ORIGINAL REPORT

Pattern of Coronary Artery Disease Risk Factors in Population Younger than 55 Years and Above 55 Years: A Population Study of 31999 Healthy Individuals

Zinat Nadia Hatmi[1], Mitra Mahdavi-Mazdeh[2], Seyed Saeid Hashemi-Nazari[3], Ebrahim Hajighasemi[3], Behnaz Nozari[4], and Azita Mahdavi[5]

[1] *Department of Community Medicine, Tehran University of Medical Sciences, Tehran ,Iran*
[2] *Department of Nephrology, Tehran University of Medical Sciences, Tehran ,Iran*
[3] *Health City Office, Tehran Municipality, Tehran ,Iran*
[4] *Research Center of Iranian Tissue Bank, Tehran, Iran*
[5] *National BEHZISTI Organization, Tehran, Iran*

Received: 17 Feb. 2010; Received in revised form: 3 Apr. 2010; Accepted: 2 Jun. 2010

Abstract- More than eighty percent of patients with coronary heart diseases (CHD) have conventional risk factors. Prevalence of well known risk factors seems to show a different pattern in younger patients and individual above 55 years. To evaluate the pattern of conventional CHD risk factors in healthy individuals in two different age groups. A large scale population based survey of 31999 individuals from ten medical centers was designed. Screening of risk factors was performed upon these protocols: taking medical history, physical examination and blood tests of complete blood cell counts, fasting blood sugar, lipid profile, urinalysis and creatinine. Prevalence of the risk factors in healthy people aged above 55 years were: 8.1% for systolic blood pressure (SBP)>140 mmHg, 3.8% for diastolic blood pressure (DBP)>90mmHg, 13.9% for fasting blood glucose (FBS)≥126 Mg/dl, 36.9% for total cholesterol>200 Mg/dl, 19.2% for triglyceride (TG)>200 Mg/dl, 67.8% for HDL-c<40 Mg/dl, 27.2% for LDL-c>130 Mg/dl, 4.72 for TC/HDL-c ratio, 2.88 for LDL-c/HDL/c ratio and 4.24 for TG/HDL-c ratio. Prevalence of risk factors in individuals younger than 55 years were: 1.7% for SBP>140 mmHg, 1.2% for DBP>90 mmHg, 5.2% for FBS≥126 Mg/dl, 31.3% for TC>200 Mg/dl, 21.5% for TG>200 Mg/dl, 69.4% for HDL-c<40 Mg/dl, 23.2% for LDL-c>130 Mg/dl, 4.7 for TC/HDL-c ratio, 2.83 for LDL-c/HDL-c ratio and 4.43 for TG/HDL-c ratio. In univariate model of analysis: prevalence of the risk factors were significantly higher in age above 55 years than in people younger than 55 years except for hypertriglyceridemia and HDL-c<40 Mg/dl. In a multivariate model of logistic regression, pattern of following CHD risk factors remained to demonstrate a statistically significance difference between two age groups: FBS≥126 Mg/dl *P*=0.006, TG>200 Mg/dl *P*= 0.002, HDL-c<40 Mg/dl *P*= 0.019, education status *P*=0.001, sex *P*=0.012, and SBP>140 mmHg *P*=0.001. Pattern of such a CHD risk factors of FBS≥126 Mg/dl, TG>200 Mg/dl, HDL-c<40 Mg/dl, education status, sex and SBP>140 mmHg demonstrated a statistically significant difference in the age above 55 years to the healthy people younger than 55 years. These results cab be implicated to set up prediction models for stratifying individuals at higher risk of CHD.

Acta Medica Iranica 2011; 49(6): 368-374.

