

Coronary Risk Factors in Patients with Coronary Artery Ectasia : A Case-Control Study from Iran

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Coronary artery ectasia is a rare finding in angiography. We investigated the prevalence of coronary artery ectasia and assessed cardiovascular risk factors as probable influencing factors in this disease in our region. This study was conducted from October 2007 to March 2010 on 2500 patients visiting Imam Reza and Qaem and Razavi hospitals, Mashhad, Iran who had chest pain and were selected for angiographic studies. The study was based on reviewing angiographic films besides filling in questionnaires. 103 coronary artery ectasia cases showing 4% prevalence for this kind of coronary involvement were selected as the study group and compared with 62 patients with atherosclerosis and no ectasia as the control group. Mean age of the study and control group was 57.6 and 54.1yrs, respectively indicating a statistically significant difference ($p=0.032$). The study and control groups showed no significant difference based on sex, smoking history and mean Body Mass Index (BMI). However, a BMI above 25 had a significantly higher prevalence in the study group ($p=0.036$). Mean hs-CRP and homocystein levels were 3.4 and 11.8 in the study group and 2.3 and 8.3 in the control group, respectively, both revealing a significant difference ($p=0.002$, $p<0.001$). Hyperlipidemia in ectasia patients in comparison to controls was significantly more prevalent ($p=0.001$). The prevalence of coronary artery ectasia was 4% and cardiovascular risk factors in ectasia cases included: hyperlipidemia, high hs-CRP, and homocystein.

Key words: Ectasia, Angiography, Coronary Artery Disease, Risk factors .

Coronary artery ectasia (CAE) is a serious cardiac involvement, defined as localized coronary dilatation which exceeds the diameter of normal adjacent segments or the diameter of the

patient's largest coronary vessel by 1.5 times. CAE varies in incidence from 1.5 to 5% in most literature; however, it has been reported to be as high as 10% in some nations. The exact etiology of coronary ectasia remains not well understood; however, a number of potential explanations for coronary dilatation have been proposed, including atherosclerosis, Kawasaki disease, Takayasu arteritis, congenital coronary artery disease, rare

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etiologies like syphilis, trauma or dissection and also iatrogenic causes¹. Atherosclerosis, either the atheromatic plaque or the localized inflammation itself can lead to loosening and destruction of the blood vessels' connective tissue and result in vascular ectasia or aneurysm²⁻⁴. Familial hypercholesterolemia causes ectasia both through the atherosclerotic mechanism and also through its direct effect^{3,5}. Regarding that high Homocysteine level is a risk factor for cardiovascular and cerebrovascular diseases, it could be considered as a risk factor for coronary artery ectasia as well^{1,6-7}. Chronic inflammation and a high CRP level have been seen in companionship with coronary artery ectasia³. A subset of patients may have no evidence of a known risk factor for coronary disease; therefore they might be recognized as having idiopathic coronary artery ectasia¹.

The prevalence of CAE, as determined by angiography, has been between 0.3% and 5.3% in earlier studies⁴. It seems that during the recent years the prevalence of CAE has increased; for instance the reported cases were as high as 10% from India in 2006⁸ and 9.9% from Turkey in 2010⁹. This rise in the prevalence of CAE as suggested by previous studies could be due to the high exposure to pesticides and fluorosis⁹.

The clinical manifestations of coronary artery ectasia include a wide spectrum of signs and symptoms. In many cases it has no specific clinical symptom and is usually accidentally diagnosed in angiography due to other indications. In cases which it becomes symptomatic, the most common symptom is acute coronary syndrome which could be the result of the ectasia itself, a thrombosis in the ectatic region or spontaneous stenosis in the involved coronary artery.

This study was designed to investigate the prevalence of coronary artery ectasia in our region. It also assessed the most common cardiovascular risk factors as probable influencing factors in this disease and in the same population.

MATERIALS AND METHOD

Subjects

This is a case-control study performed from October 2007 through March 2010 in Imam Reza, Razavi and Qaem hospitals, Mashad, Iran.

During this study 2500 patients underwent coronary artery angiography; among them 103 cases of coronary artery ectasia were diagnosed that formed the study group. 62 patients who were willing to continue the study course but had no sign of ectasia, autoimmune or collagen-vascular disease and were not receiving any steroids, were recruited as the control group. The sampling method was simple and target-based. Subsequent to diagnosis of the type of arterial involvement in the performed coronary artery angiography, the patients were divided into two groups. The study group consisted of patients with coronary artery ectasia; the exact inclusion criteria for the control group were as follows: coronary artery involvement in the form of atherosclerosis, no history of autoimmune or collagen-vascular diseases and no corticosteroid consumption. None of the patients in the study group had a history of autoimmune or collagen-vascular diseases.

The study was thoroughly conducted in line with the Declaration of Helsinki. The ethics committee of Mashhad University of Medical Sciences approved the research protocol. The aim and methodology of the study was fully explained to the patients and an informed consent was obtained from each subject prior to study entrance.

