Cigarette smoking and diabetes mellitus

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SUMMARY

Objective: To assess whether an independent relationship between cigarette smoking and type 2 diabetes exists in both men and women selected from a French population, and to assess the effects of active smoking and smoking cessation on the prevalence of diabetes.

Methods: A population-based cross-sectional study in 28,409 volunteers.

Results: After adjustment for age, BMI, waist-hip ratio (WHR) and alcohol, the risk of diabetes mellitus (estimated by the odds ratio) was 1.49 (1.13-1.96, P = 0.004) and 1.31 (1.01-1.77, P = 0.03) for current and former smoker men, respectively, as compared to non-smoker men. The risk was even higher in men aged 40 to 69. No association was found with the duration of smoking cessation. In women, the risk of diabetes associated with current smoking was much less significant [HR: 1.46 (0.92-2.22, P = 0.09)], even in women aged 40 to 69 [HR: 1.60 (1.00-2.58, P = 0.05)]. No relationship was found for past smoking in women.

In non-diabetic men, the adjusted fasting glucose was similar in current and in non smokers, but it was higher in current smokers aged 40 to 69 (99.2 ± 0.27 vs 98.7 ± 0.14 mg/dl, P = 0.05). It was higher in former than in non smokers (97.4 ± 0.20 vs 96.0 ± 0.10 mg/dl, P = 0.0001), regardless of age.

In non-diabetic women, the adjusted fasting glucose was lower in current than in non smokers (90.7 ± 0.20 vs 91.4 ± 0.12 mg/dl, P = 0.0001), even in women aged 40 to 69 (93.0 ± 0.35 vs 93.7 ± 0.18 mg/dl, P = 0.03). It was similar in former and in non smokers, regardless of the age.

Conclusions: Current and past smoking are associated with a risk of diabetes mellitus essentially in men, but much less in women, and the relationship between fasting glucose and smoking appears different in men and women. No dose-relationship between the number of cigarettes smoked and diabetes mellitus was found. Smoking cessation is not associated with a reduced risk of diabetes.

Key-words: Smoking - Diabetes mellitus - Epidemiology - Risk factors - Sex.


RÉSUMÉ

Tabagisme et diabète

Objectif : Évaluer si il existe une relation indépendante entre tabagisme actif et prévalence du diabète, chez l’homme et chez la femme d’une population française ; il était également d’évaluer si cette relation existe aussi chez les anciens fumeurs.

Méthode : Étude transversale de population.

Résultats : Après ajustement sur l’âge, de l’index de masse corporelle, le rapport taille sur hanche et l’alcool, le risque de diabète était de 1.49 (1.13-1.96, P = 0.004) et 1.31 (1.01-1.77, P = 0.03) respectivement pour les hommes fumeurs actuels ou anciens fumeurs, comparés aux non fumeurs. Le risque était encore plus élevé chez les hommes de 40 à 69 ans ; il n’y avait de relation avec la durée du tabagisme. Chez la femme, le risque de diabète était beaucoup moins significatif (1.46 [0.92-2.22], P = 0.09), même chez celles de 40 à 69 ans (1.60 [1.00-2.58], P = 0.05). Aucune relation n’a été trouvée chez les anciennes fumeuses.

Chez les hommes non diabétiques, la glycémie ajustée était similaire chez les fumeurs et les non fumeurs, mais elle était plus élevée dans le sous-groupe des fumeurs actifs de 40 à 69 ans (99,2 ± 0,27 vs 98,7 ± 0,14 mg/dl, P = 0,05). Elle était également plus élevée chez les anciens fumeurs que chez les non fumeurs (97,4 ± 0,20 vs 96,0 ± 0,10 mg/dl, P = 0,0001), quel que soit l’âge.

Chez les femmes non diabétiques, la glycémie ajustée était plus basse chez les non fumeuses que les fumeuses (90,7 ± 0,20 vs 91,4 ± 0,12 mg/dl, P = 0,0001), même chez celles âgées de 40 à 69 ans (93,0 ± 0,35 vs 93,7 ± 0,18 mg/dl, P = 0,03). Elle était similaire chez les anciennes fumeuses et les non fumeuses, quel que soit l’âge.

