Respiratory Medicine (2004) **98**, 263–270

respiratoryMEDICINE

Influence of family history and smoking habits on the incidence of self-reported physician's diagnosis of COPD

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Received 6 June 2003; accepted 3 October 2003

KEYWORDS
Chronic obstructive pulmonary disease;
Family history;
Incidence;
Smoking cessation

Summary *Background*: The incidence of chronic obstructive pulmonary disease (COPD) is little investigated. This study assessed the incidence of a self-reported physician's diagnosis of chronic bronchitis and/or emphysema (CBE) and/or COPD (CBE/COPD), and investigated the effects of a family history of CBE in 1992 and change in smoking habits (assessed in 1992 and 2000) on this incidence.

Methods: A follow-up study in 2000 of 4933 subjects who responded to a respiratory questionnaire study in 1992 was performed. Response rate was 86.8%. Odds ratios (ORs) for incident cases of CBE/COPD were calculated by multiple logistic regression.

Results: The cumulative incidence of a physician's diagnosis of CBE/COPD was 2.9%. A family history of CBE predicted incident cases of CBE/COPD, OR 2.7 (95% CI 1.5–5.1). Also continuous smoking, relapse into smoking, or having stopped smoking between 1992 and 2000 had elevated ORs for incident cases of CBE/COPD, 2.6 (1.4–4.7), 7.2 (2.7–18.7), and 2.6 (1.3–5.3), while the OR for ex-smoking in 1992 as well as 2000 was 0.9 (0.4–1.8).

Conclusions: A family history of CBE increases the risk for development of CBE/COPD. Sustained smoking cessation over many years may be required to significantly reduce the risk of developing CBE/COPD.

Introduction

A majority of studies on potential risk factors of chronic obstructive pulmonary disease (COPD) have been of a cross-sectional design. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) states that more longitudinal studies are needed to fully understand the epidemiology of the disease.[1]

There is a marked variability in the development of COPD in response to cigarette smoking,[2] but severe alpha 1-antitrypsin deficiency remains the only proven genetic risk factor for COPD.[3,4] Cross-sectional studies have found a great aggregation of COPD in families.[5–9] It would be of interest to examine whether a family history of COPD is also associated with the incidence of COPD.

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doi:10.1016/j.rmed.2003.10.006

Positive effects of smoking cessation on lung function both in smokers with and without COPD are well documented,[10–12] but the effects of change in smoking habits over time on the incidence of COPD seems to have been little examined in a random population sample.

This study has assessed the incidence of a self-reported physician's diagnosis of chronic bronchitis and/or emphysema (CBE) and/or COPD in subjects who responded to a respiratory questionnaire. The influence of a family history of CBE reported in 1992 and smoking habits reported in 1992 as well as 2000 on this incidence was examined.

Methods

Study area and population

The present study was performed in Skåne, the southern-most county of Sweden. In 1992, the study area included Malmö, the third largest city in Sweden, and all of its surrounding municipalities with a mixture of densely populated and rural regions.[13] In 2000, the study area also comprised Malmö, but only half of its surrounding municipalities.

In 1992, the questionnaire was sent to 12 071 subjects aged 20–59 years (70.1% response rate), and in 2000–11 933 to subjects aged 18–77 years. All subjects were randomly selected from the Swedish Populations Register. A follow-up study was performed in all subjects who in 1992 resided in the present study area and still were residing there ($n = 4790$) or had moved to other parts of Skåne or to some of its three neighbouring counties ($n = 143$). Since 1992, further 312 subjects had moved elsewhere, were dead, or had unknown addresses. The study was approved by the Medical Ethics Committee, Lund University, Lund.

Questionnaire

The questionnaire in 2000, entitled; "Questions about the Lungs", had the same layout as the one used in 1992.[8,13] That questionnaire was based on the questionnaire used in the OLIN studies,[14,15] and other epidemiological studies, e.g. Stjernberg et al.[16] and Lindstrom et al.[17] In turn, this questionnaire was developed from a revised version of the British Medical Research Council (BMRC) questionnaire,[18] with modifications from the American Thoracic Society[19] and Tucson.[20] The questionnaire in 2000 was complemented with specific questions about COPD and a family history of COPD (Appendix A). If no response was received within 2 weeks a first reminder was sent out, and finally, after 10 weeks, a second, reminder including a new questionnaire was mailed.

