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# Angiographic Profiling of Coronary Artery Ectasia in Relation to Matrix Metalloproteinase Enzyme

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## ABSTRACT

**Background:** Earlier literature proposed that coronary artery ectasia (CAE) might represent a manifestation of atherosclerosis, yet the connection between matrix metalloproteinase enzymes and both the presence and severity of CAE has remained insufficiently characterized.

**Objective:** This study aimed to determine the correlation between serum matrix metalloproteinase enzyme-9 (MMP-9) concentrations and the angiographically defined characteristics of CAE.

**Patients and methods:** A total of 100 cases with confirmed CAE were retrospectively analyzed for their clinical manifestations and angiographic patterns, with special emphasis on the correlation between CAE severity and serum MMP-9 levels. Evaluation of major cardiovascular risk factors was likewise performed.

**Results:** Among CAE cases, 45% exhibited elevated serum MMP-9 levels (>71 µg/dl). A substantial correlation was detected between MMP-9 levels and the extent of vascular involvement, being present in all cases with three-vessel ectasia compared to 43.38% with single-vessel disease (P = 0.035). Furthermore, higher MMP-9 levels were significantly associated with ectasia type, occurring in 83.33% of type 1 cases versus 40% of type 4 cases (P = 0.015).

**Conclusions:** Elevated serum MMP-9 levels were substantially correlated with both the occurrence of CAE and the degree of its severity.

**Keywords:** Coronary angiography, Coronary artery ectasia, Atherogenesis, Extracellular matrix, Matrix Metalloproteinase-9.

## INTRODUCTION

Coronary artery ectasia (CAE) represents a pathological dilatation of the coronary arteries, identified when the diameter of an affected segment is at least 1.5 times larger than that of an adjacent normal arterial portion [1, 2]. According to the conventional classification [3]: CAE is grouped into four types: Type I, diffuse ectatic changes in two or more vessels, type II, diffuse ectasia in one vessel associated with localized dilation in another, type III, diffuse ectasia confined to one vessel and type IV, localized segmental form. Despite extensive research, the mechanisms leading to CAE remain poorly characterized. MMPs—a group of zinc-dependent endopeptidases exhibiting proteolytic activity—are considered key mediators of abnormal extracellular matrix (ECM) degradation. These enzymes play roles in numerous physiological and pathological pathways, including embryonic development, tissue repair, reproductive function, tumor invasion, and certain dermatologic and pulmonary diseases. Emerging studies have strengthened the evidence implicating MMPs in the pathogenesis of CAE [4-7].

**Eitan and Roguin** [2] reported that the proteolytic activity of MMPs on ECM proteins, along with diminished circulating levels of their endogenous inhibitors, may underlie the pathogenesis of aortic aneurysms. Therefore, this investigation aimed to determine the relationship between serum levels of matrix metalloproteinase-9 (MMP-9) and the angiographically defined characteristics of CAE.

## PATIENTS AND METHODS

This retrospective analysis included 945 coronary angiography procedures performed at the Cardiovascular Department of Sohag Faculty of Medicine between July 2022 and August 2023. A total of 100 cases were diagnosed with CAE, yielding an estimated prevalence of 10.5%.

**Exclusion criteria:** Cases, which had a prior history of coronary angioplasty, aortocoronary bypass grafting, or existing valvular heart disease.

The collected variables included demographic information, major cardiovascular risk factors (hypertension, dyslipidemia, diabetes and smoking) and the indication for coronary angiography.

Angiographic imaging was conducted using a Philips Integris 2000 system (Philips, Harvey, IL 60426, USA) at 12.5 frames per second. The angiograms were assessed for (1) the coronary vessels affected by ectasia, (2) the number of ectatic arteries and (3) the type of ectasia (I–IV).

