TÜBİTAK

Original Article

Turk J Med Sci
2011; 41 (2): 317-324
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E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-1004-735

Distribution of coronary artery risk factors: a regional analysis

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Aim: To analyze the frequency and distribution of coronary artery risk factors in the city of Rize and its surrounding areas.

Materials and methods: This observational study included 452 patients (333 men, 119 women). In addition to demographic characteristics of the patients, conventional risk factors were also recorded. The patients were grouped according to their ages, gender, and electrocardiographic characteristics.

Results: The mean age of participants was 63 ± 13 years and 74% were male. Smoking and hypertension (HT) were seen more often (71%) in younger male patients. No difference among age groups was detected with regard to the occurrence of diabetes mellitus. The levels of HDL-cholesterol ($P < 0.001$) and the ratio of total cholesterol to HDL-cholesterol ($P < 0.05$) were found to be relatively higher in female patients. The prevalence of smoking and familial risk factors both decreased with age.

Conclusion: At least one of these risk factors was detected in 97% of patients. Therefore, our study continues to emphasize the crucial role of modification of risk factors in patients with coronary artery disease, the most important etiologic factor for morbidity and mortality.

Key words: Coronary artery disease, risk factors, regional

Koroner arter hastalığı risk faktörlerinin dağılımı: Bölgesel bir analiz

Amaç: Bu çalışmadaki amacımız, Rize ili ve civarında koroner arter risk faktörlerinin sıklık ve dağılımını incelemektir.

Yöntem ve gereç: Bu gözlemsel çalışmaya, 452 hasta (333 erkek, 119 kadın) alındı. Hastaların demografik özelliklerinin yanı sıra, geleneksel risk faktörleri kaydedildi. Hastalar yaşa, cinsiyete ve elektrokardiyografik özelliklerine göre gruplara ayrıldı.

Bulgular: Çalışmaya katılan hastaların yaş ortalaması 63 ± 13 iken, % 74'ü erkekti. Sigara kullanımı ve HT genç yaşta ve erkeklerde daha fazla görüldü (% 71). Diyabetes mellitusta yaş grupları arasında fark tespit edilmedi. Kadınlarda HDL-C ($P < 0,001$) ve Total-C/HDL-C oranı ($P < 0,05$) erkeklere göre daha yüksek bulundu. Sigara kullanımı ve aile hikayesi yaşla birlikte azalma gösterdi.

Sonuç: Hastaların % 97'sinde en az bir risk faktörü mevcuttu. Dolayısıyla çalışmamız, en önemli morbidite ve mortalite nedeni olan koroner arter hastalığında, hastalardaki risk faktör değişikliğinin ne kadar önemli olduğunu bizlere tekrar vurgulamaktadır.

Anahtar sözcükler: Koroner arter hastalığı, risk faktörleri, bölgesel

Received: 02.04.2010 – Accepted: 13.07.2010

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Introduction

Coronary artery diseases (CAD) are the most important causes of morbidity and mortality in developed and developing countries (1). Since countries differ in terms of cardiovascular risk factors, regional differences in the same population can be also observed (2,3).

Developments in the management of important modifiable risk factors such as dyslipidemia, hypertension (HT), smoking, and diabetes mellitus (DM) have significantly reduced the possibility of new coronary events (both fatal and non-fatal), and have improved the likelihood of survival. In studies performed, cases of atherosclerotic vascular diseases involving both coronary and non-coronary arteries demonstrated the utmost benefit from secondary prophylaxis (4-7).

In the management of CAD, modification of risk factors is and will continue to be an indispensable part of the treatment strategy, despite pertinent technological advances in cardiovascular therapeutics (8).

In our country, the distribution of cardiovascular risk factors has been analyzed using a randomized sampling method in the TEKHARF study. In this study, the frequency of CAD was found to be 5.8% in male and 5% in female subjects (9). Despite this availability of nationwide data concerning the frequency of CAD, adequate relevant data related to specific regions are lacking.

The purpose of this study was to determine the distribution of coronary risk factors among hospital cases diagnosed as acute coronary syndrome in our center. Furthermore, we have investigated their distribution according to age groups, gender, and subtypes of acute coronary syndrome, in order to finally update data about our geographic region.

Materials and methods

Patients suffering from acute coronary syndrome between January 2009-2010 were enrolled in the study. The diagnosis was made on the basis of medical history, electrocardiographic (ECG) findings, and cardiac enzyme levels. The patients were classified according to gender, age groups [young: ≤44 years (Group 1), middle aged: 45-64 years (Group 2), and advanced age: ≥65 years (Group 3)], and ECG findings [patients with ST elevation (Group 1), ST depression (Group 2), and without any change in ECG (Group 3)].

