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Evaluation of the Relationship between Family History and Occurrence, Anatomical Location, and Extent of Coronary Artery Disease among Patients Undergoing Coronary Angiography

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Abstract

Background: A positive family history (FH) of coronary artery disease (CAD) is considered an independent risk factor for developing CAD. However, the relationship between the occurrence, angiographic anatomical location of the stenosis, and extent of CAD and the risk factors in the patients and their relatives is not well defined. Evaluation of this relationship is our main goal in this study.

Methods: In this descriptive cross-sectional study, the FH data for CAD and premature death in first-and second-degree relatives, angiographic anatomical location of the stenosis, the extent of CAD in the patients and their relatives, as well as the relationship between other risk factors and the extent of CAD, were collected from 300 adult patients undergoing coronary angiography at Farshchian cardiovascular hospital in Hamadan (Iran) between March 2020 and 2021. SPSS 24 and the chi-square, Fisher exact, and student t tests were used to analyze data. The significance level was considered $P < 0.05$.

Results: Out of 300 patients, 185 (61.7%) were men and 115 (38.3%) were women. A total of 177 patients (59%) in maternal and 82 patients (27.3%) in paternal relatives had an FH of CAD. There was a significant relationship between the severity of coronary artery involvement and risk factors ($P < 0.001$). Moreover, there was no significant relationship between the location of coronary artery involvement of the right coronary artery, left coronary artery, and left anterior descending artery and the severity of involvement of patients undergoing coronary angiography and their first- and second-degree relatives ($P = 0.480$).

Conclusion: Our findings suggest that there was no significant relationship between the anatomical location of the stenosis and the number of vessels involved and the FH of the patients. In patients with an FH, the extent of CAD significantly increased according to their risk factors for heart disease.

Keywords: Family History, Coronary Artery Disease, Cardiac Risk Factors, Anatomical Location, Vessel Involvement

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Introduction

CAD is one of the leading causes of death all around the world, including Iran (1). It also has a significant impact on quality of life, as well as a significant financial and psychological burden (2). Initially, it was assumed that familial clustering of CAD is caused by the presence of a high prevalence of CAD risk factors such as diabetes mellitus, high blood pressure, and so forth among family members. However, a positive FH is now considered an independent risk factor for CAD development that is not related to other risk factors (3, 4). Compared with other clinical CAD risk factors, positive FH in young patients is the strongest clinical predictor of future unheralded myo-

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↑What is "already known" in this topic:
A positive family history (FH) of coronary artery disease (CAD) is considered an independent risk factor for developing CAD.

→What this article adds:
FH could not predict angiographic localization or severity of CAD. In patients with FH, the extent of CAD significantly increased according to their risk factors for heart disease.

cardial infarction (MI). Currently, the goal of medical science is to conduct genetic studies and discover genes implicated in various diseases. The heritability of CAD has been estimated to be between 40% and 60%. After accounting for traditional CAD risk variables, the age-specific incidence of CAD rose by >2-fold in people with an FH of early illness. It was found that the heritability of fatal CAD events was 0.57 for men and 0.38 for women up to >35 years. Heritable effects are most visible in children and adolescents (5, 6). Most patients with CAD undergo coronary angiography, and the accompanying knowledge of coronary anatomy and morphology has several consequences for the affected adult, but it may also refine risk prediction in children and siblings of these patients. To enable its best utilization, future prospective investigations of CAD in families should take into account the anatomic correlates of the disease in various imaging modalities as well as the potential relevance of FH in risk prediction and prognosis. Although studies to date have not definitively demonstrated a relationship with FH, traditional risk factors may predict the location of CAD. There has only been 1 study that looked at coronary angiographic localization in connection to FH in those with established coronary artery disease (CAD) and found that left mainstem and proximal disease (LMD) showed substantial heritability. This study, which was based on family pedigrees, also revealed that healthy siblings of patients with LMD were at greater risk of future coronary events, in addition to the risk of a positive FH (7). Information such as coronary artery anatomy, risk factors, and the extent of involvement, when combined with more accurate family information, can be very helpful in future screening strategies for asymptomatic relatives (8). It was reported that all-cause mortality is correlated with the location of the afflicted vessels on a coronary angiogram, the number of affected vessels, and FH. It is possible that FH information still plays a role in risk prediction and prognosis in ACS given that patients having angiography are more likely to have a premature maternal history of myocardial infarction (9, 10). In the present study, we assessed the anatomical coronary angiographic findings, the extent of CAD, and the relationship between other risk factors and the extent of CAD in patients who had a positive FH of CAD and were hospitalized in the coronary care units.

Methods

Population

This is a descriptive cross-sectional study that used a convenience-consecutive sampling method to study 300 patients who underwent coronary angiography at Farshchian cardiovascular hospital in Hamadan, Iran, from March 2020 to 2021.

