High Serum Resistin Levels in Coronary Artery Ectasia

Muhammet Raşit Sayın[1], Mehmet Ali Çetiner[2], İshak Özel Tekin[3], Mustafa Aydın[1], İbrahim Akpınar[1], Turgut Karabağ[1], Aydan Özbay[1], Serpil Boz[1]

[1] Bülent Ecevit University Faculty of Medicine, Department of Cardiology, Zonguldak, Turkey
[2] Zonguldak Karadeniz Ereğli State Hospital, Clinic of Cardiology, Zonguldak, Turkey
[3] Bülent Ecevit University Faculty of Medicine, Department of Immunology, Zonguldak, Turkey

ABSTRACT

Introduction: The etiological and pathogenic factors responsible for coronary artery ectasia (CAE) are unclear. Therefore, we aimed to compare subjects with and without CAE with respect to resistin levels and determine whether resistin plays a role in the aetiology or pathogenesis of CAE.

Patients and Methods: This study enrolled a total of 81 subjects, of whom 42 had CAE [15 female (F), mean age 60.4 ± 9.0 years] and 39 had a normal coronary anatomy (22 F, mean age 56.2 ± 10.7 years). Using coronary artery diameters of the control group as reference, subjects having coronary artery dilatation that was at least 1.5 times larger than the normal adjacent segments were considered to have CAE. Resistin levels were measured from blood samples obtained on the day of the coronary angiography.

Results: Both the groups had similar baseline characteristics. Serum resistin levels were significantly higher in the CAE group [mean 703.5 ± 828.1 ng/L, median 379.5 (40-4092) ng/L] than in the control group [mean 313.5 ± 252.6 ng/L, median 256 (30-1244) ng/L] (p= 0.001).

Conclusion: CAE and atherosclerosis share common histopathological and clinical characteristics. Resistin, a polypeptide with a known role in the development and clinical presentation of atherosclerosis, may also mediate the formation of CAE. There is a need for future studies with a larger sample size to better delineate the effect of resistin on the development of CAE.

Key Words: Ectasia; resistin; adipokine

Resistin ve Koroner Arter Ektazisi

ÖZET

Giriş: Koroner arter ektazi (KAE)'den sorumlu olan etyolojik ve patojenik etmenler belirgin değildir. Bizler KAE'si olan ve olmayan olguları resistin düzeyleri açısından kıyaslamayı, böylelikle resistinin KAE patogenezinde bir rolü olup olmadığını saptamayı amaçladık.

Hastalar ve Yöntem: Çalışma 81 olgudan oluşmaktaydı. Olguların 42'sinde (15'i kadın, ortalama yaş 60.4 ± 9.0 yıl), KAE mevcut olup, 39 olguda (22'si kadın, ortalama yaş 56.2 ± 10.7 yıl) ise normal koroner arter anatomisi vardı. Normal komşu segmentlere kıyasla en az 1.5 kat koroner arter dilatasyonu mevcut olgular KAE olarak kabul edildiler. Koroner anjiyografinin gerçekleştirildiği gün alınan kan örneklerinde resistin düzeyleri ölçüldü.

Bulgular: Her iki grubun referans özellikleri benzerdi. Serum resistin düzeyi KAE grubunda [ortalama 703.5 ± 828.2 ng/L, ortanca 379.5 (40-492) ng/L] kontrol grubuna göre (ortalama 313.5 ± 252.6 ng/L, ortanca 256 (30-1244) ng/L] anlamlı şekilde daha yüksek saptandı (p= 0.001).

Sonuç: KAE ve aterosklerozis ortak histopatolojik ve klinik özellikler arz etmektedir. Resistin, aterosklerozun gelişiminde ve klinik tablonun oluşumundaki yeri iyi bilinen bir polipeptid olup, aynı zamanda KAE oluşumunda da rol alıyor olabilir. Resistinin KAE'nin oluşumunda ki yerinin daha iyi anlaşılabilmesi için büyük ölçekli çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Ektazi; resistin; adipokin

Correspondence

Muhammet Raşit Sayın

E-mail: sayinmr@mynet.com
Submitted: 12.02.2016
Accepted: 07.03.2016

@ Copyright 2016 by Koşuyolu Heart Journal.
Available on-line at
www.kosuyoluheartjournal.com

