the percentage of predicted was employed because it is widely used in clinical settings and easy to interpret, although the use of a classification according to units of standard deviations is probably more correct from the statistical point of view [17, 18].

With regard to FEV_1/FVC, the subjects were divided into two groups: those with FEV_1/FVC ≥0.65 and those with lower values.

Other investigated variables

In addition to age, sex, and indices of ventilatory function some of the analyses included the following well-established risk factors for IHD: tobacco smoking, diabetes mellitus, blood pressure, body-mass index (BMI) and plasma-cholesterol level.

Smoking habits. Smoking habits were obtained from the questionnaire. The questions covered both previous and current smoking habits including the duration of smoking, the type of tobacco smoked, the average daily consumption of tobacco, and inhalation habits. All types of tobacco were pooled together using the following equivalents for tobacco content: one plain or filter cigarette = 1 g; one cigar = 5 g; 1 cheroot or cigarillo = 3 g; 1 g of pipe tobacco = 1 g. After preliminary analyses the following grouping was used:

SMK Group 1: current nonsmokers
SMK Group 2: current smokers who reported not inhaling
SMK Group 3: current smokers who reported inhaling and consumed <15 g of tobacco a day
SMK Group 4: current smokers who reported inhaling and consumed ≥15 g but <30 g of tobacco a day
SMK Group 5: current smokers who reported inhaling and consumed ≥30 g of tobacco a day

Blood pressure. Blood pressure was measured with the London School of Hygiene sphygmomanometer [19]. After preliminary analysis it was decided to use systolic blood pressure (SBP) in the analysis and to transform the observed levels of SBP to standardized deviates (SD) by subtracting the mean and dividing the difference by the standard deviation for the sex and 10 yr age group in question. The transformation was done to eliminate the influence of age and sex on SBP. In the final regression analysis standardized SBP was entered as a continuous variable. In the initial presentation of data, the subjects were subdivided according to standardized SBP into the following groups:

SBP Group 1: standardized SBP <-0.5 SD
SBP Group 2: -0.5 SD ≤ standardized SBP <0.5 SD
SBP Group 3: 0.5 SD ≤ standardized SBP <1.5 SD
SBP Group 4: standardized SBP ≥1.5 SD

Plasma cholesterol. Plasma cholesterol (CHOL) was measured enzymatically using non-fasting blood samples drawn from a cubital vein [15]. As with SBP the age- and sex-standardized deviates were generated and used in the analysis. After preliminary analysis the following classification was employed:
CHOL Group 1: standardized CHOL <0.75 SD
CHOL Group 2: 0.75 SD ≤ standardized CHOL <1.75 SD
CHOL Group 3: 1.75 SD ≤ standardized CHOL <2.5 SD
CHOL Group 4: standardized CHOL ≥ 2.5 SD

Body-mass index. BMI (weight×height^{-2} in kg·m^{-2}) was included using three levels: <20; 20–29, ≥30.

Diabetes mellitus. The diagnosis of *diabetes mellitus* (DM) was based on answers in the questionnaire.

Statistical analysis

The proportional hazards model of Cox was used for analysis [20]. The variables of main interest were measures of ventilatory function (FEV_1%pred, FVC%pred and FEV_1/FVC). The Cox regression model was used in two ways: 1) analytically; and 2) as a simple predictive model [21]. The analytical models comprised major risk factors for ischaemic heart disease, such as smoking habits, blood pressure, cholesterol level, BMI and diabetes mellitus, in addition to an index of ventilatory function, age and sex. Whereas smoking, diabetes and BMI can be regarded as genuine confounders because they are related to both lung function [22, 23] and to the end-points of the present study, systolic blood pressure and cholesterol were included because they are well-established risk factors for ischaemic heart disease, although they were not significantly correlated to the lung function level in this population.

The predictive models included only sex and age as covariates in addition to either FEV_1%pred, FVC%pred and FEV_1/FVC.

Separate models were developed for the three end-points: non-fatal AMI, fatal AMI, and cardiovascular death. Time was reckoned from the initial examination until the occurrence of an end-point or until the end of the observation period. The regression coefficients were estimated using the maximum likelihood method as suggested by Cox, and the hypothesis of a significant effect of a risk factor was evaluated by means of the likelihood ratio test. The results are given in terms of estimated relative risks (ERR).