All patients were examined by an experienced cardiologist immediately after hospitalization. Information obtained pertaining to family history, the presence of DM, HT, smoking, body mass index (BMI), and other demographic characteristics was recorded. Patients with a history of HT, those using antihypertensive drugs, and those with blood pressure above 140/90 mmHg on recurrent measurements were defined as hypertensive cases. Those with a history of DM, and/or hyperglycemia (as defined according to the World Health Organization (WHO) criteria) were accepted as cases with DM. Patients with at least one first degree relative having a history of CAD at an early age (<55 years for males, and <65 years for females) or sudden cardiac death (SCD) were considered as potential candidates for CAD. Patients who were using tobacco products upon referral to our hospital and those that had quit smoking within the previous year were considered smokers.

Blood samples were taken within 24 h of patient's hospitalization, after 12 h of fasting. Serum samples were subjected to centrifuge at 3000 rpm for 15 min, and conserved at -85 °C until the analysis of lipid and micro-CRP parameters. Analyses of the serum's total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL-c), and low-density lipoprotein (LDL-c) were performed using the Abbot Architect C16000 autoanalyzer.

LDL-c levels of ≥ 130 mg/dL in non-diabetics, and ≥ 100 mg/dL diabetics were considered as elevated LDL values (10).

Our hospital is a central hospital in the region. Patients from other regional hospitals were referred to our hospital, enabling us to reach a total of 452 subject. Thus, we think that the number of patients examined in our current study is sufficient for drawing conclusions.

Statistical analysis

Categorical variables were expressed as percentages and compared using the chi-square test or Kruskal-Wallis test. Continuous data were

presented as means ± standard deviation. One sample Kolmogorov-Smirnov test was performed to evaluate normal distribution of continuous variables. Differences in continuous variables between groups were determined using Student's t-test or Mann-Whitney U test for variables with or without normal distribution, respectively. Univariate correlations between 2 continuous variables were analyzed using Pearson correlation coefficients or Spearman correlation according to data distribution. Data were analysed by one-way analysis of variance (ANOVA) with a post-hoc comparison using the LSD test. A P value of < 0.05 was considered to be statistically significant. All analyses were performed using SPSS v.16.0 (SPSS Inc, USA).

Results

Our study included 452 patients (333 men, 119 women) with a mean age of 63 ± 13 years (Table 1).

Table 1. Distribution of risk factors according to all patients.

	All Patients n = 452 (%)
BMI	28±4.7
Gender, male, n (%)	333 (74)
HT, n (%)	189 (42)
DM, n(%)	95 (21)
Family history, n (%)	199 (44)
Smoking, n (%)	181 (40)
Total-c, mg/dL	185 ± 40
LDL-c, mg/dL	118 ± 33
HDL-c, mg/dL	38 ± 10
Trigliceride#, mg/dL	149 ± 76
High LDL-c¥, n (%)	194 (43)
Total-c/HDL-c	5.1 ± 1.6
Total-c/HDL-c ≥ 4.5, n (%)	282 (62)
Micro CRP#, µg/dL	2.9 ± 6.1

Evaluation of risk factors according to age groups

The general characteristics of patients according to age are shown in Table 2. Most of the patients were in the middle and advanced age groups. Levels of micro-CRP and the incidence of DM were similar in all groups. In all age groups, risk factors were more frequently seen among male patients and a statistically significant decrease in risk factors was detected to correlate with aging ($P < 0.001$). BMIs differed significantly between Groups 2 and 3 ($P < 0.001$). A significant increase in the number of hypertensive patients with age was detected. The incidence of smoking was highest in Group 1 (71%) and a statistically significant decrease in smoking was detected with aging ($P < 0.001$). Triglyceride levels were lower in Group 3, and intergroup difference was statistically significant ($P < 0.001$). Although higher LDL-c level was similar in Groups 1 and 2, the difference was statistically significant between Groups 2 and 3. In addition, the total-c/HDL-c ratio was significantly different between Groups 1 and 3 and Groups 2 and 3 ($P < 0.001$). The occurrence of a total-c/HDL-c ratio greater than 4.5 was detected to be higher in Group 1 ($P < 0.05$). When all risk factors (age, gender, family history, HT, DM, smoking, and higher LDL) were considered, at least one risk factor was detected in 97% of the patients.

Evaluation of risk factors according to gender

Smoking was more frequently seen in male patients ($P < 0.001$). Hypertension, HDL-c levels, and total-c/HDL-c ratios were higher in females ($P < 0.001$, $P < 0.01$, and $P < 0.05$, respectively). Other risk factors appeared to be similar in both genders (Table 3).