INTRODUCTION

Coronary artery ectasia (CAE) is defined as coronary artery dilatation that is at least 1.5 times larger than the normal adjacent segments or the largest coronary artery diameter[1]. The term ectasia describes diffuse dilatation of the coronary artery, and focal dilatation is termed as coronary aneurysm[2]. Primarily caused by atherosclerosis (50% of cases), it mainly occurs secondary to congenital malformations, connective tissue diseases, vasculitic syndromes and collagenopathies and following the coronary artery revascularization procedures[3]. Histopathologically, ectatic segments are characterized by a marked degradation of medial collagen and elastin fibrils and the disruption of internal and external elastic laminae[4]. In addition, alterations resembling advanced atherosclerosis have also been described, including lymphocyte and monocyte infiltration in the media and adventitia layers, neovascularization and intramural haemorrhage[5]. Enzymatic degradation of the media layer is the key pathogenetic factor for the development of CAE. Other factors related to the etiopathogenesis of the disorder include inflammatory factors (adhesion molecules, C-reactive protein, leukotrienes and adipokines), rennin-angiotensin system, nitric oxide and homocysteine[6].

Adipokines are a group of inflammatory proteins released primarily by adipocytes or the adipose tissue. Resistin (resistance to insulin) was first detected in 2001, when it was defined as a protein that serves as a bridge between obesity and diabetes by leading to insulin resistance[7]. It is released by the adipose tissue in mice, whereas its primary sources in humans are peripheral blood mononuclear cells, macrophages and bone marrow cells[8,9]. Human resistin is a 12.5 kDa cysteine-rich peptide with a 108-amino-acid-long mature sequence[10]. A large number of recent studies have suggested that resistin plays a role in many mechanisms responsible for atherosclerosis, including thrombosis, angiogenesis, smooth muscle cell migration and proliferation, endothelial dysfunction and inflammation, the latter two being the leading causes. In addition, in vitro experimental and clinical studies have investigated the role of resistin in the pathogenesis of atherosclerosis and coronary artery disease and in the prediction of major adverse cardiovascular events.

To the best of our knowledge, however, there are no other studies examining the role of resistin in CAE, a condition known to share a similar etiopathogenesis with coronary artery disease. The aim of this study was to explore resistin levels and investigate whether it plays a role in the etiopathogenesis of the disease.

PATIENTS and METHODS

Patient Population

The study subjects were selected from a patient population that underwent coronary angiography at our clinic between May 2012 and June 2013. Forty-two patients were diagnosed to have CAE, whereas 39 patients with angiographically normal coronary arteries were included as the control group. The study was approved by the local ethics committee and conducted in compliance with the Helsinki declaration. All the study subjects were informed about the study and provided written informed consent.

Inclusion Criteria

Forty-two patients having coronary arteries that were ≥ 1.5 times larger than the segments regarded as normal in a generalized manner along the coronary tree were placed in the ectasia group. The control group comprised 39 patients with similar risk factors and demographic properties and angiographically normal coronary arteries and flow properties.

Exclusion Criteria

In addition to the patients with acute coronary syndrome or a history of coronary revascularization, patients with connective tissue diseases, Kawasaki disease, inflammatory bowel disease, vasculitis, malignancy, heart failure (EF < 50%), chronic renal failure, chronic liver disease, chronic obstructive lung disease, infections or coronary plaques > 20% in coronary angiography were excluded from the study.

Study Design

The demographic characteristics of the patients were recorded and their medical history was taken. The risk factors for atherosclerosis and current drugs used by the patients were questioned. All the patients underwent a routine physical examination and blood pressure measurements were taken in addition to length, weight, waist circumference and body mass index measurements. Complete blood count, serum biochemistry, serum lipid panel and resistin levels were measured. The ejection fraction of the heart was calculated using Vivid 7.0 (GE Ultrasound, Horten, Norway) by the Simpson's biplane method of discs in a 2-dimensional echocardiographic examination.

Assessment of CAE with Coronary Angiography

Coronary angiography was performed via femoral artery puncture using the Philips Angioscop X-Ray device (Integris BH5000, Philips Medical Systems, Best, The Netherlands) in all the patients. All coronary angiography procedures were performed using the Judkins technique and 6F catheters but without any coronary vasodilator. The coronaries were imaged from the cranial and caudal angles to acquire right and left anterior oblique images. Two senior cardiologists, who were blinded to the demographic and clinical features as well as the biochemical results of the patients, reviewed all the angiographic sequences. Iohexol (Omnipaque, Ireland) was used as the contrast agent in all the patients. By convention, coronary arteries that were at least 1.5 times larger than the adjacent normal segments or the greatest coronary artery diameter were considered ectatic[1]. CAE patients were divided

into subgroups in accordance with the Markis classification system as follows: Type 1 CAE, diffuse ectasia in two or three vessels; Type 2 CAE, diffuse ectasia in one vessel and localized ectasia in at least one other vessel; Type 3 CAE, diffuse ectasia in one vessel; Type 4 CAE, localized and segmentary ectasias.