To determine serum MMP-9 levels, venous blood samples were collected nearly within one month after cases discharge. The specimens were centrifuged for 10 minutes at 4 °C, after which the serum was aliquoted and frozen at −20 °C. Quantification of MMP-9 was carried out using a Human MMP-9 ELISA kit (RayBioPantech,



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Norcross, GA 30092, Germany) based on the direct sandwich enzyme-linked immunosorbent assay method.

**Ethical considerations: This study was conducted after approval from the Research Ethics Committee of the Faculty of Medicine, Sohag University. Written informed consents were obtained from all participants prior to inclusion in the study. The consent form clearly stated their voluntary participation and agreement to the use and publication of anonymized data while ensuring full confidentiality and privacy of personal information. The study procedures adhered to the ethical principles outlined in the Declaration of Helsinki for research involving human subjects.**

**Statistical analysis**

All statistical analyses were conducted using STATA software version 14.2 (StataCorp LP, College Station, TX, USA). Continuous variables were presented as mean ± SD and compared using Student's t-test, whereas categorical variables were expressed as counts and percentages and analyzed with the Chi-square test. Graphical representations were generated using Microsoft Excel or STATA. A two-tailed P value ≤ 0.05 was considered indicative of statistical significance.

**RESULTS**

The studied population had a mean age of 52.24 ± 10.02 years. Males represented the majority (65%), while females accounted for 35%. Hypertension was present in 53% of participants, and diabetes mellitus in 43%. Smokers constituted 34%, whereas 66% were non-smokers. Dyslipidemia was observed in 52% of the study population (Table 1).

**Table (1):** Demographic data and risk factors

| Variable | Statistics/ percentage |
|---|---|
| **Age/year (**Mean ± SD*) | 52.24±10.02 |
| **Gender** | |
| Male | 65 (65%) |
| Female | 35 (35%) |
| **Hypertension** | |
| Hypertensive | 53 (53%) |
| Not hypertensive | 47 (47%) |
| **Diabetes** | |
| Diabetic | 43 (43%) |
| Not Diabetic | 57 (57%) |
| **Smoking** | |
| Yes | 34 (34%) |
| No | 66 (66%) |
| **Dyslipidemia** | |
| Yes | 52(52%) |
| No | 48(48%) |

***SD:** Standard deviation.

Regarding clinical characteristics, most patients presented with chronic coronary syndrome (64%), whereas acute coronary syndrome (ACS) was detected in 36%. The majority had single-vessel disease (83%), followed by two-vessel (14%) and three-vessel involvement (3%). The right coronary artery was the most frequently affected (55%), followed by the left anterior descending (48%) and left circumflex (17%) arteries. Based on Markis classification [3], type 4 ectasia was the predominant angiographic pattern (70%), while types 1, 2 and 3 represented 6%, 11%, and 13% respectively. The mean ± SD of MMP-9 was 176.18 ± 174.86 ng/ml with elevated levels found in 45% of patients (Table 2).

**Table (2):** Clinical presentation, angiographic criteria and MMP-9 level

| Variable | Statistics /percentage |
|---|---|
| **Clinical presentation** | |
| Acute coronary syndrome | 36 (36%) |
| Chronic coronary syndrome | 64 (64%) |
| **Number of ectatic vessels** | |
| One | 83 (83%) |
| Two | 14(14%) |
| Three | 3 (3%) |
| **Site of ectasia** | |
| Right coronary | 55 (55%) |
| Left anterior descending | 48 (48%) |
| Left circumflex | 17 (17%) |
| **Type of ectasia** | |
| Type 1* | 6 (6%) |
| Type 2† | 11 (11%) |
| Type 3‡ | 13 (13%) |
| Type 4 § | 70 (70%) |
| **MMP-9**¦ Mean ± SD (ng/ml) | 176.18±14.86 |
| **MMP-9 level** | |
| Elevated | 45 (45%) |

¦MMP-9: Matrix metalloproteinase-9, SD: Standard deviation, *: Type 1 – diffuse ectasia of two or three vessels, †: Type 2 – diffuse ectasia in one vessel and localized disease in another vessel, ‡: Type 3 – diffuse ectasia in one vessel only, §: Type 4 – localized or segmental involvement.

