The Egyptian Journal of Hospital Medicine (July 2022) Vol. 88, Page 2917-2922

Relationship between Monocyte to High Density Lipoprotein Cholesterol Ratio and Coronary Artery Tortuosity

Tarek Ahmed Naguib, El Sayed Mohamad Farag, Mohammad Abd Allah El Tahlawi, Ahmed Fathy Shawky
Department of Cardiology, Faculty of Medicine, Zagazig University, Egypt
***Corresponding Author:** Ahmed Fathy Shawky, **Mobile:** (+20)01004474020, **Email:** shawky_82@hotmail.com

ABSTRACT

Background: Coronary artery tortuosity (CorT) is a prevalent angiographic finding commonly associated with aging, hypertension, atherosclerosis and other cardiovascular conditions. It has been suggested that coronary artery tortuosity causes alteration in blood flow and reduction in coronary artery pressure distal to the tortuous segment and can thus lead to ischemia.

Objective: This study aimed to find the relationship between monocytes to high density lipoprotein cholesterol ratio (MHR) and isolated coronary artery tortuosity (CorT) without obstructive coronary artery disease (CAD). **Patients and Methods:** This study is an observational retrospective case control study that was performed in National Heart Institute and Zagazig University Hospital between January 2018 and January 2020 for patients with stable coronary artery disease that underwent coronary angiography. In this study 60 patients with chronic stable angina were enrolled, 30 patients showed Cor-T without obstructive CAD (cases) on coronary angiography, while the other 30 patients showed normal coronaries (Control).

Results: The most two predictable factors for the detection of Cor-T are MHR and C-reactive protein (CRP). In Cor-T group there was a significant positive correlation between the number of tortuous vessels and the MHR with P-value <0.001, the more number of tortuous vessels the higher MHR.

Conclusions: The relationships between the noninvasive laboratory index MHR and coronary artery tortuosity is significant. These findings consider MHR as an accurate, quantitative, non-invasive, highly available and non-expensive parameter for the prediction and detection of Cor-T and may be useful for risk stratification.

Keywords: Coronary artery disease, Coronary artery tortuosity, MHR, Monocyte to High Density Lipoprotein Cholesterol ratio.

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of both morbidity and mortality worldwide. It encompasses a wide clinical spectrum ranging from silent ischemia to sudden death[(1)].

Arterial tortuosity is characterized by multiple elongations in arteries, especially coronary arteries. It is usually detected during angiography. Few studies have evaluated this phenomenon and its etiology, signs, and complications have not yet been fully understood. Some studies have shown that coronary artery tortuosity (CorT) without coronary artery obstruction or atherosclerosis may cause angina pectoris during activity or exercise test[(2)].

Coronary artery tortuosity (CorT) is a prevalent angiographic finding commonly associated with aging, hypertension, atherosclerosis and other conditions. Preliminary evidence suggests that degradation of elastin, a key component of extracellular matrix in the vascular wall, may be responsible for the development of CorT. The clinical significance of CorT should be considered in several aspects[(3)].

Therefore, it has been suggested that coronary artery tortuosity causes alteration in blood flow and reduction in coronary artery pressure distal to the tortuous segment and can thus lead to ischemia. Severe tortuosity in coronary arteries facilitates atherosclerosis. As a result, atherosclerosis is more common in patients with coronary artery tortuosity[(2)]. Hemodynamic shear stress in tortuous arteries may enhance the formation and rupture of atherosclerotic plaques and prepare better conditions for developing acute coronary syndrome[(4)].

It has been shown that high monocyte count and low HDL-C levels may be relevant to inflammation[(5)] and oxidative stress[(6)], and it has been reported that the MHR is a new prognostic marker in several CVDs [(7)].

In the present study, we aimed to find the relationship between monocytes to high density lipoprotein cholesterol ratio (MHR) and isolated coronary artery tortuosity (CorT) without obstructive coronary artery disease.

PATIENTS AND METHODS

This study is a retrospective observational case control study that was performed in National Heart Institute and Zagazig University Hospital between January 2018 and January 2020 for patients with stable coronary artery disease that underwent coronary angiography. The study included 60 patients and they were divided into two groups; the case group consisted of 30 persons who had tortuous coronaries without obstructive CAD and the control group consisted of 30 persons who had normal coronaries.

Inclusion criteria:

Patients with chronic stable angina with evidence of myocardial ischemia in the form of treadmill electrocardiogram, dobutamine stress echo or nuclear perfusion stress imaging.

