Original Article

The Association of Smoking with Components of the Metabolic Syndrome in Non-diabetic Patients

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Abstract

Introduction: There is limited evidence about the association between smoking and metabolic syndrome (MS). The aim of this study was to assess the association of smoking with MS components. Materials and Methods: As part of the baseline survey of a community-based study, we studied 5573 non-diabetic men. All participants were interviewed and underwent physical examinations and blood collection. Results: The study participants comprised 1625 smokers and 3948 non-smokers, with a mean age of 38.07 ± 14.85 years. Serum low-density lipoprotein-cholesterol (LDL-C) and triglycerides (TG) were higher in smokers than in non-smokers (LDL-C: 115.34 ± 39.03 vs 112.65 ± 40.94 mg/dL, respectively, *P* = 0.015 and TG: 175.13 ± 102.05 vs 172.32 ± 116.83 mg/dL, respectively, *P* = 0.005). Body mass index, waist circumference and waist-hip ratio were lower in smokers than in non-smokers. Mean systolic and diastolic blood pressures were significantly lower in smokers than in non-smokers (systolic: 112.06 ± 15.888 vs 117.25 ± 17.745 mmHg, respectively, *P* = 0.000; diastolic: 73.66 ± 10.084 vs 76.23 ± 10.458 mmHg, respectively, *P* = 0.000). The percentage of individuals with 2 MS components was higher in smokers than in non-smokers (39.64% vs 33.00%, respectively, *P* = 0.000). However, the percentage of non-smokers with 3 MS components was higher than in smokers (49.62 % vs 43.82%, respectively, *P* = 0.000). Conclusions: Our findings support the hypothesis that lifestyle factors such as smoking can adversely affect MS components. However, we should acknowledge that these differences may have resulted from the large sample sizes studied and may not be clinically significant. The lower prevalence of some MS components in smokers than in non-smokers might be because of their lower anthropometric measures.

Ann Acad Med Singapore 2008;37:919-23

Key words: Anthropometric indexes, Biochemical factors

Introduction

Metabolic syndrome (MS) is conceptualised as a constellation of physiologic or anthropometric abnormalities.[1] Typically, it includes excess weight, hyperglycaemia, elevated blood pressure, low concentration of high-density lipoprotein cholesterol (HDL-C), and hypertriglyceridaemia.[2] It is estimated that at least 47 million Americans, or about 1 in 5 people, have this condition.[3] The prevalence of MS is high not only in Western communities, but also in Asian populations.[4] Each abnormality promotes atherosclerosis independently, but when they accumulate, the metabolic disorders become increasingly atherogenic and increase the risk of cardiovascular morbidity and mortality.[1] MS is an important risk factor for subsequent development of type II diabetes and cardiovascular diseases (CVDs).[4]

Unhealthy lifestyle habits might increase the risk of CVDs.[5-7] These habits include physical inactivity, calorie-dense diets, habitual alcohol drinking, smoking and psychosocial stress.[8] Previous studies have demonstrated the adverse effect of smoking on CVDs, e.g. tobacco use increases triglycerides (TG) and decreases HDL-C levels. It has also been shown that total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and TC/HDL-C

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ratio are strongly related to smoking.[9] Another study revealed significant improvements in LDL-C, HDL-C and the HDL-C-to-LDL-C ratio 8 weeks after cutting down on smoking.[10]

An increasing body of evidence suggests that oxidative stress is involved in the pathogenesis of CVD.[11] Cigarette smoke contains large amounts of free radicals. In addition, smokers have lower antioxidant vitamins intake and/or higher antioxidant turnover rates. These conditions increase oxidative stress in smokers compared to non-smokers.[10-13] Previous studies have demonstrated the adverse effect of smoking on serum lipid profile; however, there is limited evidence on the association of smoking and MS components such as lipid profile and obesity. Dysglycaemia is an important component of MS; it leads to endothelial dysfunction, and could be a confounder of the effect of smoking on MS components. Hence, we set out to examine lifestyle factors such as smoking, which could adversely affect MS components, as defined by the Adult Treatment Panel III (ATP III) guideline.[2]