MMP-9 level showed a significant association with the number of ectatic vessels (P = 0.035). Patients with three ectatic vessels demonstrated elevated MMP-9 in all cases (100%), whereas those with one or two vessels had lower rates of elevation (43.38% and 42.86% respectively) (Table 3).

**Table (3):** Relation between MMP-9 level and number of ectatic arteries

| | Number of ectatic arteries | | | P value |
|---|---|---|---|---|
| | One n=83 | Two n=14 | Three n=3 | |
| **MMP-9*** | | | | |
| Normal | 47 (56.62%) | 8 (57.14%) | 0 | ***0.035*** |
| Elevated | 36 (43.38%) | 6 (42.86%) | 3 (100%) | |

*MMP-9: Matrix metalloproteinase-9

MMP-9 level was also significantly related to the type of ectasia (P = 0.015*). Elevated MMP-9 was most frequent among type 1 ectasia (83.33%), followed by type 2 (54.55%), type 3 (46.16%) and type 4 (40%) (Table 4 & Figure 1).

**Table (4):** Relation between MMP-9 level and type of ectasia

| | Type of ectasia | | | | P value |
|---|---|---|---|---|---|
| | Type 1* n=6 | Type 2† n=11 | Type 3‡ n=13 | Type 4§ n=70 | |
| **MMP-9¦** | | | | | |
| Normal | 1 (16.67%) | 5 (45.45%) | 7 (53.84%) | 42 (60%) | **0.015** |
| Elevated | 5 (83.33%) | 6 (54.55%) | 6 (46.16%) | 28 (40%) | |

¦MMP-9: Matrix metalloproteinase-9, *: Type 1 – diffuse ectasia of two or three vessels, †: Type II – diffuse ectasia in one artery together with localized disease in another, ‡: Type III – diffuse ectasia limited to a single artery, §: Type IV – segmental or localized ectatic change.

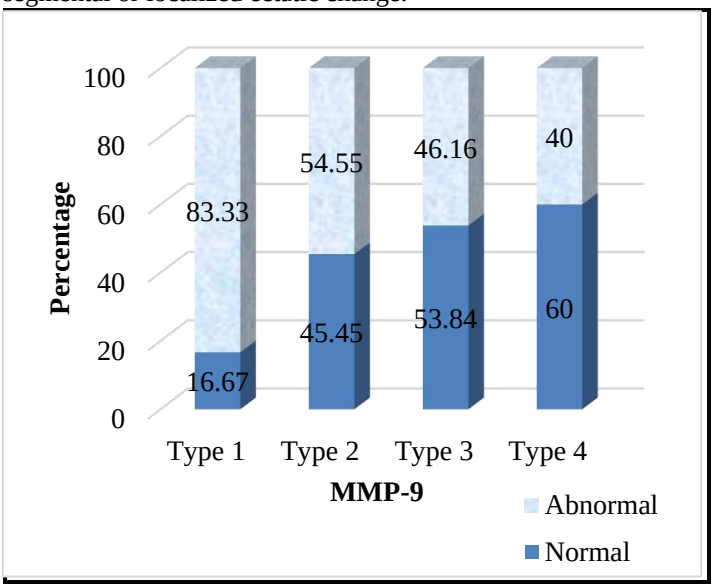


**Figure (1):** Relation between MMP-9 level and Type of ectasia.

## DISCUSSION

The present study investigated the association between specific serum matrix metalloproteinase (MMP-9) levels and angiographically defined patterns of coronary artery ectasia (CAE). The findings demonstrated a significant correlation between elevated MMP-9 concentrations and both the number of ectatic vessels and the Markis classification of ectasia type, suggesting that enzymatic degradation of the extracellular matrix may contribute to disease progression and severity. These results are consistent with the growing body of evidence linking MMP activity to vascular remodeling and atherogenesis, thereby reinforcing the role of MMP-9 as a potential biomarker of ectatic vessel pathology.

