Comparison of Traditional Risk Factors, Angiographic Findings, and In-Hospital Mortality between Smoking and Nonsmoking Turkish Men and Women With Acute Myocardial Infarction

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ABSTRACT

Background: The prevalence of smoking is high in Turkey. However, there are no data available evaluating the differences between smokers and nonsmokers according to their sex in patients with acute myocardial infarction (AMI) in Turkey.

Hypothesis: The aim of the study was to determine the prevalence of smoking and its relationship to age, localization, and extension of coronary heart disease (CHD), and other risk factors in Turkish men and women with first AMI.

Methods: This study included, 1502 patients with first AMI from 3 different cities in Turkey. The baseline characteristics and traditional risk factors for CHD, Coronary angiographic results, and in-hospital outcome were recorded.

Results: The proportion of male smokers was significantly higher than that of women (68% vs 18%, $P < 0.001$). Smokers were younger by almost a decade than nonsmokers ($P < 0.001$). Male nonsmokers were younger than females; however, the mean age of first AMI was similar in male and female smokers. In both genders, prevalence of hypertension and diabetes mellitus was significantly lower in smokers than in nonsmokers ($P < 0.001$). Smokers had less multivessel disease and less comorbidity as compared to nonsmokers. Although the in-hospital mortality rate was lower in smokers, smoking status was not an independent predictor of mortality.

Conclusions: Smoking, by decreasing the age of first AMI in women, offsets the age difference in first AMI between men and women. The mean age of first AMI is lower in Turkey than most European countries due to a high percentage of smoking.

Introduction

Ischemic coronary heart disease (CHD) is the leading cause of death in both men and women worldwide.[1] However, there are significant gender-specific differences in its natural history, pathophysiology, prevalence, and clinical outcome. Although the mean age of the initial presentation of CHD is lower by almost a decade in men than in women and it is 2 to 5 times more common among men, women present a greater symptom burden; higher rate of functional disability and mortality; and a lower prevalence of obstructive CHD, as seen by coronary angiography, as compared to men.[2–6] There was also substantial gender-related variability in the prevalence of risk factors for CHD.[7]

Turkey is a large country and has a young population; nevertheless, the prevalence of atherosclerotic vascular disease is unexpectedly high and the mean age of patients with CHD is the youngest in Europe.[8] This may be due to the higher prevalence for some of the risk factors for CHD in this country. It is well established that cigarette smoking is a major and powerful contributor to the risk of acute myocardial infarction (AMI) in both men and women.[9,10] In Turkey, the prevalence of smoking, especially among young adults, is higher than in most European countries, and its

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prevalence has been increasing, especially in women.[11–13] According to the Turkish Diabetes Epidemiology Study (TURDEP), a large population-based study, the prevalence of smoking was 51% in men and 11% in women.[14]

Although several studies have described the prevalence of risk factors among women and men in different populations, we still have limited data to show the impact and the gender-related differences of smoking on acute ischemic CHD in Turkish patients. Therefore, the aim of the present study was to determine the prevalence of smoking, and its relationship to age, localization, and extension of CHD, and other risk factors in Turkish men and women with first AMI.

Methods

Between 2003 and 2008, patients with the diagnosis of first AMI were consecutively included from 3 different Turkish cities (Ankara, Konya, and Kayseri) in this cross-sectional observational study. Acute myocardial infarction was diagnosed by typical electrocardiographic findings (≥1 mm ST elevation in at least 2 contiguous derivations) and the elevation of myocardial necrosis markers in the presence of typical chest pain lasting 30 minutes or more.[15] The exclusion criteria included: previous myocardial infarction (MI) and the presence of left bundle branch block or paced-rhythm in electrocardiography on admission.

Information about demographic characteristics (age, gender) and risk factors known to be traditional risk factors for ischemic CHD (history of hypertension [HT] and diabetes mellitus [DM], smoking, and family history) were acquired and blood samples were taken to analyze lipid levels. Hypertension was defined as a history of HT and/or antihypertensive drug therapy,[16] and DM was defined as a history of DM and/or usage of antidiabetic drugs before hospital admission.[17] Blood pressure and fasting glucose levels were also recorded during the in-hospital period and patients with high blood pressure (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) or high fasting blood glucose levels (≥126 g/dL) in sequential measurements were recorded as hypertensive or diabetic patients, respectively.[16,17] Family history of premature cardiovascular disease was defined as at least 1 first-degree relative with premature CHD or sudden cardiac death (onset age ≤55 years in a male relative, ≤65 years in a female relative).[18] Current smokers were defined as patients reported to have smoked cigarettes or other tobacco products in previous years and those who quit smoking during the last year.[9]

Fasting blood samples (12 h) for lipid profile were taken within the first 24 hours of onset of symptoms. Total cholesterol (total-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were quantified by a cholesterol oxidase colorimetric assay of the supernatant from the precipitation of non-HDL lipoproteins with heparin and manganese chloride (Beckman Coulter, Inc, Fullerton, CA). Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald equation (LDL-C = [total-C] − [HDL-C + TG/5]).[19] High LDL-C was defined as LDL-C ≥130 mg/dL in nondiabetic patients and as LDL-C ≥100 mg/dL in diabetic patients.[20] The lipid profiles were not available in 127 patients because of early death or emergency coronary artery bypass surgery.