Inclusion Criteria

All patients had an FH of premature death or CAD in first- and second-degree relatives who had previously undergone coronary angiography before death. Patients with an FH of sudden death at a young age—for women younger than 55 years and men younger than 45 years old—were considered cases with a positive FH and thus were included in the study.

Exclusion Criteria

In the absence of relatives' angiographic data, the patients were excluded from the study except those with an FH of premature death.

Ethical Consideration

Informed consent was obtained from all study participants. All patient information will remain strictly confidential.

Disease Definition

Positive FH is defined as the presence of CAD in first-degree relatives in women younger than 65 years and in men younger than 55 years. By definition, premature CAD occurs in women younger than 55 years and in men younger than 45 years. The proposed CAD is obstructive CAD, which is defined by the evidence of stenosis of >70% of coronary arteries in coronary angiography.

Measurements

We examined the relationships between the occurrence, anatomical location, and extent of CAD in the patients and their relatives, as well as the relationship between other risk factors and the extent of CAD.

In the case of a history of coronary angiography in Farshchian hospital (angiography video or angiography report sheet), the data were taken from the hospital archives and the angiographic results, including age at the time of angiography, gender, and the relationship between the patients and their relatives were listed in a checklist. However, in the case of angiography in other medical centers, its information (coronary angiography video or angiography report sheet) and other necessary data would be received and recorded on a checklist.

The checklist also contained questions about independent cardiovascular risk factors such as diabetes, dyslipidemia, smoking, and blood pressure. The patient's data were obtained directly, and the patient's relative data were obtained by telephone (if possible) or through the primary patient.

Coronary angiography of patients and their relatives was reported by our interventional cardiologists at Farshchian cardiovascular hospital. Coronary artery stenosis of patients and their relatives were classified into the main groups of coronary artery disease, including single-vessel disease (LAD, LCX, and RCA), LM, and multivessel disease. Main artery stenosis was divided into different subgroups according to the SYNTAX score: proximal, mid, and distal parts. In the case of the patient's relatives with a history of coronary artery bypass graft (CABG) and premature death, we classified them as multivessel diseases. Moreover, the relationship between the occurrence, anatomical location (eg, the location of coronary artery stenosis in maternal, paternal, or other relatives) and extent of coronary artery stenosis and the type of patient's family relationship (sisters, brothers, and children) was measured in this study.

Data Analysis

SPSS 24 and the chi-square, Fisher exact, and student t tests were used to analyze the data. The significance level was set at $P < 0.05$.

Results

Demographic and Risk Factors

The mean age of patients was 55.54 ± 12.57 years, 185 (61.7%) of whom were men and 115 (38.3%) were women. In terms of cardiovascular risk factors, 92 (30.7%) were smokers, and the prevalence of diabetes, hypertension, and dyslipidemia were 66 (22%), 211 (70.3%), and 190 (63.3%), respectively. Among the relatives of patients, 82 (27.3%) were paternal and 177 (59%) were maternal. In addition, 41 (13.7%) were their children, brothers, or sisters. Table 1 shows the demographic information of the patients and their relatives in this study. As shown in Table 1, 177 patients (59%) in maternal and 82 patients (27.3%) in paternal relatives had an FH of CAD or premature deaths. These findings suggest that the proportion of maternal relatives can contribute to the development of CAD in patients. Hypertension and dyslipidemia were both important risk factors for patients and their relatives for CAD.

Anatomic Location of Stenosis

A total of 228 patients were involved in RCA with stenosis (34.2% proximal, 35% mid part, and 30.7% distal). Table 2 shows the RCA coronary artery stenosis frequency in patients and their relatives. Based on the chi-square statistics, there was no significant relationship between the area of involvement of the RCA branch in the patients and their relatives ($P = 0.480$).

In total, 224 patients had LAD with stenosis (32.6% proximal, 33.9% medial, and 33.5% distal). As shown in Table 3, there was no statistically significant relationship between the location of LAD stenosis and patients' FH ($P = 0.793$).

LCX coronary artery stenosis was observed in 208 patients, which 51.9% were in the distal region and 48.9% in the proximal region. There was no significant relationship between their first- and second-degree relatives ($P = 0.710$) (Table 4).