Keywords: Coronary artery disease; Risk factors; Cross-sectional study; Primary prevention

Introduction

80% to 90% of patients with Coronary Heart Disease (CHD) have conventional risk factors (1). Novel and conventional factors play a crucial role in developing and progression of atherosclerosis (1, 2). Frequency and distribution of known risk factors of CHD in younger patients (men≤55 years and women≤65 years) (1) and the older patients have been shown a different pattern (1). On the other hand premature CHD is related to diabetes and cigarette smoking in woman and cigarette smoking in men (1). Prevalence of the conventional risk factors of cigarette smoking, diabetes, dyslipidemia and hypertension are related to age (1). 85% to 90% of patients with premature CHD have encompassed one conventional CHD risk factor (1). It has been demonstrated an increasing trend in lacking any of these conventional risk factors in patients older than 65 years

Corresponding Author: Zinat Nadia Hatmi
Department of Epidemiology, Tehran University of Medical Sciences, Tehran ,Iran
Tel: +98 912 3788790, Fax: +98 21 88962357, E-mail: znhatmi@yahoo.com

(1). Screening and treatment of modifiable risk factors reduce mortality and morbidity related to CHD (1).

Regarding the epidemic situation in our population we performed and analyzed this research to determine the pattern of CHD risk factors in a population of 31999 healthy individuals comprises of two age groups, above 55 years and younger than 55 years.

Patients and Methods

A large scale population based survey of 31999 individuals were performed by the Mahdavi-Mazdeh *et al*. in Tehran municipality health center titled as Medical Screening of Taxi Drivers in Tehran (MSTDT) in 2007.

Study design

A population based cross-sectional study with 31999 healthy people from ten medical clinics extracted from ten different part of the capital city was conducted.

Study population

Participants of MSTDT were taxi drivers or applicants of purchasing taxi who were introduced to the medical screening program.

Screening protocol consisted of

1. Taking medical history (smoking, hypertension), gathering such demographic characteristics as age, gender, and education.
2. Physical examination by a measurement of blood pressure, weight and height.
3. Blood Tests: After 12 hours overnight fasting, blood samples were gathered to perform: complete blood cell counts, fasting blood sugar, urinalysis, lipid profile and creatinine.

Fasting plasma glucose level was detected enzymatic-ally via glucose oxidize method with auto-analyzer BT3000 (Biotechnical, Italy) by locally generated kits (Pars Azmoon, Co Ltd.). Serum cholesterol and triglyceride were measured by calorimetric method using the above same auto-analyzer.

Statistical analysis

Processed data was analyzed with SPSS V. 14.0. The statistical tests were used, consist of chi-square test, independent sample *t*-test and odds ratios (OR) for univariate analysis. Logistic regression model was fitted to evaluate multivariate- adjusted relationships between pre-specified variables. Relationships were considered significant, at $P<0.05$.

Results

Overall distribution of the factors and calculated ratios in 31999 study samples demonstrated in table 1.

Table 1. Overall distribution of factors and ratios

Factors		Distributions (Frequency or mean ± SD)
Gender	Female	507 (1.6%)
	Male	31489 (98.4%)
Cigarette smoking	Yes	7743 (24.2%)
	No	24256 (75.8%)
Age		43.76 ± 11.31
BMI		25.91 ± 3.92
HB		14.88 ± 1.33
HCT		44.74 ± 3.82
MCV		88.01 ± 6.15
Systolic blood pressure (SBP)		117.80 ± 12.51
Diastolic blood pressure (DBP)		76.11 ± 8.32
Height(cm)		172.85 ± 7.12
Weight(kg)		77.44 ± 12.75
Fasting blood glucose (FBS)		96.53 ± 31.55
Total cholesterol (TC)		188.88 ± 38.65
HDL-C		41.09 ± 9.95
LDL-C		111.65 ± 33.21
Triglyceride (TG)		169.04 ± 91.06
TC/HDL-C ratio		4.70 ± 1.25
LDL-C/HDL-C ratio		2.84 ± 1.00
TG/HDL-C ratio		4.40 ± 2.72