Coronary angiography was performed on 94% of the patients during the hospitalization period. Angiographic images were assessed by 1 independent cardiologist. The infarct-related artery was determined angiographically, and significant stenoses in the major coronary arteries was also recorded. A modified Gensini score was used to evaluate the extent of CHD.[21] The left ventricular ejection fraction (LVEF) was calculated with the modified Simpson's method by echocardiography. Death during hospitalization period was also recorded.

Statistical Analysis

Statistical analyses were performed with SPSS for Windows 13.0 software (SPSS Inc, Chicago, IL). Continuous variables were expressed as mean ± standard deviation. A Student *t* test was used to compare continuous variables and categorical variables were compared using a χ^2 test. To determine the influence of various factors on mortality a logistic regression analysis was performed, including age, gender, history of HT and DM, smoking, the number of vessels involved, Killip class (≥II, on admission), systolic blood pressure, LVEF, and heart rate on admission. The odds ratios (OR) and 95% confidence intervals (CI) were also calculated. A P value of <0.05 was considered statistically significant.

Results

From 2003 to 2008, 1502 patients were admitted to hospitals with a confirmed diagnosis of first AMI. The number and general characteristics of the patients are shown in Table 1. Approximately one-fifth of the patients were female. The mean age at first AMI was 57 ± 11 years in men and 64 ± 12 years in women, regardless of smoking status ($P < 0.001$). The proportion of smokers among men was significantly greater than among women (68% vs 18%, $P < 0.001$). Male smokers were 11 years younger and women smokers were 10 years younger compared to nonsmokers ($P < 0.001$ for both values). There was a small, but statistically significant difference between the mean age of nonsmoking men and women ($P = 0.011$). Interestingly, there was no statistically significant difference between the mean age of smoking men and women ($P = 0.39$). The proportion of smokers was higher in younger patients and decreased proportionally in older patients, both among men and women (Figure 1). In the ≤45 age group, 92% of the male patients and 60% of the female patients were smokers.

Table 1. Distribution of Risk Factors for MI in Turkish Nonsmokers and Smokers

	Men			Women		
	Nonsmokers n = 389	Smokers n = 809	*P* Value	Nonsmokers n = 250	Smokers n = 54	*P* Value
Age, yrs	64 ± 11	54 ± 10	<0.001	66 ± 11[a]	55 ± 12[b]	<0.001
⩽45 yrs	16 (4)	172 (21)		10 (4)	15 (28)	
46–65 yrs	198 (51)	536 (66)		111 (44)	30 (56)	
>65 yrs	175 (45)	101 (13)		129 (52)	9 (17)	
History of HT	164 (42)	170 (21)	<0.001	173 (69)	24 (44)	0.001
History of DM	95 (24)	96 (12)	<0.001	112 (45)	13 (24)	0.003
Family history	56 (14)	229 (28)	<0.001	43 (17)	18 (33)	0.008
Total-C, mg/dL	181 ± 47	185 ± 43	0.103	194 ± 53	196 ± 44	0.794
TG, mg/dL	117 ± 98	131 ± 90	0.018	133 ± 119	144 ± 103	0.563
HDL-C, mg/dL	38 ± 9	36 ± 9	0.005	42 ± 12	43 ± 9	0.701
LDL-C, mg/dL	120 ± 37	123 ± 37	0.180	124 ± 41	126 ± 37	0.805
High LDL-C[c]	158 (44)	333 (44)	0.447	126 (56)	24 (50)	0.274
Total-C/HDL-C	4.9 ± 1.4	5.3 ± 1.6	<0.001	4.8 ± 1.6	4.7 ± 1.0	0.577
Total-C/HDL-C ⩾4.5	218 (60)	519 (68)	0.005	120 (53)	26 (53)	0.542

Abbreviations: DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; HT, hypertension; LDL-C, low-density lipoprotein cholesterol; total-C, total cholesterol; TG, triglyceride.
The values are expressed mean ± SD or n (%) where appropriate.
[a] $P < 0.011$ in comparison to male nonsmokers.
[b] $P = 0.365$ in comparison to male smokers.
[c] High LDL-C was defined as LDL-C ⩾130 mg/dL in nondiabetic patients and as LDL-C ⩾100 mg/dL in diabetic patients.