Conclusions : Le tabagisme actuel et le tabagisme ancien sont associés à une risque de diabète essentiellement chez les hommes, mais beaucoup moins chez les femmes, et la relation entre glycémie et tabagisme apparaît différent chez l’homme et chez la femme. Aucune relation dose-réponse entre le nombre de cigarettes fumées et le risque de diabète n’a été trouvée. L’arrêt du tabagisme n’est pas associé à un risque réduit de diabète.

Mots-clés : Tabagisme - Diabète - Epidémiologie - Facteur de risque - Sexe.

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Received: November 17th, 2003; revised: February 23rd, 2004
Insulin resistance is a major component of type 2 diabetes. In the past decade, the increase in the incidence of type 2 diabetes mellitus has emerged as one of the most challenging health problems in western countries. No overall strategy has been defined to reduce the epidemic. However, it is recommended that all factors associated with insulin resistance should be identified and treated.

Interestingly, several studies have shown that insulin sensitivity is impaired in current smokers [1-4], which led some investigators to study the relationship between cigarette smoking and diabetes mellitus. Studies in Northern Europe (United-Kingdom, Holland, Sweden), in Japan and in the United States suggest that cigarette smoking can trigger the development of diabetes [5-12]. However, these populations have very different genetic backgrounds compared to the French population and the incidence of diabetes mellitus is usually higher in these countries than in France. It therefore remains to be demonstrated whether such an association exists in the French population. Moreover, most of these studies were carried out in men, and female populations were rarely studied [13-15]. Confusing parameters such as weight, hip and waist measurements, alcohol consumption were not systematically evaluated, and the influence of smoking cessation is still a matter of debate.

The goals of the present study were: 1) to assess whether a relationship between cigarette smoking and type 2 diabetes could be found in a sample of male and female volunteers consulting for examination in French health centers (IRSA), after adjustment for sex, age, body mass index (BMI), waist/hip ratio (WHR), and alcohol consumption, and 2) to evaluate the effects of active smoking and smoking cessation on the prevalence of diabetes.

**Subjects and methods**

**Subject selection**

From January 1 to June 30 1998, 28,409 volunteers (aged 20 to 69) were examined at the Institut régional pour la Santé (IRSA, Regional Institute for Health). Volunteers were drawn from nine departments in Western and Central France (4.5 million inhabitants, the vast majority being Caucasians). The subjects were offered a routine medical examination and blood tests provided by their medical insurance (caisse primaire d’assurance maladie). Most of those screened were individuals basically in good health who were just looking for a general check-up. All subjects were interviewed by a trained nurse who completed a standardized questionnaire regarding personal medical history, current treatments, and life-style behaviors (especially alcohol and smoking habits). Complete information regarding personal and medical history was available in 27,777 out of 28,409 of subjects (97.8%).

Non-smokers were defined as individuals who had never smoked, current smokers were active chronic cigarette smokers, and former smokers were those who had ceased smoking at least one month prior to the examination.

A physician recorded clinical parameters, including age, weight, height, and hip and waist measurements. Body mass index (BMI) and waist/hip ratio (WHR) were calculated. Overweight and obesity were defined as a BMI between 25.1 and 30.0 kg/m² and above 30 kg/m², respectively. Diabetes mellitus was defined as fasting glucose levels > 7.0 mmol/l or as subjects treated with an oral anti-diabetic agent or insulin.

**Statistical analysis**

Results were expressed as means ± standard deviations and percentages. Unadjusted means were compared using Student’s t tests, and qualitative parameters were compared using a Chi² test or Fisher’s exact test as appropriate. In order to determine if current or former smoking was an independent risk for diabetes, a logistic regression was carried out by using an adjustment on age, BMI, WHR, and alcohol consumption (yes/no).

Multivariate regression analysis was carried out to assess the mean fasting glucose after adjustment for age, BMI, WHR and alcohol ratio in current smokers, former smokers and non smokers among non-diabetic men and women.

The risk of diabetes related to smoking was expressed using odds ratio (with 95 % confidence interval). Analyses were performed using SAS (SAS Institute Inc., Cary, NC, USA).