BMI=body mass index, HB=hemoglobin, HCT=hematocrite, MCV=mean corpuscular volume, FBS=fasting blood glucose, TC=total cholesterol, HDL-C=high density lipoprotein, LDL-C=low density lipoprotein, TG= triglyceride, cm=centimeter, kg=kilogram

Table 2. Distribution of the factors and ratios by age groups

Factors (Frequency or Mean ±SD) / Age groups		Under 55 years	Above 55 years	*P* value
gender	Female	492 (1.8%)	-	0.001
	Male	26206 (98.2%)	-	
Age		40.41 ± 8.7	61.57 ± 5.08	0.001
BMI		25.92 ± 3.97	25.81 ± 3.64	0.067
HB		14.93 ± 1.32	14.62 ± 1.36	0.001
HCT		44.85 ± 3.78	44.19 ± 4.01	0.001
MCV		87.87 ± 6.07	88.73 ± 6.54	0.001
Systolic blood pressure (SBP) mmHg		116.52 ± 11.62	124.51 ± 14.76	0.001
Diastolic blood pressure (DBP) mmHg		75.63 ± 8.19	78.69 ± 8.54	0.001
Height (cm)		173.33 ± 7.08	170.35 ± 6.82	0.001
Weight (kg)		77.92 ± 12.95	74.90 ± 11.42	0.001
Fasting blood glucose (FBS)		94.73 ± 28.80	105.97 ± 42.18	0.001
Total cholesterol		187.87 ± 38.52	193.83 ± 38.80	0.001
HDL-C		40.98 ± 9.95	41.72 ± 9.91	0.001
LDL-C		110.93 ± 33.16	115.41 ± 33.20	0.001
Triglyceride (TG)		169.61 ± 93.05	165.81 ± 79.36	0.007
TC/HDL-C ratio		4.70 ± 1.26	4.72 ± 1.16	0.20
LDL-C/HDL-C ratio		2.83 ± 1.01	2.88 ± 0.96	0.003
TG/HDL-C ratio		4.43 ± 2.80	4.24 ± 2.28	0.001

BMI = body mass index, HB=hemoglobin, HCT=hematocrite, MCV=mean corpuscular volume, FBS=fasting blood glucose, TC=total cholesterol, HDL-C=high density lipoprotein, LDL-C=low density lipoprotein, TG= triglyceride, cm=centimeter, kg=kilogram

The prevalence of the conventional CHD risk factors by two age groups and calculated informative ratios compared in table 2. these variables distributed for 31999 individuals, 26699 of whom formed the under 55 years old group and 5021 were located in above 55 years old group. Pattern of conventional risk factors between two age groups mostly were statistically different.

Gender related distribution of the risk factors presented in table 3.

Table 3. Pattern of risk factors and ratios by sex

Factors (Frequency or Mean ±SD) / Sex	Female	Male	*P* value
Cigarette smoking	0%	24.2%	0.001
Age	39.70 ± 8.73	43.83 ± 11.34	0.001
BMI	26.48 ± 4.50	25.90 ± 3.91	0.005
Systolic blood pressure	111.48 ± 8.27	117.90 ± 12.54	0.001
Diastolic blood pressure	69.98 ± 7.57	76.20 ± 8.30	0.001
Fasting blood sugar	90.09 ± 18.46	96.64 ± 31.71	0.001
Total Cholesterol	178.23 ± 37.52	189.05 ± 38.64	0.001
HDL-C	40.03 ± 10.66	41.11 ± 9.93	0.028
LDL-C	112.99 ± 33.29	111.62 ± 33.21	0.37
Triglyceride	130.54 ± 64.31	169.66 ± 91.30	0.001
HB	12.94 ± 1.33	14.91 ± 1.31	0.001
HCT	40.21 ± 3.65	44.82 ± 3.78	0.001
MCV	87.78 ± 7.39	88.01 ± 6.13	0.49
TC/HDL-C ratio	4.65 ± 1.26	4.70 ± 1.24	0.32
LDL-C/HDL-C ratio	2.97 ± 1.04	2.84 ± 1.00	0.004
TG/HDL-C ratio	3.61 ± 2.31	4.41 ± 2.73	0.001

