

Original Research

Effects of Smoking on Heart Rate at Rest and During Exercise, and on Heart Rate Recovery, in Young Adults

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Introduction: There is an established link between smoking, abnormal heart rate (HR) values, and impaired cardiovascular health in middle-aged or older populations. The purpose of this study was to examine the effects of smoking on resting HR and on HR responses during and after exercise in young adults.

Methods: A sample of 298 young adults (159 men), aged 20-29 years old, were selected from a large population of health-science students based on health status, body mass index, physical activity, and smoking habit. All subjects underwent a maximal Bruce treadmill test and their HR was recorded during, at peak, and after termination of exercise.

Results: Smokers had significantly higher resting HR values than non-smokers. Both female and male smokers showed a significantly slower HR increase during exercise. Female smokers failed to reach their age-predicted maximum HR by 6.0 bpm and males by 3.6 bpm. The actual maximum HR achieved (HR_{max}) was significantly lower for both female smokers (191.0 bpm vs. 198.0 bpm) and male smokers (193.2 bpm vs. 199.3 bpm), compared to non-smokers. Heart rate reserve was also significantly lower in female (114.6 bpm vs. 128.1 bpm) and male smokers (120.4 bpm vs. 133.0 bpm). During recovery, the HR decline was significantly attenuated, but only in female smokers. Females had a higher resting HR and showed a higher HR response during sub-maximal exercise compared to males.

Conclusions: Smoking was found to affect young smokers' HR, increasing HR at rest, slowing HR increase during exercise and impairing their ability to reach the age-predicted HR_{max}. In addition, smoking was associated with an attenuated HR decline during recovery, but only in females.

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S moking is a major risk factor for cardiovascular morbidity and mortality, and is considered to be the leading preventable cause of death in the world. Based on WHO estimates, tobacco continues to kill nearly 6 million people each year, including more than 600,000 passive smokers, through heart disease, lung cancer, and other illnesses; that is one and a half million more than the corresponding estimate for 1990.¹ If current

trends continue, the death toll is projected to reach more than 8 million per year by 2030.¹ Smoking is associated with an increased risk of all types of cardiovascular disease, including coronary heart disease, ischemic stroke, peripheral artery disease and abdominal aortic aneurysm.² Internationally, 25% of middle-aged cardiovascular deaths are attributable to smoking.^{1,2} The European Society of Cardiology reported recently that smoking causes 28%

of cardiovascular deaths in men and 13% in women aged 35 to 69 years.²

There is an established link between heart rate (HR) and cardiovascular health.^{3,4} HR is a very important, non-invasive and easy-to-measure index of myocardial work.⁵ HR response during exercise⁶ and post-exercise HR decline⁷ are also very good markers of cardiac autonomic control. There is a plethora of studies suggesting that the findings of a blunted HR elevation during progressive exercise (chronotropic incompetence)⁸⁻¹¹ and attenuated HR decline during recovery¹¹⁻¹³ are important surrogates for an underlying autonomic dysfunction associated with increased cardiovascular morbidity and mortality. A high resting HR (HR_{rest}) and abnormal HR responses during or after exercise may precede manifestations of cardiovascular disease and may contribute to the early identification of persons at high risk.^{8,11} Despite these indications, the use of HR in clinical practice for monitoring cardiovascular function has been undervalued.^{3,4}

Smoking has been associated with higher HR_{rest} ¹⁴ and chronotropic incompetence.^{15,16} In addition, smoking prevalence is significantly higher in populations with a blunted HR increase during exercise⁸⁻¹¹ or an attenuated HR decline during recovery.¹¹⁻¹³ Overall, HR responses to cigarette smoking may be implicated in the link between smoking and cardiovascular disease. However, although the effects of smoking on HR seem to be age-dependent,¹⁷ relatively little is known about how smoking affects HR in young adults. The purpose of this study was to examine the effects of smoking on resting HR and on HR responses during and after exercise in young male and female smokers.