Received: 24/1/2022
Accepted: 23/3/2022

Exclusion criteria:

Patients with acute coronary syndrome (ACS) (STEMI or NSTEMI). Patients with left ventricular systolic dysfunction (left ventricular ejection fraction (LVEF) < 40%). Patients with malignancy. Patients with known liver diseases or elevated liver function tests (SGPT > 56 units/l and SGOT > 40 units/l) [8]. Patients with kidney diseases (serum creatinine more than 1.5 mg/dl) [8]. Patients with other acute or chronic inflammatory diseases. Patients that had previously undergone percutaneous coronary intervention or coronary artery bypass grafting.

All patients in the study were subjected to full history taking, full clinical examination and laboratory investigations including: CBC with differential count, CRP, T. cholesterol, TG, LDL, HDL, MHR, PLR, SGOT, SGPT, creatinine and HbA1c.

Echocardiography: 2D (including parasternal long-axis view, parasternal short-axis view, apical 4 – chamber view, apical 2 – chamber view and apical 5– chamber view), M-mode, pulsed wave Doppler and tissue Doppler imaging (TDI) were obtained for all patients to assess left ventricular (LV) systolic function and LV dimensions, LV diastolic function, interventricular septal (IVS) and posterior wall (PW) thickness, regional wall motion abnormalities (RWMA) and left ventricular mass index (LVMI).

(A) LV systolic function was calculated by Simpson's method as; End-diastolic volume minus end-systolic volume) divided by (end-diastolic volume). (B) LV diastolic function was assessed by pulsed wave Doppler and TDI. (C) IVSd and PWd thickness were measured in M-Mode. (D) LVMI was calculated for each patient as follows; LVMI (LV Mass Indexed to Body Surface Area) = LV Mass / BSA. LV Mass = 0.8 x (1.04 x ((LVEDD + IVSd +PWd)3 - LVEDD3) + 0.6.

Coronary Angiography:

Coronary angiography was done to all patients using GE, Toshiba and Siemens catheterization machines. The standard Judkins technique and 6Fr catheters was used to perform baseline angiography through the femoral or the radial artery. Coronary arteries were demonstrated in the left and right oblique planes in the cranial and caudal angles as well the lateral plane. All the angiograms were evaluated by two experienced physicians for the presence of tortuosity or not. CorT is defined as a fixed ≥3 bends during both systole and diastole, with each bend ≥45°. All patients were divided into two groups according to the presence of coronary tortuosity (CorT); Group 1 (Tortuous group) without coronary lesions and, Group 2 (Non-tortuous group) with normal coronaries.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were collected, tabulated, verified, revised and then edited on a personal computer. The data was then analyzed statistically by using SPSS statistical package version 16. Continuous data were expressed as mean ± standard deviation, and the categorical data were expressed as frequency and percentages. Continuous variables were tested for normal distribution using Kolmogorov-Smirnov test. Both groups were compared using chi-square test for qualitative variables, and independent t-test for normally distributed continuous variables. Pearson test was used in the correlation analysis between parametric variables. P value was considered significant if < 0.05.

RESULTS

Table (1) shows the demographic characteristics of the studied groups. There was a significant difference between the case and the control group as regard BMI where BMI was higher in group I. There was a significant difference between the two groups as regard gender. In group I, female cases represented 83.3% and male 16.7%. There was also a significant difference between the two groups as regard HTN where HTN was more in group I.

Table (1): Demographic characteristics of the studied groups

		Group I (No. 30)	**Group II** (No. 30)	Test of significance	P-value
Age (years) (Mean ± SD)		54.2 ± 6.8	54.23 ± 6.4	t = 0.019	0.98
BMI (kg/m^2) (Mean ± SD)		32.06 ± 2.27	29.52 ± 2.51	t = 4.103	P<0.001**
Gender	Male	5 (16.7%)	13 (43.3%)	X^2 = 5.07	0.024*
	Female	25 (83.3%)	17 (56.7%)	OR (95% CI) 0.26 (0.079-0.87)	
HTN	YES	24 (80%)	6 (20%)	X^2 = 21.6	<0.001**
	NO	6 (20%)	24 (80%)	OR (95% CI) 16 (4.5-56.6)	
DM	YES	13 (43.3%)	19 (63.3%)	X^2 = 2.41	0.12
	NO	17 (56.7%)	11 (36.7%)	OR (95% CI) 0.44 (0.15 – 1.24)	
Family History Of IHD	YES	5 (16.7%)	4 (13.3%)	X^2 = 0.13	0.71
	NO	25 (83.3%)	26 (86.7%)	OR (95% CI) 1.3 (0.3-5.4)	
Smoking	YES	5 (16.7%)	9 (30%)	X^2 = 1.49	0.22
	NO	25 (83.3%)	21 70%)	OR (95% CI) 0.46 (1.35-1.6)	

*: Significant, **: Highly significant

Table (2) shows the laboratory markers of the study groups. T. cholesterol and LDL were significantly higher in group I whereas HDL was significantly lower in group I.

