

The Role of a History of Coronary Heart Disease among Second Degree Relatives for Predicting Coronary Artery Disease

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Abstract

Introduction: The history of atherosclerotic disease among second degree family members of patients as a risk factor has not been properly explained. The present study aimed to assess this role in the Iranian population.

Methods: This case-control study was performed on 500 consecutive patients, who were candidates for coronary angiography. The presence of Coronary Heart Disease (CHD) history among first and second degree relatives were determined by interviewing the participants.

Results: In total, 450 patients were shown to have CHD as the case group and 50 without CHD as the control group. Family history of CHD among first degree relatives was 39.1% for cases and 22.0% for the controls with a significant difference ($P = 0.018$), however the history of CHD among second degree relatives was not statistically different in the case group and the control group (17.8% vs. 8.0%, $P = 0.079$). In total, 80 patients had CHD with simultaneous history of disease among their second degree relatives, while 370 with CHD had no history of disease among their second degree relatives. Our study could not find a significant difference between the two CHD groups with and without history of disease among second degree relatives in terms of cardiovascular risk profile.

Conclusions: Despite the powerful effect of the presence of family history of CHD in first degree relatives on risk of CHD and its severity, the presence of this history among second degree relatives cannot predict the risk for CHD.

INTRODUCTION

Coronary Heart Disease (CHD) is the most common cause of death in the world and a multi-factor disease influenced by several genetic and environmental factors. Several studies have shown that a family history of ischemic heart disease is a very important predictor for CHD that can estimate the increased risk for coronary heart disease and thus can be useful for primary prevention of the disease [1-4]. Many studies have been conducted on family history of ischemic heart disease as a main determinant for CHD. In fact, family history reflects the involvement of both genetic and ecological factors that affect the metabolic profile as well as lifestyle of families and individuals, simultaneously [5, 6]. By definition, a positive family history of CHD refers only to the presence of disease among first-degree relatives [7, 8]; however, a his-

tory of atherosclerotic disease among second degree family members of the patients, as a risk factor, has not been properly explained. Because of limited available studies on the role of positive family history of CHD among second degree relatives, as a risk profile for disease, the present study aimed to assess this role in the Iranian population. In other words, in this researched we aimed to determine whether the presence of family history of CHD among second degree family members of patients could predict the risk for disease in these patients.

METHODS

This case-control study was performed on 500 consecutive patients, who were candidates for coronary angiography to confirm or rule out of documented CHD defined as the pres-

ence of at least one involved coronary vessel with more than 50% stenosis in coronary angiography report. In this regard, the patients were categorized as the case group with evident Coronary Artery Disease (CAD) and the control group without significant coronary disease. The baseline characteristics and clinical data of the subjects including the presence of cardiovascular risk profiles were collected by reviewing the recorded hospital files or interviewing the patients. Also, the presence of CHD history among first and second degree relatives was determined by interviewing the participants.

Results were presented as mean \pm Standard Deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnov test. Categorical variables were compared using the chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than five were observed. Quantitative variables were also compared with t test or Mann-Whitney U test. For the statistical analysis, the SPSS version 16.0 statistical software for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant. The institutional review board approved the study protocol and patients provided informed written consent.

RESULTS

In total, 450 patients with CHD were included in the case group and 50 without CHD made up the control group. Comparing the two groups (Table 1), indicated higher mean age as well as higher male gender frequency in the CHD group than in the control group. Regarding cardiovascular common risk factors, the prevalence of diabetes was 33.1% and 26.0% in the case and control group, respectively, with no difference between the two groups ($P = 0.308$). Also, 56.4% and 52.0% were hypertensive, 40.9% and 36.0% were dyslipidemic and 33.8% and 22.0% were smokers in the case and control group, respectively, without between-group differences. A history of previous myocardial infarction (53.3% vs. 2.0%), previous Coronary Artery Bypass Grafting Surgery (CABG) (19.1% vs. 0.0%), and previous Percutaneous Coronary Intervention

(PCI) procedures (56.0% vs. 2.0%) were more common in the case group compared with the control group. In electrocardiography assessment, ST-T changes were found in 72.2% of the patients in the case group and 60.0% in the control group with a slight difference ($P = 0.072$), however pathologic Q wave was significantly higher in those with documented CHD (33.6% vs. 8.0%, $P < 0.001$). Also, indications of branch blocks were more evident in the case than in the control groups (14.0% vs. 6.0%). Echocardiography assessment also indicated higher prevalence of left ventricular dysfunction as well as higher rate of wall motion abnormality among cases when compared to the controls ($P < 0.001$).

Family history of CHD among first degree relatives was found in 39.1% of the cases and 22.0% of the controls with a significant difference ($P = 0.018$), however the history of CHD among second degree relatives was not statistically different in the case group and the control group (17.8% vs. 8.0%, $P = 0.079$).

In total, 80 patients had CHD with simultaneous history of disease among their second degree relatives, while 370 with CHD had no history of disease among their second degree relatives. Our study could not find a significant difference between the two CHD groups with and without history of disease among second degree relatives in terms of gender ($P = 0.587$), diabetes mellitus ($P = 0.514$), smoking ($P = 0.190$), previous myocardial infarction ($P = 0.284$), history of cerebrovascular disease ($P = 0.610$), and history of CABG ($P = 0.592$) or PCI ($P = 0.149$). However, those with a history of CHD among their second degree relatives were younger (mean age: 56.84 years vs. 60.62 years, $P = 0.005$) with lower prevalence rates of hypertension (42.5% vs. 52.5%, $P = 0.006$) and dyslipidemia (22.5% vs. 36.8%, $P = 0.015$) (Table 2). Also, there was no difference in the number of involved coronary vessels between the CHD groups with and without family history among second degree relatives ($P = 0.181$). The risk for CHD significantly increased among patients with a family history among first degree relatives (OR = 2.27, 95%CI: 1.13 to 4.57), however the presence of CHD among second degree relatives could not predict the increased risk for CHD among the patients (OR = 2.49, 95%CI: 0.87 to 7.11).