Prevalence and incidence of a physician's diagnosis of CBE/COPD

The prevalence of a physician's diagnosis of CBE or COPD was assessed from the questions: "Have you been diagnosed by a doctor as having chronic bronchitis and/or emphysema?", or COPD?" There was no question on COPD in 1992.

The cumulative incidence of physician's diagnosis of CBE/COPD, was assessed from a positive answer in 2000 regarding a physician's diagnosis of CBE/COPD, but negative answers in 1992 on the questions on both self-reported CBE, and self-reported physician's diagnosis of CBE as well as a negative answer on the question: "Do you usually have cough with phlegm on most days during periods of at least three months during at least two successive years?", i.e. analogous to the definition of chronic bronchitis.[21]

Smoking habits

Subjects with a positive answer to the question "Do you smoke?" or: "Have you stopped smoking during the last 12 months?" were classified as current smokers. Subjects who had smoked but stopped smoking more than a year ago were classified as ex-smokers.

Social position

Statistics Sweden has elaborated a socio-economic classification system.[22] In its most aggregated form, the classification of the economically active population consists of six groups (Appendix B). Like in a previous study,[23] the economically active population was further merged into the two groups "low social position" and "middle/high social position".

Statistical analyses

The prevalence of a disease or a symptom was calculated as percentage of positive answers to a question. Non-responders to a single question were quoted as having answered: "No/do not know". Univariate logistic regression analysis was used to test potential associations between separate factors reported in 1992 and the incidence of a physician's diagnosis of CBE/COPD between 1992 and 2000. Multiple logistic regression analysis

(forward conditional) was used to assess the simultaneous influence of conceivable factors on the incidence of a self-reported physician's diagnosis of CBE/COPD. The results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Factors for which the univariate logistic regression analysis showed an association with the incidence of a physician's diagnosis of CBE/COPD with a P value of <0.15 were included as covariates in the multiple regression model. Age, gender, and social position were controlled for in this analysis. In addition, interaction terms between age, gender, a family history of CBE in 1992, and smoking habits were tested in all different combinations in the multiple regression analysis. For smoking habits, a categorical variable, ''change in smoking habits'', was created, categorized into six categories based on smoking habits reported in 1992 and 2000, i.e: ex–ex (sustained quitting), current–ex (stopped smoking), never–current (started smoking), ex–current (relapse into smoking), current–current (continuous smoking), and never smoked. The latter category was reference. The variable number of smoked cigarettes per day was categorized into three categories with smoking of <5 cigarettes/day as reference.

A non-response analysis in the follow-up study group was performed by comparing basic demographics and answers to the questionnaire in 1992 between non-responders and responders. A similar analysis was made in the 312 subjects not eligible for the study in 2000. Chi-squared analysis was used for comparison of prevalence rates between different groups. Differences by age were tested by analysis of variance (ANOVA). A P-value of <0.05 was considered statistically significant. The computer-based analysis-program SPSS version 10.1 was used for all calculations.

Results

Participation

In 2000, in total 9316 individuals (78.1%) returned the questionnaire. Of the 4933 subjects who received the questionnaire in 1992 as well as in 2000 (the follow-up study group), 4280 subjects (86.8%) responded at both occasions.