Table (2): Laboratory markers of the studied groups

	Group I (No. 30) (Mean ± SD)	**Group II** (No. 30) (Mean ± SD)	**t**	**P**
T. Cholesterol (mg/dl)	190.86 ± 19.74	175.6 ± 23.27	2.7	**0.008****
T.G (mg/dl)	154.1 ± 8.12	125.6 ± 31.4	1.8	**0.75**
HDL (mg/dl)	33.67 ± 7.4	42.68 ± 8.21	-4.4	**<0.001****
LDL (mg/dl)	122.89 ± 17.2	111.19 ± 22.18	2.2	**0.026***
Creatinine (mg/dl)	0.92 ± 0.15	0.89 ± 0.15	0.78	**0.43**

*: Significant, **: Highly significant

Table (3) shows the inflammatory markers of the study groups. There was a significant difference between the two groups as regard CRP, monocytes and MHR, they were higher in group I.

Table (3): Inflammatory markers of studied groups

	Group I (No. 30) (Mean ± SD)	**Group II** (No. 30) (Mean ± SD)	**t**	**P**
CRP (mg/l)	11.7 ± 4.5	6.4 ± 1.48	6.07	**<0.001****
Monocytes 10^9/µL)	550 ± 40	360 ± 10	6.02	**<0.001****
Platelets (10^9/µL)	252100± 5900	276000 ± 7400	1.46	**0.14**
Lymphocytes (10^9/µL)	2420 ± 60	2100 ± 50	1.52	**0.13**
MHR	16.8 ± 3.97	8.4 ± 1.75	10.53	**<0.001****
PLR	116.3 ± 9.1	142.3 ± 5.14	1.9	**0.054**

**: Highly significant

Table (4) shows that there was a significant difference between the two groups as regard IVSd and PWd, which were higher in group I.

Table (4): EF, LV wall thickness, LV diastolic dysfunction and RWMA of the study groups

		Group I (No. 30)	**Group II** (No. 30)	**Test of significance**	**P**
IVSd (cm) (Mean ± SD)		1.07 ± 0.13	0.97 ± 0.11	t = 3.08	**0.003****
PWd (cm) (Mean ± SD)		1.01 ± 0.14	0.89 ± 0.12	t = 3.5	**0.001****
LV EF (%) (Mean ± SD)		62.83 ± 4.2	61 ± 5.3	t = 1.46	**0.14**
LV diastolic dysfunction	**Yes**	21 (70%)	5 (16.7%)	$X^2 = 0.64$	**0.42**
	No	9 (30%)	25 (83.3%)		
RWMA	**Yes**	11 (36.7%)	8 (26.7)	$X^2 = 3.7$	**0.054**
	No	19 (63.3)	22 (73.3)		

**: Highly significant

Table (5) shows that in males and females there was a significant higher value of LVMI in group I.

Table (5): LVMI of studied groups

	Group I (No. 30) (Mean ± SD)	**Group II** (No. 30) (Mean ± SD)	**T**	**P**
LVMI (Males) g/m^2	119.4000±26.51	107.3846±24.5123	4.167	**0.001****
LVMI (Females) g/m^2	96.3200±21.1235	92.3529±19.6142	2.396	**0.021****

**: Highly significant

Table (6) shows that there was 16 cases had tortuous LAD-LCX (53.3%). Also the most common vessel to have tortuosity was the left circumflex artery (LCX) (found tortuous in all the 30 cases (100% of cases)) then the left anterior descending artery (LAD) (found tortuous in 25 cases (83.3% of cases)) then the right coronary artery (RCA) (found tortuous in 12 cases (40% of cases)).

Table (6): Types of tortuous vessels in group I

Type of Cor-T	**Number of Cases**	**Percentage %**
LAD- LCX	16	53.3%
LAD-LCX-RCA	9	30%
LCX	2	6.7%
LCX-RCA	3	10%

Table (7) shows significant positive correlation between the number of tortuous vessels and the MHR, the more number of tortuous vessels the higher was MHR.

Table (7) Correlation between the number of tortuous vessels in Cor-T groups and MHR

		MHR
Number of Cor-T	Pearson Correlation (r)	0.865**
	Sig. (2-tailed) (P)	<0.001
	N	30

DISCUSSION

In this study we found a non-significant difference between the case group and the control group as regard age. On the other hand, previous studies revealed that coronary tortuosity may be associated with increased age [9,10].

