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Not smoking is associated with lower risk of hypertension: results of the Olivetti Heart Study

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Background: Few epidemiological investigations evaluated the role of smoking cessation on blood pressure (BP), and the results are not univocal. Therefore, the aim of this study was to assess the effect of smoking cessation on the risk to develop hypertension (HPT) and on BP values. **Methods:** This longitudinal study, with a follow-up period of 8 years, included the participants of the Olivetti Heart Study. Participants were 430 untreated normotensive non-diabetic men with normal renal function, examined twice in 1994–95 and in 2002–04. The sample included current smokers (S, $n = 212$), former smokers (ES, $n = 145$) and never smokers (NS, $n = 73$) at baseline. **Results:** Basal body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher in ES than in S (ES vs. S; BMI: 27.0 ± 2.5 vs. 26.1 ± 2.9 kg/m^2; $P < 0.01$; SBP/DBP: $121.2 \pm 9.3/80.0 \pm 5.8$ vs. $19.1 \pm 9.9/77.4 \pm 6.7$ mm Hg; $P < 0.05$; M ± SD). After 8 years of follow-up, BP changes (Δ) were significantly lower in ES than in S (ΔSBP/DBP: $12.6 \pm 13.4/7.9 \pm 8.1$ vs. $16.0 \pm 14.9/10.3 \pm 10.1$ mm Hg; $P < 0.05$; M ± SD), also after adjustment for potential confounders. Moreover, at the last examination, the overall HPT prevalence was 33%, with lower values in ES than in S (25 vs. 38%, $P = 0.01$). After accounting for age, BP and BMI at baseline, and changes in smoking habit over the 8-year period, ES still had significant lower risk of HPT than S (odds ratio 0.30, 95% confidence interval 0.15–0.58; $P < 0.01$). **Conclusions:** In this sample of healthy men, smoking cessation was associated with lower BP increment and minor HPT risk, independently of potential confounders.

Introduction

The worldwide prevalence of smoking is high, in both Western and developing countries, in men as well as in women.[1–3] Strong evidence supports the association between smoking and risk of cardiovascular events.[4,5]

Tobacco smoking is associated with a number of adverse effects on the cardiovascular system: alterations of the lipidemic profile,[6] insulin resistance,[7] higher incidence of diabetes[8] and metabolic syndrome.[9] Cigarette smoking also increased platelet activation[10] and plasma levels of inflammatory markers,[11] and it impaired vasodilatation due to decreased nitric oxide synthesis.[12] Altogether, these alterations contribute to the onset and progression of the atherosclerotic process.[13,14] Moreover, several studies showed that tobacco smoking leads to endothelial dysfunction,[7,14] increases arterial stiffness[15,16] and causes sympathetic system activation.[17]

The results of cross-sectional investigations on the relationship between smoking and blood pressure (BP) are not univocal, with some studies showing a positive[18,19] and others an inverse association.[20] Only few reports describe the possible predictive role of smoking status on the risk of hypertension (HPT), and their results suggest an association only in selected subgroup of subjects.[11,21,22] Some observational studies detected an increase in BP values and HPT prevalence after smoking cessation in men[23] and women.[24] Moreover, large epidemiological investigations found a similar weak risk to develop HPT in former and current smokers compared with never smokers.[11,21] While accounting for waist girth increments after smoking cessation, who quit smoke was associated with lower risk of HPT.[11] Therefore, the aim of this study was to assess the effect of cigarette smoking cessation on BP changes and on the risk to develop HPT in an 8-year follow-up investigation of an adult male population sample in Southern Italy (the Olivetti Heart Study, OHS).

Methods

Study population

The OHS is an occupational investigation of the male workforce of the Olivetti factories in Southern Italy (Pozzuoli-Naples and Marcianise-Caserta). A total of 1085 individuals aged 25–74 years (51.5 ± 7.2 years) were examined in 1994–95.