A P value < 0.05 was considered significant.

**Results**

**Characteristics of population (Tab I)**

**Men**

Forty-five percent of the subjects were men and 55% were women.

The prevalence of diabetes mellitus in the male population, was 3.5%, 36.8% of subjects being overweight and 9.3% obese. Current smokers accounted for 36% of subjects and former smokers 24%. Fifty-eight percent of subjects were regular alcohol consumers. Current smokers were younger...
and had a lower BMI, and the percentage of regular alcohol consumers was lower in this group than in former- and non-smokers.

**Women**

The prevalence of diabetes mellitus in the female population was 1.8%, 21.1% being overweight and 10.9% obese; 30.6% were regular alcohol consumers. Current smokers accounted for 24% of subjects and former smokers for 10%. Current smokers were younger and had a lower BMI. The percentage of regular alcohol consumers in current smokers was lower than in former and non-smokers.

### Table I

Baseline characteristics of population (27,777 subjects).

<table>
<thead>
<tr>
<th></th>
<th>Men (12,417 subjects) (45%)</th>
<th>Women (15,360 subjects) (55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never smokers</td>
<td>Former smokers</td>
</tr>
<tr>
<td>Number</td>
<td>4958</td>
<td>2959</td>
</tr>
<tr>
<td>Percentage of population (%)</td>
<td>39.92</td>
<td>23.83</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.5 ± 12.3</td>
<td>46.8 ± 11</td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>5.38 ± 0.82</td>
<td>5.63 ± 0.11</td>
</tr>
<tr>
<td>Diabetes mellitus prevalence (%)</td>
<td>2.68</td>
<td>5.65</td>
</tr>
<tr>
<td>Number of cigarettes by day</td>
<td>—</td>
<td>19.1 ± 11.8</td>
</tr>
<tr>
<td>Duration of smoking (years)</td>
<td>—</td>
<td>17.7 ± 9.9</td>
</tr>
<tr>
<td>Number of pack-years</td>
<td>—</td>
<td>17.3 ± 15.8</td>
</tr>
<tr>
<td>Duration of smoking cessation (years)</td>
<td>—</td>
<td>11.0 ± 8.7</td>
</tr>
<tr>
<td>Alcohol drinkers (%)</td>
<td>61.4</td>
<td>68.7</td>
</tr>
<tr>
<td>Alcohol consumption (g/day)</td>
<td>24.8 ± 19.5</td>
<td>37.4 ± 11.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.0 ± 3.6</td>
<td>26.7 ± 3.7</td>
</tr>
<tr>
<td>BMI &gt; 25-29.9 (%)</td>
<td>37.7</td>
<td>47.2</td>
</tr>
<tr>
<td>BMI &gt; 30 (%)</td>
<td>8.4</td>
<td>14.2</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.91 ± 0.07</td>
<td>0.93 ± 0.07</td>
</tr>
</tbody>
</table>

### Association between smoking and diabetes mellitus

**Univariate analysis in men**

In each age group, the prevalence of diabetes mellitus was higher in current and former smokers than in non-smokers [with the exception of the 20-29 years age group (Fig 1a)]. The prevalence of diabetes mellitus for each BMI class was higher in current and former smokers than in non-smokers, and for overweight and obese subjects; it was higher in former smokers than in current smokers. More-

![Figure 1](image1.png)

**Figure 1**

Diabetes mellitus percentage according to age (A), and BMI (B) among never smokers (NS), former smokers (FS), and current smokers (CS), in the male population.
over, in each BMI class the prevalence of diabetes mellitus was higher in former smokers than in current smokers (Fig 1b). No dose-effect relationship was found between the number of cigarettes smoked and the prevalence of diabetes mellitus.

Univariate analysis in women
In women aged 40-69 years, the prevalence of diabetes mellitus was higher in former smokers and non-smokers than in current smokers, and for overweight and obese women it was higher in former smokers and non-smokers than in current smokers.