Also in this study we found a significant difference between the case and the control group as regard BMI. On the contrary higher BMI was not associated with CorT in a study by **Ismail *et al.*** [11] in postmenopausal females.

In our study female patients have more significant Cor-T compared to male genders. In this study we found a highly significant difference between the Cor-T and non Cor-T groups regarding the presence of hypertension. Some authors suggested that Cor-T is a common finding seen with hypertension due to elongation and dilatation of the arteries associated with left ventricular hypertrophy[10, 12-14].

In our study the prevalence of LVH was more observed in the Cor-T group, and there was a significant difference between both groups regarding IVSd and PWd and a significant difference regarding LVMI. Coronary tortuosity has also been linked to the changes in the left ventricular geometry—namely concentric hypertrophy[15].

In our study there was no significant difference between the Cor-T and non Cor-T groups regarding the presence of DM, family history of IHD and smoking. In the study by **Levent and Zeynep**[10] Cor-T was independently associated with diabetes mellitus. Smoking has been shown as the probable risk factors of coronary tortuosity by other researchers[16].

Also in our study we found a significant difference between the two groups as regard CRP level. **Ismail *et al.*** [11] found that higher levels of hs-CRP were associated with the presence of Cor-T in a cohort of postmenopausal females. This may reflect heightened inflammatory state associated with Cor-T and provide indirect link between Cor-T and adverse cardiovascular events.

We studied the lipid profile of our patients and it was found that patients with Cor-T have significant higher levels of T. cholesterol and LDL and significant lower level of HDL while triglycerides did not differ significantly between the two groups. In other studies, raised LDL were associated with increased incidence of Cor-T. [13]. Cor-T patients had higher total cholesterol and LDL, and there was also a trend for higher HDL and triglycerides[17].

In a previous study conducted by **El Tahlawi *et al.*** [18], it showed that Cor-T was associated with subclinical atherosclerosis and increased coronary artery calcium score even in the absence of significant obstructive lesion.

In our study Cor-T group was associated with significant higher monocytes count **vs** non Cor-T group. Also in this study Cor-T group was associated with significant higher monocyte to high-density lipoprotein cholesterol ratio compared to non Cor-T group. Another study reported that high MHR values are associated with a greater severity and occurrence of isolated coronary artery ectasia[19]. It can be then hypothesized that there may be an association between a high monocyte count and a low HDL-C level in relation to the development coronary tortuosity.

In our study other marker of inflammation did not differ significantly between the two groups e.g. platelets, lymphocytes and platelet-to-lymphocyte ratio. On the other hand **Levent and Zeynep**[10] found that Cor-T was associated with increased PLR, even in the absence of coronary artery disease.

In this study, a multivariate analysis was done to show the most two predictable factors for the detection of Cor-T, they were MHR then CRP. We identified the cut off values for MHR (10.71) with 93% sensitivity and 94% specificity, while the cut off values for CRP (9.3) with 80% sensitivity and 97% specificity.

The current study demonstrates that higher monocyte to HDL-C ratio (MHR) was associated with the presence of Cor-T, this may add to the literature on the incompletely understood mechanism of Cor-T as a new marker, found to be related to Cor-T. The main pathophysiological links between MHR and Cor-T can be endothelial dysfunction and inflammation [19].

In our study the most common vessel to have tortuosity was the LCX (found tortuous in all the 30 cases) then the LAD (found tortuous in 25 cases) then the RCA (found tortuous in 12 cases). In agreement with our study, coronary tortuosity was most often observed in the left circumflex artery (LCX), followed by the left anterior descending artery (LAD), and the right coronary artery (RCA) [20].

This study was done on elective patients; some of them underwent stress testing before the coronary angiography. All patients with Cor-T who had an earlier stress test showed a positive test result for ischemia while having insignificant CAD. This may denote ischemia at a microvascular level, which suggests that Cor-T is not entirely benign. It is clear from the present study and other studies that Cor-T without significant CAD produces clinical symptoms like chronic stable angina with objective evidence of myocardial ischemia [20].

CONCLUSION

In conclusion, the study found that the relationships between the noninvasive laboratory index MHR and Coronary artery tortuosity is significant. These findings consider MHR as an accurate, quantitative, non-invasive, highly available and non-expensive parameter for the prediction and detection of Cor-T and may be useful for risk stratification.

The study recommends that using the monocytes to high density lipoprotein cholesterol ratio (MHR) as laboratory parameter for prediction and detection of

coronary artery tortuosity severity. More studies are needed to assess coronary artery tortuosity regarding causes, prediction and management. More studies are needed to assess MHR as a novel inflammatory marker. More studies are needed to assess MHR in coronary artery tortuosity on a larger scale of patients.