Results

The distribution of subjects according to the different levels of the investigated variables and the observed number of new cases of AMI and of cardiovascular deaths are given in table 2. The unadjusted incidence of the investigated end-points, especially the incidence of cardiovascular deaths, increased with decreasing FVC%pred. A similar, although less pronounced trend was observed for FEV_1%pred and FEV_1/FVC. The incidence of all three end-points increased with age, systolic blood pressure, cholesterol level, BMI and with the amount of tobacco smoked. The incidence was higher in men than in women and higher among subjects with diabetes than in the non-diabetic subjects.

Both analytical and predictive proportional hazards models were developed for each one of the investigated end-points using either FEV_1%pred, FVC%pred or FEV_1/FVC as the index of ventilatory function. In the analytical models, all of the variables describing other

Table 2. – Distribution of the subjects according to the levels of the investigated variables and end-points

Variable	Subjects at risk n	Cardiovascular deaths n (% of all)	Non-fatal AMI n (% of all)	Fatal AMI n (% of all)
FEV_1%pred				
≥80	9408	244 (2.6)	167 (1.8)	89 (0.9)
60–79	2327	88 (3.8)	55 (2.4)	33 (1.4)
<60	776	56 (7.2)	16 (2.1)	11 (1.4)
FVC%pred				
≥80	10471	278 (2.7)	197 (1.9)	97 (0.9)
60–79	1740	84 (4.8)	34 (2.0)	29 (1.7)
<60	300	26 (8.7)	7 (2.3)	7 (2.3)
FEV_1/FVC				
≥0.65	11460	324 (2.8)	214 (1.9)	117 (1.0)
<0.65	1051	64 (6.1)	24 (2.3)	16 (1.5)
Sex				
Women	6856	113 (1.6)	78 (1.1)	101 (1.5)
Men	5655	275 (4.9)	160 (2.8)	32 (0.6)
Age				
30–49 yrs	4441	25 (0.6)	30 (0.7)	11 (0.2)
50–59 yrs	4479	92 (2.1)	86 (1.9)	34 (0.8)
60–69 yrs	2865	170 (5.9)	98 (3.4)	58 (2.0)
70+ yrs	726	101 (13.9)	24 (3.3)	30 (4.1)
Diabetes mellitus				
No	12298	367 (3.0)	230 (1.9)	122 (1.0)
Yes	213	21 (9.9)	8 (3.8)	11 (5.2)
Body-mass index				
<20	863	21 (2.4)	7 (0.8)	7 (0.8)
20–29	10121	300 (3.0)	194 (1.9)	103 (1.0)
≥30	1527	67 (4.4)	37 (2.4)	23 (1.5)
Systolic blood pressure				
SBP group 1	4116	92 (2.2)	52 (1.3)	31 (0.8)
SBP group 2	4867	134 (2.8)	94 (1.9)	47 (1.0)
SBP group 3	2440	96 (3.9)	60 (2.5)	30 (1.2)
SBP group 4	1088	66 (6.1)	32 (2.9)	25 (2.3)
Cholesterol				
CHOL group 1	10071	291 (2.9)	147 (1.5)	98 (1.0)
CHOL group 2	1852	66 (3.6)	62 (3.3)	24 (1.3)
CHOL group 3	400	17 (4.3)	15 (3.8)	7 (1.8)
CHOL group 4	188	14 (7.4)	14 (7.4)	4 (2.1)
Smoking habits				
SMK group 1	4541	112 (2.5)	61 (1.3)	11 (0.2)
SMK group 2	2127	91 (4.3)	33 (1.6)	32 (1.5)
SMK group 3	2265	62 (2.7)	47 (2.1)	23 (1.0)
SMK group 4	3015	98 (3.3)	77 (2.6)	34 (1.1)
SMK group 5	563	25 (4.4)	20 (3.6)	33 (5.9)

AMI: acute myocardial infarction; FEV_1%pred: forced expiratory volume in one second as percentage of predicted; FVC%pred: forced vital capacity as percentage of predicted; FEV_1/FVC: ratio between FEV_1 and FVC; SBP: systolic blood pressure; CHOL: cholesterol; SMK: smoking. For definition of different groups see text.