Multivariate analysis in men
The risk of diabetes mellitus (estimated by the odds ratio) associated with age, BMI, WHR and regular alcohol consumption in men was 1.07 (95% confidence interval: 1.06-1.08, P < 0.0001), 1.14 (1.11-1.17, P < 0.0001), 1.04 (1.02-1.05, P < 0.0001) and 0.66 (0.53-0.83, P < 0.0001) respectively. After adjustment for age, BMI, WHR and alcohol consumption, the risk of diabetes mellitus was 1.49 (1.13-1.96, P = 0.004) and 1.31 (1.01-1.73, P = 0.03) for current and former smokers, respectively, as compared to non-smokers (Tab II).

When analysis was restricted to men aged 40 to 69, the risk of

Table II
Effect of smoking habits and other variable on risk of diabetes mellitus among 12,417 men and 15,360 women.

<table>
<thead>
<tr>
<th></th>
<th>Men 20-69 years</th>
<th>Men 40-69 years</th>
<th>Women 20-69 years</th>
<th>Women 40-69 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never smokers</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Former smokers</td>
<td>1.31 (1.01-1.70) p = 0.0383</td>
<td>1.33 (1.02-1.74) p = 0.0362</td>
<td>1.46 (0.92-2.22) p = 0.0936</td>
<td>1.60 (1.00-2.58) p = 0.0496</td>
</tr>
<tr>
<td>Current smokers</td>
<td>1.49 (1.13-1.96) p = 0.0043</td>
<td>1.45 (1.08-1.95) p = 0.0061</td>
<td>0.89 (0.54-1.39) p = 0.6156</td>
<td>0.88 (0.47-1.51) p = 0.6539</td>
</tr>
<tr>
<td>Age</td>
<td>1.07 (1.06-1.08) p &lt; 0.0001</td>
<td>—</td>
<td>1.07 (1.04-1.08) p &lt; 0.0001</td>
<td>—</td>
</tr>
<tr>
<td>BMI</td>
<td>1.14 (1.11-1.17) p &lt; 0.0001</td>
<td>—</td>
<td>1.14 (1.11-1.16) p &lt; 0.0001</td>
<td>—</td>
</tr>
<tr>
<td>WHR</td>
<td>1.04 (1.02-1.05) p &lt; 0.0001</td>
<td>—</td>
<td>1.06 (1.04-1.07) p &lt; 0.0001</td>
<td>—</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.66 (0.53-0.83) p = 0.0003</td>
<td>—</td>
<td>0.73 (0.54-0.99) p = 0.049</td>
<td>—</td>
</tr>
</tbody>
</table>

Multivariate analysis controlling for former and current smokers, age, BMI, Waist/Hip Ratio, alcohol consumption (yes/no) [Odds ratio (confidence interval at 95%) p value].
diabetes mellitus was even higher in current and former smokers (Tab II). No relationship was found between the duration of cessation of smoking and the risk of diabetes mellitus.

**Multivariate analysis in men**

The risk of diabetes mellitus associated with age, BMI, WHR and alcohol consumption in women was similar to that found in men. However, diabetes mellitus was not significantly associated with current or former smoking, even when analysis was restricted to women aged 40 to 69 (Tab II).

**Association between fasting glucose and smoking in non-diabetic subjects**

In non-diabetic men, the adjusted fasting glucose was similar in current and in non-smokers, but it was higher in current smokers aged 40 to 69 (99.2 ± 0.27 vs 98.7 ± 0.14 mg/dl, P = 0.05). It was higher in former than in non smokers (97.4 ± 0.20 vs 96.0 ± 0.10 mg/dl, P = 0.0001), regardless of age. In non-diabetic women, the adjusted fasting glucose was lower in current than in non smokers (90.7 ± 0.20 vs 91.4 ± 0.12 mg/dl, P = 0.0001), even in women aged 40 to 69 (93.0 ± 0.35 vs 93.7 ± 0.18 mg/dl, P = 0.03). It was similar in former and in non smokers, regardless of the age.

