TWO-YEAR INCIDENCE OF ACUTE FATAL AND NON-FATAL CORONARY EVENTS AND STROKE: IRANIAN POPULATION OVER 35 YEARS OLD

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ABSTRACT

Introduction: Cardiovascular diseases and stroke constitute an important cause of death in most developed and developing countries. Identification of the major risk factors of coronary accidents and stroke and understanding of the relative risk posed by each of these risk factors are critical points for prevention, control and management of this health problem.

Methods: 6542 individuals aged over 35 years from the cities of Isfahan, Arak and Najafabad were followed for two years. The individuals were chosen from among the population of 12800 people, selected in a multistage sampling manner to participate in Isfahan Healthy Heart Program (IHHP). Pregnant women, mentally retarded individuals, and those with acute systemic diseases were excluded. Risk factors were extracted based on definition, and the degree of risk posed by each risk factor was determined.

Results: The incidence of acute coronary events was studied in 3970 (60.7%) healthy individuals participating in IHHP, who were followed over a two years period. 60 deaths (1.5% of the population) were reported during the two years, 1% of which were caused by myocardial infarction (MI). There were 115 instances of fatal and non-fatal cardiac events (2.9% of the population). Strokes were seen in half of the cases. A positive history of smoking was accompanied by reduced survival of subjects in this study. The incidence of non-fatal cardiac events also increased with diastolic hypertension and triglyceride level. In this study, the greatest risk of cardiac events was associated with hypertension, diabetes, metabolic syndrome, and positive history of smoking.

Discussion: In this study, the two-year incidence of cardiac events was higher than that of European countries. The relative risk of risk factors such as diabetes, positive history of smoking, and hypertension was also notably higher than that of similar studies. In light of the higher risk of cardiac events compared with similar studies, preparing a risk chart based on geographical and cultural features for evaluation of the risk of cardiac events seems imperative.

Key Words: Risk chart, Fatal cardiac accidents, Non-fatal cardiac accidents, stroke, Cardiovascular risk factors, Iran

ARYA Journal 2005, 1(1): 9-14

INTRODUCTION

Today, programs for primary prevention of coronary artery diseases (CAD) emphasize correct evaluation and management of cardiovascular disease risk factors[1]. Previous retrospective cohort studies have implicated the effects of factors such as gender, age, smoking, hypertension, and high blood cholesterol level in the development of coronary diseases[2]. Clinical trials following initial studies have stressed the effect of treating hypercholesterolemia and hypertension on reducing the incidence of coronary diseases[3, 4].

However, the main problem in clinic concerns the application of the findings of multiple clinical trials and cohort studies as basic evidence to be used in treatment and management of patients[2], which is mainly due to the yet unknown effect of the presence of multiple risk factors in patients[1, 2]. Hence, the multiplicity of coronary disease risk factors calls for assessment of the overall risk of cardiovascular diseases by clinical specialists[5].

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Efforts made during the past two decades towards solving this problem by preparing a risk chart for cardiovascular diseases have yielded evidence upon which clinical decisions for high-risk patients can be made[6-10].

Cardiovascular diseases (CVD) account for 80% of deaths in develop ping countries[11]. Studies conducted in Iran are also indicative of the high mortality and morbidity due to CVD[12]. Given that every individual stands his/her own unique chance of developing CVD, it seems necessary to prepare a risk chart consistent with regional conditions, which enables appropriate evaluation of the risk of cardiac accidents[13].

In the first stage of the ten-year plan for evaluation of the incidence of cardiac accidents in the population under study in Isfahan Healthy Heart Program (IHHP) [14] in the cities of Isfahan and Najaf-Abad (as an interventional area) and in the city of Arak (as a reference area), the two-year incidence of cardiac evente and the relative risk of CVD risk factors are studied.

METHODS

This two-year cohort study was conducted between 2000 and 2002 in three provincial cities of Isfahan, Arak, and Najaf-Abad[14].

Given the minimum rate of coronary accidents and stroke (0.3% per year for acute coronary accidents and myocardial infarction), the incidence of these events was considered at 0.2% and the sample size in the over-35 population in the 3 provincial cities was calculated at 6000 people, with an accuracy of 0.0036.