BMI = body mass index, HB=hemoglobin, HCT=hematocrite, MCV=mean corpuscular volume, FBS= fasting blood glucose, TC= total cholesterol, HDL-C=high density lipoprotein, LDL-C=low density lipoprotein, TG= triglyceride

Table 4. Overall prevalence of conventional CHD risk factors among 31999 individuals

Prevalence of Risk factors	Total number (%)
Systolic blood pressure (SBP)>140 mmHg	863 (2.7%)
Diastolic blood pressure (DBP)>90 mmHg	494 (1.6%)
SBP>120 mmHg	6328 (20.1%)
DBP>80 mmHg	19983 (63.5%)
Fasting blood sugar≥126 Mg/dl	2090 (6.6%)
Total cholesterol (TC)>200 Mg/dl	10284 (32.3%)
TC>170 Mg/dl	20961 (65.9%)
Triglyceride (TG) >200 Mg/dl	6698 (21.2%)
HDL-C<40 Mg/dl	17518 (69.1%)
LDL-C>130 Mg/dl	5932 (23.9%)

FBS= fasting blood glucose, TC= total cholesterol, HDL-C=high density lipoprotein, LDL-C=low density Lipoprotein, TG= triglyceride

Continuous traditional CHD risk factors also treated as categorical variables upon standard measures, and resulted in table 4. Table 4 demonstrated the overall prevalence of risk factors in whole population of 31999 with different cut off points of the variables. The prevalence of conventional CHD risk factors and estimated crude odds ratios among people younger than 55 years and older than 55 years have been tabulated (Table 5).

Prevalence of the conventional risk factors were significantly higher in age above 55 years than in people younger than 55 years except the frequency of HDL-c< 40 mg/dl. Hypertriglyceridemia and age demonstrated a reverse relationship, that is the frequency of hypertriglyceridemia was significantly (*P*=0.001) higher in individuals younger than 55 years.

Prevalence of the CHD risk factors by sex and estimated odds ratios (OR) and 95% confidence intervals (CI) from univariate logistic regression model demonstrated in table 6. For most risk factors the prevalence were significantly higher in men than in women. The prevalence of HDL-c<40 mg/dl and LDL-c>130 mg/dl showed a higher frequency in women, that were not statistically significant (*P*>0.05).

Multivariate Analysis

In a logistic regression model that controlled for confounding variables, the pattern of CHD conventional risk factors by age above 55 years and under 55 years remained to demonstrate a significantly statistical differences in SBP>120 mmHg (*P*=0.001), DBP>80 mmHg (*P*=0.021), FBS≥126 Mg/dl (*P*=0.006), TG>200 mg/dl (*P*=0.002), HDL<40 Mg/dl (*P*=0.019), education status (*P*=0.001), sex (*P*=0.012), height (*P*= 0.048), HB (*P*=0.001), HCT (*P*=0.022), MCV (*P*=0.001) and SBP>140 mmHg (*P*= 0.001).

Table 5. Prevalence of the conventional CHD risk factors by two age groups along side estimated odds ratios and 95% confidence intervals

Risk factors	Under 55 years N (%)	Above 55 years N (%)	*P* value	Odds ratios and 95% confidence intervals
SBP>140 mmHg	465(1.7%)	401(8.1%)	0.001	5.00(4.36-5.74)
DBP>90 mmHg	304(1.2%)	187(3.8%)	0.001	3.36(2.79-4.04)
SBP>120 mmHg	4198(16%)	2069(41.9%)	0.001	3.79(3.55-4.04)
DBP>80 mmHg	16141(61.41%)	3674(74.4%)	0.001	1.82(1.70-1.95)
FBS≥126 Mg/dl	1373(5.2%)	690(13.9%)	0.001	2.95(2.67-3.25)
TC>200 Mg/dl	8323(31.3%)	1845(36.9%)	0.001	1.28(1.20-1.36)
TC>170 Mg/dl	17183(64.7%)	3575(71.5%)	0.001	1.36(1.28-1.46)
TG>200 Mg/dl	5673(21.5%)	954(19.2%)	0.001	0.86(0.80-0.93)
HDL-C<40 Mg/dl	14823(69.4%)	2603(67.8%)	0.062	0.93(0.86-1.04)
LDL-C>130 Mg/dl	4860(23.2%)	1030(27.2%)	0.001	1.23(1.14-1.33)