Table 1: Baseline Characteristics and Clinical Data of Study Participants

Item	CHD Group (n=450)	Non-CHD Group (n=50)	P value
Male gender	282 (62.7)	22 (44.0)	0.010
Age, year	59.95 \pm 11.07	51.96 \pm 12.06	< 0.001
Diabetes mellitus	149 (33.1)	13 (26.0)	0.308
Hypertension	254 (56.4)	26 (52.0)	0.548
Dyslipidemia	154 (40.9)	18 (36.0)	0.504
Smoking	152 (33.8)	11 (22.0)	0.092
Myocardial infarction	240 (53.3)	1 (2.0)	< 0.001
Cerebrovascular disease	23 (5.1)	1 (2.0)	0.329
Previous CABG	86 (19.1)	0 (0.0)	0.001
Previous PCI	252 (56.0)	1 (2.0)	< 0.001
Family history of CAD (first relatives)	176 (39.1)	11 (22.0)	0.018
Family history of CAD (second relatives)	80 (17.8)	4 (8.0)	0.079

CHD: coronary heart disease; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention; CAD: coronary artery disease.

Data in table are presented as No. (%).

Table 2: Baseline Characteristics and Clinical Data in the Groups with and without Family History of CHD among Second Degree Relatives

	CHD Group with History of CHD Among Second Degree Relatives (n=80)	CHD Group without History of CHD Among Second Degree Relatives (n=370)	P value
Male gender	48 (60.0)	234 (63.2)	0.587
Age, year	56.84 ± 10.10	60.62 ± 11.16	0.005
Diabetes mellitus	24 (30.0)	125 (33.8)	0.514
Hypertension	34 (42.5)	220 (59.5)	0.006
Smoking	18 (22.5)	136 (36.8)	0.015
Smoking	22 (27.5)	130 (35.1)	0.190
Myocardial infarction	47 (58.8)	193 (52.2)	0.284
Cerebrovascular disease	5 (6.2)	18 (4.9)	0.610
Previous CABG	17 (21.2)	69 (18.6)	0.592
Previous PCI	39 (48.75)	213(60.27)	0.149
Number of involved coronaries			0.181
None	13 (16.2)	57 (15.4)	
Single vessel	12 (15.0)	93 (25.1)	
Two vessels	28 (35.0)	96 (25.9)	
Three vessels	27 (33.8)	124 (33.5)	

CHD: coronary heart disease; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention
Data in table are presented as No. (%) or Mean ± SD.

DISCUSSION

This case-control study showed that the presence of coronary heart disease among first degree relatives predict CHD (OR = 2.27) but this history in second degree relatives cannot predict the risk for CHD.

Reviewing the literature showed no similar comprehensive research on the association between the presence of family history of CHD among second degree relatives and increased risk for disease. However, several studies could demonstrate the definitive role of family history of CHD among first degree relatives for predicting CHD and its severity and prognosis. As shown by Leander et al. [1], family history was a strong risk factor for myocardial infarction interacting with other cardiovascular risk factors. A male candidate with one or more affected parents or siblings has an increased risk of myocardial infarction by more than two times compared with no family history of coronary heart disease. In a female candidate this increase is 2.1 times. When two or more parents or siblings are affected, the adjusted odds ratio of myocardial infarction was 3.4 and 4.4 for males and females, respectively. Family history of coronary heart disease in current female smokers had a synergistic effect with high quotient between low-density lipoprotein and high-density lipoprotein cholesterol. Hawe et al. [9] showed that the hazard ratio of CHD for males with a family history of CHD was 1.73 compared to those without a family history; and this was independent of other classic risk factors. In a systematic review by Prabhakaran et al. [10], after pooling the case-control studies (involving 17,202 cases and 30,088 controls) unadjusted odds ratio of 2.03 was yielded, whereas after pooling the cohort studies (including 313,837 individuals), relative risk for future coronary heart disease of 1.60 was yielded. All published papers focused on the predictive role of family history of CHD in first degree relatives and could also show its synergistic effects when they interacted with other cardiovascular

risk factors, however the role of family history in second degree relatives was not approved, which was also shown by our study. In fact, the presence of family history of CHD in second degree relatives might not have enough power to predict an increased risk for CHD. It seems that the hereditary transfer of polymorphisms related to CHD is mainly done between first degree relatives of the patients.

However, it seems that the employed small sample size and therefore partially low power of our study could potentially affect the results. Also, one of the other main limitations of the study was lower prevalence of some cardiovascular risk factors such as advanced ages, hypertension, and diabetes in the group with a family history of CHD in second degree relatives that affected the validity of our findings. In fact, this finding may rule out the synergistic effect of family history of CHD in second degree relatives and other risk factors.

Overall, it seems that despite the powerful effect of the presence of family history of CHD in first degree relatives on risk of CHD and its severity, the presence of this history among second degree relatives cannot predict the risk of CHD. Also, the synergistic effects of this parameter with other cardiovascular risk profiles are not predicted.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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