Prevalence of a physician's diagnosis as well as a family history of CBE (in 1992) and CBE/COPD (in 2000)

A physician's diagnosis of CBE/COPD was more frequently reported in 2000 than a physician's diagnosis of CBE in 1992 ($P<0.05$) (Table 1). CBE (in 1992) as well as CBE/COPD (in 2000) were more common among women than men at both occasions. Also, more women than men were smokers, both in 1992 and 2000, $P<0.05$ and $P<0.001$, respectively. The prevalence of smoking was significantly lower in 2000 compared with 1992. There was no statistical difference in report of a family history of CBE between 1992 and 2000, but significantly more women than men reported a family history of CBE ($P<0.001$). In 1992, as well as

Table 1 Prevalence (%) and 95% CIs of a self-reported physician's diagnosis as well as a family history of CBE (in 1992), and CBE/COPD (in 2000), and of current and ex-smokers in 1992 and 2000 ($n = 4280$).

	1992			2000		
	All ($n = 4280$)	Men ($n = 1972$)	Women ($n = 2308$)	All ($n = 4280$)	Men ($n = 1972$)	Women ($n = 2308$)
Diagnosis of CBE (in 2000 CBE/COPD)	3.7 3.2–4.2	3.3 2.6–4.1	4.1 3.3–4.9	4.3 3.8–4.9	3.8 2.9–4.6	4.7 3.8–5.5
Family history of CBE (in 2000 CBE/COPD)	8.6 7.8–9.4	6.0 4.9–7.0	10.8 9.6–12.1	9.3 8.1–10.5	7.0 5.8–8.1	11.4 10.1–12.7
Current smokers	32.8 31.4–34.2	30.9 28.9–33.0	30.9 28.9–33.0	26.3 25.0–27.6	24.4 23.1–25.6	27.7 26.4–28.9
Ex-smokers	24.8 23.5–26.1	27.0 25.0–28.9	22.9 21.2–24.6	30.7 29.3–32.1	32.7 30.6–34.8	28.9 27.1–30.8

in 2000, 33% of the subjects in the follow-up study group were classified as having a ''low social position''. Of subjects who in 2000 stated a physician's diagnosis of CBE, and COPD, respectively, 79.7% and 92.5%, reported recurrent or permanent breathing problems. Corresponding figures for symptoms of chronic bronchitis, i.e. ''cough with phlegm during at least three months during at least two successive years of the last years'' were 36.8% and 40.4%, respectively.

Incidence of a physician's diagnosis of CBE/COPD

The cumulative incidence of a physician's diagnosis of CBE/COPD in the follow-up study group was 2.9% (48 males and 64 women). This corresponds to an estimated annual incidence of 0.36%. Of these subjects, 45% were current smokers and 36% were ex-smokers. The highest numerical incidence of CBE/COPD among women was noted in the age group 48–57 years, while the highest numerical incidence among men was found in oldest age group (58–67 years) (Table 2). The incidence of a physician's diagnosis of CBE/COPD increased by an increasing number of cigarettes smoked per day in 1992. For those who smoked >14 cigarettes/day, the incidence was 6.6%.

Influence of a family history of CBE and change in smoking habits

Results of the univariate logistic regression analyses of potential associations between different factors reported in 1992 and incident cases of a physician's diagnosis of CBE/COPD are shown in Table 3.

According to multiple logistic regression analysis a family history of CBE in 1992 was a predictor of incident cases of a self-reported physician's diagnosis of CBE/COPD (Table 4). Also increase in age, continuous smoking, relapse into smoking, and stopped smoking between 1992 and 2000, were associated with an elevated OR for the incidence of CBE/COPD. For subjects who were ex-smokers both in 1992 and 2000 (sustained quitters) the OR was 0.9 (0.4–1.8). Statistically, no significant interactions were found between age, gender, smoking habits, and report of a family history of CBE in 1992.

The prevalence of smoking was significantly higher in subjects who reported a family history of CBE or CBE/COPD than in the rest of the follow-up group in 1992 as well as in 2000, 38.0% vs. 32.3% and 31.8% vs. 25.8%, respectively. In addition, smokers with a family history of CBE/COPD reported a consumption of >14 cigarettes/day more frequently than the rest of the smokers, 41.2% vs. 29.0%, in 2000.

Table 2 Cumulative incidence rates (%) and 95% CIs of self-reported physician's diagnosis of CBE/COPD between 1992 and 2000 by age (in 2000), and gender ($n = 4280$).