The required study data were gathered through angiography films and specifically-designed questionnaires. This specifically-designed questionnaire consisted of sex, age, weight, height, and BMI of each individual patient which were measured by a single clinician. A complete history was taken from each patient including hypertension, diabetes, hyperlipidemia and smoking history. The diagnosis of hypertension, diabetes and hyperlipidemia was based on their history and type of current medication. A patient was defined as a smoker he/she had been smoking for over 6 months; based on the World Health Organization's definition. Also patients having quit smoking for over 6 months were considered as quitters. Since none of the studied cases had quit smoking for at least 6 months, they were divided into two groups of smokers and non-smokers.

Data analysis

The data were analyzed with the application of the SPSS software (version 11.5) and by using statistical tests including Kolmogorov-

Smirnov test, Chi-square test, Mann-Whitney test and t- test. Significance level stood at 0.05.

RESULTS

The prevalence of coronary artery ectasia was estimated as 4% in this study.

The coronary risk factors and clinical features among the study and control groups are shown in table 1.

Body Mass Index was compared between the two groups according to Harrison's Principles of Internal Medicine's categorization¹⁰ which is shown in table 2. Mann-Whitney test showed a significant difference between the two groups (P=0.036).

Serum levels of high sensitivity C-reactive protein and concentration of homocysteine were also compared among the two

groups according to their categorization in **Braunwald's Heart Disease for hs-CRP and the referred laboratory normal ranges for homocysteine**¹¹. The results are demonstrated in tables 3 and 4. A significant difference was seen between the two groups in hs-CRP (P= 0.002, Mann-Whitney test) and homocysteine (P= 0.00, Chi-Square test).

The odds ratio for different risk factors was as follows: 4.3 for hyperlipidemia, 1.5 for hs-CRP, 1.4 for Homocysteine level, 1.03 for Body Mass Index level and 0.9 for both age and platelets count.

DISCUSSION

The prevalence of coronary artery ectasia was estimated as 4% in this study which is higher than the similar report in text books (1-3%)¹¹. Hashemvali and colleagues in Egypt estimated the

Table 1. Risk factors in the study and control groups

Item	Study group (n=103)	Control group(n=62)	Sig.
Age (mean ± standard deviation)	54.1±9.4	57.6±11.2	P=0.032 (t- test)
Gender	85 (82.8%) Male 18 (17.5%) Female	52 (83.9%) Male 10 (16.1%) Female	P=0.823 (Chi-Square test)
Body Mass Index (mean ± standard deviation)	26.3±4	25.3±3.5	P=0.128 (t- test)
Smoker	34 (33%)	14 (22.6%)	P= 0.162 (Chi-Square test)
Diabetes	10 (9.7%)	10 (16.1%)	P=0.325 (Chi-Square test)
Hypertension	62 (60.2%)	44 (71%)	P=0.182 (Chi-Square test)
Hyperlipidemia	43 (41.7%)	10 (16.1%)	P = 0.001 (Chi-Square test)
hs-CRP (mean ± standard deviation)	3.4 ± 3.2	2.3 ± 2.3	P = 0.000 (Mann-Whitney test)
Homocysteine (mean ± standard deviation)	11.8 ± 5.8	8.3 ± 2.9	P= 0.002 (Mann-Whitney test)
White Blood Cells count	7197.1 ± 1904.4	8128.4 ± 1982.4	P=0.404 (t- test)
Platelets count	225223.3 ± 79648.1	245129.1 ± 63670.1	P= 0.011 (Mann-Whitney test)

Table 2. Comparing Body Mass Index between the two groups

Body Mass Index	Study group (n=103)	Control group(n=62)
<20	6 (5.8%)	2 (3.2%)
20-25	31 (30.1%)	32 (51.6%)
25-30	49 (47.6%)	22 (35.5%)
30-40	17 (16.5%)	6 (9.7%)

Table 3. Comparing the Serum level of high sensitivity CRP between the two groups

Serum hs-CRP	Study group (n=103)	Control group(n=62)
< 1 mg/l (low risk)	10 (9.7%)	14 (22.6%)
1-3 mg/l (medium risk)	44 (42.7%)	32 (51.6%)
>3 mg/l (high risk)	49 (47.6%)	16 (25.8%)

Table 4. Comparing the concentration of Homocysteine between the two groups

Homocysteine	Study group (n=103)	Control group(n=62)
Normal Homocysteine	85 (82.5%)	62 (100%)
Abnormal Homocysteine	18 (17.5%)	0 (0.00%)

prevalence of coronary artery ectasia as 16.4%¹², whereas in three clinical trials conducted by the cardiology research center of Singapore's National University², Japan⁵ and Aristotle University of Greece⁸ the same value was estimated as 1.2%, 2.3% and 2.7%, respectively. The wide difference between our study and the prior reports could be due to the following issues: a different social, economical and cultural basis in our studied population, difference in the basic health level and the genetic background or a different general prevalence due to any etiology; these could only be proven by further and more precise researches.