At the present examination, we excluded participants who presented, at baseline, with a diagnosis of HPT [systolic blood pressure (SBP) ≥140 mm Hg, diastolic blood pressure (DBP) ≥90 mm Hg or current antihypertensive therapy] ($n = 478$), altered renal function [glomerular filtration rate (GFR) <60 ml/min] ($n = 15$) or evidence of diabetes mellitus (fasting blood glucose level ≥126 mg/dl or anti-diabetic therapy) ($n = 37$), as well as subjects whose demographic and anthropometric characteristics and cardiometabolic risk factors were not available at baseline ($n = 60$). According to these selection criteria, we included 495 individuals, 430 (87%) of whom had also been examined in 2002–04 and had been considered eligible for the present analysis (Supplementary Appendix 1). They were stratified into three groups: smokers (S, $n = 212$), ex-smokers (ES, $n = 145$) and never smokers (NS, $n = 73$). In particular, ES had mean age of 50.1 years; 67% of participants were overweight, 14% were obese and 10% had central obesity and median of years since quitting was 3 (interquartile range (IQR): 2–4). S aged 49.8 years; 54% were overweight, 9% were obese and 12% had central obesity. Finally, NS had mean age of 47.6 years, 55% were overweight, 10% were obese and 8% had central obesity (table 1).

Table 1 Baseline characteristics of study participants

Variable	Total	Ex-smokers	Smokers	Never smokers
N	430	145	212	73
Age (years)	49.5 ± 6.6	50.1 ± 5.4****	49.8 ± 6.6	47.6 ± 8.3***
BMI (Kg/m^2)	26.4 ± 2.8	27.0 ± 2.5**,****	26.1 ± 2.9	26.0 ± 2.9
Overweight (%)	58	67**	54	55
Obesity (%)	11	14**	9	10
SBP (mm Hg)	119.8 ± 9.9	121.2 ± 9.3*	119.1 ± 9.9	118.9 ± 10.9
DBP (mm Hg)	78.5 ± 6.5	80.0 ± 5.8**	77.4 ± 6.7	78.7 ± 6.7
Heart Rate (b/min)	60.2 ± 7.6	61.6 ± 7.9**	59.2 ± 7.5	60.4 ± 7.0
Optimal BP (%)	34	29	37	33
Normal BP (%)	52	53	51	52
High-Normal BP (%)	14	18	12	15
Abdominal circumference (cm)	92.7 ± 8.0	94.1 ± 6.1*,****	92.4 ± 8.4	91.0 ± 9.8
Central obesity (%)	11	10	12	8
GFR (ml/min)[a]	87.1 ± 1.2	91.2 ± 1.2	88.0 ± 1.2	91.2 ± 1.0
HOMA index (U)[a]	1.7 ± 1.6	1.8 ± 1.7	1.7 ± 1.6	1.8 ± 1.6
CRP (mg/l)[a,b]	1.1 ± 2.5	0.9 ± 2.3**	1.3 ± 2.4	0.9 ± 3.0***
Hypercholesterolaemia (%)	81	82	80	79
Hypertriglyceridaemia (%)	41	39	46	30***
Physical activity (%)	32	35	32	27
Alcohol use (%)	81	85****	83	68***

Data are expressed as means ± SD, or as percentages; CRP: high-sensitive C-reactive protein; SBP, systolic blood pressure; DBP, diastolic blood pressure.
a: Geometric mean.
b: Analysis based on 340 participants.
Ex-smokers vs. smokers: *$P<0.05$, **$P<0.01$. Never smokers vs. smokers: ***$P<0.05$.
Ex-smokers vs. never smokers: ****$P<0.05$.

The local Ethics Committee approved the study protocol, and the participants provided their informed consent to participate.

Study protocol

The OHS study procedures have been previously described.[25] The examination at the baseline and at the end of the study was performed between 08:00 and 11:00 h, in a quiet and comfortable room, with the participants having fasted for at least 13 h. The participants had been instructed to pursue their normal activities but to avoid vigorous exercise and abstain from smoking and drinking alcohol, coffee, tea or any other beverages containing caffeine starting the evening before the visit.

The visit included a physical examination, the measurements of anthropometric parameters, a blood test, a fasting timed urine collection and the administration of a questionnaire including information on medical history, physical activity at work and during leisure time and alcohol consumption.