FBS= fasting blood glucose, TC= total cholesterol, HDL-C=high density lipoprotein, LDL-C=low density lipoprotein, TG= triglyceride, SBP=systolic blood pressure, DBP= diastolic blood pressure

Table 6. Prevalence of risk factors by sex and estimated crude odds ratios with 95% confidence intervals

Risk factors	Female N (%)	Male N (%)	Significance level	Odds ratios an 95% confidence intervals
SBP>140 mmHg	1 (0.2%)	862 (2.8%)	0.008	14.27 (2.00-101.65)
DBP> 90 mmHg	0 (0%)	494 (1.6%)	0.004	-
SBP>120 mmHg	28 (5.6%)	6300 (20.3%)	0.001	4.30 (2.93-6.30)
DBP>80 mmHg	138 (27.6%)	19843 (64.1%)	0.001	4.67 (3.83-5.69)
FBS≥126 Mg/dl	13 (2.6%)	2077 (6.7%)	0.001	2.68 (1.54-4.67)
TC>200 Mg/dl	125 (24.9%)	10159 (32.4%)	0.001	1.45 (1.18-1.78)
TC>170 Mg/dl	277 (55.1%)	20683 (66%)	0.001	1.58 (1.32-1.89)
TG>200 Mg/dl	58 (11.6%)	6640 (21.3%)	0.001	2.06 (1.56-2.71)
HDL-c<40 Mg/dl	340 (71.3%)	17176 (69.1%)	0.30	0.90 (0.73-1.09)
LDL-c>130 Mg/dl	126 (26.8%)	5806 (23.8%)	0.12	0.85 (0.69-1.04)

FBS= Fasting blood glucose, TC= Total cholesterol, HDL-C=High density lipoprotein, LDL-C=Low Density Lipoprotein, TG= Triglyceride, SBP=Systolic Blood Pressure ,DBP= Diastolic Blood Pressure

Discussion

In our study the prevalence of conventional CHD risk factors were at such a high level, which can lead in convince authorities for developing control measures, for the most preventable disease of our time (CHD).The overall pattern of the risk factors revealed that, the prevalence of CHD risk factors have a range from 20.1% of SBP>120 mmHg to over sixty percent for elevating total cholesterol (TC) and HDL-c< 45 mg/dl.

The ratio of TC/HDL-c was 4.70 ± (1.25). Our observation of comparison of the CHD conventional risk factors above 55 years and people younger than 55 years showed that, cigarette smoking, systolic blood pressure, diastolic blood pressure fasting blood sugar, total cholesterol, triglyceride, LDL-c, and ratio of TG/HDL-C were significantly higher in older individuals (above 55 years). Lower level of HDL-C and large ratio of LDL-c/HDL-c were higher in younger people (under 55 years) than people with age older than 55 years. The ratio of TC/HDL-C and BMI were equally high but did not show a statistically significant difference. There is few evidence to support the role of LDL-C and HDL-C in association with CAD in old age (3). Our study indicates that low levels of HDL-C was higher among people younger than 55 years and possibly play a role in the development of premature CHD. In concordance with other investigations (4) we observe that the prevalence of CHD risk factors continue to increase with progress age.