Coronary Vessels Involved in Patients and Their Relatives

As mentioned earlier, 300 participants were included in the study, of whom 114 patients (37.9%) had a single-vessel disease and 187 patients (62.1%) exhibited 2- or 3-vessel disease. Among the relatives of the patients whose information was obtained by studying their case summary, a single-vessel disease was observed in 84 patients (27.9%) and the remaining 217 patients (72.1%) showed a multivessel disease. This study considered the history of the sudden death of relatives to be equivalent to multivessel disease. Table 5 shows the number of coronary arteries involved in patients and their relationship to their relatives. There was no significant relationship between

Table 1. Demographic information of patients and their relatives in the study

Patients			Relatives		
Variable		Number (%)	Variable		Number (%)
Gender	Men	185 (61.7)	Family Relationship	Paternal	82 (27.3)
	Female	115 (38.3)		Maternal	177 (59)
				Others	41 (13.7)
Smoking	Yes	92 (30.7)	Smoking	Yes	61(20.3)
	No	208 (69.3)		No	239 (79.7)
Diabetic	Yes	66 (22)	Diabetic	Yes	74 (24.7)
	No	234(78)		No	226 (75.3)
Hypertension	Yes	211(70.3)	Hypertension	Yes	210 (70)
	No	89(29.71)		No	90 (30)
Dyslipidemia	Yes	190 (63.3)	Dyslipidemia	Yes	194 (64.7)
	No	110(36.7)		No	106 (35.3)

Table 2. Frequency of RCA coronary artery lesions in patients and their first- and second-degree relatives

RCA Lesions in Relatives	RCA Lesions in Patients				*P value
	Normal	Proximal	Midpart	Distal	0.483
Normal	19	19	16	23	
Proximal	15	24	22	17	
Midpart	17	19	16	17	
Distal	21	16	26	13	
Total	72	78	80	70	

* Pearson Chi-Square

Table 3. Frequency of LAD coronary artery lesions in patients and first- and second-degree relatives

LAD lesions in Relatives	LAD lesions in Patients				*P Value
	Normal	Proximal	Midpart	Distal	0.792
Normal	26	17	20	19	
Proximal	18	25	20	21	
Midpart	21	9	15	19	
Distal	11	22	21	16	
Total	76	73	76	75	

* Pearson Chi-Square

Table 4. Frequency of LCX coronary artery lesions in patients and their first- and second-degree relatives

LCX lesions in Relatives	LCX lesions in Patients			*P value
	Normal	Proximal	Distal	0.710
Normal	30	3\2	27	
Proximal	40	46	51	
Distal	22	22	30	
Total	92	100	108	

* Pearson Chi-Square

Table 5. Patients with coronary artery disease and its relationship with lesions in first- and second-degree relatives

Number of diseased coronary artery in patients	Number of diseased coronary artery in Relatives			*P* value
	one artery	More than one artery	Total	
one artery	25	89	114	0.063
More than one artery	59	127	186	
Total	84	216	300	

Table 6. Frequency of risk factors for coronary disease according to the number of diseased coronary artery

Risk Factors		Single Vessel Disease	Multivessel Disease	*P* Value*
Smoking	Yes	20	72	<0.001
	No	94	114	
Diabetes	Yes	102	132	<0.001
	No	12	54	
Hypertension	Yes	93	118	<0.001
	No	21	68	
Dyslipidemia	Yes	95	95	<0.001
	No	19	91	

the number of diseased vessels in patients and the number of diseased vessels in their first- and second-degree relatives ($P = 0.063$).

Relationship Between Coronary Vessels Involved and Risk Factors in Patients

Another aim of this study was to investigate the relationship between different risk factors and the number of coronary arteries involved in patients with a positive FH. As shown in Table 6, a statistically significant relationship was observed between the risk factors of hypertension, diabetes, smoking, and dyslipidemia in patients with a positive FH and the number of vessels involved in CAD.

Discussion

The present study demonstrates that hypertension and dyslipidemia are both important risk factors for patients and their relatives for CAD. In Harpaz et al study (11), patients with positive FH were on average younger (53 years versus 64 years), most of whom were men, smokers, and more likely to have dyslipidemia. Patients without an FH of CAD had a lower history of DM and hypertension. These findings were consistent with our results. Harpaz et al reported that patients with positive FH had a lower rate of heart failure during hospitalization. During hospitalization, coronary angiography, percutaneous coronary intervention, and CABG were performed more frequently in the group of patients with positive FH. Coronary angiographic findings were also compared, and it was found that the coronary anatomy and extent of CAD involvement were similar between the 2 groups. However, on average, patients with positive FH suffered from myocardial infarction 1 decade earlier than patients without an FH of CAD, and the extent of CAD was similar with older people (11). Although the present study did not investigate the long-term outcome of the disease, the mean age of the patients included in the study was 55 years, which was similar to the mean age of their relatives at the time of sudden death or coronary events.

