European Journal of Clinical Investigation (1997) **27**, 427–433

Long-term use of smokeless tobacco and physical performance in middle-aged men

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Received 11 September 1996; accepted 11 January 1997

Abstract. To determine the influence of prolonged nicotine exposure on maximal physical working capacity, a study of clinical measures of physical fitness and cardiovascular response to exercise was performed in 144 healthy men, 35–60 years old, subdivided into smokeless tobacco users, smokers and non-users of tobacco. Regular users of smokeless tobacco, with exposures of more than 20 years, showed similar maximal oxygen uptake (mean 3·48 L min^{-1}, SD 0·49, $n = 48$) to non-users (mean 3·51 L min^{-1}, SD 0·51, $n = 65$). In smokeless tobacco users, higher blood pressure and heart rate values were observed at rest and at submaximal work, after exposure to tobacco shortly before the exercise test, but not at maximal work. However, significantly lower maximal oxygen uptake was found for smokers (mean 2·88 L min^{-1}, SD 0·49, $n = 31$) compared with non-users ($P < 0·001$). Plasma concentration of cotinine, the main metabolite of nicotine, was significantly higher in smokeless tobacco users (mean 347 ng mL^{-1}, SD 175, $n = 48$) than in smokers (mean 253 ng mL^{-1}, SD 153, $n = 31$, $P < 0·001$). The findings indicate that long-term use of smokeless tobacco does not significantly influence exercise capacity in healthy, physically well-trained subjects.

Keywords. Exercise test, nicotine, oxygen consumption, physical fitness, smokeless tobacco, smoking.

Introduction

The use of oral smokeless tobacco, mostly in the form of 'snuff dipping', is practised by approximately 20% of all Swedish males. The regular use of smokeless tobacco results in blood levels of nicotine similar to those observed in cigarette smokers [1,2]. Cigarette smoking has been associated with poor physical fitness, and smokers show reduced cardiovascular endurance in comparison with non-smokers [3–6]. The acute effects of smokeless tobacco during exercise have been studied in habitual users, mostly aged around 20 years [6–10]. The findings indicate an elevated heart rate at rest, during exercise at submaximal workloads and during recovery after exercise, but not at maximal exercise.

Although these studies delineate the acute response to the use of smokeless tobacco after a brief period of abstinence, they provide no information on the possible effects on maximal physical performance after exposure to smokeless tobacco for many years. Such information would be of interest in view of the reported positive correlation between increased heart rate at rest and the risk of developing cardiovascular disease [11]. It would also help to elucidate the role of nicotine in the progress of cardiovascular disease. We have previously found an increased mortality from cardiovascular disease among smokeless tobacco users in a long-term cohort study of 135 000 construction workers [12]. However, in a case–control study of post-myocardial infarction patients and control subjects, contradictory results were found [13]. Higher levels of systolic and diastolic blood pressure have been found in smokeless tobacco users compared with non-users [14], as well as increased plasma catecholamine concentrations [15,16] following nicotine exposure.

The purpose of the present study was to examine further the possible influence of long-term exposure to smokeless tobacco on cardiovascular and pulmonary function as evaluated by determinations of heart rate, blood pressure and pulmonary oxygen uptake at rest and during exercise at gradually increasing workloads in groups of smokeless tobacco users, cigarette smokers and non-users.

Patients and methods

Subjects

From the Stockholm City Fire Brigade, with 269 employed firemen between 35 and 60 years of age, 151 men (56%) were recruited to participate in an extended examination of physical working capacity. A compulsory fitness test is performed annually by all firemen and, some time before the test, subjects were asked to participate in the present study. Non-participating subjects,

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Table 1. Classification of the study population into major tobacco habit groups