Methods

Selection criteria

A systematic search for confounding factors has shown that age,^{7,18} body mass index (BMI),^{19,20} excessive consumption of coffee or alcohol,^{21,22} educational level,²³ resting blood pressure,²⁴ and physical fitness^{10,20,24} are potential confounders in the relation between smoking and cardiac function. In this series, healthy college students, 20-29 years of age, of normal weight ($18.5 \text{ kg/m}^2 \leq \text{BMI} \leq 24.9 \text{ kg/m}^2$), and normotensive (systolic blood pressure: $\text{SBP} < 140 \text{ mmHg}$; diastolic blood pressure: $\text{DBP} < 90 \text{ mmHg}$), with a low consumption of coffee (up to two cups per day) and

alcohol (up to seven drinks per week), were eligible for the study. Health status was assessed by a physician and a cardiologist through medical history, physical and clinical examination. All subjects underwent baseline ECG and echocardiographic examinations to exclude cardiac abnormalities and confirm normal left ventricular function at baseline. Students with metabolic diseases, such as diabetes, hyperlipidaemia and thyroid disease, physical disability, recent illness, pregnancy and a history of alcohol or drug abuse, were not included in the study population. An elevated resting HR_{rest} is directly related with abnormal HR responses during and after exercise,¹⁰⁻¹² and is an independent risk factor for cardiovascular morbidity and mortality.²⁵⁻²⁸ In this study, the cut-off limit for tachycardia was set at $\geq 90 \text{ bpm}$ for women and $\geq 85 \text{ bpm}$ for men.^{4,29} All individuals with a higher HR_{rest} were excluded.

Physical activity and exercise capacity as measures of physical fitness are strongly associated with cardiac function and cardiovascular health, both in young adults³⁰ and in healthy middle-aged individuals.^{10,20} In order to control for these potential confounders, the physical activity level of the subjects was evaluated using the Greek version of the short International Physical Activity Questionnaire (IPAQ-Gr), which has shown good to high reliability³¹ and adequate validity³² properties in young adults. The individuals eligible for the study were those with a low physical activity profile, according to IPAQ physical activity classification criteria.³¹ In order to control for exercise capacity, the statistical outcomes were corrected for subjects' maximal exercise test duration. Finally, smokers were defined as those who had smoked 20 or more cigarettes per day for at least three smoking years. Non-smokers had never smoked.

Study population

The participants were selected from a large population of physical therapy students at the Technological Educational Institute of Athens (TEI-A). A standardised self-addressed questionnaire was given to all 3rd and 4th year students during 5 consecutive years. Based on the selection criteria, 421 students were invited for baseline evaluation, but finally 298 (159 men) completed all measurements and tests (Table 1). The rest (123 students, 29%) either did not meet the baseline criteria for HR, SBP and DBP at rest (22%), or did not complete the protocol (7%).

Table 1. Personal characteristics, baseline and exercise data of study population.

	Females		Males	
	Non-Smokers (n=79)	Smokers (n=60)	Non-Smokers (n=86)	Smokers (n=73)
Age (yrs)	22.3 ± 1.3	22.8 ± 1.7*	22.6 ± 1.9	23.2 ± 1.9*
Height (cm)	165.1 ± 5.4	164.3 ± 5.5*	178.9 ± 5.6	178.4 ± 6.0*
Weight (kg)	57.0 ± 5.3	57.3 ± 5.8*	74.2 ± 6.4	74.2 ± 6.6*
BMI (kg/m ²)	20.9 ± 1.5	21.2 ± 1.6*	23.2 ± 1.4	23.3 ± 1.4*
HR _{rest} (bpm)	70.0 ± 5.8	76.4 ± 6.4 [†]	66.3 ± 6.1	72.8 ± 6.1 [†]
Age-predicted HR _{max} (bpm)	197.7 ± 1.3	197.2 ± 1.7*	197.4 ± 1.9	196.9 ± 1.9*
SBP _{rest} (mmHg)	119.4 ± 8.2	117.4 ± 8.0*	125.1 ± 8.1	124.3 ± 8.2*
DBP _{rest} (mmHg)	72.9 ± 6.4	72.5 ± 6.5*	76.4 ± 6.4	77.1 ± 6.5*
Smoking	Never smoke	≥ 20 cigarettes/day	Never smoke	≥ 20 cigarettes/day
Smoking yrs	Never smoke	4.7 ± 1.7	Never smoke	5.8 ± 2.3
PA [‡]	Low	Low	Low	Low
IPAQ score [‡]	342	326*	352	337*
Exercise test duration (min)	9.4 ± 0.8	8.5 ± 0.8 [†]	11.4 ± 0.9	9.9 ± 0.8 [†]

*Non-significant differences between smokers and non-smokers. [†]p<0.01 for smokers vs. non-smokers. [‡]Scoring and classification criteria were based on IPAQ committee guidelines.³¹ Values are expressed as mean ± SD.