Materials and Methods

Study Population

This cross-sectional study was performed as part of the baseline survey of a community-based interventional programme entitled the Isfahan Healthy Heart Programme (IHHP) in 3 cities in Iran (Isfahan, Najafabad, Arak); the IHHP methodology has been previously described in detail;[14] we report it in brief here. The participants were selected from among 12,318 people comprising 6300 men and 6300 women registered in the IHHP between 2000 and 2001. The selected subjects were 5573 non-diabetic men with a mean age of 38.07 ± 14.85 years. As the contribution of several metabolic disorders to MS is different in men and women, we selected only non-diabetic men. To compare the effect of smoking on MS components and lipid profile, we assigned the subjects to 2 groups which included 1625 smokers (29.2%) and 3948 non-smokers (70.8%). The MS components according to the ATP III criteria guideline,[2] and anthropometric and laboratory findings were compared between the 2 groups. In smokers, it seems reasonable to presume that an increased production of free radicals aggravates the complications of MS. Also, as 4 of the 5 components of MS (i.e. obesity, hyperglycaemia, hypertension and hypertriglyceridaemia) are characterised by high oxidative stress and all of the subjects in this study were non-diabetic, only those components were evaluated in the present study. To exclude diabetic patients, in addition to known cases of diabetes, those individuals with fasting blood glucose (FBG) of more than 110 mg/dL and 2-hour post-load plasma glucose of more than 200 mg/dL were excluded from the analysis.

Anthropometric Measurement

Anthropometric measurements were performed by a well-trained team using a portable stationmaster. Height (Ht) was measured with participants standing without shoes to the nearest 0.5 cm using a secured metal ruler, while weight (Wt) was measured to the nearest 0.1 kg in light clothing using calibrated balance beam scales. Body mass index (BMI) was calculated by dividing Wt (kg) by Ht squared (m^2). Waist circumference (WC) measurements were conducted at the end of normal expiration to the nearest 0.1 cm, measuring from the narrowest point between the lower borers of the rib cage and the iliac crest and the hip at the level of the trochanter. The waist-to-hip ratio (WHR) was calculated by dividing WC by hip circumference.[14]

Measurement of Clinical and Laboratory Findings

Laboratory tests were performed in routine clinical visits. Blood pressure (BP) was measured twice by a nurse or technician using a standard mercury sphygmomanometer after 5 to 10 minutes of rest in the supine position. The average of the 2 measurements was recorded. Laboratory tests were performed in the morning after at least 8 hours of overnight fasting. All blood samples were collected from respective centres in the 3 cities of Najafabad, Arak and Isfahan. They were immediately frozen at -20°C until assayed within 72 hours at the central laboratory of Isfahan Cardiovascular Research centre (a WHO Collaborating centre), which meets the criteria of the national reference laboratories (a WHO Collaborating Centre in Tehran, Iran) and which is under the quality control of the University of Leuven, Belgium. Reference samples were obtained at the beginning of the study and included in daily laboratory analyses. Measurements of FBG and 2-hour post-load plasma glucose and plasma lipid profile was performed with standard procedures. FBG and the 2-hour post-load plasma glucose test were performed on fresh blood samples. After obtaining the initial venous blood sample, the participants drank 389 mL of Lucozade (equivalent to 75 g anhydrous glucose) over 5 minutes. A second blood sample was taken 2 hours later and analysed using the electrochemical glucose oxidase method. HDL-C, LDL-C, TC and TG were measured in fasting blood samples. TG was measured by enzymatic colorimetric methods and HDL-C was determined after dextran sulphate-magnesium chloride precipitation of non-HDL-C; LDL-C level was derived using the Friedewald equation in individuals with TG <400 mg/dL.[14]

Statistical Analysis

Data obtained from non-diabetic men were included in the analysis. The results are provided as means ± standard

deviation (SD). Comparisons between the groups were conducted by the Mann-Whitney U-test. Chi-square test was used to compare categorical variables and the prevalence of MS in smokers and non-smokers. *P* values of less than 0.05 were considered as statistically significant.