	Non-users ($n = 68$)	Smokeless tobacco users ($n = 50$)	Smokers ($n = 33$)	Years of tobacco use Median (25th, 75th percentiles)
Never-users of tobacco	42	–	–	0
Ex-users for ≥5 years*	15	–	–	13 (10–20)
Ex-users for ≤ 5 years†	11	–	–	24 (20–29)
Smokeless tobacco users‡	–	29	–	25 (19–27)
Ex-smokers, now smokeless tobacco§	–	21	–	24 (17–31)
Smokers¶	–	–	26	28 (20–30)
Smoking and smokeless tobacco use**	–	–	5	30 (20–31)
Ex-smokeless, now smoking††	–	–	2	32 (30–35)

* Stopped smoking or using smokeless tobacco more than 5 years before examination.
† Stopped smoking or using smokeless tobacco less than 5 years before examination.
‡ Daily smokeless tobacco use for more than 6 months.
§ Stopped smoking more than 6 months ago; daily smokeless tobacco users for more than 6 months.
¶ Daily smoking for more than 5 years.
** Daily smoking plus daily or occasional smokeless tobacco use.
†† Stopped using smokeless tobacco more than 6 months ago; daily smokers for more than 6 months.

mostly because of the lack of a suitable schedule, were equally distributed among the nine different fire departments and were later examined by the company physician. Tobacco habits were categorized into non-users, smokeless tobacco users and smokers according to the subgroups shown in Table 1, where the duration of the tobacco habit is also shown.

Questionnaire

In connection with the physical examination, a questionnaire was filled out under the supervision of a nurse. Physical activity during work was divided into active, i.e. fireman duties and compulsory physical training during work time, or sedentary, i.e. no physically demanding duties. Leisure-time exercise was divided into two exercise levels: low, ≤ once a week; medium/high, 2–4 times a week. Alcohol and coffee habits were registered as self-reported low, medium or high consumption. Symptoms and family history of angina pectoris, hypertension or myocardial infarction were registered as yes/no answers, as was ongoing medication and a family history of parental death before the age of 60 years.

All subjects were informed of the nature, purpose and possible risks of the study before giving their voluntary consent to participate. The study protocol was approved by the ethics committee of Karolinska Hospital.

Procedures

Before testing, after 5 min rest, heart rate was measured by palpation, and blood pressure was measured in the supine position from the right upper arm by standard sphygmomanometry.

The exercise investigation was performed as a graded maximal exercise test on a MedGraphics computerized test bicycle (Medical Graphics, St Paul, MN, USA). The initial workload was 50 W, increased by 20 W every minute until volitional exhaustion. Heart rate, ECG and respiratory rate were recorded continuously. Oxygen uptake and carbon dioxide production were measured continuously, and respiratory gases were sampled via a mouthpiece, using the pulmonary gas exchange system CPX/MAX from MedGraphics. Systolic blood pressure was recorded every third minute. Heart rate and systolic blood pressure were also measured at the 190 W workload level.

The ECG recordings were all evaluated by the same investigator, without knowledge of the subject's tobacco status. Horizontal ST segment depression ≥1 mm during exercise was regarded as a sign of myocardial ischaemia. ST segment changes of < 1 mm were registered, but not classified as pathological. Arrhythmias before, during and after work were noted.

One day before the exercise test, a venous blood sample was drawn from an antecubital vein after overnight fasting and 8 h abstinence from any tobacco use. The determination of nicotine and cotinine (the primary metabolite of nicotine) in blood plasma was performed by capillary gas chromatography after a single-step liquid–liquid extraction procedure of the plasma sample. Nicotine and cotinine were detected by means of a nitrogen-selective detector giving high selectivity and sensitivity [17]. The limit of detection was 0·2 ng of nicotine and 1·3 ng of cotinine. Cotinine levels were used to estimate the intake of nicotine [18]. Cotinine, with a half-life of about 18 h, is a good quantitative indicator of habitual nicotine intake [19,20].

All subjects were told to use their habitual amount of tobacco before the exercise test. The time interval between the last intake of tobacco and the exercise test was noted.