BMI – body mass index; DBP_{rest} – resting diastolic blood pressure; HR – heart rate; IPAQ score – total weekly physical activity score based on International Physical Activity Questionnaire; PA – physical activity; SBP_{rest} – resting systolic blood pressure;

Study protocol

All tests and measurements were conducted during morning hours, under constant conditions of temperature and humidity. Before their first appointment day, the participants familiarised themselves with the lab and exercise test equipment and signed a written informed consent. At baseline, HR_{rest}, SBP, and DBP were obtained with the subjects lying supine, after ten minutes of rest. If eligible, the students were given an appointment for their exercise test evaluation. The study protocol followed the principles of the Helsinki Declaration and its later amendments and was approved by the research committee of TEI-A.

Exercise test

All participants exercised with the standard Bruce maximal treadmill test. The maximal exercise test duration was used as an indirect measure of participants' exercise capacity. The exercise testing procedures followed the guidelines set out by the American Heart Association.³³ In summary, participants abstained from heavy eating, coffee and alcohol, and smokers from smoking, for at least 6 hours before the exercise test. During testing, subjects were not using the hand-rails for support. Those participants who were able to continue to the fourth stage of the Bruce protocol exercised in a running mode. Age-predicted target HRs

were not used as predetermined endpoints. Testing was terminated at maximal effort, when symptoms such as intense exhaustion, fatigue, dyspnoea, or intense leg pain occurred. All subjects were placed supine immediately after termination of the exercise test for a 5-min recovery period. Neither the cardiologist who supervised the exercise tests nor the assisting examiner were aware of the subjects' smoking status.

Heart rate evaluation

The same examiner of the research team obtained all HR measurements with the use of a 12-lead ECG. HR_{rest} was obtained with the subjects lying supine, after 10 minutes of rest. During the Bruce test, HR values were recorded at the end of every minute (e.g. HR₁). The HR value at a fixed sub-maximal aerobic workload was defined as HR_{submax} (e.g. end of stage one - HR₃, end of stage two - HR₆). The percentage HR increase until a given minute ($\Delta HR\%$) was used as a representative index of HR response during exercise and was calculated as follows: $\Delta HR\% = (\Delta HR_v / HR_{rest}) \times 100$, where $\Delta HR_v = HR_v - HR_{rest}$. In addition, the percentage HR increase between the 3rd and 6th min of exercise ($\Delta HR_{6,3}\%$) was computed. The highest HR achieved at maximal effort was defined as the actual maximum HR (HR_{max}). The age-predicted HR_{max} was determined as 220 minus the participant's age. In order to account for age and

HR_{rest} , heart rate reserve (HRR) and the percentage of the age-predicted HRR achieved (HRR%) were used and computed as follows: $HRR = HR_{max} - HR_{rest}$ and $HRR\% = [HRR / (\text{age-predicted } HR_{max} - HR_{rest})] \times 100$.^{6,15} The HR recovery (HR_{rec}) was recorded during the 5-min post-exercise period. Two indexes of HR_{rec} were computed: 1) the HR difference between HR_{max} and a given min of recovery, $\Delta HR_{recv} = HR_{max} - HR_{recv}$, as a measure for comparison with previously published data; and 2) the percentage HR decline until a given min of recovery, $\Delta HR_{recv}\% = (\Delta HR_{recv} / HR_{max}) \times 100$. For the purposes of the present study, HR values at rest, during sub-maximal exercise, at peak exercise, and during the first two minutes of recovery were used for comparisons between groups.

Data analysis

Statistical analysis of the data was performed using the IBM® SPSS® version 19 software package (2010 SPSS Inc., Chicago, IL, USA). Age, BMI, BP, HR values and maximal exercise test duration were normally distributed (Kolmogorov–Smirnov test) and are presented as mean \pm standard deviation. Analysis of variance for personal, baseline and exercise data, and the chi-square test for IPAQ score were used to examine possible differences between groups.

For the detection of significant HR differences between smokers and non-smokers, multivariate analysis of variance (general linear model, full factorial - type III) was used. Smoking was considered the independent variable (fixed factor) and all HR values were set as the dependent variables. Preliminary stepwise multiple regression analysis was used in order to determine which of the personal characteristics (age, sex, BMI, smoking, total weekly PA and maximal exercise test duration: independent variables) were significantly associated with each one of the examined HR values (dependent variables). Smoking was a significant determinant of HR in all cases. Total IPAQ score and BMI were not found to have any relation with HR responses and were therefore excluded from the final multivariate model. Maximal exercise test duration and age were related with most HR values and they both entered the final MANCOVA model as covariates. Gender was found to significantly affect HR responses and, since it was our intension to examine the effects of smoking on HR in both sexes, the results are presented separately for men and women. The level of significance was set as a p-value <0.05.