Results

TG and LDL-C were significantly higher in smokers (triglyceride: 172.3 ± 116.8 vs 175.1 ± 102.05 mg/dL, respectively, $P = 0.005$; LDL-C: 115.3 ± 39 vs 112.6 ± 40.9 mg/dL, respectively, $P = 0.015$). HDL-C was significantly lower in smokers than in non-smokers (44 ± 10.3 vs 45.8 ± 12.2 mg/dL, respectively, $P = 0.000$). Although TG was higher in smokers than in non-smokers, the difference was not significant. Other parameters such as BMI, WC, WHR, and mean systolic and diastolic BP were significantly lower in smokers than in non-smokers (BMI: 23.9 ± 4.4 kg/m^2 vs 24.5 ± 4.6 kg/m^2, respectively, $P = 0.029$; WC: 86.83 ± 11.61 vs 88.38 ± 11.89 cm, respectively, $P = 0.000$; WHR: 0.89 ± 0.008 vs 0.9 ± 0.088, respectively, $P = 0.029$; systolic BP: 112.06 ± 15.89 vs 117.25 ± 17.75 mmHg, respectively, $P = 0.000$; diastolic: 73.66 ± 10.08 vs 76.23 ± 10.46 mm/Hg, respectively, $P = 0.000$) (Table 1).

To evaluate the association of smoking with the number of MS components, we compared these components between 2 groups. Furthermore, the participants were divided into 4 categories based on the number of MS components and the results are displayed as the percentage of subjects in each category. Since all subjects were non-diabetic, the dysglycaemia component was not included in the analysis. The percentage of smokers with 2 MS components was greater than that of non-smokers, nonetheless, the percentage of non-smokers with 3 MS components was higher (Table 2).

To determine the most prevalent MS components in smokers, we compared these components between the 2 groups. The percentage of individuals with 2 MS components (TG ≥150 mg/dL and HDL-C <40 mg/dL) was higher in smokers than in non-smokers. The frequency of individuals with other MS components such as increased WC (>102 cm) and high BP (≥130/85 mmHg) was higher in non-smokers (WC: 67.97% in smokers vs 56.12% in non-smokers, respectively, $P < 0.0001$; high blood pressure: 12.91% in smokers vs 8.51% in non-smokers, respectively, $P < 0.0001$). Hypertriglyceridaemia was the most prevalent MS component in both smokers and non-smokers (Table 3).

Discussion

Our findings support the hypothesis that lifestyle factors such as smoking adversely affect MS components. Our results showed an association between smoking and elevated serum LDL-C and TG, as well as low HDL-C. However, we should acknowledge that these significant differences may have resulted from the large sample size and are probably not clinically significant. A similar study demonstrated that smoking was not related to diabetes mellitus, TC and/or LDL-C.[3] Although some studies revealed that smoking habits could change endothelial function.[15-17] In contrast, another study revealed that

Table 1. Laboratory and Anthropometric Indices in Smokers and Non-smokers: Isfahan Healthy Heart Programme (IHHP)

Laboratory parameters	Non-smokers	Smokers	*P*
LDL cholesterol (mg/dL)	112.65 ± 40.94	115.34 ± 39.03	0.015
HDL cholesterol (mg/dL)	45.88 ± 12.28	44.01 ± 10.35	0.000
Total cholesterol (mg/dL)	192.75 ± 61.69	193.48 ± 46.51	0.079
Triglyceride (mg/dL)	172.32 ± 116.83	175.13 ± 102.05	0.005
FBS (mg/dL)	78.65 ± 10.04	77.89 ± 9.97	0.005
2-hour post-load plasma glucose	89.86 ± 21.65	87.21 ± 19.29	0.000
Anthropometric parameters			
BMI (kg/m^2)	24.59 ± 4.69	24.42 ± 4.63	0.029
Waist circumference (cm)	88.38 ± 11.89	86.83 ± 11.61	0.000
Waist-to-hip ratio	0.9 ± 0.088	0.89 ± 0.008	0.029
Clinical parameters			
Systolic blood pressure (mmHg)	117.25 ± 17.75	112.06 ± 15.89	0.000
Diastolic blood pressure (mmHg)	76.23 ± 10.46	73.66 ± 10.08	0.000

BMI: body mass index; FBS: fasting blood glucose; HDL: high-density lipoprotein; LDL: low-density lipoprotein
*Values are expressed as means ± standard deviation (SD)

Table 2. Number of Metabolic Syndrome Components in Smokers and Non-smokers: IHHP