Statistical methods

Means and standard deviations were computed for each of the outcome measures in the three separate groups

Table 2. Measured characteristics of the study population (means ± standard deviations) and comparisons of tobacco users with non-users

	Non-users ($n=68$)	Smokeless tobacco users ($n=50$)	Smokers ($n=33$)
Age (years)	44 ± 7	45 ± 6	48 ± 6*
Height (cm)	181 ± 7	180 ± 6	180 ± 5
Weight (kg)	84·2 ± 8·1	82·6 ± 8·8	81·9 ± 7·6
BMI (kg $(m^2)^{-1}$)	26 ± 2	26 ± 2	25 ± 2
Waist/hip ratio (cm cm^{-1})	0·89 ± 0·05	0·89 ± 0·05	0·92 ± 0·06**
Hb ($g L^{-1}$)	143 ± 9	145 ± 10	147 ± 9

n, total number in each group; BMI, body mass index; Hb, haemoglobin. Comparisons made with non-users, significance level of analysis of variance (ANOVA): *$P<0·05$; **$P<0·01$.

and, where appropriate, medians and 25th and 75th percentiles. Prevalence odds ratios and 95% confidence intervals were used for comparisons of proportions in the questionnaire analysis and for ECG remarks. Analysis of variance (ANOVA) was used to determine any differences in basic characteristics between the tobacco habit groups and non-users, and Fisher's protected least significant difference (PLSD) test was used as a *post hoc* test of significance. For the results of the exercise test, adjustments for differences in age, body mass index, waist–hip ratio, alcohol consumption, physical training and physical demands of the job between the three groups were made with multiple regression analysis. Significance for differences was tested with Student's *t*-test. Linear regression analysis was used to examine the relationship between two variables.

Results

Seven of the 151 subjects participated in the baseline physical examination only and did not perform the bicycle ergometer test in association with the study. Three were non-users, two were smokeless tobacco users and two were smokers. The reason for not participating was lack of time because of professional duties.

Comparing non-users and smokeless tobacco users, no significant differences were observed with regard to age, height, weight, body mass index, waist–hip ratio or blood haemoglobin, as shown in Table 2. Smokers were slightly but significantly older than the two other groups, and also showed a significantly higher waist–hip circumference ratio.

The results of the questionnaire analysis, presented in Table 3, showed no significant differences between smokeless tobacco users and non-users. Among smokers, significantly higher prevalences of family history of myocardial infarction were found, as were the prevalences of more sedentary occupation, low physical training level and higher alcohol consumption compared with non-users.

The average consumption of tobacco was 27 ± 15 g day^{-1} for smokeless tobacco users, i.e. approximately half a 50-g can daily, and 17 ± 10 cigarettes day^{-1} for smokers. Quantitatively, this represents a lower total intake of nicotine for smokers than for smokeless tobacco users, who also exhibited higher levels of cotinine compared with smokers. After overnight abstinence, the mean blood cotinine levels were significantly ($P<0·001$), and on average 37%, higher among smokeless tobacco users compared with smokers (see Table 4). Cotinine values below 10 ng mL^{-1} were considered to confirm non-user status.

The mean total duration of tobacco consumption was more than 24 years for both smokers and smokeless tobacco users, as presented in Table 1. Smokeless tobacco users who were former smokers had stopped smoking on average 12 years (SD ± 8) before the investigation. Before the exercise test, all tobacco users were instructed to use their usual amount of tobacco. A total of 79% of the smokeless tobacco users and 77% of the

Table 3. Prevalence of questionnaire characteristics of the study population

	Non-users ($n=68$) Percentage	OR	Smokeless tobacco users ($n=50$) Percentage	OR	CI	Smokers ($n=33$) Percentage	OR	CI
Family history of MI	25·0	1·0	20·0	0·8	(0·3–1·8)	42·4	2·2	(0·9–5·3)
Parent dead ≤ 60 years of age	19·1	1·0	18·0	0·9	(0·4–2·4)	39·4	2·8	(1·1–6·9)
Sedentary occupation	10·3	1·0	4·0	0·4	(0·1–1·8)	39·4	5·7	(2·0–16·2)
Low physical training	13·2	1·0	10·0	0·7	(0·2–2·3)	51·5	7·0	(2·6–18·5)
Alcohol intake (medium/high)	70·6	1·0	76·0	1·3	(0·6–3·0)	94·0	6·5	(1·4–29·5)

OR, odds ratio, comparisons made with non-users as reference group. CI, 95% confidence interval. MI, myocardial infarction.