Supporting our results, **Eitan and Roguin** [2] as well as **Dahhan** [8] highlighted that the clinical implications of CAE—a condition of notable prevalence—have only been recognized in recent years. Data from earlier studies suggest that CAE affects between 1.4% and 7.4% of cases who undergo coronary angiography, with men being more frequently affected, as documented by **Giannoglou *et al.*** [9] and **Pinar *et al.*** [10].

A notable proportion of cases with CAE had major cardiovascular risk factors, with HTN detected in 85.1% of cases. Prior studies have described an inverse correlation between diabetes mellitus (DM) and coronary aneurysms. Although DM is a key risk factor for atherosclerosis, it appears to be less common among cases with coronary aneurysms, possibly due to its preference for inducing contraction-type over expansion-type vascular remodeling. This could explain the underrepresented diabetes in our study patients. These findings are in accordance with those of **Androulakis *et al.*** [11] and **Yetkin *et al.*** [12].

The Right coronary artery (RCA) demonstrated the greatest frequency of ectatic involvement, with the left anterior descending (LAD) and left circumflex (LCX) arteries affected to a lesser extent, whereas the left main coronary artery (LMCA) was rarely involved. These patterns align with previous reports by **Mavrogeni** [13] and **Lamblin *et al.*** [14].

CAE may present with variable clinical features and is frequently identified incidentally during evaluation for coronary artery disease (CAD) or ACS. According to **Akyürek *et al.*** [15], myocardial infarction and angina pectoris are considerably more prevalent in CAE ectasia, while **Baman *et al.*** [16] linked these ischemic events to disturbed coronary flow patterns. **Brunetti *et al.*** [17] and **Kuramochi *et al.*** [18] further suggested that slow or stagnant flow in dilated coronary segments can activate platelets, trigger the coagulation cascade, and favor thrombus formation.

In the current study, chronic coronary syndrome (64%) and ACS (36%) were the predominant reasons for coronary angiography with chronic coronary syndrome represented the major clinical manifestations of CAE.

Evidence from **Dogan *et al.*** [19] and **Dendramis *et al.*** [20] indicates that ECM imbalance and enzymatic remodeling play a key role in CAE pathogenesis. These

enzymes drive abnormal ECM degradation in response to biochemical and hemodynamic perturbations, resulting in excessive expansive remodeling and vessel dilation characteristic of CAE.

Within our study population, 45% of cases exhibited increased MMP-9 levels, which rose markedly in relation to the extent of vessel involvement and the degree of ectasia. Given that CAE and CAD often coexist and share overlapping histological features, CAE was historically regarded as a variant of atherosclerosis. Nonetheless, contemporary studies suggest that CAE represents an independent pathological entity. Although both conditions produce similar myocardial insults and clinical presentations, CAE exhibits an inverse correlation with age and DM. Additionally, CAE cases have higher serum MMP levels (correlated significantly with its type and number of ectatic vessels) and a greater tendency for right coronary artery involvement compared to those with CAD [21].

## LIMITATIONS

This study had some limitations. First, its retrospective design and relatively small sample size may limit the generalizability of the findings. Second, serum MMP-9 levels were measured at a single time point after hospital discharge, which may not fully reflect dynamic fluctuations during disease evolution. Finally, the single-center nature of the study may introduce selection bias, and further large-scale prospective studies are warranted to validate these results.

## CONCLUSIONS

Although the precise pathogenic mechanisms underlying CAE remain incompletely understood, ECM-degrading enzymes such as MMPs appear to play a crucial role in its pathogenesis. The present findings suggest a potential association between elevated MMP-9 levels and both the presence and extent of CAE.

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