A fasting venous blood sample was obtained for the determination of serum glucose, insulin, creatinine, high-sensitive C-reactive protein (CRP) and lipids. Blood specimens were immediately centrifuged and stored at −70°C until analysis. Serum total cholesterol, triglyceride, glucose and CRP levels were measured with automated methods (Cobas-Mira; Roche, Milan, Italy). Serum insulin concentrations were measured by radioimmunoassay (Insulina Lisophase; Technogenetics, Milan, Italy). Insulin sensitivity was estimated by the homeostasis model assessment (HOMA) using the following formula: fasting plasma insulin (μU/ml) × fasting plasma glucose (mmol/l)/22.5.

GFR (expressed as ml/min) was assessed by the following formula: [140 − age (years) × weight (kg)]/[72 × serum creatinine (mg/dl)].

Baseline smoking status was investigated by a previously validated questionnaire comprising 11 questions.[26] The questionnaire classified the participants into current smokers, never smokers and ex-smokers, and reported the number of cigarettes per day, the duration of smoking habits and the number of years since cessation.

SBP and DBP (phase V) were measured three times, 2 min apart, with a random zero sphygmomanometer (Gelman Hawksley Ltd., Sussex, UK) after the subject had been sitting for at least 10 min. The average of the second and third reading was recorded.

The diagnosis of incident HPT during the 8-year follow-up period was defined as SBP ≥140 and/or DBP ≥90 mm Hg or current use of antihypertensive drug treatment (according to European Society of Hypertension/European Society of Cardiology guidelines).[27] Moreover, we also adopted more stringent criteria to detect HPT occurrence at follow-up (i.e. SBP ≥160 and/or DBP ≥95 mm Hg or current antihypertensive treatment at follow-up). These criteria were adopted to avoid the HPT prevalence overestimation, which would be possible because BP was measured only one time in the clinical visit.

Physical activity level was expressed according to whether the participant habitually engaged at least 30 min/day of aerobic exercise (YES/NO). Participants were also classified according to their alcohol intake into two groups: at least one glass of wine (or an equivalent amount of other alcoholic beverages per day) (YES) or no alcohol consumption (NO).

Hypercholesterolaemia was defined as a fasting blood total cholesterol level ≥190 mg/dl or use of lipid-lowering medication (YES), and hypertriglyceridaemia as fasting blood triglyceride levels ≥150 mg/dl or use of lipid-lowering medication (YES).[27]

Body weight, height and abdominal circumference were measured as described.[25] Overweight was defined as a body mass index (BMI) ≥25 kg/m^2 and obesity as a BMI ≥30 kg/m^2. Central obesity was given by a abdominal circumference value ≥102 cm.[27]

Statistical analysis

Statistical analyses were performed using the SPSS software, version 15 (SPSS Inc., Chicago, IL). As the distributions of HOMA index, GFR and CRP (based on 340 participants) were skewed (Kolmogorov–Smirnov test: $P<0.01$), we based our analyses on the log-transformed values of HOMA index (Kolmogorov–Smirnov test: $P=0.28$), GFR (Kolmogorov–Smirnov test: $P=0.23$) and CRP (Kolmogorov–Smirnov test: $P=0.94$).

To assess differences between group means, analysis of variance was used, followed by the Bonferroni correction for multiple comparisons, whereas chi-squared test was used to evaluate differences

between categorical variables. Bivariate relationships between the variables under investigation were evaluated by Pearson correlation analysis. Multiple linear regression analysis was used to determine the independent effect of smoking on BP levels, adjusting for baseline age, BMI, BP, heart rate and antihypertensive therapy and cigarette smoking at follow-up, and additional model, based on 340 subjects, was also accounted for CRP. Binary logistic regression analysis was used to estimate the role of cigarette smoking on incidence of HPT, adjusting for baseline age, BMI or changes in BMI, SBP and heart rate, and cigarette smoking at follow-up. Further model based on 340 participants was adjusted also for CRP.

It was estimated that 134 subjects were required in each arm to detect a true difference of 3.4 mm Hg in SBP changes over time, and to provide 80% power at 5% probability level (two-sided).

The results are reported as mean or geometric mean ± SD or SE or as percentages or as odds ratio (OR) and 95% confidence interval (CI), unless otherwise indicated. Two-sided $P < 0.05$ was considered statistically significant.

Results

In the whole population sample of the OHS in the 1994–95 examination, the current smokers were 43%, ex-smokers 37% and never smokers 20%. This distribution was slightly higher than that reported by official Italian registries, matching for gender, age and year[28,29] (figure 1).