Number of metabolic syndrome component	Non-smokers (%)	Smokers (%)	*P*
At least one component	8.63	7.82	0.000
Two components	33.00	39.64	0.000
Three components	49.62	43.82	0.000

Table 3. Frequency of Individuals with Metabolic Syndrome Components in Smokers and Non-smokers: IHHP

Metabolic syndrome components	Non-smokers	Smokers	*P*
Waist circumference >02 cm	67.97%	56.12%	0.000
Triglycerides ≥150 mg/dL (1.695 mmol/L)	83.05%	87.59%	0.000
HDL cholesterol <40 mg/dL (1.036 mmol/L)	18%	21%	0.000
Blood pressure ≥130/85 mmHg	12.91%	8.51%	0.000

smoking had a dyslipidaemic effect and can increase TC, LDL-C and TG; furthermore, it can decrease serum HDL-C level.[4,18] In our study, mean systolic and diastolic BP in smokers were lower in smokers than in non-smokers.[4] Previous studies have reported such a negative relationship between cigarette smoking and diastolic/systolic BP.[4] The cumulative incidence of hypertension in smokers is shown to be lower than in non- and ex-smokers.[19] The adjusted mean change in BP of smokers is reported to be significantly lower than in non- and ex-smokers.[20] Contrary to our results, some studies have shown that cigarette smoking may also induce an increase in abdominal obesity.[21] In our study, BMI, WHR and WC in smokers were significantly lower than in non-smokers. Some other studies have demonstrated lower BMI in current and smoking status.[22] Some studies have shown that tobacco cessation leads to considerable weight gain.[23] The association between smoking and relative weight is modified by social factors such as age, education, marital status, hypertension and glucose intolerance.[22]

Unlike our findings, some studies have reported a higher percentage of symptoms of MS in young male smokers compared to non-smokers.[24] Given the cumulative effect of CVD risk factors, the Kuopio study clearly demonstrated that the highest CVD risk is found in obese smokers, especially those with abdominal fat accumulation.[25] Current smoking was also found to be a significant independent risk factor for MS in both men and women, which is consistent with previous cross-sectional studies.[25-27]

In the current study, the percentage of individuals with 2 MS components was greater in smokers and the frequency of those with 3 components was unexpectedly higher in non-smokers. This may be accounted for by the diminution of anthropometric measures and BP in smokers. The 2 most common components of MS in smokers were hypertriglyceridaemia and low HDL-C.

Study Limitations

This cross-sectional study could not establish causal relations, but could generate a hypothesis that can be evaluated by future prospective studies. Therefore, the results are merely reflective of associations observed between smoking and clinical/biochemical parameters. The possible interference with smoking of other variables, such as dietary habits should not be overlooked. Moreover, the quality and quantity of smoking were not evaluated. Thus, treatment of patients with MS will most likely require lifestyle and when necessary, pharmacological interventions that will control the individual components of MS. Longitudinal studies with long-term follow-up among smokers, as well as experimental studies of the levels of oxidative stress in smokers are recommended.

Acknowledgements

The Isfahan Healthy Heart Programme is supported by grant (No. 31309304) from the Iranian budget and programming organisation, the Deputy of Health of the Ministry of Health and Medical Education in the Islamic Republic of Iran, Isfahan Cardiovascular Research Centre and Isfahan Provincial Health Centre, both affiliated with Isfahan University of Medical Sciences. We thank the personnel of Isfahan and Arak Provincial Health Offices for their cooperation. We would also like to thank Dr Asgary, Head of basic department and Dr Naderi, Head of Laboratories of the Isfahan Cardiovascular Research Centre, who designated this project as a model in the region. It is indexed as code No. 86 in the Canadian Heart Health Promotion Projects: www.med.mun.com.