A comparison between the results and that of the previous report in our population (5), indicate that the prevalence of the most risk factors in the present study of the healthy taxi drivers are lower than the general population. This discrepancy can be elaborate as healthy worker effect. Prevalence of the CHD risk factors in taxi drivers are lower than the general population. However, the conventional CHD risk factors still remained at high level of prevalence and, it is compatible with the epidemic situation in our population. Comparison of the pattern of CHD risk factors between female and male demonstrated that, cigarette smoking, SBP, DBP, FBS≥ 126 mg/dl, high level of TC and TG, and the ratios of LDL-C/HDL-C and TG/HDL-C were significantly higher in men than in women. Whereas, body mass index, HDL-C and ratio of TC/HDL-C were greater in women than in men. Comparison of our study of the population based healthy individuals with hospital based investigation among patients with CHD (1) demonstrated explicit different patterns of the risk factors, especially between women and men.

In the term of strength of associations ,the most related risk factors with age above 55 years to age under 55 years in the order of odds ratios including: SBP>140 mmHg, SBP>120 mmHg, DBP>90 mmHg, FBS≥126 Mg/dl, DBP> 80 mmHg, TC>170 Mg/dl, and LDL-C> 130 Mg/dl However, the male to female odds ratios revealed this respectively pattern of, SBP> 140 mmHg, DBP>80 mmHg, SBP>120 mmHg, FBS≥126 Mg/dl, TG>200 Mg/dl and TC>170 Mg/dl.

Beyond the role of these conventional risk factors that is common and consistence with development of CAD and plaques formation (6), the risk assessment of the population at risk for CHD, needs for additional cumulative effect of the novel risk factors including: inflammatory markers (2,7-9), homeostasis markers (2, 10-12), and lipid related factors (2,13-16).

Development of national risk education program upon present situation and the results of our investigation should be addressed. Recent evidences

have been shown, there is no doubt that management of the modifiable and life style related CHD risk factors lead in reduce future cardiovascular events. Wise investigator may consider the impact of these programs much larger than commonly considered, just for individuals with CHD risk factors. The offspring of people with risk factors either in primary prevention and/ or secondary prevention may enjoy the implementing of the result of the modification of CHD risk factors (17,18).

In concordance with the results of an international large study in 44 countries reported that the conventional CHD risk factors are mainly under controlled in many part of the universe (19), our finding confirmed that the CHD risk factors are under detected, non-treated and non-controlled in our population.

Strengths and limitations

Limitations: This is a large scale survey estimated the prevalence of conventional CHD risk factors. Because of the role of Novel risk factors, we strongly recommend, designing and performing surveys addressing both novel and conventional CHD risk factors.

Strength: Evaluation of the prevalence of conventional CHD risk factors upon a large scale, 31999 samples of healthy people using valid and standardized methods. In conclusion, pattern of CHD conventional risk factors in two age groups of above 55 years and under 55 years demonstrated a significant differences. The risk factors that differ were: SBP>120 mmHg, DBP >80 mmHg, FBS≥126 Mg/dl, TG>200 Mg/dl, HDL-C< 40 Mg/dl, education status, sex, and SBP>140 mmHg. These results cab be implicated to set up prediction models for stratifying individuals at higher risk of CHD.

Acknowledgement

This project was supported by a grant from the Tehran Municipality Health Center titled as MSTDT in 2007.