Baseline relevant characteristics of the sample are reported in table 1. The prevalence of overweight was 58%, obesity 11% and central obesity 11%. Mean duration of smoking habit was 29 years [median: 30 years, (IQR: 25–35)] and mean number of cigarettes per day 18 [median: 20, (IQR: 10–25)]. During the study, 20% ($n = 42$) of S quit smoking and nobody started smoking. The comparison, at baseline, between ES and S showed that BMI, SBP, DBP, heart rate and abdominal circumference were significantly higher in ES than in S (ES vs. S; BMI: 27.0 ± 2.5 vs. 26.1 ± 2.9 kg/m^2, $P < 0.01$; SBP: 121.2 ± 9.3 vs. 119.1 ± 9.9 mm Hg, $P < 0.05$; DBP: 80.0 ± 5.8 vs. 77.4 ± 6.7 mm Hg, $P < 0.01$; heart rate: 61.6 ± 7.9 vs. 59.2 ± 7.5 b/min, $P < 0.05$; abdominal circumference 94.1 ± 6.1 vs. 92.4 ± 8.4 cm, $P < 0.05$). Besides, CRP was significantly lower in ES (ES vs. S: 0.9 ± 2.3 vs. 1.3 ± 2.4 mg/l, $P < 0.01$) (table 1).

Otherwise the comparison between ES and NS indicated a significantly lower age, BMI, abdominal circumference and alcohol consumption in NS (NS vs. ES: age, 47.6 ± 8.3 vs. 50.1 ± 5.4, $P < 0.05$; BMI: 26.0 ± 2.9 vs. 27.0 ± 2.5 kg/m^2, $P < 0.05$; abdominal circumference: 91.0 ± 9.8 vs. 94.1 ± 6.1 cm, $P < 0.05$; alcohol use: 68 vs. 85%, $P < 0.05$).

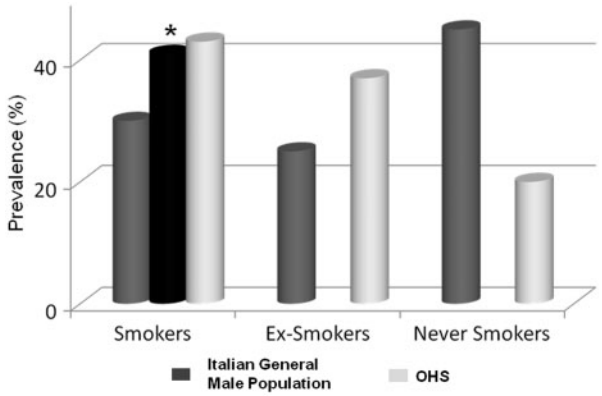

Figure 1 Prevalence of smokers in the Olivetti Heart Study (OHS) at baseline (1994–95) and in Italian general male population in 1994–95 (data from Italian registries[28,29]). *Data of Italian general male population matched for age (data available only for smokers)

Finally, the comparison between NS and S subjects showed that NS were younger, consumed less alcohol and had lower CRP and hypertriglyceridaemia than S (NS vs. S: age 47.6 ± 8.3 vs. 49.8 ± 6.6, $P < 0.05$; alcohol use: 68 vs. 83%, $P < 0.05$; CRP: 0.9 ± 3.0 vs. 1.3 ± 2.4 mg/l, $P < 0.05$; hypertriglyceridaemia: 30 vs. 46%, $P < 0.05$).

After the 8-year follow-up, the changes (Δ) in BP were significantly lower in ES than in S (ES vs. S; ΔSBP: 12.6 ± 13.4 vs. 16.0 ± 14.9 mm Hg, $P = 0.03$; ΔDBP: 7.9 ± 8.1 vs. 10.3 ± 10.1 mm Hg, $P = 0.02$); in addition, in a full multivariate model, after accounting for all potential confounders, SBP changes remained significantly lower in the ES group. On the contrary, DBP changes did not reach statistical significance (table 2). In addition, also BMI, abdominal circumference, HOMA index, GFR and CRP were not significantly different between ES and S during the follow-up.