The distribution of risk factors varied significantly between smokers and nonsmokers.

In both genders, the history of HT and DM was more frequently observed in nonsmokers, whereas there was a high prevalence of family history in smokers. In men, TG levels and total-C/HDL ratio were higher and HDL-C levels were lower in smokers as compared to nonsmokers. In women, no significant difference was observed in lipid parameters between smokers and nonsmokers.

Clinical and coronary angiographic characteristics of the patients is shown in Table 2. There was no significant difference between smokers and nonsmokers regarding the localization of the MI and infarct-related artery in women and men. In both genders, single-vessel disease was more frequently observed in smokers, whereas multivessel disease was more common in nonsmokers. Gensini score, an indicator of the extent of CHD, was also higher in nonsmokers among men and women as compared to smokers. Left ventricular ejection fraction was lower in nonsmokers than in smokers.

The overall mortality rate in our study was 11.3% and there was a significant difference between men and women (4.4% vs 11.8%, $P < 0.001$) as well as between smokers and nonsmokers (3.6% vs 9%, $P < 0.001$). The percentage of death was higher in nonsmokers than in smokers in both genders, but the statistical significance was observed only between male smokers and male nonsmokers (Table 2). The logistic regression analysis identified Killip class, history of DM, systolic blood pressure, LVEF, and heart rate on admission as significant independent predictors of in-hospital death (Table 3). However, smoking was not an independent predictor of mortality.

Discussion

In this geographically defined cohort, smoking was highly prevalent in younger AMI patients in both men and women. Both smoker men and women had experienced their first AMI about a decade earlier compared with nonsmokers. Other findings of this study were that the prevalence of well-known risk factors for AMI such as history of HT and

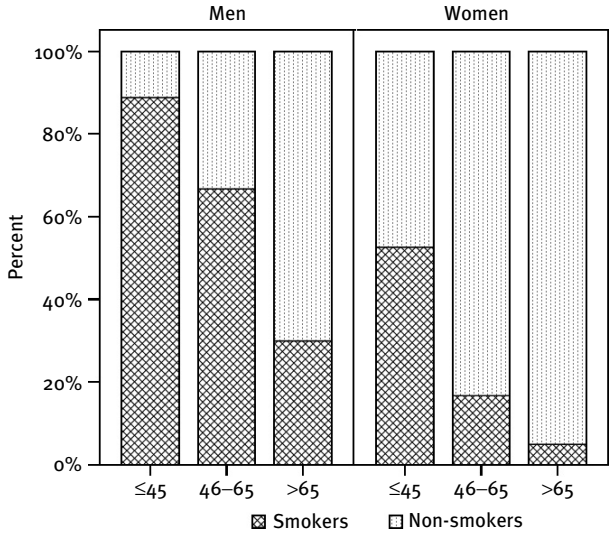

Figure 1. Prevalence of male and female smokers in patients with first acute myocardial infarction according to age group.

DM were lower in smokers and that nonsmokers had more extensive CHD and a worse prognosis than smokers.

Cigarette smoking and/or use of other tobacco products is one of the most important risk factors of morbidity and mortality in both developing and developed countries. Regular smokers who die of a smoking-related disease lose approximately 16 years of life expectancy compared to nonsmokers.[22] Atherosclerotic vascular diseases are the most common smoking-related diseases and there is consistent evidence supporting the causal role of smoking in the development of atherosclerosis and cardiovascular disease.[23–25] In the INTERHEART (A Global Study of Risk Factors in Acute Myocardial Infarction) study, it was reported that smoking was one of the most powerful risk factors for AMI and it was associated with a 3-fold increase in odds of a nonfatal AMI, compared with those who never smoked. In addition, the magnitude of risk was linearly related to the number of smoked cigarettes.[26] The authors emphasized that there was no safe level of smoking. Indeed, several other studies also demonstrated that light-smoking and/or heavy-smoking impair coronary microvascular functions, by decreasing the coronary flow velocity reserve, by causing endothelial dysfunction, by decreasing the release of tissue plasminogen activator, and by increasing platelet thrombus formation resulting in an increase risk of atherosclerosis and AMI.[27,28]

Table 2. Clinical and Coronary Angiographic Characteristics of Nonsmokers and Smokers