Age group (age in 2000) (years)	All ($n = 4280$)	Men ($n = 1972$)	Women ($n = 2308$)
28–67 (All)	2.9 (2.4–3.4)	2.7 (1.9–3.4)	3.1 (2.3–3.8)
28–37	1.9 (1.0–2.7)	1.5 (0.3–2.6)	2.2 (0.9–3.4)
38–47	2.9 (1.8–4.0)	3.2 (1.5–4.8)	2.7 (1.2–4.1)
48–57	2.5 (1.5–3.5)	1.1 (0.1–2.0)	3.9 (2.2–5.6)
58–67	4.2 (3.0–5.5)	4.9 (2.9–6.9)	3.6 (2.0–5.2)

Table 3 Odds ratios and *P*-values according to univariate logistic regression analyses for incident cases of a physician's diagnosis of CBE/COPD between 1992 and 2000 of different factors reported in 1992.

	n	OR	*P*-value
Being a man vs. woman	1972	0.9	0.266
Having a smoker in the home	658	0.9	0.423
Living close to heavy traffic	1426	1.3	0.056
Low social position vs. middle/high position	1411	1.5	0.055
A family history of CBE	368	2.8	<0.001
A family history of asthma	744	1.5	0.053
A family history of allergic rhinitis	1173	1.3	0.166
Being an ex-smoker vs. never smoker	1060	1.2	0.521
Being a current smoker vs. never smoker	1405	2.6	<0.001

Table 4 ORs and 95% CIs for incident cases of self-reported physician's diagnosis of CBE/COPD between 1992 and 2000 according to stepwise multiple logistic regression (forward conditional) controlling for age, gender and smoking.

	n	OR	95% CI
A family history of CBE in 1992	368	2.7	1.5–5.1
Never smoked (reference)	1785	1.0	
Stopped smoking	448	2.6	1.3–5.3
Relapse into smoking	85	7.2	2.7–18.7
Continuous smoking	957	2.6	1.4–4.7
Smoking of >14 cigarettes/day in 1992	560	4.0	1.1–14.9

A family history of asthma and living close to heavy traffic, were included as covariates in the model, but due to a final *P*-value of >0.05 their results are not displayed.

Non-response analysis

Of the 653 subjects who did not participate in 2000, 382 subjects were men and 271 were women. More non-responders than responders were current smokers in 1992, 41.5% vs. 32.8% ($P<0.001$). Non-responders in 2000 had a higher prevalence of self-reported symptoms of chronic bronchitis in 1992 than responders, 7.8% vs. 5.7% ($P=0.025$). There were no differences between non-responders and responders regarding the prevalence of ex-smokers, a physician's diagnosis of CBE, or a family history of CBE in 1992.

No significant differences emerged between the 312 subjects, who were not eligible for the study in 2000 and the rest of the follow-up group regarding age, gender, smoking habits and a physician's diagnosis of CBE in 1992.

Discussion

This study of a general population sample found an estimated incidence of a self-reported physician's diagnosis of CBE/COPD of 0.36%. A family history of CBE was an independent predictor of this incidence. Continuous smoking as well as relapse into smoking was associated with an elevated incidence of CBE/COPD. This was also the case for having stopped smoking between 1992 and 2000, while for sustained ex-smokers (i.e. those who had quit before 1992), the OR for incident cases of CBE/COPD was similar to that for never smokers.

The found incidence of a physician's diagnosis CBE/COPD is of a similar order of magnitude as in a few studies, which have evaluated the incidence of COPD, both with spirometry. A Finnish study performed between 1961 and 1971 found an annual incidence of a ratio between forced expiratory volume in 1 s (FEV_1) and vital capacity (VC) of <0.6 of 0.2%.[24] A study from Poland found an incidence of COPD, defined as $FEV_1<$ 65% of predicted, of about 0.5%.[25]