Table 4. Tobacco consumption characteristics of the study population with medians and, within brackets, 25th and 75th percentiles

	Non-users ($n=68$)	Smokeless tobacco users ($n=50$)	Smokers ($n=33$)
Tobacco (g day^{-1} or cig day^{-1})	0	21 (14–36)*	15 (10–21)†
Blood nicotine (ng mL^{-1})‡	0 (0–0·3)	3·2 (1·6–4·8)	3·2 (1·7–8·2)
Blood cotinine (ng mL^{-1})‡	4·0 (0·7–5·8)	333 (232–421)	213 (163–359)

* Grams of smokeless tobacco per day.
† Cigarettes smoked per day.
‡ After overnight abstention.

smokers had consumed tobacco less than 2 h before the test.

The results of the exercise tests, adjusted for differences in age, body mass index, waist–hip ratio, alcohol consumption and level of physical training and physical demands of the job in the three groups, are presented in Table 5. In smokeless tobacco users, no significant differences were observed for maximal oxygen uptake or maximal work compared with non-users. In smokers, both maximal workload and oxygen uptake were significantly lower, by approximately 15%, compared with non-users. In Fig. 1, box plots of the maximal oxygen uptake in the three groups are presented, and maximal workload and maximal oxygen uptake in the different age groups are shown in Fig. 2.

Over the age groups, smokeless tobacco users did not differ significantly from non-users either in maximal work or in oxygen uptake, whereas smokers performed significantly lower maximal workloads and also had significantly less oxygen uptake in all age groups compared with non-users.

An analysis of the influence of intake of tobacco less than 2 h or more than 2 h before the test was performed in the smokeless tobacco group. Use of tobacco < 2 h before the test led to a heart rate on average 6 beats min^{-1} higher, a systolic blood pressure 10–15 mmHg higher and a diastolic blood pressure 6 mmHg higher compared with those who had their last intake of tobacco more than 2 h before the test, as shown in Table 6. These differences remained both at the 190-W workload and at maximal workload, but did not influence the achieved level of maximal oxygen uptake or workload. Similar differences were also observed for smokers, although less pronounced (not shown).

There was a significant correlation between increasing age and decrease in maximal workload ($r=0·55$, $P<0·001$) and maximal oxygen uptake ($r=0·53$, $P<0·001$). A reduction of 5–10% for every 5-year period was observed in all three groups.

In smokeless tobacco users, no correlation was observed between the reported amount of tobacco consumed and maximal workload. In contrast, in smokers there was a significant negative correlation between the maximal workload and the number of cigarettes smoked per day ($r=-0·53$, $P<0·01$).

The ECG recordings were analysed with regard to the

Table 5. Results of the exercise test (adjusted means† ± standard deviations) and comparisons of tobacco users with non-users