	Men			Women		
	Nonsmokers n = 389	Smokers n = 809	*P* Value	Nonsmokers n = 250	Smokers n = 54	*P* Value
Anterior AMI	170 (44)	369 (46)	0.269	122 (49)	22 (41)	0.178
Heart rate on admission, beat/min	77 ± 19	76 ± 19	0.231	83 ± 22	76 ± 20	0.089
Killip class (⩾II, on admission)	55 (21)	102 (20)	0.334	54 (28)	7 (27)	0.539
Ejection fraction, %	45 ± 9	47 ± 9	0.011	45 ± 10	50 ± 9	0.002
In-hospital mortality	24 (6.3)	27 (3.4)	0.019	32 (13.1)	3 (5.7)	0.092
Single-vessel disease	190 (51)	471 (62)	<0.001	126 (54)	39 (75)	0.003
2-vessel disease	126 (34)	219 (29)	0.043	58 (28)	8 (15)	0.104
Multivessel disease	54 (15)	71 (9)	0.006	52 (22)	5 (10)	0.027
Gensini score	125 ± 52	117 ± 48	0.021	136 ± 60	104 ± 43	0.002
Infarct related artery			0.843			0.573
LMCA	1 (0.3)	2 (0.3)		2 (0.9)	0 (0)	
LAD	168 (45.8)	360 (47.4)		118 (50.2)	22 (42.3)	
LCx	42 (11.4)	95 (12.5)		25 (10.6)	8 (15.4)	
RCA	156 (42.5)	302 (39.8)		90 (38.3)	22 (42.3)	

Abbreviations: AMI, acute myocardial infarction; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; LMCA, left main coronary artery; RCA, right coronary artery.
The values are expressed mean ± SD or n (%) where appropriate.

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Table 3. The Results of Logistic Regression Analysis for Prediction of In-Hospital Outcome

		95% Confidence Interval		
Predictors	Odds Ratio	Lower	Upper	*P* Value
Killip class on admission	4.706	2.146	10.318	<0.001
Diabetes mellitus	2.915	1.344	6.322	0.007
Systolic blood pressure on admission	0.974	0.958	0.990	0.002
Ejection fraction	0.953	0.912	0.995	0.029
Heart rate on admission	1.019	1.001	1.037	0.040

In our study investigating patients who suffering from first AMI, prevalence of smoking was higher in men than in women, which is consistent with population-based studies from Turkey.[13] It was notably higher in younger patients than in older patients, for both sexes. Smoking was the most prevalent risk factor in patients ⩽45 years of age in both men and women. In our study, it was found that male smokers suffered from first AMI 10 years before male nonsmokers, whereas female smokers suffered from first AMI 11 years before female nonsmokers. Consistent with the previous literature data, females were older than males in nonsmokers. However, an interesting finding of the study was that the mean age of first AMI was similar between male and female in smokers. This finding suggests the hypothesis that smoking might remove some of the relative advantages of premenopausal women. Moreover, the percentage of smoking in our study was higher than in all regions in the INTERHEART study.[26] This situation may explain the reason why the first experienced AMI is earlier in Turkey.

One of the other findings in our study is that well-known risk factors such as history of HT and DM are lower in smokers than in nonsmokers. The explanation for this is that smokers experienced their first AMI earlier. Cigarette smoking increases inflammation and oxidation of LDL-C, which plays a pivotal role in the pathophysiology of atherosclerosis.[29] Smoking is more strongly associated with occlusive thrombus formation causing AMI with the disruption of vulnerable plaque and alteration of platelet function in the early stages of atherosclerotic disease, particularly in young people.[30,31] Consistent with this, in our study, we found that Gensini score, an indicator of the extent of CHD and multivessel disease, was lower in smokers than in nonsmokers, for both men and women.

In the present study, in-hospital mortality was lower in smokers compared to nonsmokers. Although several previous studies have demonstrated that smoking increases the risk of AMI and death from CHD, the unadjusted short-term clinical outcome of smokers is better than nonsmokers, a phenomenon called the smoking paradox.[31,32] This paradox results from smokers tending to have lower comorbities such as a history of HT and DM, more favorable clinical and angiographic baseline characteristics with younger ages, higher ejection fraction, and less multivessel coronary artery disease compared to nonsmokers.[33,34] In our study, the characteristics of the patients were the same. Smoking was not an independent predictor of in-hospital mortality in logistic regression analysis.

Study Limitations

There are several limitations in this study. Second hand tobacco smoke, a risk factor for AMI, was not interrogated in our study. And also, the degree of smoking was not recorded. Another limitation was that a control group was not included in the study.

Conclusion

There are 2 results that can be drawn from this study. Smoking, by decreasing the age of first experienced AMI in women, offsets the mean age of first AMI between men and women. The age difference in first AMI is lower in Turkey than reported in the literature due to the high percentage of smoking.

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