**Discussion**

The results of the present investigation in a large cohort of French subjects suggest that there is a significant association between smoking and diabetes mellitus in men. The risk of diabetes mellitus was elevated after adjustment for age, BMI, WHR and alcohol consumption. Other findings were of interest: the relationship between smoking and the prevalence of diabetes was evident in men, but was much less significant — if any — in women. Moreover, adjusted fasting glucose was higher in former than in non smoker men, whereas it was paradoxically lower in current than in non smoker women; the difference remained significant even when the analysis was restricted to women 40 to 69. Finally, the association to diabetes was similar in current and in former smokers, and no dose-effect relationship was found.

The present investigation is the first to our knowledge to be carried out in France focusing on the association between smoking and the prevalence of diabetes mellitus. It has previously been suggested that smoking can increase abdominal fat distribution in men and women, without increasing weight, and this could be interpreted as a smoking-induced increase in insulin resistance with abdominal fat tissue accumulation [16-18]. In this study we similarly found that smokers had a lower BMI than non-smokers but similar WHR. However, the relationship between tobacco use and diabetes mellitus remained significant after adjustment for BMI and WHR, indicating an effect independent of body changes.

The hyperglycaemic mechanisms of tobacco use have been explored, but have not been clearly identified. It was initially shown that tobacco consumption induces an increase in free fatty acids [2]. Shepherd et al. [19] suggested that this might be a cause of insulin resistance [20, 21] by impairment of insulin stimulated translocation of GLUT4 in skeletal muscles. Moreover, cigarette smoking may release oxygen-free radicals which could reduce insulin sensitivity [22]. It has been demonstrated that tobacco use can stimulate hyperglycaemic hormone production (primarily epinephrine and norepinephrine) [23, 24]. A direct toxic effect on pancreatic cells has also been suggested [12]. Other studies have been performed with nicotine patches and gums. Users of nicotine patches or gum have lower insulin sensitivity, suggesting that the effect of smoking on insulin sensitivity might be mediated by nicotine [25, 26, 27]. Admittedly, other tobacco compounds may also be involved.

The impact of tobacco is more difficult to assess in women and few studies have been published involving this gender. Tobacco use was not associated with diabetes mellitus in the present study; in contrast, it is interesting to note that classical risk factors such as age, BMI and WHR were still risk factors for diabetes in women. Two American studies published by Will et al. [15] and Rimm et al. [13] respectively, found an increase in prevalence of diabetes in smoking women. The relative risks were 1.42 and 1.21, respectively, and a dose-effect relationship was identified. However, it should be noted that cigarette consumption was higher in these two studies than in our own study (daily consumption above 20 cigarettes for Will’s study [15] and above 25 cigarettes for Rimm’s study [13]) and that the risk of diabetes was no longer significant for lower cigarette consumption. Moreover, WHR was not taken into account in the multivariate analysis [13, 15]. The difference between men and women could be explained by a protective effect of oestradiol on beta-pancreatic cells. Indeed, Ostrgren et al. [28] showed a deterioration of beta-pancreatic cell function in smoking men but not in smoking women. Brussard et al. [29] described an improvement in glycaemic balance in menopausal women treated with oestrogens.

BMI and WHR were higher in former smokers than in current and non-smokers [30, 31], which could enhance insulin resistance. The relationship between former smokers and diabetes mellitus is in accordance with earlier reports in the literature [6, 8-11]. The fact that the association persisted on multivariate analysis suggests that a history of tobacco use is an independent risk factor of diabetes, independent of age, WRH and BMI.

As there was no follow-up, the incidence of diabetes mellitus could not be calculated. The population was selected from people who were medically insured and may not be representative of the French population: the examination was free and the subjects agreed to undergo the clinical examination and blood tests. Important parameters such as...
physical activity, eating habits, social status and family his-
tory of diabetes were not available. However, the most im-
portant risk factors were studied. It is thus probable that the
association between smoking and diabetes mellitus, espe-
cially in men, can be generalized to the French population.

Further studies are needed and we are currently plan-
ing to set up a longitudinal study including the above-
mentioned and other parameters.

It should be remembered that the effects of smoking on
health last much longer than the duration of smoking, and
that cigarette smoking is increasing among college students
[32]. The epidemic of diabetes mellitus may be just begin-
ing. Tobacco use should therefore be better controlled by
preventive medicine and requires the development of incen-
tives to cease smoking while providing psychological sup-
port.

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