Another finding of this study suggests that the proportion of maternal relatives can contribute to the development of CAD in patients. Sintonen et al addressed the FH as a risk factor for CAD in patients younger than 60 years who survived a recent acute myocardial infarction. They revealed that FH was an important risk factor for CAD, but this risk is higher in female patients (12). Our study showed similar CAD patterns in maternal relatives (the mother and her sisters and brothers) were more than the same pattern in the paternal family (the father and his sisters and brothers)—a result that is consistent with the Sintonen et al study. However, these differences were not statistically significant. Comparable CAD patterns, however, were uncommon in the patients' sisters and brothers. Regarding the effect of genetics on cardiovascular diseases, in a study by McPherson et al (2016) on 100 genetic relations and analysis of gene loci, 28% of patients confirmed the effect of genetics in CAD. Therefore, the genetic risk score can be used to predict CAD risk beyond classic cardiovascular risk factors. They also help identify the people who benefit most from specific treatments, including statins (13). Thus, the case-control study on CAD and myocardial infarction genetics by Dai et al and the meta-analysis on gene locus (14) conducted by Vanderharst et al both revealed CAD-related gene loci and even the impact of genetics on restenosis inside coronary stents (15). Hence, genetics has a great effect not only on the onset of CAD but also on the response to treatment (14-16). In addition, calculating the genetic score of CAD risk would help detect susceptible and non-susceptible individuals to cardiovascular and non-cardiovascular diseases (17). Even the morphological features of stenosis leading to sudden coronary death are related to an FH of premature CAD (18). According to the results of Marcus et al, LMD was frequently shared by siblings with CAD.

Moreover, in apparently healthy siblings of patients with LMD, this heritable component results in a risk increase for future events that is greater than that of a strong positive FH by itself (19). In a study by Zhang et al (2016), the FH of premature CAD and the morphology of Culprit stenosis in cases of sudden cardiac death who experienced autopsy were evaluated. They showed that in cases of sudden death if there is a positive FH, culprit stenosis is more likely to be plaque erosion (20). With regard to the sudden death of relatives as one of the signs of multivessel CAD, the present study demonstrated that multivessel CAD is more common in the next generation of such patients. One of the interesting parts of this study was determining the anatomical location of stenosis in patients and their relatives. Although no strong statistical relationship was observed between the location of the coronary artery stenosis of the patients and their relatives, a similar pattern was frequently observed in the patient's relatives, especially since these similar findings were more common in the maternal relatives.

This study also showed a higher frequency of multivessel CAD in patients with an FH of multivessel CAD. In addition, there was no significant difference between patients with multivessel CAD and their relatives. Moreover, Harper et al evaluated the role of CAD and prognosis in patients who survived the first attack of acute myocardial infarction and showed that positive FH was an independent risk factor for CAD (11). Although our study did not deal with long-term survival and outcome and our statistical population was limited, it was found that the cardiac risk factors in the group with multivessel CAD were significantly higher than in the single-vessel CAD group.

Overall, our results were somewhat consistent with the results of a study by Amitava et al, where they concluded that FH data do not predict angiographic localization of coronary disease in patients presenting with acute coronary syndrome (ACS). Maternal stroke and maternal myocardial infarction may affect ACS in women by a mechanism unrelated to atherosclerosis or coronary anatomy (21). However, FH data may still be useful in the risk prediction and prognosis of ACS. Therefore, the researcher strongly recommends future studies be conducted using a larger sample size using the prospective cohort method on the relatives of patients with CAD for evaluation of CAD.

Conclusion

In summary, hypertension and dyslipidemia appear to be 2 main risk factors for patients and their relatives for CAD. There was no significant relationship between the anatomical location of stenosis and number of vessels involved and the FH of the patient. However, statistically significant relationships were observed between the risk factors of hypertension, diabetes, smoking, and dyslipidemia in patients with a positive FH and the number of vessels involvement in CAD. With various contradictory results, FH is still considered a risk indicator for cardiovascular diseases. To enable its best use, future prospective investigations of FH in CAD should take into account the anatomic correlates of disease in various imaging modalities as well as the potential relevance of FH in risk prediction and prognosis.

Authors' Contributions

In this study, Amirhossein Yazdi (MD) played a role in performing and reporting coronary angiography, Vahid Ashrafi (MD) collected data, and Maryam Farhadian (PhD) performed the statistical analysis.

Abbreviations

- ✓ CVD: cardiovascular disease
- ✓ CAD: coronary artery disease
- ✓ MI: Myocardial infarction
- ✓ CABG: Coronary artery bypass graft
- ✓ FH: Family history
- ✓ LMCA: left main coronary artery
- ✓ LAD: Left Anterior Descending Coronary Artery
- ✓ RCA: right coronary artery
- ✓ CT: computed tomography
- ✓ DM: Diabetes melitus
- ✓ HTN: Hypertension

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Conflict of Interests

The authors declare that they have no competing interests.

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