Results

Baseline data

Two hundred and ninety-eight young healthy adults with a mean age of 22.7 years participated in the present study (Table 1). Non-significant differences were found between smokers and non-smokers regarding age, height, weight, BMI and physical activity level in both sexes. In addition, non-significant differences were found for resting SBP and DBP between smokers and non-smokers of both sexes (Table 1). However, smokers had significantly higher HR_{rest} compared with non-smokers in both female (76.4 bpm vs. 70.0 bpm, $p=0.001$) and male (72.8 vs. 66.3, $p=0.004$) participants (Tables 2 & 3). Regarding sex differences, males had a lower HR_{rest} than females (69.2 bpm vs. 72.7 bpm, $p<0.001$), but their resting SBP and DBP were significantly higher (data not shown).

HR during exercise

In females, non-significant differences were found in HR_{submax} between smokers and non-smokers (Table 2). However, female smokers had a significantly lower HR increase ($p=0.001$) until a given minute of sub-maximal exercise than non-smokers ($\Delta HR_3\%$: 74.6% vs. 85.9% and $\Delta HR_6\%$: 118.0% vs. 137.2%). In addition, the percentage HR increase between the 3rd and 6th min of exercise was significantly lower for female smokers ($\Delta HR_{6-3}\%$: 24.9% vs. 27.7%, $p=0.003$). Moreover, as exercise intensity increased, the rate of HR increase slowed in female smokers. At rest, their HR was 9.1% higher than that of non-smokers, but this dropped to 2.5% (3rd min) and to 0.3% at the end of stage two (6th min).

Male smokers had a significantly higher HR_{submax} at the end of the 3rd min than non-smokers (HR_3 : 121.6 bpm vs. 128.5 bpm, $p=0.027$), but non-significant differences were found at the end of the 6th min (Table 3). Male smokers had a significantly lower HR increase until the end of the 6th minute of sub-maximal exercise than did non-smokers ($\Delta HR_6\%$: 108.7% vs. 121.7%, $p=0.001$). Moreover, the percentage HR increase between the 3rd and 6th min of exercise was significantly lower for male smokers ($\Delta HR_{6-3}\%$: 17.7% vs. 20.3%, $p=0.001$). As exercise intensity increased, the rate of HR increase slowed in male smokers. At rest, their HR was 9.8% higher than that of non-smokers, but this dropped to 5.7% (3rd min) and to 3.4% (6th min).

Regarding sex differences, females showed a

Table 2. Multivariate analysis of the effects of smoking on heart rate values at rest, during sub-maximal exercise, at peak exercise and during recovery in young females.

	Non Smokers (n=79)	Smokers (n=60)	Significance			
			F-value	p	Mean difference	(95% CI)
Rest:						
HR _{rest} (bpm)	70.0 ± 5.8	76.4 ± 6.4	12.01	0.001	-6.39	(-8.44 to -3.34)
Submax exercise:						
HR ₃ (bpm)	129.5 ± 7.8	132.7 ± 8.4	0.76	NS	-3.23	(-5.96 to -0.50)
ΔHR _{3%} (%)	85.9 ± 14.0	74.6 ± 13.2	16.62	0.001	11.32	(6.69 to 15.95)
HR ₆ (bpm)	165.2 ± 9.0	165.6 ± 8.9	1.89	NS	-0.41	(-3.44 to 2.62)
ΔHR _{6%} (%)	137.2 ± 17.6	118.0 ± 17.8	28.32	0.001	19.15	(13.17 to 25.13)
ΔHR _{6-3%} (%)	27.7 ± 4.4	24.9 ± 4.6	8.86	0.003	2.76	(1.24 to 4.28)
Peak exercise:						
HR _{max} (bpm)	198.0 ± 2.7	191.0 ± 2.8	148.36	<0.001	7.04	(6.11 to 7.97)
HRR (bpm)	128.1 ± 5.8	114.6 ± 7.0	72.64	<0.001	13.43	(11.29 to 15.57)
HRR% (%)	100.2 ± 1.8	95.0 ± 2.2	150.82	<0.001	5.28	(4.60 to 5.95)
Recovery:						
ΔHR _{rec1} (bpm)	50.0 ± 7.7	39.1 ± 7.4	17.71	<0.001	10.85	(8.29 to 13.41)
ΔHR _{rec1%} (%)	25.3 ± 3.8	20.5 ± 3.8	10.30	0.002	4.74	(3.47 to 6.02)
ΔHR _{rec2} (bpm)	68.0 ± 6.9	57.2 ± 6.8	26.53	<0.001	10.82	(8.50 to 13.15)
ΔHR _{rec2%} (%)	34.3 ± 3.3	29.9 ± 3.4	13.65	<0.001	4.40	(3.26 to 5.54)