Table 3. – Estimated effects of FEV_1%pred, FVC%pred and FEV_1/FVC on cardiovascular mortality, fatal, and non-fatal AMI

Covariate	Cardiovascular deaths ERR (95% CI)	Non-fatal AMI ERR (95% CI)	Fatal AMI ERR (95% CI)
FVC%pred	p<0.001	p>0.1	p=0.09
≥80	1.0	1.0	1.0
60–79	1.4 (1.1–1.7)	0.8 (0.5–1.1)	1.3 (0.9–2.0)
<60	2.2 (1.5–3.4)	0.9 (0.4–2.0)	1.7 (0.8–3.6)
FEV_1%pred	p<0.001	p>0.1	p>0.01
≥80	1.0	1.0	1.0
60–79	1.2 (0.9–1.5)	1.1 (0.8–1.5)	1.2 (0.8–1.8)
<60	1.8 (1.4–2.4)	0.8 (0.5–1.4)	0.9 (0.5–1.7)
FEV_1/FVC	p<0.05	p>0.1	p>0.1
≥0.65	1.0	1.0	1.0
<0.65	1.3 (1.0–1.7)	0.7 (0.5–1.1)	0.9 (0.5–1.4)

Estimated relative risks (ERR) derived from a proportional hazards model of Cox of the analytical type including sex, age, diabetes mellitus, systolic blood pressure, cholesterol level, body-mass index (BMI) and smoking habits as other covariates. 95% CI: 95% confidence interval. For other abbreviations see legend to table 2.

Table 4. – Estimated effect of the covariates included together with FEV_1%pred in the analytical proportional hazards model of Cox

Covariate	Cardiovascular deaths ERR	p	Non-fatal AMI ERR	p	Fatal AMI ERR	p
Sex		<0.001		<0.001		<0.001
Women	1.0		1.0		1.0	
Men	2.5		2.2		3.1	
Age		<0.001		<0.001		<0.001
30–49 yrs	1.0		1.0		1.0	
50–59 yrs	4.1		3.4		3.5	
60–69 yrs	13		7.5		10	
70+ yrs	37		9.2		25	
Diabetes mellitus		<0.01		0.08		<0.01
no	1.0		1.0		1.0	
yes	1.9		1.4		3.3	
Systolic blood pressure		<0.001		<0.001		<0.001
Increase in risk per 1 SD	1.4		1.3		1.4	
Cholesterol		<0.01		<0.001		<0.05
CHOL group 1	1.0		1.0		1.0	
CHOL group 2	1.2		2.2		1.3	
CHOL group 3	1.4		2.5		1.7	
CHOL group 4	3.1		5.4		2.3	
Smoking habits		<0.001		<0.001		<0.001
SMK group 1	1.0		1.0		1.0	
SMK group 2	1.3		1.0		1.8	
SMK group 3	1.5		1.9		2.0	
SMK group 4	2.1		2.5		2.4	
SMK group 5	2.7		3.3		3.8	

SBP: systolic blood pressure. For further abbreviations see legends to tables 2 and 3. For definition of different groups see text.

Table 5. – Estimated effects of FEV_1%pred, FVC%pred and FEV_1/FVC on cardiovascular mortality, fatal, and non-fatal AMI

Covariate	Cardiovascular deaths ERR (95% CI)	Non-fatal AMI ERR (95% CI)	Fatal AMI ERR (95% CI)
FVC%pred	p<0.001	p>0.1	p=0.05
≥80	1.0	1.0	1.0
60–79	1.5 (1.2–1.9)	0.9 (0.4–1.9)	1.5 (1.0–2.2)
<60	2.5 (1.7–3.7)	1.0 (0.7–1.4)	2.4 (1.3–4.7)
FEV_1%pred	p<0.001	p>0.1	p=0.05
≥80	1.0	1.0	1.0
60–79	1.4 (1.1–1.9)	1.2 (0.9–1.6)	1.4 (1.0–2.0)
<60	2.0 (1.5–2.7)	0.9 (0.6–1.5)	1.2 (0.8–2.2)
FEV_1/FVC	p<0.05	p>0.1	p>0.1
≥0.65	1.0 p<0.05	1.0 p>0.1	1.0 p>0.1
<0.65	1.4 (1.1–1.9)	0.9 (0.6–1.3)	1.0 (0.6–1.6)

Estimated relative risks (ERR) derived from a predictive proportional hazards model of Cox including sex and age as other covariates. For abbreviations see legends to tables 2 and 3.

potential risk factors than ventilatory function were included as covariates. In these models, the risk of cardiovascular death increased significantly with decreasing levels of FVC%pred, FEV_1%pred and FEV_1/FVC (table 3). In contrast, the risk of AMI was not significantly related to the lung function, although the ERR for fatal AMI were consistently higher than 1 for reduced levels of FVC%pred. The ERR for the covariates describing male sex, diabetes, systolic blood pressure, cholesterol level, and smoking habits derived from the models including FEV_1%pred are given in table 4. In the models including FVC%pred or FEV_1/FVC, the ERR for these variables were almost identical. After inclusion of all covariates in the regression models, BMI was not significantly related to any of the investigated end-points.