The comparison between ES vs. NS showed that both groups had similar ΔBP values (ES vs. NS: ΔSBP 12.6 ± 13.4 vs. 11.9 ± 11.6 mm Hg - ΔDBP: 7.9 ± 8.1 vs. 8.5 ± 8.5).

According to European Society of Hypertension/European Society of Cardiology guidelines, the incidence of HPT after 8 years of follow-up was 54%, whereas according to the more stringent criteria of HPT, incidence was 33%, and was significantly different only between ES and S (ES = 25%, S = 38%, $P = 0.01$). This difference was confirmed by a logistic regression analysis, also accounting for baseline age, BMI, SBP, heart rate and smoking habit at follow-up (ES vs. S, OR 0.30, 95% CI 0.15–0.58, $P < 0.01$). In addition, adjusting for CRP, HPT risk remained significantly lower in ES subjects (OR 0.28, 95% CI 0.14–0.57, $P < 0.01$). The predictive role of cigarette smoking remained statistically significant also in a model including BMI changes throughout the study (table 3).

Finally, the analysis of the possible relationship between duration of smoking habit, number of cigarette smoked per day or duration of smoking cessation and changes in BP during the observational period did not show significant associations.

Discussion

For the first time, an epidemiological study shows that in people who quit smoking, BP and risk of HPT over time are similar to those of never smokers and significantly lower than those of current smokers. These results are not affected by duration of smoking cessation.

Two large prospective studies have investigated the relationship between cigarette smoking and risk of HPT. One of them involved

Table 2 Eight-year changes in blood pressure in ex-smokers compared with smokers

Model	Changes in SBP $\beta \pm$ SE	*P*-value
Unadjusted	−3.40 ± 1.54	0.028
Multivariate Model 1[a]	−5.49 ± 2.02	0.007
Multivariate Model 1 bis[b]	−5.66 ± 2.04	0.006
Model	**Changes in DBP $\beta \pm$ SE**	***P*-value**
Unadjusted	−2.37 ± 1.01	0.019
Multivariate Model 2[c]	−1.46 ± 1.32	0.267
Multivariate Model 2 bis[d]	−1.62 ± 1.33	0.222

SBP, systolic blood pressure; DBP, diastolic blood pressure.
a: Adjusted for baseline age, BMI, SBP (rank), heart rate and antihypertensive therapy and cigarette smoking at follow-up.
b: Model 1 plus baseline CRP (high-sensitive C-reactive protein): based on 340 participants).
c: Adjusted for baseline age, BMI, DBP (rank), heart rate and antihypertensive therapy and cigarette smoking at follow-up.
d: Model 2 plus baseline CRP (high-sensitive C-reactive protein): based on 340 participants.

Table 3 Eight-year risk of incident hypertension in ex-Smokers compared with smokers

Model	Risk of incident hypertension OR (95% CI)	*P*-value
Unadjusted	0.55 (0.35–0.88)	0.013
Multivariate Model 1[a]	0.30 (0.15–0.58)	0.001
Multivariate Model 1 bis[b]	0.28 (0.14–0.57)	0.001
Multivariate Model 2[c]	0.38 (0.19–0.76)	0.006
Multivariate Model 2 bis[d]	0.37 (0.18–0.74)	0.005

OR, odds ratio of ex-smokers vs. smokers; SBP, systolic blood pressure.
a: Adjusted for baseline age, BMI, SBP and heart rate, and cigarette smoking at follow-up.
b: Model 1 plus baseline CRP (high-sensitive C-reactive protein): based on 340 participants.
c: Adjusted for baseline age, SBP and heart rate, BMI changes and cigarette smoking at follow-up.
d: Model 2 plus baseline CRP (high-sensitive C-reactive protein): based on 340 participants.

13 000 male participants and found that compared with never smokers, past smokers and current smokers had similar risk of HPT.[11] The other study included 28 000 female participants, and it found a weak, but greater, risk of HPT in former smokers than in never smokers.[21] However, these two investigations were based on self-reported BP and anthropometric values, and furthermore, did not adjust for changes in weight during the follow-up, nor did they provide information on smoking cessation. Conversely, our results are based on direct measurement of BP values in both examinations and take into account the changes in body weight during follow-up as covariate in the multivariate model.