Sampling was conducted among a population of 12800 individuals who were participating in IHHP in the provincial cities of Isfahan, Najaf-Abad and Arak. The population under study in IHHP was selected among individuals aged over 19 years, 6542 of whom were older than 35. Of this number, 3197 individuals were from the cities of Isfahan and Najaf-Abad (70% from Isfahan, 30% from Najaf-Abad, matching the proportion of the original population).

Ten percent of the population under study in Isfahan was from rural areas and 90% from urban areas. 40% of the population under study in Najaf-Abad was from rural areas and 60% from urban areas. Of 3345 over-35 people studied in Arak, 60% were from urban areas and 40% from rural areas. In two cities, sampling was conducted in a multistage method and by considering the socioeconomic status of the subjects.

In this study, the major risk factors were determined based on data from IHHP. The risk factors included hypertension, as defined in the second panel of the third conference on control of blood lipids, and the most recent set of guidelines on diabetes control[15, 17].

All of the over-35 subjects or their families were called and asked about the occurrence of cardiovascular events (e.i. MI, Stroke or Cardiac death) using a telephone questionnaire[9]. The addresses and telephone numbers of all the participants in IHHP are available in a database. Criteria of exclusion from the study included pregnancy, mental retardation, suffering from hemorrhagic diseases, and having lived for less than 6 months in the city where the study was conducted. In this study, the incidence of documented cases of fatal and non-fatal myocardial infarctions (MI) and stroke were determined based on data from the disease registry unit of Isfahan Cardiovascular Research Center.

The extracted figures are similar to those of most other studies conducted in this area. [1, 18-20] The extracted data were analyzed using SPSS11 software. Cox's regression model was used to determine and predict the adjusted relative risk posed by each of the risk factors in the incidence of acute coronary events in subjects at the start of the study, compared with those without risk factors. Two-year incidence rate of these events was calculated.

RESULTS

A total of 3970 individuals were available during follow up. The participation of responders to the questionnaires is shown in Table 1. The mean and standard deviation of the age of the studied population was 51.5±11.8 years in Isfahan, 48±11 years in Najaf-Abad, 52.11±11.5 years in Arak, and 50.7±11.7 years in the cities where interventions were made (Isfahan and Najaf-Abad). Fatal MI was seen in 1%, non-fatal MI in 1.95%, and stroke in 0.5% of the studied subjects. A total of 60 deaths (1.5%) occurred in subjects during two years of the study (Table 2).

The incidence of fatal and non-fatal MI and stroke had a rising trend, increasing with age until the age of 74 in intervention cities of Isfahan and Najaf-Abad and in the non-intervention city of Arak, and slightly decreasing after the age of 75, owing to the reduction of the number of subjects in this age group. Positive history of smoking, metabolic syndrome, hypertension, hyperglycemia, and dyslipidemia were associated with the highest relative risk of fatal and non-fatal MI and stroke (Table 3).

Table 1: Characteristics of Sex and Location of Follow up Persons

Variables	Isfahan N (%)	Najaf-Abad N (%)	Isfahan+Najaf-Abad N (%)	Arak N (%)	Total
	n=2162	n=1035	n=3197	n=3345	n=6542
Male	676(50.4)	242(47.5)	918(49.1)	1040(49.5)	1958(49.3)
Female	676(49.6)	267(52.5)	953(50.9)	1059(50.5)	2012(50.7)
Urban	1331(97.7)	267(52.5)	1598(85.4)	1498(70.9)	3087(77.8)
Rural	31(2.3)	242(47.5)	273(14.6)	610(29.1)	883(22.2)
	1362(63)	509(49.2)	1871(58.5)	2099(62.8)	3970(60.7)