A significant difference was observed between the two groups based on age ($p=0.032$); The mean age of the ectasia cases was less than the control group. This was similar to the study performed in China by Li *et al*¹³ but differed from the one conducted by Waly *et al* in Egypt where the mean age of the ectasia cases was higher than the controls¹².

Regarding that the study and control groups were matched for sex, no significant difference was observed on this basis ($p=0.823$). To note, 82.8% and 83.9% of the cases and controls were males, respectively. Although similar to findings from other reports, this could be due to the close relationship between coronary artery ectasia with atherosclerosis and underlying cardiovascular disorders which have a higher prevalence in males; it consequently results in more angiographic interventions in this gender.

When comparing the Total Body Mass index (BMI) in the study and control group by applying t-

test, no meaningful difference was detected ($p=0.182$), whereas after categorizing the cases based on Harrison's BMI grouping system, Mann-Whitney test showed a significant difference. It was seen that almost all the patients with coronary artery ectasia had a BMI over 25

while most of the controls had a normal BMI (20-25). The same results were achieved in Waly *et al* study¹².

Considering that smoking is a confirmed risk factor in cardiovascular diseases; it was also investigated in this research, where no significant difference was observed between the study and control groups (33% vs. 22.6%). Although this finding was in agreement with those from similar studies, but it could be said that as smoking is a major risk factor in cardiovascular diseases, therefore a remarkable divergence between patients with coronary artery ectasia and the controls with different degrees of atherosclerosis is not expected.

Since hypertension is a well-known risk factor for cardiovascular diseases, it was also taken into account in the current study. 58%, 54.7% and 31% of the patients in Lam, Mabuchi and Li^{2,5,13} studies had confirmed hypertension, respectively. None of the mentioned studies revealed any significant difference between the study and control groups. In the current study, 60.2% of the ectasia cases had hypertension but with no significant difference between the two groups ($p=0.182$). Hence, it seems that hypertension is not a specific risk factor for coronary artery ectasia, still a well-known risk factor for all cardiovascular diseases.

In the recent studies having been conducted worldwide, diabetes has been introduced as a protective factor against the development and progression of ectasia¹⁴⁻¹⁵. We expected a small number of diabetic cases among the ectasia patients, which it was also supported statistically with only 9.7% of the ectasia cases having diabetes concomitantly.

In the study performed in Singapore's National University 63% of the ectasia cases had hyperlipidemia² while in the study conducted in China by Li *et al*¹³, it was diagnosed in 16% of the ectasia cases. In the current study, hyperlipidemia had a 2.5 times higher prevalence in cases with coronary artery ectasia in comparison to controls (41.7% vs 16.1%). This finding was statistically significant based on the Chi-square test ($P=0.001$).

Regarding the findings from previous studies mentioning the role of inflammation in coronary artery ectasia, inflammatory factors such as hs-CRP were investigated in both the study

and control group which confirmed the expected significant difference between cases and controls in their level of hs-CRP ($P=0<001$). This finding was similar to those reported by Li *et al*¹³ and Yilmaz *et al*⁷ from China and Turkey, respectively.

In a research conducted in 2005 by Satran *et al*, the level of Homocysteine in the coronary artery ectasia cases was higher than the controls (14.9 mmol/L vs 8.6 mmol/L)¹⁶. In our study, the same level was higher in the ectasia cases in comparison to controls and the difference was statistically significant ($P=0.002$). The lowest Homocysteine level was 4.5 μ mol/L and 5.5 μ mol/L in males and females, respectively. The highest serum Homocysteine level was 355 μ mol/L and 195 μ mol/L in males and females respectively, which shows a higher Homocysteine concentration in males with coronary artery ectasia.

No significant difference was detected between the study and control group in their white blood cell count. However, the mean count was higher in the controls. In the study by Li *et al* a significant rise in white blood cell count was observed in coronary artery ectasia cases while no other report on this issue was found in the literature¹³.

CONCLUSION

The findings of this study show that hyperlipidemia, hs-CRP, and Homocysteine levels were 4.3, 1.5, 1.4 times higher in coronary ectasia cases in comparison to controls, respectively. Therefore, hyperlipidemia, high hs-CRP, and Homocysteine levels are introduced as cardiovascular risk factors in patients with ectasia in our region. Mean age and platelet count ratio in the study versus the control group was 0.9. This fact suggests that patients with a lower age and platelet count have a higher tendency for developing coronary artery ectasia.

Further studies are required in order to better clarify the role of various risk factors and the changes in different laboratory tests in patients with coronary artery ectasia and therefore provide a better path to understanding its etiology and subsequently the best possible predictors and methods required for its prevention.

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