	Non-users ($n=65$)	Smokeless tobacco users ($n=48$)	Smokers ($n=31$)
Vo_2 max (L min^{-1})	3·51 ± 0·51	3·48 ± 0·49	2·88 ± 0·49***
Vo_2 max (mL min^{-1} kg^{-1})	42·4 ± 6·3	43·9 ± 6·0	38·3 ± 5·7***
Maximal workload (W)	325 ± 39	320 ± 42	266 ± 43***
RQ at max work	1·21 ± 0·08	1·17 ± 0·06	1·26 ± 0·1
HR at rest (beats min^{-1})	57 ± 9	54 ± 9	61 ± 10
HR at 190 W (beats min^{-1})	130 ± 15	130 ± 13	139 ± 18*
HR max (beats min^{-1})	171 ± 12	168 ± 10	168 ± 15
HR 10 min after work (beats min^{-1})	90 ± 12	86 ± 9	90 ± 11
Systolic BP at rest (mmHg)	124 ± 12	126 ± 13	123 ± 16
Systolic BP at 190 W (mmHg)	184 ± 23	191 ± 28	198 ± 24*
Systolic BP max (mmHg)	216 ± 23	210 ± 29	213 ± 27
Systolic BP 10 min after work (mmHg)	124 ± 10	121 ± 12	122 ± 11
Diastolic BP at rest (mmHg)	79 ± 8	76 ± 9	80 ± 9
Diastolic BP 10 min after work (mmHg)	75 ± 9	73 ± 8	74 ± 9

† All values are adjusted for differences in age, BMI, waist/hip ratio, alcohol consumption, level of physical training and physical demands of the job within the three groups. Comparisons made with non-users, significance level by Students *t*-test: no indication, comparison not significant; *$P<0·05$; ***$P<0·001$.

HR, heart rate; BP, blood pressure; Vo_2, oxygen uptake; RQ, respiratory quotient = CO_2/O_2.

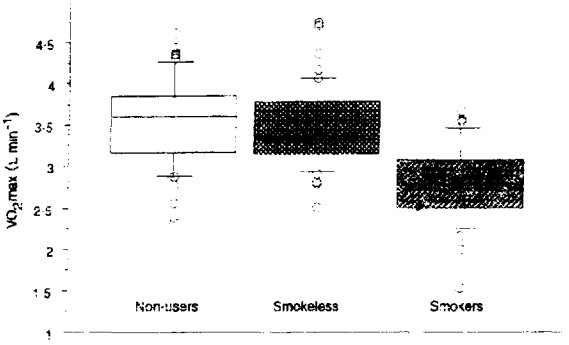

Figure 1. Box plot showing the 10th, 25th, 50th, 75th and 90th percentiles of maximal oxygen uptake in the three groups. Values above and below the 10th and 90th percentiles are plotted separately.

presence of significant ST depressions, arrhythmias or other pathological findings. Three subjects (two non-users and one smokeless tobacco user) showed a pathological ECG recording with signs of ischaemia, i.e. horizontal ST segment depression ≥1 mm during exercise, but were normal at rest and 10 min after exercise. The ECG recordings were normal in 80% of the non-users, in 73% of the smokeless tobacco users and in 71% of the smokers. ST segment changes < 1 mm were also registered and were observed in 8% of the non-users, in 15% of the smokeless tobacco users and in 23% of the smokers. The intergroup comparisons were not statistically significant.

Discussion

In the present study of physical fitness, no significant differences were found in physical performance between middle-aged smokeless tobacco users and non-users of tobacco, in spite of more than 20 years of smokeless tobacco use. This is in agreement with the findings of previous studies, in which younger subjects, mostly with acute exposure to smokeless tobacco, were investigated [6–10,21]. The results for smokers confirmed the findings from other studies of significantly lower maximal working capacity and oxygen uptake compared with non-users [3–6]. These findings also remained when the level of physical training and occupational physical activity were taken into account.

Acute nicotine exposure is likely to explain the observed higher heart rate and blood pressure both at rest and at work in smokeless tobacco users and smokers, exposed to tobacco shortly before (i.e. < 2 h) the exercise test compared with those not recently exposed (i.e. > 2 h). Although the difference was not statistically significant, it can be hypothesized that long-term repetitive exposure to nicotine might influence the activation of the autonomic nervous system and its influence on the heart, resulting in an increased risk of sudden cardiac events [11]. In an 11-year follow-up study of 6000 smokeless tobacco users, the relative risk of death from cardiovascular disease was twice as high in middle-aged smokeless tobacco users as in non-users [12], while a case–control study of myocardial infarction failed to demonstrate any increased risk among smokeless tobacco users [13].