A self-report of a physician's diagnosis relies on individual recall as well as on the accuracy of the diagnosis. It would have been of interest to validate the self-reported physician's diagnosis of CBE/COPD by performing spirometry, but this was not feasible. The sensitivity of a physician's diagnosis of CBE/COPD is probably low, which is shown by the considerable underdiagnosis of COPD,[15] in particular of mild-to-moderate COPD.[1] However, the specificity of a self-reported physician's diagnosis of CBE/COPD may be relatively good and useful for evaluation of risk associations in epidemiological studies. This has been concluded in a cohort study in nurses,[26] but may need confirmation also in a general population sample. In the present study, a majority of subjects with a physician's diagnosis of CBE or COPD reported problems with their breathing, which is characteristic for COPD. Also the fact that the incidence of a physician's diagnosis of CBE/COPD was associated with increase in age, smoking, and high cigarette consumption supports the specificity of a self-reported physician's diagnosis of CBE/COPD. We also believe that a predominant part of the subjects who reported a physician's diagnosis of CBE/COPD indeed had a *clinically significant* disease, i.e. of sufficient severity to prompt a visit to a physician. This thought is in accordance with GOLD.[1] COPD may sometimes be confused with asthma, but there are in fact some individuals with both diseases. It is unknown how great this percentage is. In the present study, about 19% of the subjects with CBE/COPD reported a concomitant asthma.

One may speculate whether the incidence rate found in the study may be overestimated due to an increasing focus on COPD in recent years. However, this may be counterbalanced by fact that the prevalence of current smokers in 1992 was greater among non-responders than responders, which thus may instead have led to an underestimation of the incidence.

The present results support that a family history of COPD is an important risk factor for the

development of COPD. However, it still remains to be clarified to what extent a family history of COPD really reflects genetic risk factors. A questionnaire cannot cover all conceivable questions on environmental risk factors, and in addition, it cannot adequately measure the degree of different exposures. Furthermore, recognised risk factors such as childhood infections,[3] poor socio-economic status,[27] and environmental tobacco smoke in the family[28] may have had an effect before the first questionnaire study, and could then have led to an increased familial risk of CBE/COPD. Also, having a family member with CBE or COPD may lead to an increased knowledge of these conditions and to an increased awareness when known disease symptoms occur, which might have resulted in a bias.

Subjects with a family history seemed to have somewhat more ''heavy'' smoking habits than the rest of the study population which suggests that smokers with a family history of CBE/COPD is a particular target group for smoking cessation.

Subjects who had stopped smoking between 1992 and 2000 had an OR for the incidence of a physician's diagnosis of CBE/COPD similar to that for continuous smokers. This might to some extent be explained by the fact that subjects who received a diagnosis of CBE/COPD may have been more motivated to stop smoking, i.e. were more frequently ex-smokers in 2000. However, those who reported that they were ex-smokers at both occasions (sustained quitters) had an OR similar to that of never smokers. This seems to indicate that a successful smoking cessation in a random sample of smokers can lead to a substantial reduction in the risk of developing a clinically significant COPD, but that it may take several years until the full effect is achieved. The beneficial long-term effect of smoking cessation is also shown by the American Lung Health Study.[12] Of smokers who quit in the beginning of the study, only 10% had an FEV_1 of less than 60% of predicted after 11 years, while this occurred in 38% of the continuous smokers.

Relapse into smoking appeared to be associated with a somewhat higher incidence of CBE/COPD than continuous smoking. The former group was, however, relatively small and this result should therefore be interpreted with caution. The finding is line with the a study from Tucson,[29] where subjects who attempted to quit smoking but started again had a more rapidly declining FEV_1 than continuously smoking and ex-smoking subjects. However, in the American Lung Health Study, subjects who made several attempts to quit smoking had less loss of lung function.[30]

Conclusion

In conclusion, the estimated incidence of a physician's diagnosis of CBE/COPD, which may represent a clinically significant COPD was 0.36% in a random population sample. A family history of CBE is an independent predictor for the development of CBE/COPD. A successful smoking cessation over many years may be required to achieve a significant reduction in the risk of developing CBE/COPD.