Evaluation of risk factors on the basis of ECG findings

The prevalence of smoking was significantly higher in male and female subjects in Group 1 as compared to Groups 2 and 3 ($P < 0.002$). Age and micro-CRP levels were statistically significant ($P < 0.05$) (Table 4).

Table 2. Distribution of risk factors according to age groups.

Parameters	Group 1 n = 34 (%)	Group 2 n = 204 (%)	Group 3 n = 214 (%)
BMI	28 ± 3.9	29 ± 4.6	27 ± 4.8^{c***}
Gender, male, n (%)	32 (94)	175 (86)	126 (59)^{b***c***}
HT, n (%)	4 (12)	75 (37)^{a**}	110 (51)$^{b***\ c**}$
DM, n(%)	6 (18)	21 (43)	46 (22)
Family history, n (%)	19 (56)	98 (48)	82 (38)^{b*c*}
Smoking, n (%)	24 (71)	110 (54)	47 (22)^{b***c***}
Total-c, mg/dL	194 ± 38	190 ± 38	179 ± 42^{b*c**}
LDL-c, mg/dL	125 ± 35	120 ± 31	114 ± 34^{b*c*}
HDL-c, mg/dL	35 ± 5.6	37 ± 9	39 ± 10.7^{b**c*}
Triglyceride#, mg/dL	180 ± 89	165 ± 83	129 ± 61^{b***c***}
High LDL-c¥, n (%)	16 (47)	102 (50)	77 (36)^{b*c**}
Total-c/HDL-c	5.69 ± 1.31	5.42 ± 1.89	4.74 ± 1.24^{b***c***}
Total-c/HDL-c ≥ 4.5, n (%)	27 (79)	137 (67)	118 (55)^{b**c*}
Micro CRP#, µg/dL	3.04 ± 4.63	2.30 ± 3.67	3.44 ± 7.86

Data were analyzed by one-way analysis of variance (ANOVA) with a post-hoc comparison using the LSD test. Comparison of patients with Group 1 vs. Group 2, (a) Group 1 vs. Group 3 (b) and Group 2 vs. Group 3 (c)
Sign shows the parameter with nonparametric distribution; * 0.0 5 > P, ** 0.005 > P and *** 0.001 > P
¥ High LDL-c indicates the sum of LDL-c ≥ 100 mg/dL for diabetic patients and LDL-c ≥ 130 mg/dL for non-diabetic patients

Table 3. Distribution of risk factors according to gender.

Parameters	Male n = 333 (%)	Female n = 119 (%)	P
BMI	28 ± 4.1	29 ± 6.0	0.062
Age, year	63 ± 13	62 ± 13	0.350
HT, n (%)	123 (37)	66 (55)	0.001
DM, n (%)	73 (22)	22 (19)	0.430
Family history, n (%)	150 (45)	49 (41)	0.466
Smoking, n (%)	170 (51)	11 (9)	0.001
Total-c, mg/dL	184 ± 40	187 ± 42	0.435
LDL-c, mg/dL	117 ± 32	119 ± 33	0.556
HDL-c, mg/dL	37 ± 9.4	40 ± 10.3	0.001
Triglyceride#, mg/dL	153 ± 82	139 ± 58	0.091
High LDL-c¥, n(%)	146 (44)	48 (40)	0.507
Total-c/HDL-c	4.86 ± 1.23	5.22 ± 1.72	0.050
Total-c/HDL-c ≥ 4.5, n(%)	214 (64)	68 (57)	0.169
Micro CRP#, µg/dL	2.53 ± 3.97	3.92 ± 9.81	0.330

¥ High LDL-c indicates the sum of LDL-c ≥ 100 mg/dL for diabetic patients and LDL-c ≥ 130 mg/dL for non-diabetic patients.
Sign shows the parameter with nonparametric distribution

Table 4. Distribution of risk factors according to ECG findings.

Parameters	Group 1 n = 156 (%)	Group 2 n = 78 (%)	Group 3 n = 218 (%)
Age, year	61 ± 14	65 ± 12[a*]	63 ± 12
BMI	27 ± 4.1	27 ± 5.8	28 ± 4.6[b*]
Gender, male, n (%)	126 (81)	46 (59)[a***]	161 (74)[b** c*]
HT, n (%)	70 (45)	32 (41)	87 (40)
DM, n(%)	28 (18)	15 (19)	52 (24)
Family history, n (%)	60 (39)	32 (41)	107 (49)
Smoking, n (%)	81 (52)	19 (25)[a***]	81 (37)[b*** c*]
Total-c, mg/dL	185 ± 42	187 ± 45	184 ± 38
LDL-c, mg/dL	117 ± 32	120 ± 36	117 ± 33
HDL-c, mg/dL	38 ± 8.4	39 ± 10.4	38 ± 10.5
Trigliceride[#], mg/dL	149 ± 87	134 ± 58	154 ± 74
High LDL-c[¥], n (%)	72 (46)	38 (44)	88 (40)
Total-c/HDL-c	5.16 ± 1.98	5.01 ± 1.46	5.14 ± 1.35
Total-c/HDL-c ≥ 4.5, n (%)	90 (58)	49 (63)	143 (66)
Micro CRP[#], µg/dL	3.2 ± 4.8	4.3 ± 11.3	2.2 ± 3.8[b*]