Values are expressed as mean ± SD. Significance values were adjusted for age and maximal exercise test duration.

CI – confidence interval; HR – heart rate; ΔHR% – percentage heart rate increase until a given min of exercise; ΔHR_{6-3%} – percentage heart rate increase between 3rd and 6th min of exercise; HR_{max} – maximum heart rate; HRR – heart rate reserve; HRR% – percentage of the age-predicted heart rate reserve achieved; ΔHR_{rec} – heart rate difference between HR_{max} and a given min of recovery; ΔHR_{rec%} – percentage of heart rate decline until a given min of recovery.

Table 3. Multivariate analysis for the effects of smoking on heart rate values at rest, during sub-maximal exercise, at peak exercise and during recovery in young males.

	Non Smokers (n=79)	Smokers (n=60)	Significance			
			F-value	p	Mean difference	(95% CI)
Rest:						
HR _{rest} (bpm)	66.3 ± 6.1	72.8 ± 6.1	8.59	0.004	-6.50	(-8.41 to -4.59)
Submax exercise:						
HR ₃ (bpm)	121.6 ± 7.9	128.5 ± 7.8	4.98	0.027	-6.95	(-9.42 to -4.49)
ΔHR _{3%} (%)	84.4 ± 14.0	77.5 ± 14.2	2.37	NS	6.89	(2.45 to 11.32)
HR ₆ (bpm)	146.1 ± 8.8	151.0 ± 8.4	0.25	NS	-4.92	(-7.62 to -2.21)
ΔHR _{6%} (%)	121.7 ± 16.9	108.7 ± 16.2	10.46	0.001	13.07	(7.85 to 18.29)
ΔHR _{6-3%} (%)	20.3 ± 4.4	17.7 ± 4.9	11.09	0.001	2.66	(1.21 to 4.11)
Peak exercise:						
HR _{max} (bpm)	199.3 ± 2.9	193.2 ± 3.2	66.55	<0.001	6.13	(5.18 to 7.08)
HRR (bpm)	133.0 ± 6.7	120.4 ± 6.7	39.61	<0.001	12.63	(10.51 to 14.74)
HRR% (%)	101.4 ± 2.1	97.1 ± 2.3	65.15	<0.001	4.31	(3.63 to 4.99)
Recovery:						
ΔHR _{rec1} (bpm)	50.2 ± 7.5	39.6 ± 7.8	2.118	NS	10.63	(8.23 to 13.02)
ΔHR _{rec1%} (%)	25.2 ± 3.6	20.5 ± 3.9	0.381	NS	4.71	(3.53 to 5.89)
ΔHR _{rec2} (bpm)	69.1 ± 7.1	58.1 ± 8.8	3.74	NS	11.04	(8.63 to 13.45)
ΔHR _{rec2%} (%)	34.7 ± 3.4	30.0 ± 4.1	0.59	NS	4.62	(3.45 to 5.80)

Values are expressed as mean ± SD. Significance values were adjusted for age and maximal exercise test duration. Abbreviations as in Table 2.

higher HR response during sub-maximal exercise compared to males. Both sub-maximal HR values and percentage HR increase during exercise were significantly higher in females in all subgroups examined.

HR at peak exercise

The age-predicted HR_{max} was similar in smokers and non-smokers, for both sexes. However, the actual

HR_{max} was significantly lower ($p < 0.001$) for both female (191.0 bpm vs. 198.0 bpm, Table 2) and male smokers (193.2 bpm vs. 199.3 bpm, Table 3) compared to non-smokers. Both female and male smokers failed to reach their age-predicted HR_{max} , with female smokers falling short by 6.0 bpm, and male smokers by 3.6 bpm. In contrast, female non-smokers achieved their age-predicted HR_{max} (Tables 1,2), while male non-smokers exceed it by 1.9 bpm (Tables 1,3). Heart rate reserve was significantly lower ($p < 0.001$) in both female (114.6 bpm vs. 128.1 bpm) and male smokers (120.4 bpm vs. 133.0 bpm) compared to non-smokers. In addition, the percentage of HRR achieved (HRR%) was also significantly lower in smokers ($p < 0.001$). Female smokers reached 95% of their age-predicted HRR, while female non-smokers achieved 100.2%. Male smokers reached 97.2% of their age-predicted HRR, compared with 101.4% for male non-smokers.