Two other prospective studies focalized the investigation on smoking cessation, and found that it was positively associated with both risk of HPT and changes in BP during weight variations.[23,24] Janzon et al examined only current smokers, who were divided on the basis of their changes in smoking habits during follow-up. This study showed that the women who quit smoking had higher weight gain with greater BP increase and risk of HPT than never smokers or current smokers.[24] On the contrary, our results showed that weight increases during follow-up were similar between ex-smokers, current smokers and never smokers; furthermore, although we adjusted for changes in smoking habit during follow-up, ex-smokers were considered those who were former smokers at baseline.

In a study evaluating only male individuals, the participants who quit smoking had higher risk of HPT and BP increase than current smokers and non-smokers, also after stratification by weight changes.[23] In addition, Lee et al indicated a similar risk of HPT between current smokers and non-smokers. These results were based on single BP determination during the 4 years of follow-up, and the authors considered as ex-smokers those who quit smoking during the follow-up. Our investigation, which was based on an 8-year follow-up, considered the average of three BP measurements, both at baseline and at follow-up, and included as ex-smokers the subjects who had quit smoking before the baseline examination, and in the multivariate model, we also adjusted for changes in smoking habit during follow-up.

Finally, a longitudinal investigation of a relatively small cohort of middle-aged men reported an inverse association between smoking cessation and the risk of HPT, although this association achieved statistical significance only after adjustment for basal waist girth and/or changes in waist girth during follow-up.[11] On the contrary, our study found this inverse association not only after adjustment for covariates, but also in the linear model.

In conclusion, our study is the first prospective investigation of the relationship between cigarette smoking and risk of HPT based on direct measurement of BP, anthropometric indexes and related biochemical variables at both baseline and follow-up examinations. To the best of our knowledge, this is the first investigation to demonstrate a significant association between smoking cessation at baseline and subsequent rate of HPT and BP decline, independently of age, BP, BMI, physical activity, alcohol intake, kidney function, insulin resistance, heart rate and CRP at baseline, and of intercurrent changes in body weight and smoking habits.

An ancillary finding of our study was that DBP at baseline was significantly higher in ES than in S, as also reported in other epidemiological studies[20,30] and in a case–control study on hypertensive individuals.[31] In our opinion, this significant difference could be traced to the direct association between DBP and BMI, which, in turn, was higher in the ES than in the S group.

The second important result of our study is the association between cigarette smoking cessation and BP changes during the 8-year follow-up. This result is in agreement with previous studies reporting that smoking could affect central hemodynamic parameters and arterial stiffness.[15,32] It is important to note that our investigation found similar changes in BP and risk to develop HPT in the ES and NS groups. This result confirms previous investigations showing a significant reduction of cardiovascular risk in former smokers compared with current smokers after 1 year of smoking cessation.[33]

With regard to the duration of smoking cessation, the analysis did not show association with BP over time. These results were supported by the homogeneity of duration of smoking cessation in the sample participants (and by the stability of the changes in BP and in body weight over the years).

Our study has some limitations. Firstly, it addressed white adult male individuals only, hence its results can only be generalized to a white adult male population. Secondly, as intermediate BP measurements from baseline to end of observation were not available, time-to-event analyses on incidence of HPT are not feasible.

The strengths of this investigation are the prospective design of the study with a relatively long follow-up observation period, direct measurement of BP and related variables at both baseline and follow-up, stringent criteria for diagnosis of incident HPT, careful standardization of data collection and inclusion of an unselected population sample.

The results of our study showed a favourable association between smoking cessation and BP decrease over time and risk to develop HPT in an adult sample of generally healthy men.

These results support the recommendations to abstain from smoking or stop smoking to reduce cardiovascular risk and, in particular, to prevent HPT development and increase BP levels with age.

Supplementary Data

Supplementary data are available at *EURPUB* online.

Conflict of interest: None declared.

Key points

- This investigation shows that smoking cessation protects from HPT risk.
- This article underlines for the first time that smoking cessation prevents from BP increments in general male population, independently of changes in body weight.
- These results support the recommendations to abstain from or to stop smoking to reduce cardiovascular risk. In addition, they underline the necessity of smoking cessation to prevent the development or the worsening of the cardiovascular risk determined by HPT.

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