Data were analyzed by one-way analysis of variance (ANOVA) with a post-hoc comparison using the LSD test. Comparison of patients with Group 1 vs. Group 2 (a), Group 1 vs. Group 3 (b), and Group 2 vs. Group 3 (c)
[#] Sign shows the parameter with nonparametric distribution; * 0.0 5 > P, ** 0.005 > P and *** 0.0001 > P
[¥] High LDL-c indicates the sum of LDL-c ≥ 100 mg/dL for diabetic patients and LDL-c ≥ 130 mg/dL for non-diabetic patients.

Discussion

From the perspective of preventive medicine, in addition to the recognition of modifiable and non-modifiable risk factors that influence CAD, consideration of regional differences is of crucial importance. The aim of this study was to determine the distribution pattern of well-known cardiovascular risk factors in our region in order to contribute to the development of primary and secondary regional prophylactic strategies for CAD.

Cases of coronary and atherosclerotic vascular diseases constitute the group at highest risk for mortality and morbidity. The purpose of primary and secondary prophylaxis in these cases is to decrease morbidity and mortality while increasing the patient's quality of life, and life expectancy (11). The effectiveness of secondary prophylaxis in patients with CAD correlates directly with a recognition of the risk factors in affected individuals.

Our study is the first investigation analyzing coronary artery risk factors in our region for different subtypes of CAD based on electrocardiographic data. The results of this study show that in the younger age group, the most frequently encountered risk factors were smoking, family history positivity, and a total-c/HDL-c ratio of ≥ 4.5, while in the advanced age group DM and HT were the most frequently detected risk factors. In addition, higher LDL-c values were detected in the younger age group. When all risk factors were considered, another important outcome of this study was that 97% of the patients had at least one modifiable risk factor. In a similar subgroup analysis of the study performed by Khot et al. in Cleveland clinics, 85% of the patients had at least one risk factor (12).

Advanced age is an important non-modifiable risk factor for CAD, which is the most frequently encountered fatal disease both in men and women

aged ≥ 65 years (13). In our study, 47% of our patients aged ≥ 65 years, and only 8% of our cases aged ≤ 44 years. In ECG subgroup analyses, the group with ST-elevation was younger than that with ST-depression with a significant difference in terms of the presence of risk factors. In our study, HT is revealed as an important influential risk factor for morbidity and mortality, with an incidence increasing with age.

In studies performed, differences have been demonstrated between male and female patients with regard to the frequency of CAD, its clinical outcomes, and associated risk factors. CAD was seen 2-5 times more frequently in men. Furthermore, important differences in the prevalence of modifiable risk factors between genders have been revealed (14). In our study, 74% of our patients were male, a group which constituted a higher percentage (81%) of patients with STEMI, and 59% of cases with ST depression ($P < 0.001$). Some authors have reported higher percentages of modifiable risk factors in men. Others have indicated that risk factors such as DM and HT were the most important predisposing factors for the development of CAD in men while acute myocardial infarction held this position for women (15). In our study, HT, HDL-c, and Total-c/HDL-c were more frequently seen in women ($P < 0.001$), while smoking was more prevalent among male patients. No other significant differences in risk factors were detected.

Although preliminary studies reported controversial data concerning the family histories of the patients, more recent investigations have determined them to be an important risk factor especially for males and those female patients aged < 60 years (16). In accordance with the results of our study, the INTERHEART study also demonstrated family history positivity to be a more important risk factor in younger age group ($P < 0.05$) (2).

It was shown that with modification of modifiable risk factors in patients with coronary artery disease, the incidence of non-fatal coronary events could be reduced, and the number of fatal CVS cases could be halved (17). Despite the abundance of scientific data, however, the incidence of smoking, HT, and, most especially, dyslipidemia rank at higher levels than anticipated, particularly in developed countries (18). This phenomenon is attributed partly to the inability of physicians to follow-up with their patients properly and the insufficient compliance of patients to the recommendations of their physician (19).