HR during recovery

Both absolute HR decline and percentage HR decline during the first two minutes of recovery were significantly lower for female smokers compared to non-smokers (Table 2, Figure 1). At the first post-exercise minute, $\Delta HR_{rec1}\%$ was 20.5% for female smokers vs. 25.3% for non-smokers ($p = 0.002$). At the second post-exercise min, $\Delta HR_{rec2}\%$ was 29.9% for female smokers vs. 34.3% for non-smokers ($p < 0.001$). However, HR recovery values were not found to be significantly different between smokers and non-smokers in males (Table 3, Figure 2).

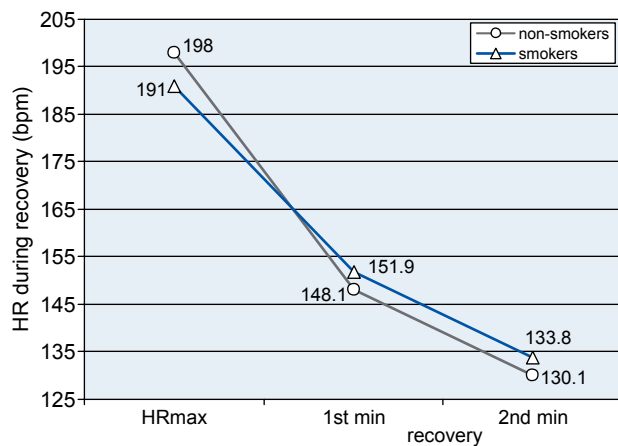


Figure 1. Heart rate (HR) decline during the first two minutes of recovery in young females. HR (beats per min) is expressed in terms of mean values.

Discussion

In the present study, smoking was found to affect the resting and exercise HR responses in both male and female young smokers. Smokers had elevated HR_{rest} , a slower HR increase during exercise, impaired ability to reach their age-predicted HR_{max} , and female smokers had an attenuated HR decline during recovery.

Heart rate at rest

In our study, the HR_{rest} in females was 3.5 bpm higher than in males; this agrees with the average HR_{rest} difference of 3-7 bpm between sexes found in most studies.^{4,21,25,29} Our findings also indicate that both female and male young smokers had significantly higher HR_{rest} than non-smokers. These results are in line with previously published data from young populations,^{21,34-36} and they are also in agreement with many HR-related studies of healthy middle-aged populations, where smoking has been associated with increased resting HR values.^{26,27} Smoking is associated with autonomic dysfunction¹⁴ and with selective alterations in cardiac autonomic control.^{37,38} More specifically, smoking, acting at peripheral sympathetic sites, increases circulating levels of catecholamines,³⁹ augments sympathetic outflow,^{17,40} and causes a long-term reduction in vagal drive.³⁸ This sympathetic predominance, seen even in young heavy smokers,³⁸ is also associated with impaired baroreflex function,^{37,40} leading to a marked increase in HR_{rest} .

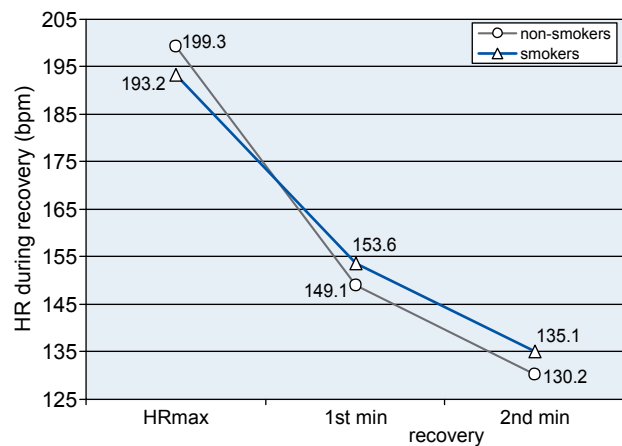


Figure 2. Heart rate (HR) decline during the first two minutes of recovery in young males. HR (beats per min) is expressed in terms of mean values.