Table 2: Incidence of Cardiovascular Events in Study Population

Variables	Isfahan N (%)	Najaf-Abad N (%)	Arak N (%)	P.value	Isfahan+Najaf-Abad N (%)	P.value
Cardiovascular events						
Non fatal MI	28(36.8)	14(18.4)	34(44.7)	0.22	42(55.3)	0.15
Fatal MI	14(35.9)	4(10.3)	21(53.8)	0.88	18(46.2)	0.51
Stroke	5(27.8)	7(38.9)	6(33.3)	0.004	12(66.7)	0.076
Chest pain	22(25.9)	14(16.5)	49(57.6)	0.21	36(42.4)	0.27
Etiology of death						
Alive persons	1343(98.6)	503(98.8)	2064(98.3)	p>0.05	1864(98.7)	p>0.05
Myocardial infarction	14(1)	4(0.8)	21(1)	p>0.05	———	p>0.05
Stroke mortality	2(0.1)	———	2(0.1)	p>0.05	2(0.1)	p>0.05
Cancer mortality	1(0.1)	2(0.4)	3(0.1)	p>0.05	3(0.2)	p>0.05
Other cause of mortality	2(0.1)	———	9(0.4)	p>0.05	2(0.1)	p>0.05

Corrected relative risk based on Cox's model used to predict the survival of patients before cardiac accidents is shown in (Table 4).

Figures 1 and 2 show the survival of patients with fatal MI and stroke, versus the presence of positive history of smoking as a risk factor.

DISCUSSION

In the present study, 60.7% of the population under study was followed by phone and correspondence. Several other studies have reported a success rate varying between 38% and 83% in following subjects.[5]

The risk factors investigated in the present study were similar to those studied by Prim and PROCAM in their 5-year and 10-year studies.[21] In the 5-year study conducted by Prim, 120 cardiac accidents were reported in a population of 2399 people within the age range of 50 to 59 years.[21] In this study, 115 instances of fatal and non-fatal cardiac accidents were seen among 3970 over-35 individuals followed for two years. In a study of individuals aged between 30 and 74 years by Framingham, there were 383 cases of cardiac accidents during a 10-year period.[21]

However, some studies have suggested that the Framingham study has overestimated the risk of cardiac accidents in some European countries[22-23]. The current two-year study showed that death from MI accounts for 1% of all deaths in the population of healthy individuals in the cities of Isfahan, Najaf-Abad and Arak.

In this study, a positive history of smoking was associated with the highest relative risk of fatal coronary events and strokes.

Figures 1 and 2 clearly show the high relative risk posed by smoking in post-MI patients with a history of smoking, and patients who had not suffered stroke and had a history of smoking. In the study by Framingham, positive history of smoking is also accompanied by a two-fold increase in the relative risk of cardiac accidents; as in the present study, the study by Framingham shows that this risk is higher in women than men [24]. Also in this study, hypertension was associated with a higher relative risk of fatal and non-fatal cardiac accidents and stroke.

Relative risks varied with location and gender, ranging between 2.1 and 8.2 for non-fatal cardiac accidents, between 3.4 and 7 for fatal cardiac accidents, and between 3.1 and 4.6 for stroke.

The relative risk associated with hypertension was 2.4 in the Framingham study[24]. The highest relative risk was reported in a study of the black race conducted by Erik, with a relative risk measuring 8.8 times higher than the normotensive population[24].

Table 3: Relative Risk of Cardiovascular Events based on Sex and Area in Study Populations