Table 5 shows the ERR for the FVC%pred, FEV_1%pred and FEV_1/FVC obtained using the simple predictive models, which only included age and sex as covariates. Both FEV_1%pred and FVC%pred were significant predictors of cardiovascular mortality and fatal AMI, whereas FEV_1/FVC was only significantly related to cardiovascular mortality. None of the investigated lung function variables were significant predictors of non-fatal AMI.

Discussion

Our study showed that whilst ventilatory impairment in a simple predictive model was significantly related to both cardiovascular mortality and fatal AMI, it was only related to cardiovascular mortality in a regression model including major risk factors for cardiovascular disease. In neither type of regression model was FEV_1, FVC or FEV_1/FVC significantly related to non-fatal AMI, suggesting that ventilatory impairment is not causally related to IHD.

The effects of variables like tobacco smoking, blood pressure, cholesterol level, BMI and diabetes were similar to those observed in other populations and have been discussed in another report [24].

There are several possibilities of bias connected with the definition of the end-points used in the present analysis. Whereas it is likely that the use of WHO criteria for diagnosis of AMI yields high sensitivity and specificity [24], the diagnosis of cardiovascular death is probably less certain. Previous studies on the reliability of the Danish Death Register indicated that cardiovascular deaths including deaths from heart disease are likely to be overestimated [25]. If some of the deaths registered as cardiovascular deaths were in fact due to lung disease, this could result in an overestimation of the effect of ventilatory function impairment.

Previous studies of the relationship between ventilatory function impairment and cardiovascular mortality showed a significantly higher risk of mortality in subjects with impaired FEV_1 [1, 6, 8], FEV_1/FVC [4], and FVC [26]. However, in a recent paper comparing four large surveys, in only one of the surveys was the risk of cardiovascular death among subjects with moderately or severely reduced FEV_1 significantly higher than among those with normal or slightly reduced FEV_1 [27]. In the present study, the risk of cardiovascular death among subjects with reduced ventilatory function was only moderately raised. In comparison, subjects with a similar lung function impairment had a more than 50 times higher risk of death from obstructive lung disease than those with normal lung function [28]. Whereas there is little doubt that the latter association is causal, the mechanisms beyond the observed association between ventilatory impairment and cardiovascular mortality remain speculative. In fact, the ERR of death from cardiovascular disease were lower than the ERR for total mortality in subjects with a similar FEV_1 reduction [28].

With regard to AMI, the models including major coronary risk factors showed that ventilatory impairment was not significantly associated with the risk of first AMI. However, there was a trend towards an increased risk of

fatal AMI among subjects with reduced FVC. In fact, the ERR for fatal AMI in subjects with reduced FVC%pred were not very different from the ERR for cardiovascular mortality and the lack of significance was probably due to the low number of fatal AMI.

The lack of a significant independent association between reduced ventilatory function and AMI is in accordance with some [29–31], but not with other studies, where there was a significant, although relatively weak association between a measure of the ventilatory function and risk of AMI [32–34]. In the Framingham Study [26] reduced FVC was associated with the risk of AMI only in women. In the multiple risk factor intervention trial (MRFIT) study, KULLER *et al.* [35] observed that reduced FEV_1 was associated with increased risk of coronary heart disease mortality, but not with the risk of non-fatal myocardial infarction. The latter findings are quite similar to ours.

In their paper on respiratory risk factors and mortality TOCKMAN and COMSTOCK [12] discussed two possible mechanisms for the association between reduced ventilatory function and cardiovascular mortality: 1) a mechanism leading from reduced pulmonary function through chronic hypoxaemia to excess cardiovascular mortality; and 2) a mechanism implying that early heart failure through pulmonary vascular and interstitial congestion and probably through the enlargement of the heart leads to lung function reduction which, therefore, is associated with cardiovascular morbidity and mortality. Only the first mechanism insinuates causality. TOCKMAN and COMSTOCK [12] did not consider that the association between lung function reduction and cardiovascular mortality may be caused by smoking, as in their study this association was also present in lifetime nonsmokers. In contrast, in the Honolulu Heart Programme [36] the association between ventilatory function and coronary heart disease was present in past and current smokers, but not in lifetime nonsmokers.