Heart rate at sub-maximal workload

The HR value at a fixed sub-maximal aerobic workload (HR_{submax}) is directly related with the increased metabolic demands imposed by the specific workload intensity.⁶ Thus, HR_{submax} can be considered as an important marker of myocardial work,⁵ being inversely associated with exercise capacity^{41,42} and cardiovascular health.^{43,44}

Our data indicated that no differences were found between young smokers and non-smokers regarding their sub-maximal HR values, with the exception of HR_3 in males, where smokers had significantly higher HR values. There are few studies examining the effects of smoking on HR_{submax} in healthy young adults. The results are confusing, since in some studies smoking was found to increase men's HR at a fixed sub-maximal workload,^{15,24} whereas elsewhere it was suggested that smokers have lower HR at sub-maximal exercise,^{45,46} and others found no differences.^{36,47} Differences in methodology (e.g. definition of sub-maximal workload, HR evaluation protocol, selection criteria for smokers, etc.) might have contributed to these divergent findings.

In the present study, the effects of smoking on HR_{submax} at the end of stage I were sex-specific. It is likely that the significant differences found between the sexes in smoking years and exercise capacity (greater differences in maximal exercise test duration were observed between smokers and non-smokers in males than in females) may partially explain our findings. Bernaards et al similarly reported that the effect of smoking on HR_{submax} and cardiovascular fitness was more pronounced in male smokers than in female smokers, a finding that is possibly explained by the lower number of pack-years in women.⁴⁶ In the Framingham Heart Study, Lauer et al found that the effect of smoking on HR_{submax} was sex-dependent at younger ages (<40 yrs).¹⁵ The authors reported that male smokers had higher HR_{submax} (at 6th min of Bruce exercise test) than non-smokers, but female smokers had significantly lower values than non-smokers. This is consistent with the finding of Shalnova et al that smoking had a significant negative association with HR_{submax} at a fixed treadmill workload, but only in females.⁴¹ Clearly, further research is needed to thoroughly examine the association between smoking and HR_{submax} in young adults and the possible effect of gender.

Heart rate increase during exercise

During exercise, the increased metabolic demands are met by an increased cardiac output, achieved

through an augmentation in HR and stroke volume. The elevation of HR—confounded by age, HR_{rest} and exercise capacity^{5,6}—is regulated by exercise-induced autonomic control, where sympathetic activity increases and vagal tone is reduced. The HR elevation peaks at maximal exercise, when healthy subjects achieve an actual HR_{max} close (± 10 bpm) to their age-predicted HR_{max} .⁶ An impaired HR response to exercise and failure to reach >80% of the age-predicted HRR, known as chronotropic incompetence,⁶ are associated with autonomic imbalance and are important prognostic markers of cardiovascular health.^{8-11,48}

In the present study, both female and male smokers showed a significantly slower HR increase during treadmill testing compared to non-smokers. Although chronotropic incompetence was not observed in any of the subgroups examined, significantly more smokers failed to reach their age-predicted HR_{max} . Smokers had a lower HR_{max} by 7.0 bpm in females and 6.1 bpm in males, similar to the 7.0 bpm difference between smoking and non-smoking groups reported by Sandvik et al in healthy middle-aged men.¹⁰ Our results are also in line with many HR-related epidemiological studies in healthy middle-aged^{8-10,49} or younger⁴⁸ populations, where smoking was always significantly associated with an impaired HR increase during exercise, a lower HRR or a lower HR_{max} achieved. Analysis of our data showed that the effects of smoking on $\Delta HR\%$, HR_{max} , HRR and HRR% were more pronounced in female smokers. These sex-specific findings are similar to those reported by Lauer¹⁵ and Sidney,⁴⁵ supporting the suggestion that smoking may be associated with a higher cardiovascular risk in young women than in men.²³

It has been reported that smoking blunts HR elevation during progressive exercise, posing an increased risk to smokers' health.^{15,16} Adaptations to chronic smoking, such as down-regulation of β -adrenergic receptors, have been used in order to explain smokers' blunted HR response to exercise.^{15,46} Long-term smoking has been found to decrease the density of lymphocyte or adipose tissue β -receptors, down-regulating the β -receptors of the cardiovascular system.³⁹ The down-regulation of β -adrenergic receptors may explain why β -adrenergic blockers are not so effective in smoking cardiac patients who, despite β -adrenergic blockade, have higher HR_{submax} compared with non-smoking cardiac patients.⁵⁰ However, it is questionable whether these adaptations, which usually refer to middle-aged or older-aged smokers,

can explain the chronic effects of smoking on HR response during exercise in healthy young adults. In addition, it must be considered whether it may be the smokers' impaired exercise capacity that results in their inability to achieve a good exercise response⁵¹ and thus an adequate HR increase.