	Outcome	Isfahan+Najaf-Abad N (%)	Arak N (%)	Female N (%)	Male N (%)	Total
Family history N (%) RR CI95%	**Non fatal MI**	17(40.5) 0.5(0.2-0.97)	13(38.2) 1.3(0.6-2.7)	15(37.5) 0.6(0.3-1.2)	15(41.7) 1.1(0.6-2.3)	30(39.5) 0.8(0.5-1.3)
	Fatal MI	7(38.9) 0.4(0.2-1.2)	2(9.5) 0.2(0.05-1)	7(35) 0.5(0.2-1.4)	2(10.5) 0.2(0.04-1)	9(23.1) 0.4(0.2-1)
	Stroke	8(66.7) 1.5(0.4-5.2)	2(33.3) 1(0.2-6)	3(60) 1.5(0.2-9.5)	7(53.8) 1.9(0.6-5.8)	10(55.6) 1.6(0.6-4.2)
Diabetes RR CI95%	**Non fatal MI**	6(14.3) 1.6(0.6-3.8)	6(17.6)* 2.9(1.1-7.1)	5(12.5) 1.4(0.5-3.8)	7(19.4)* 3(1.3-7.1)	12(15.8)* 2.1(1.1-4)
	Fatal MI	5(27.8)* 3.7(1.6-10.6)	2(9.5) 1.4(0.3-6)	4(20) 2.5(0.8-7.8)	3(15.8) 2.3(0.6-8.1)	7(17.9)* 2.4(1-5.6)
	Stroke	5(41.7)* 6.9(2.1-22.1)	1(16.7) 2.6(0.3-2.2)	1(20) 2.5(0.2-23)	5(38.5)* 7.9(2.5-24.7)	6(33.3)* 5.6(2-15.2)
Hyperlipidemia RR CI95%	**Non fatal MI**	35(83.3)* 2.6(1.15-5.9)	27(79.4)* 2.7(1.1-6.2)	31(77.5)* 2.3(1.1-4.8)	31(86.1)* 3.4(1.3-8.9)	62(81.6)* 2.7(1.5-4.8)
	Fatal MI	14(77.8) 1.8(0.59-5.5)	14(66.7) 1.3(0.5-3.4)	16(80) 2.6(0.8-8)	12(63.2) 0.9(0.3-2.3)	38(71.8) 1.5(0.7-3.1)
	Stroke	11(91.7) 5.6(0.7-4.4)	4(66.7) 1.3(0.2-7.6)	5(100)* 3.3(2-12)	10(76.9) 1.8(0.5-6.6)	15(83.3)* 3(0.8-10.4)
Lack of regular exercise N (%) RR CI95%	**Non fatal MI**	38(90.5) 1.7(0.6-4.8)	29(85.3) 1(0.3-2.6)	36(90) 1.1(0.3-3)	31(86.1) 1.4(0.5-3.8)	67(88.2) 1.3(0.6-2.6)
	Fatal MI	16(88.9) 1.4(0.3-6.3)	21(100) 0.85(0.83-0.86)	20(100) 2.48(0.4-22)	17(89.5) 2(0.4-8.8)	37(94.9) 3.2(0.7-13.7)
	Stroke	9(75) 0.5(0.14-2)	5(83.3) 0.8(0.1-7.4)	4(80) 0.4(0.05-4.4)	10(76.9) 0.8(0.2-2.8)	14(77.8) 1.6(0.8-1.8)
Ex-Smoking N (%) RR CI95%	**Non fatal MI**	3(7.1) 1.08(0.3-3.5)	4(11.8) 1.9(0.6-5.7)	2(5) 3.2(0.7-14.2)	5(13.9) 1.2(0.4-3.2)	17(9.2) 1.4(0.6-3.2)
	Fatal MI	5(27.8)* 5.6(1.9-15.9)	4(19)* 3.5(1.1-10.6)	2(10)* 7(1.5-31.5)	7(36.8)* 4.6(1.7-11.8)	9(23.1)* 4.4(2-9.4)
	Stroke	5(41.7)* 10.4(3.2-33.4)	2(33.3)* 7.4(1.3-40.9)	1(20)* 15(1.6-14)	6(46.2)* 6.7(2.2-20.2)	7(38.9)* 9.3(3.6-24.4)
BMI≥30 RR CI95%	**Non fatal MI**	13(31) 1.2(0.6-2.3)	4(11.8) 1.9(0.6-5.7)	12(30) 0.9(0.4-1.8)	5(13.9) 1(0.3-2.5)	17(22.4) 0.96(0.5-1.6)