As found in this study (see Table 4), higher levels of cotinine are usually found in smokeless tobacco users [1,22] compared with smokers, although the levels of blood nicotine are about the same. This is thought to reflect a higher absorption of nicotine through the gastrointestinal mucosa caused by swallowing, followed by a first-pass liver metabolism of nicotine, not reaching the central circulation and the central nervous system until metabolized to pharmacologically inactive cotinine [16,22].

Smokeless tobacco users did not exhibit any obvious differences in body stature, physical training level or coffee and alcohol intake compared with non-users, whereas smokers were generally less physically trained and consumed more coffee and alcohol. Smokers also showed a significant tendency to central

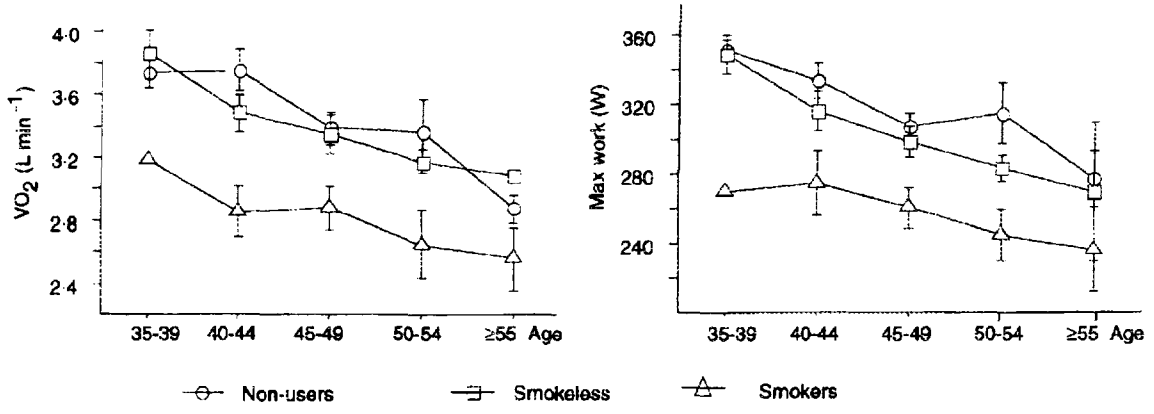

Figure 2. Maximal oxygen uptake (left) and maximal working capacity (right) and standard errors (SEM) in different age groups, for non-users, smokeless tobacco users and smokers. Comparisons with non-users (ANOVA and Fisher's PLSD test) were significant for smokers ($P < 0.05$) in all age groups, except ≥ 55 years. Significances remained after adjusting for differences in basic characteristics.

Table 6. Comparisons of exercise test results in smokeless tobacco users, with and without smokeless tobacco use less than 2 h before the test (adjusted means† ± standard deviations)

	Smokeless tobacco use >2 h before exercise test ($n=10$)	Smokeless tobacco use <2 h before exercise test ($n=37$)
Vo_2 max (L min^{-1})	3·54 ± 0·59	3·56 ± 0·47
Vo_2 max (mL min^{-1} kg^{-1})	45·2 ± 6·4	45·1 ± 6·0
Maximal workload (W)	305 ± 49	310 ± 40
RQ at max work	1·14 ± 0·06	1·14 ± 0·05
HR at rest (beats min^{-1})	52 ± 6	56 ± 10
HR at 190 W (beats min^{-1})	126 ± 12	133 ± 13
HR max (beats min^{-1})	156 ± 7	163 ± 10
HR 10 min after work (beats min^{-1})	77 ± 6	85 ± 10*
Systolic BP at rest (mm Hg)	116 ± 11	126 ± 13*
Systolic BP at 190 W (mm Hg)	178 ± 21	194 ± 29
Systolic BP max (mm Hg)	191 ± 25	209 ± 29
Systolic BP 10 min after work (mm Hg)	115 ± 11	124 ± 12*
Diastolic BP at rest (mm Hg)	68 ± 8	75 ± 9
Diastolic BP 10 min after work (mm Hg)	72 ± 7	78 ± 8*

† All values are adjusted for differences in age, BMI, waist/hip ratio, alcohol consumption, level of physical training and physical demands of the job within the two groups. Comparisons made by Student's *t*-test of adjusted mean values: *$P<0·05$.