Conflict of interest: The authors declare no conflict of interest.

Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution: Authors contributed equally in the study.

REFERENCES

1. **Welch T, Yang E (2012):** Modern management of acute myocardial infarction. Curr Probl Cardiol., 37(7):237–310.
2. **Zegers E, Meursing B, Zegers E *et al.* (2007):** Coronary tortuosity: a long and winding road. Neth Heart J., 15(5):191-5.
3. **Chiha J, Mitchell P, Gopinath B *et al.* (2017):** Gender differences in the prevalence of coronary artery tortuosity and its association with coronary artery disease. Int J Cardiol Heart Vasc., 14: 23–27.
4. **Turgut O, Yilmaz A, Yalta K *et al.* (2007):** Tortuosity of coronary arteries: an indicator for impaired left ventricular relaxation? Int J Cardiovasc Imaging, 23: 671-677.
5. **Bolayir A, Gokce S, Cigdem B *et al.* (2017):** Monocyte high density lipoprotein ratio predicts the mortality in ischemic stroke patients. Neurologia I Neurochirurgia Polska, 52(2): 150–155.
6. **Acikgoz N, Kurtoğlu E, Yagmur J *et al.* (2017):** Elevated monocyte to high-density lipoprotein cholesterol ratio and endothelial dysfunction in Behçet disease. Angiology, 69(1): 65–70.
7. **You S, Zhong C, Zheng D *et al.* (2017):** Monocyte to HDL cholesterol ratio is associated with discharge and 3-month outcome in patients with acute intracerebral hemorrhage. Journal of the Neurological Sciences, 372: 157–161.
8. **Davis C, Shiel W (2022):** Liver function tests (Normal, low, and high levels and results). Medicine Net. https://www.medicinenet.com/liver_blood_tests/article.htm
9. **Satish G, Nampoothiri S, Kappanayil M (2008):** Images in cardiovascular medicine. Arterial tortuosity syndrome: phenotypic features and cardiovascular manifestations. Circulation, 117: 477–478.
10. **Levent C, Zeynep C (2017):** Relationship between coronary tortuosity and plateletcrit coronary tortuosity and plateletcrit. Cardiovasc J Afr., 28(6): 385–388.
11. **Ismail I, El-Sayed F, Mohamed T *et al.* (2020):** Relationship between sclerostin and coronary tortuosity in postmenopausal females with non-obstructive coronary artery disease. International Journal of Cardiology, 322: 29-33.
12. **Hutchins G, Bulkley B, Miner M *et al.* (1977):** Correlation of age and heart weight with tortuosity and caliber of normal human coronary arteries. Am Heart J., 94: 196–202.
13. **McEniery C, Wallace S, Mackenzie I *et al.* (2004):** C-reactive protein is associated with arterial stiffness in apparently healthy individuals. Arterioscler Thromb Vasc Biol., 24:969–74.
14. **Yang, Naifeng L, Zhong-ze G *et al.* (2012):** Coronary tortuosity is associated with reversible myocardial perfusion defects in patients without coronary artery disease. Chin Med J., 125(19): 3581–3583.
15. **Jakob M, Spasojevic D, Krogmann O *et al.* (1996):** Tortuosity of coronary arteries in chronic pressure and volume overload. Cathet Cardiovasc Diagn., 38:25–31.
16. **Khosravani-Rudpishi M, Joharimoghadam A, Rayzan E (2018):** The significant coronary tortuosity and atherosclerotic coronary artery disease; what is the relation? J Cardiovasc Thorac Res., 10(4):209-213.
17. **Elamragy A, Yakoub S, AbdelGhany M *et al.* (2021):** Coronary tortuosity relation with carotid intima-media thickness, coronary artery disease risk factors, and diastolic dysfunction: is it a marker of early atherosclerosis? Egypt Heart J., 73: 34-39.
18. **El Tahlawi M, Sakrana A, Elmurr A *et al.* (2016):** The relation between coronary tortuosity and calcium score in patients with chronic stable angina and normal coronaries by CT angiography. Atherosclerosis, 246:334–337.
19. **Kundi H, Kiziltunc E, Cetin M *et al.* (2016):** Association of monocyte/HDL-C ratio with SYNTAX scores in patients with stable coronary artery disease. Herz., 41: 523–9.
20. **Gupta A, Panda P, Sharma Y *et al.* (2018):** Clinical profile of patients with coronary tortuosity and its relation with coronary artery disease. International Journal of Cardiovascular Research, 4(2): 66-71.