	Fatal MI	3(16.7) 0.5(0.1-1.8)	1(4.8) 0.2(0.02-1.5)	4(20) 0.5(0.1-1.6)	0(0)	4(10.3) 0.3(0.1-1)
	Stroke	3(31) 0.9(0.2-3.3)	1(16.7) 0.8(0.1-7.1)	1(20) 0.5(0.06-4.8)	3(23.1) 1.8(0.5-6.6)	4(22.2) 0.9(0.3-2.9)
WC≥102 male N (%) WC≥88 female N (%) RR CI95%	**Non fatal MI**	25(59.5) 1.04(0.5-1.9)	16(47.1) 1.12(0.5-2.2)	32(80) 1.07(0.5-2.3)	9(25) 1.1(0.5-2.5)	41(53.9) 1.1(0.7-1.7)
	Fatal MI	8(44.4) 0.5(0.2-1.4)	7(33.3) 0.6(0.2-1.5)	11(55) 0.3(0.1-0.7)	4(21.1) 0.9(0.3-2.8)	15(38.5) 0.5(0.3-1.1)
	Stroke	5(41.7) 0.5(0.1-1.5)	2(33.3) 0.6(0.1-3.4)	4(80) 1.07(0.1-9.6)	3(23.1) 1(0.2-3.8)	7(38.9) 0.6(0.2-1.5)
WHR≥1 male WHR≥ 0.85 female RR CI95%	**Non fatal MI**	28(66.7) 1.7(0.9-3.3)	17(50) 1.19(0.6-2.3)	35(87.5) 1.3(0.5-3.4)	10(27.8)* 2.4(1.1-5)	45(59.2) 1.4(0.9-2.3)
	Fatal MI	8(44.4) 0.6(0.2-1.7)	13(61.9) 1.9(0.8-4.7)	15(75) 0.5(0.2-1.6)	6(31.6)* 2.8(1-7.6)	21(53) 1.1(0.6-2.2)
	Stroke	5(41.7) 0.6(0.1-1.9)	2(33.3) 0.5(0.1-3.2)	5(100) 0.95(0.6-14)	2(15.4) 1.1(0.2-5)	7(38.9) 0.6(0.2-1.7)
Metabolic syndrome n(%) RR CI 95%	**Non fatal MI**	22(52.4)* 2.5(1.3-4.7)	12(35.3) 1.6(0.8-3.3)	23(57.5)* 1.9(1.02-3.6)	11(30.6)* 2.8(1.4-5.9)	34(44.7)* 2.1(1.3-3.3)
	Fatal MI	6(33.3) 1.1(0.4-3)	6(28.2) 1.1(0.4-3)	10(50) 1.4(0.58-3.4)	2(10.5) 0.7(0.2-3.2)	12(30.8)* 1.1(0.5-2.3)
	Stroke	8(66.7)* 4.6(1.3-15.3)	1(16.7) 0.5(0.06-5)	4(80)* 5.6(0.6-50)	5(38.5)* 4(1.3-12.4)	9(50)* 3.6(2.6-6.6)
High Blood Pressure N (%) RR CI 95%	**Non fatal MI**	30(71.4)* 8.2(4.1-16.2)	13(38.2)* 2.1(1.06-4.3)	23(57.5)* 3.8(2.7.3)	20(55.6)* 5(2.6-9.9)	43(56.6)* 4.4(2.7-7.9)
	Fatal MI	8(44.4) 2.5(0.9-6.3)	14(66.7)* 7(2.8-17.4)	11(55)* 3.4(1.4-8.3)	11(57.9)* 5.4(2.1-13.7)	22(56.4)* 4.3(2.2-8.1)
	Stroke	6(50)* 3.1(1.005-9.7)	3(50) 3.4(0.6-17)	2(40) 1.2(0.31-11.1)	7(53.8)* 4.6(1.5-13.8)	9(50)* 3.2(1.3-8.3)
Current-smoker N (%) RR C I95%	**Non fatal MI**	4(9.5) 0.5(0.18-1.4)	4(11.8) 0.7(0.2-2)	0(0)	8(22.2) 0.6(0.3-1.4)	8(10.5) 0.6(0.3-1.2)
	Fatal MI	2(11.1) 0.6(0.1-2.6)	3(14.3) 0.9(0.2-3.2)	0(0)	5(26.3) 0.8(0.2-2.3)	5(12.8) 0.7(0.3-2)
	Stroke	1(8.3) 0.4(0.05-3.4)	1(16.7) 1.1(0.13-9.8)	0(0)	2(15.4) 0.4(0.09-1.9)	2(11.1) 0.6(0.1-2.8)