HR, heart rate; BP, blood pressure; Vo_2, oxygen uptake; RQ, respiratory quotient = CO_2/O_2.

obesity compared with non-users, also affirming findings by other investigators among smokers [23,24].

In the analysis of the ECG recordings, the small number of subjects with pathological signs of myocardial ischaemia did not permit any conclusive interpretation. However, it is notable that ST segment depressions of < 1 mm were observed in twice as many smokeless tobacco users (15%) and three times as many smokers (23%) compared with non-users (8%). Whether this reflects an influence of nicotine on the myocardial circulation or on the autonomic nervous system remains, however, to be elucidated further.

The inclusion of only firemen in the study group was because of practical reasons. This professional group has a high prevalence of smokeless tobacco use among middle-aged men (30% vs. approximately 15% in these age groups among all Swedish men) and is available for medical examination in connection with their annual compulsory fitness test. This group represents a selection of extremely fit subjects. In Table 7, the average maximal working capacity from this study group is compared with the results of two other studies. The exercise capacity consistently exceeded what has been found in a study of over 2000 middle-aged men active in sports by about 17% for every 5-year age interval [25]. Compared with a random sample of Swedish men from the same age groups, the present study population performed on average more than 50% better [26]. This 'healthy worker effect' [27] might reduce the possibility of identifying negative cardiovascular influences of long-term nicotine exposure.

Table 7. Maximal work (W), comparisons of three different study populations (means and standard deviations)

Age group	Nordenfelt *et al.** ($n=58$)	Bovens *et al.*† ($n=1957$)	Present study‡ ($n=144$)
30–39	211 ± 30	–	348 ± 35
40–49	199 ± 37	259 ± 44	303 ± 42
50–59	172 ± 28	238 ± 42	273 ± 44

* Randomly selected subjects, citizens of a medium-sized Swedish town (Int J Sports Med 1993;14:66–71).

† Volunteers for sports medical check-up (Clin Physiol 1985;5:161–172).

‡ Firemen.

By studying a single professional group, some confounding from socioeconomic differences could be avoided. Nevertheless, smokers were heavier consumers of alcohol and coffee, and they also showed higher prevalences of family history of cardiovascular diseases compared with non-users. Other factors than smoking, like behavioural factors and lack of motivation for physical challenges, cannot be excluded as contributing to the reduced physical performance in smokers [6]. However, in our study all the subjects achieved a similar maximal heart rate, indicating that motivation was not correlated with tobacco habit.

The findings of the present study do not suggest nicotine exposure to be of major importance in reducing physical performance in healthy subjects. Whether chronic nicotine exposure might negatively affect coronary blood flow, myocardial function and excitability is, however, still largely unknown. Further studies are needed to investigate the health consequences of an added stress caused by combining nicotine exposure with prolonged aerobic exercise both for healthy subjects and for those affected by cardiovascular diseases. Most of the clinical consequences of chronic smoking do not appear until after the age of 65 years, and even if smokeless tobacco use appears to have fewer negative health effects than smoking, potential long-term adverse effects cannot yet be dismissed.

Acknowledgements

The analysis of plasma levels of nicotine and cotinine were kindly performed by Pharmacia, Helsingborg, Sweden. The project was funded by grants from the Swedish National Institute of Public Health (project 34121:220) and the Swedish Heart–Lung Foundation (projects 15505, 45002, 55003).

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