In Turkey, the TEKHARF study, which was performed in order to detect the prevalence of heart disease and associated risk factors in the adult population, has provided us with very important information (20,21). As a result of the study, DM, HT, smoking, and elevated LDL levels were accepted as the most important parameters among well-known modifiable risk factors contributing to the increased risk of CAD.

Especially in women, the incidence of acute myocardial infarction increases in the presence of DM and HT. In the INTERHEART study, the frequency of DM was determined to be 26% in women and 16% in men (2). The incidence of DM in patients with CAD as documented angiographically by Sönmez et al. was found to be 31% in women and 18% in men, while Aygül et al. detected corresponding rates in patients with AMI as 38% and 16%, respectively (22,23). In our study, the frequency of DM in male and female patients was determined to be 19% and 22%, respectively.

The incidence of hypertension in our study was found to be 55% in men and 37% in women, figures that are similar to the percentages reported for the INTERHEART study (53%, 35%), and the 2 other above-mentioned studies (60%, 37% and 65%, 28%) (25,26). In the INTERHEART study, HT and DM were reported to be highly influential risk factors, ranking just behind smoking and apolipoprotein B/apolipoprotein A1 ratio (2).

As demonstrated in the MRFIT (Multiple Risk Factor Intervention Trial) study, a strong correlation was found between total cholesterol and CAD, which was more prominent in patients with total cholesterol values above 200 mg/dL (24). When compared with European countries, the TEKHARF study revealed a higher incidence of coronary morbidity and mortality with lower levels of total and LDL cholesterol in the overall Turkish population. This phenomenon was attributed to the lower levels of HDL cholesterol found in the Turkish population (5,7,25). In the Turkish Heart Study, total and LDL cholesterol values were found to be different in 6 discrete regions which were categorized according to dietary habits while

HDL cholesterol levels were detected to be lower in all regions, independent of dietary habits (26). In the cited study, HDL-c levels in male subjects ranged between 34 and 38 mg/dL, which were 10 mg/dL lower than the national average when compared with our American and European counterparts. Similar findings were detected in Turks living in Europe and the USA and genetic factors became prominent because of higher hepatic lipase activity found in the Turkish population (27). In our study, mean HDL cholesterol level was determined to be 37 ± 9.4 mg/dL in men and 40 ± 10.3 mg/dL in women, a finding which is consistent with the data from the TEKHARF study.

Higher LDL-cholesterol levels were detected in 45% of the patients, which paralleled with the data previously attained. The total-c/HDL-c ratio which has been used for the evaluation of CAD risk in patients with normal LDL cholesterol levels is a parameter dependent upon variations in HDL cholesterol levels. In a study conducted by Onat et al. in the Turkish population, the mean total-c/HDL-c ratio was found to be 5.18 in men and 4.25 in women, while the corresponding values were detected to be 5.17, and 5.05 in the presence of CAD (28). In the Turkish Heart Study, the mean total-c/HDL-c ratio was detected to be 5.4 in men and 3.9 in women (29); in our study, however, the corresponding values were 4.86 ± 1.23 and 5.22 ± 1.72, respectively. This discrepancy is thought to originate from significant gender differences with regard to HDL-c concentrations ($P < 0.001$).

In the etiopathogenesis of acute coronary syndrome, smoking is revealed as the most important modifiable risk factor in both male and female patients. Tobacco use is a serious health problem in Turkey and one that is increasingly prevalent. In this country, smoking has been shown to be the most frequently encountered risk factor, especially in the younger age group. In the TEKHARF study, the incidence of smoking was 43% and 18% in men and women, respectively, while the corresponding percentages in our own study were found to be 45% and 41% (30). In the younger age group, an even higher rate (71%) was detected. The INTERHEART study also demonstrated that smoking increased the incidence of non-fatal myocardial infarction 3-fold, a figure which increased linearly with the number of cigarettes smoked (2).

Study limitations

The lack of any control group constituted the main limitation of our study. We chose not to use a control group, however, since the aim of our investigation was to determine regional distribution of traditional risk factors.

Conclusions

This investigation is the first epidemiological study performed with the intention of evaluating the distribution of conventional risk factors in patients hospitalized with the diagnosis of CAD in the eastern Black Sea region**.** At least one risk factor was detected in 97% of our patients. More specifically, in the younger age group, family history positivity, tobacco use, hypercholesterolemia, decreased HDL, and lower total-c/HDL-c ratios were more prevalent, while lower values for HT and HDL-c levels were detected in the same age group. These findings have demonstrated the crucial role of modification of risk factors in the avoidance and prevention of CAD, especially in the younger age group.

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