Table 4: Adjusted relative risk for patients' survival based COX-model

Variables	β	SE	P value	R	Exp(β)	CI95%
Survive before non fatal MI						
Triglyceride	0.0036	0.0001	0.03	0.05	1.003	1.003-1.006
Systolic blood pressure	0.023	0.0094	0.012	0.07	1.02	1.005-1.04
Survive after fatal MI						
EX-smoking	-1.05	0.42	0.012	0.1	0.34	0.15-0.79
Urbanization	-0.74	0.38	0.05	0.06	0.47	0.22-1.01
Survive before stroke event						
EX-smoking	-1.57	0.56	0.005	-0.18	0.2	0.06-0.6
Fasting blood sugar	0.004	0.0019	0.014	0.14	1.004	1.0009-1.0084

In the present study, the average systolic and diastolic blood pressure of patients with fatal and non-fatal cardiovascular events and stroke was higher than the rest of the population; this resembles the findings of similar studies, however, average blood pressures (especially diastolic pressure) was higher than similar studies.[18] In this study, diabetes was associated with a higher relative risk, especially of stroke, varying with location and gender between 5.6 and 7.9. The risk was particularly notable in males.

Diabetics also posed a 2.1 times higher relative risk of non-fatal cardiac accidents. In the ten-year study by Framingham and a study by Glostrop, diabetics stood a 2.36 and 2.62 times higher relative risk of non-fatal cardiac accidents, respectively.[10] In this study, metabolic syndrome was associated with a 1.9, and 2.8 times higher relative risk of non-fatal cardiac accidents in women and men, respectively, and a 4 times higher relative risk of stroke in men. In light of the higher incidence of fatal and non-fatal cardiac accidents in this two-year study, as compared with similar cohort studies in Europe and the Americas,[21,23-25] and the higher relative risk of CVD risk factors (esp. hypertension, diabetes, history of smoking, and metabolic syndrome) compared with other studies, it seems necessary to devise a tool that can assess the absolute and relative risk of fatal and non-fatal cardiac accidents, while matching the risk factors, as well as the geographical and cultural characteristics of the Iranian population. Moreover, provided the success of IHHP in evaluating the relative and absolute risk of the incidence of fatal and non-fatal cardiac accidents and stroke over a 10-year period, it will complete the unfinished work of Enberg et al. in studying the effect of interventions in reducing the incidence of cardiac accidents in the community.[21]

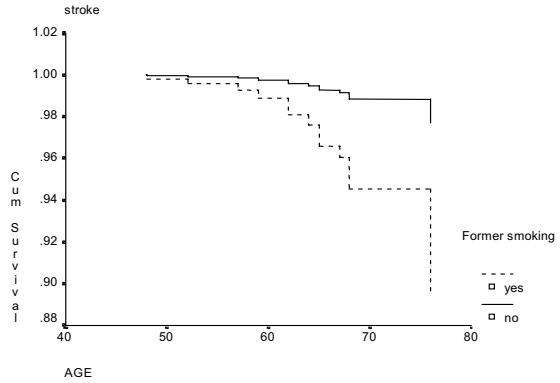

Figure1: Survival of Former Smoker before Stroke Event

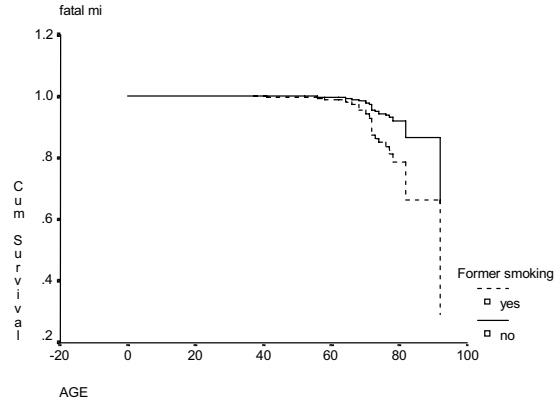

Figure2: Survival of Former Smoker with Fatal MI

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