Our findings agree best with the second mechanism proposed by TOCKMAN and COMSTOCK [12] as FVC%pred was more strongly related than FEV_1%pred to the investigated end-points. This is in accordance with FVC being a more sensitive indicator of congestive heart disease than FEV_1 and may reflect that subjects with existing heart disease are more likely to die from either AMI or other cardiovascular disease than subjects without heart disease [26]. In addition, our findings of no association between the reduction of ventilatory function and incidence of non-fatal AMI in both the analytical and the predictive regression model speak against ventilatory impairment being causally related to IHD.

Recently, WEISS [37] suggested that decreased pulmonary function being a marker of centripetal obesity may, through elevated levels of insulin, be linked to cardiovascular mortality and morbidity. In our population, the relationship between lung function impairment and cardiovascular mortality remained significant after controlling for BMI, whereas BMI was not significantly related to cardiovascular death in the analytical models. As we have no data on the distribution of body fat in our subjects, we cannot exclude that the hypothesis of Weiss may explain at least some of the observed association between ventilatory function and cardiovascular mortality, but we think that the lack of an association between ventilatory variables and non-fatal myocardial infarction speaks against it.

Still another hypothesis explaining the association between ventilatory impairment and cardiovascular mortality has been proposed by the Framingham study group [13, 26]. They suggest that as well as being a specific index of pulmonary status, ventilatory function, especially in the elderly, can be regarded as a measurement of the overall fitness and health status. This signifies that serious diseases of any kind are more likely to have fatal outcome in subjects with poor ventilatory function than in subjects with preserved lung function. Also, this hypothesis is in accordance with the findings of the present study and with the poorly understood, but highly significant association between total mortality and ventilatory impairment. We conclude that, after controlling for major risk factors for cardiovascular disease, ventilatory impairment is significantly related to cardiovascular mortality, but not to the development of myocardial infarction. This indicates that although ventilatory impairment may be a predictor of the course of established ischaemic heart disease [38], it should not be regarded as a risk factor for its development.

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Limitation de la fonction ventilatoire et risque de mort cardiovasculaire et d'infarctus myocardique fatal ou non fatal.
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RÉSUMÉ: Les relations entre la fonction ventilatoire et les accidents cardiovasculaires ont été étudiées chez 12.511 hommes et femmes, inclus en 1976–78 dans une étude prospective de population. A la fin 1983, 388 sujets étaient morts de maladie cardiovasculaire, dont 133 dans les 30 jours faisant suite à un infarctus du myocarde (infarctus myocardique fatal); 238 ont souffert d'infarctus myocardique non fatal. L'on a utilsé les modèles de risques proportionnels de Cox pour l'analyse.

Dans les modèles incluant la consommation de tabac, le niveau de cholestérol, la pression sanguine, le diabète sucré, et l'index de masse corporelle comme covariantes, le VEMS en % des valeurs prédites (VEMS%p), la capacité vitale forcée en % des valeurs prédites (CVF%p), et la relation VEMS/capacité vitale forcée, s'avèrent en relation significative avec le risque de mort cardiovasculaire. Donc, par comparaison avec les sujets dont VEMS%p ou CVF%p est supérieur ou égal à 80, le risque de mort d'affection cardiovasculaire parmi les sujets dont FEV_1%p ou FVC%p est inférieur à 60, s'avère deux fois plus élevé. Il n'y a pas d'augmentation sigificative du risque d'infarctus myocardique aigu en rapport avec la réduction de CVF%p. Il n'y a pas de relation significative entre l'altération fonctionnelle ventilatoire et le risque d'infarctus myocardique. Dans les modèles de régression, qui n'incluaient que l'âge et le sexe comme covariantes, un abaissement de CVF%p et de VEMS%p s'avère significativement en relation à la fois avec la mortailité cardiovasculaire et l'infarctus fatal du myocarde, mais non en relation avec l'infarctus non fatal, alors que la relation VEMS/CVF n'est pas en relation avec l'infarctus du myocarde fatal ou non fatal.

Nos résultats suggèrent que, quoiqu'une fonction ventilatoire altérée soit un prédicteur significatif du décès par infarctus du myocarde et d'autres maladies cardiovasculaires, elle ne doit pas être considérée comme un facteur de risque autonome pour la maladie cardiaque ischémique.
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