Heart rate decline during recovery

After the termination of exercise, sympathetic activity is withdrawn and vagal reactivation mediates the rate at which HR declines. HR decline during recovery is a useful marker of cardiac autonomic control, being directly associated with the intensity of post-exercise parasympathetic activity.^{7,52} Attenuated HR_{rec} is defined as abnormal if it declines by ≤ 12 bpm in the first post-exercise minute for tests that use a cool-down protocol, or by ≤ 18 bpm for protocols that stop exercise abruptly.^{7,52} Abnormal HR_{rec} following a maximal exercise test is directly related with a higher risk of cardiovascular disease,^{7,13} being also an independent predictor of mortality.^{8,11,12,52}

In our study, there were no signs of abnormal HR_{rec} observed in any of the subgroups examined. However, the HR decline during recovery was attenuated in young smokers of both sexes, but these changes were significant only in female smokers. In many epidemiological HR-related studies in healthy middle-aged populations, smoking was inversely associated with HR decline during recovery.^{12,13} There are very few studies that have examined the association between smoking and HR_{rec} in young adults. Kobayashi et al reported that young smokers had attenuated HR decline after sub-maximal exercise.³⁶ In our study, smoking was negatively related with HR decline after maximal exercise. In contrast, in the CARDIA study the prevalence of smoking was significantly lower in the slower HR_{rec} quartiles.³⁰ The important differences in the research design of the studies just mentioned, such as the workload intensity at termination of exercise (maximal vs. sub-maximal) and the recovery protocol (cool down vs. abrupt cessation of exercise) may explain the discrepancy between the results.

There is a direct correlation between the HR_{max} achieved at peak exercise test and the subsequent HR decline during recovery.^{11,13,30,52} This relationship may partially explain our results in females, where smokers had a significantly lower HR_{max} and blunted HR_{rec} comparing to non-smokers. In addition, it has been found that an attenuated HR_{rec} may also rep-

resent a marker of decreased exercise capacity, independently of health.^{7,52} Indeed, the CARDIA study reported a significant direct p-trend towards a decreased exercise capacity as HR_{rec} slowed.³⁰ These observations may explain the gender-specific smoking effects on HR_{rec} found in the present study, where smoking was associated with an attenuated HR_{rec} only in females. As shown in Table 1, females' exercise capacity was significantly lower compared to males in both smoking and non-smoking groups. However, as these gender-specific effects are not fully explained, further studies are needed in the future to thoroughly examine and establish these findings.

Limitations – future suggestions

The main strengths of this study were the strict selection criteria used for the enrolment of subjects from a well defined and homogeneous target population, and the examination of the smoking-HR relationship separately for men and women. In addition, the single-blind design (neither the cardiologist nor the examiner were aware of subjects' smoking status), and the control for potential confounders added statistical power to our results. On the other hand, the size of the sample and the non-randomised design are the main limitations. In addition, it can be argued that it is preferable to use objective measures in order to define smoking selection criteria, such as serum nicotine or cotinine levels, rather than formal questionnaires. However, standardised questionnaires are widely used in most smoking-related studies.^{12,18,19,50,51} Finally, our target population consisted of healthy young higher education students. Socio-economic status, smoking years, dietary habits, as well as other factors might differ from the general population. Therefore, the extent to which the present results could be generalized to a more unselected population cohort is unclear.

Given the grave consequences of smoking for cardiovascular health, the early detection of its effects on resting HR and on HR responses during exercise is of great importance and supports the need for prompt cessation of the smoking habit, especially in young people. Although there appears to be a general agreement that smoking increases resting HR, further research is needed for a thorough evaluation of the effects of tobacco on HR changes during and after exercise, since abnormal HR responses may serve as an important prognostic factor for future cardiovascular morbidity.

Conclusions

Smoking was found to affect young smokers' HR, increasing HR at rest, slowing HR increase during exercise, and impairing their ability to reach the age-predicted HR_{max}. In addition, smoking was associated with an attenuated HR decline during recovery, but only in females. Concerning sex differences, females had a higher resting HR and showed a higher HR response during sub-maximal exercise compared to males.

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