Acknowledgements

The present study is supported by the Swedish Research Council, the Medical Faculty of Lund University, the Vårdal Foundation, and the Swedish Heart Lung Foundation, to whom we are most grateful.

Appendix A

Questionnaire (''Questions about the Lungs'' in 1992)

Answer by crossing on the relevant line if no other instructions are given.

1. Have any of your parents, brothers or sisters, or children had:
   a) Asthma.
   b) Allergic eye-/nose catarrh (hay-fever)
   c) Chronic bronchitis and/or emphysema
2. Have you now, or have you had, any of the following diseases:
   a) Asthma
   b) Allergic eye/nose catarrh (hay-fever
   c) Chronic bronchitis and/or emphysema
   d) Any other lung or airways disease
   e) If yes, which?……..)
4. Have you been diagnosed by a doctor as having chronic bronchitis (bronchitis) and/or emphysema?
8. Do you usually have phlegm when coughing, or do you have phlegm on your chest which is difficult to bring up?
   If yes:
   a Do you bring up phlegm when coughing on most days during periods of at least three months?

b Have you had such periods during at least two successive years?

12. How would you characterise your breathing?
    a) I very seldom have problems with my breathing.
    b) Occasionally I have problems when breathing
    c) My breathing is never quite well.

13 Do you smoke? (smokers also include those who smoke a few cigarettes or pipe fills a week, and those who have stopped smoking during the last year)
If yes:
How many cigarettes do you smoke per day?
    a) Less than 5
    b) 5–14
    c) 15 or more
If no:
    d) Have you been a smoker but stopped smoking more than a year ago?
    e) Does anyone else in your family smoke?

14 Do you live close to a road with heavy traffic?

Questionnaire (''Questions about the Lungs'' in 2000)

Answer by crossing on the relevant line if no other instructions are given.

1.. Have any of your parents, brothers or sisters, or children had:
    a) Asthma
    b) Allergic eye-/nose catarrh (hay-fever)
    c) Chronic bronchitis and/or emphysema
    d) Chronic obstructive pulmonary disease (COPD)

3. Have you now, or have you had, any of the following diseases:
    a) Asthma
    b) Allergic eye/nose catarrh (hay-fever)
    c) Chronic bronchitis and/or emphysema
    d) Chronic obstructive pulmonary disease (COPD)
    e) Any other lung or airways disease
    f) If yes, which? ……)

5. Have you been diagnosed by a doctor as having chronic bronchitis (bronchitis) and/or emphysema?

6. Have you been diagnosed by a doctor as having chronic obstructive pulmonary disease (COPD)?

11. Do you usually have phlegm when coughing, or do you have phlegm on your chest which is difficult to bring up?
If yes:
    a) Do you bring up phlegm when coughing on most days during periods of at least three months?
    b) Have you had such periods during at least two successive years?

15. How would you characterise your breathing?
Answer with a cross at the relevant line
    a) I very seldom have problems with my breathing.
    b) Occasionally I have problems when breathing.
    c) My breathing is never quite well.

16. Do you smoke? (smokers also include those who smoke a few cigarettes or pipe fills a week, and those who have stopped smoking during the last year)
If yes:
How many cigarettes do you smoke per day?
    a) Less than 5
    b) 5–14
    c) 15 or more
If no:
    d) Have you been a smoker but stopped smoking more than a year ago?
    e) Does anyone else in your family smoke?

17. Do you live close to a road with heavy traffic?

Appendix B

Statistics Sweden has elaborated a socio-economic classification system (22). In its most aggregated form the classification of the economically active population consists of six groups:

1. Unskilled and semiskilled workers.
2. Skilled workers.
3. Assistant non-manual employees.
4. Intermediate non-manual employees.
5. Employed and self-employed professionals, higher civil servants and executives.
6. Self-employed (other than professionals).

In our analyses the economically active population was further merged into the two groups ''low social position'' and ''middle/high social position'', where low social position was defined by groups 1 and 2, whereas middle/high social position was defined by groups 3–6.

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