References

1. Khot UN, Khot MB, Bajzer CT, Sapp SK, Ohman EM, Brener SJ, Ellis SG, Lincoff AM, Topol EJ. Prevalence of conventional risk factors in patients with coronary heart disease. JAMA 2003;290(7):898-904.
2. Hackam DG, Anand SS. Emerging risk factors for atherosclerotic vascular disease: a critical review of the evidence. JAMA 2003;290(7):932-40.
3. Weverling-Rijnsburger AW, Jonkers IJ, van Exel E, Gussekloo J, Westendorp RG. High-density vs low-density lipoprotein cholesterol as the risk factor for coronary artery disease and stroke in old age. Arch Intern Med 2003;163(13):1549-54.
4. Sewell JL, Malasky BR, Gedney CL, Gerber TM, Brody EA, Pacheco EA, Yost D, Masden BR, Galloway JM. The increasing incidence of coronary artery disease and cardiovascular risk factors among a Southwest Native American tribe: the White Mountain Apache Heart Study. Arch Intern Med 2002;162(12):1368-72.
5. Hatmi ZN, Tahvildari S, Gafarzadeh Motlag A, Sabouri Kashani A. Prevalence of coronary artery disease risk factors in Iran: a population based survey. BMC Cardiovasc Disord 2007;7:32.
6. Faletra FF, Klersy C, D'Angeli I, Penco M, Procaccini V, Pasotti E, Marcolongo A, Pedrazzini GB, De Castro S, Scappaticci M, Moccetti T, Auricchio A. Relation between coronary atherosclerotic plaques and traditional risk factors in people with no history of cardiovascular disease undergoing multi-detector computed coronary angiography. Heart 2009;95(15):1265-72.
7. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med 2002;347(20):1557-65.
8. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997;336(14):973-9.
9. Boekholdt SM, Hack CE, Sandhu MS, Luben R, Bingham SA, Wareham NJ, Peters RJ, Jukema JW, Day NE, Kastelein JJ, Khaw KT. C-reactive protein levels and coronary artery disease incidence and mortality in apparently healthy men and women: the EPIC-Norfolk prospective population study 1993-2003. Atherosclerosis 2006;187(2):415-22.
10. Kerlin B, Cooley BC, Isermann BH, Hernandez I, Sood R, Zogg M, Hendrickson SB, Mosesson MW, Lord S, Weiler H. Cause-effect relation between hyperfibrinogenemia and vascular disease. Blood 2004;103(5):1728-34.
11. Danesh J, Lewington S, Thompson SG, Lowe GD, Collins R, Kostis JB, Wilson AC, Folsom AR, Wu K, Benderly M, et al; Fibrinogen Studies Collaboration. Plasma fibrinogen level and the risk of major cardiovascular diseases and nonvascular mortality: an individual participant meta-analysis. JAMA 2005;294(14):1799-809.
12. Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, Kovacs G, Mitchell M, Lewandowski B, Kovacs MJ. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med 2003;349(13):1227-35.

13. Tsimikas S, Brilakis ES, Miller ER, McConnell JP, Lennon RJ, Kornman KS, Witztum JL, Berger PB. Oxidized phospholipids, Lp(a) lipoprotein, and coronary artery disease. N Engl J Med 2005;353(1):46-57.
14. Suk Danik J, Rifai N, Buring JE, Ridker PM. Lipoprotein(a), measured with an assay independent of apolipoprotein(a) isoform size, and risk of future cardiovascular events among initially healthy women. JAMA 2006;296(11):1363-70.
15. Bennet A, Di Angelantonio E, Erqou S, Eiriksdottir G, Sigurdsson G, Woodward M, Rumley A, Lowe GD, Danesh J, Gudnason V. Lipoprotein(a) levels and risk of future coronary heart disease: large-scale prospective data. Arch Intern Med 2008;168(6):598-608.
16. Lamarche B, Tchernof A, Mauriège P, Cantin B, Dagenais GR, Lupien PJ, Després JP. Fasting insulin and apolipoprotein B levels and low-density lipoprotein particle size as risk factors for ischemic heart disease. JAMA 1998;279(24):1955-61.
17. Shaukat N, de Bono DP, Jones DR. Like father like son? Sons of patients of European or Indian origin with coronary artery disease reflect their parents' risk factor patterns. Br Heart J 1995;74(3):318-23.
18. Wannamethee SG, Shaper AG, Walker M, Ebrahim S. Lifestyle and 15-year survival free of heart attack, stroke, and diabetes in middle-aged British men. Arch Intern Med 1998;158(22):2433-40.
19. Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, Goto S, Liau CS, Richard AJ, Röther J, Wilson PW; REACH Registry Investigators. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. JAMA 2006;295(2):180-9.