REFERENCES

1. Meigs JB. Epidemiology of the metabolic syndrome. Am J Manag Care 2002;8:S283-S92.
2. Ford ES, Mokdad AH, Giles WH, Brown DW. The metabolic syndrome and antioxidant concentrations: findings from the Third National Health and Nutrition Examination Survey. Diabetes 2003;52:2346-52.
3. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287:356-9.
4. Kelishadi R, Derakhshan R, Sabet B, Sarrafzadegan N, Kahbazi M, Sadri GH, et al. The metabolic syndrome in hypertensive and normotensive subject: The Isfahan Healthy Heart programme. Ann Acad Med Singapore 2005;34:243-9.
5. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 2002;288:2709-16.
6. Kannel WB, McGee DL, Gordon T. A general cardiovascular risk profile: the Framingham Study. Am J Cardiol 1976;38:46-51.
7. Wood D. Established and emerging cardiovascular risk factors. Am Heart J 2001;141:49-57.
8. Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C, Toutouzas PK. Risk stratification of coronary heart disease through established and emerging lifestyle factors, in a Mediterranean population: CARDIO2000 Epidemiological Study. J Cardiovasc Risk 2001;6:329-39.

9. Tsujii S, Kuzuya H. The significance of lifestyle as a risk factor for the metabolic syndrome Nippon Rinsho 2004;62:1047-52.
10. Rahman I, MacNee W. Oxidant/antioxidant imbalance in smokers and chronic obstructive pulmonary disease. Thorax 1996;51:348.
11. Marangon K, Herbeth B, Lecomte E, Paul-Dauphin A, Grolier P, Chancerelle Y, et al. Diet, antioxidant status, and smoking habits in French men. Am J Clin Nutr 1998;67:231-9.
12. Cross CE, Van der Vliet A, Eiserich JP. Cigarette smokers and oxidant stress: a continuing mystery. Am J Clin Nutr 1998;67:184-5.
13. Cia H, Harrison DG. Endothelial in cardiovascular disease the role of oxidant stress. Circ Res 2000;87:840-4.
14. Sarraf-zadegan N, Sadri G, Malek Afzali H, Baghaei M, Mohammadifard N, Shahrokhi S, et al. Isfahan Healthy Heart programme: a comprehensive integrated community-bases programme for cardiovascular disease prevention and control. Design, methods and initial experience. Acta Cordial 2003;58:309-20.
15. Kim SH, Kim JS, Shin HS, Keen CL. Influence of smoking on markers of oxidative stress and serum mineral concentrations in teenage girls in Korea. Nutrition 2003;19:240-3.
16. Guthikonda S, Sinkey C, Barenz T, Haynes WG. Xanthine oxidase reverses endothelial dysfunction in heavy smokers. Circulation 2003;107:416-21.
17. Winkelmann BR, Boehm BO, Nauck M. Cigarette smoking is independently associated with markers of endothelial dysfunction and hyperinsulinaemia in nondiabetic individuals with coronary artery disease. Curr Med Res Opin 2001;17:132-41.
18. Shimokata H, Muller DC, Anders R. studies in the distribution of body fat, III. Effect of cigarette smoking. JAMA 1989;261:1169-73.
19. Freund KM, Belanger AJ, Agostino DRB, Kannel WB. The health risks of smoking. The Framingham Study: 34 years of follow-up. Ann Epidemiol 1993;3:417-24.
20. Reaven G. Metabolic syndrome: pathophysiology and implication for management of cardiovascular disease. Circulation 2002;106:286-8.
21. Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM. Insulin resistance an cigarette smoking. Lancet 1992;339:1128-30.
22. Okubo Y, Suwazono Y, Kobayashi E, Nogawa K. An association between smoking habits and blood pressure in normotensive Japanese men: a 5-year follow-up study. Drug Alcohol Depend 2004;73:167-74.
23. Rodu B, Stegmayr B, Nasic S, Cole P, Asplund K. The influence of smoking and smokeless tobacco use on weight amongst men. J Intern Med 2004;255:102-7.
24. Tahtinen TM, Vanhala MJ, Oikarinen JA, Keinanen-Kiukaaniemi SM. Effect of smoking on the prevalence associated cardiovascular risk factors of insulin resistance among Finnish men in military service. J Cardiovasc Risk 1998;5:319-23.
25. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. Arch Intern Med 2003;163:427-36.
26. International Obesity Task Force. Asia-Pacific Perspective: Redefining Obesity and its Treatment. Western Pacific Region. Sydney: Health Communications, 2000.
27. Tahtinen TH, Vanhala MJ, Oikarinen JA, Keinanen-Kiukaanniemi SM. Effect of smoking on the prevalence of insulin resistance-associated cardiovascular risk factors among Finnish men in military service. J Cardiovasc Risk 1998;5:319-23.