Resistin Measurement

Serum samples were collected after coronary angiography, centrifuged at 14000 rpm for 5 min, and stored at -70°C until the assay. A double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) method using the Human Resistin ELISA kit (Hangzhou Eastbiopharm, China) was used to measure the serum resistin levels.

Statistical Analysis

Study data were analysed using SPSS for Windows 16.0 (Chicago, Ill, USA). Here the mean ± standard deviation or median (minimum-maximum) are used for expressing the continuous variables, whereas the numbers and percentages are used for the categorical variables. The chi-square test was used to compare categorical variables, whereas the Kolmogorov-Smirnov test was used to test the normality of data. Groups were compared using the Independent t-test or Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

RESULTS

Among the 81 subjects enrolled, 42 (15 F, mean age 60.4 ± 9.0 years) formed the ectasia group and 39 (22 F, mean age 56.2 ± 10.7 years) formed the control group. There were no significant differences between the groups with respect to the demographic variables and atherosclerosis risk factors. No significant differences were observed between both the groups with regard to waist circumference, body mass index, fasting serum glucose and lipid panel. Ejection fractions of both the groups were similar (Table 1). Although the rate of cardiovascular drug use for any reason was higher in the ectasia group, the difference did not reach statistical significance (Table 2).

According to the Markis classification, 15 patients were placed in Group 1, 12 patients in Group 2, 8 patients in Group 3 and 7 patients in Group 4. The rate of CAE was 2.02 ± 0.8, with the left anterior descending artery being the most common vessel to be involved (81%). The corresponding rates for the right coronary artery and circumflex artery were 64% and 57%, respectively. Serum resistin levels were significantly higher in the CAE group than those in the control group [mean 703.5 ± 828.1 ng/L, median 379.5 (40-4092) ng/L and mean 313.5 ± 252.6 ng/L, median 256 (30-1244) ng/L, respectively; p= 0.001).

Table 1. Clinical characteristics of the study population

	Ectasia group n= 42	Control group n= 39	p value
Age (years)	60.4 ± 9.0	56.2 ± 10.7	0.064[a]
Sex (F) (n, %)	15 (36%)	22 (56%)	0.062[b]
SBP (mmHg)	133.9 ± 16.9	127.0 ± 14.3	0.053[a]
DBP (mmHg)	74.7 ± 10.0	71.0 ± 8.7	0.088[a]
WC (cm)	109.5 ± 10.3	109.2 ± 10.1	0.911[a]
BMI (kg/m^2)	30.4 ± 4.6 30.5 (23.0-39.6)	30.0 ± 6.2 28.4 (21.3-44.9)	0.542[c]
HT (n, %)	28 (67%)	18 (46%)	0.063[b]
DM (n, %)	14 (33%)	7 (18%)	0.114[b]
Smoking (n, %)	12 (29%)	12 (31%)	0.829[b]
DL (n, %)	12 (29%)	7 (18%)	0.260[b]
Family history (n, %)	10 (24%)	12 (31%)	0.482[b]
FBG (mg/dL)	127.2 ± 60.5 105 (72-330)	114.1 ± 37.5 104 (74-256)	0.567[c]
LDL-C (mg/dL)	105.3 ± 29.5	120.2 ± 45.8	0.154[a]
HDL-C (mg/dL)	40.2 ± 8.7	45.5 ± 10.6	0.053[a]
TC (mg/dL)	181.1 ± 32.3 181.5 (114-241)	197.3 ± 57.0 178 (136-354)	0.572[c]
TG (mg/dL)	175.7 ± 89.1	161.7 ± 67.7	0.528[a]
EF	62.7 ± 4.4	62.9 ± 4.2	0.884[a]

[a] Independent t-test, [b] Chi-square test, [c] Mann-Whitney U test.
BMI: Body mass index, DBP: Diastolic blood pressure, DM: Diabetes mellitus, DL: Dyslipidemia, EF: Ejection fraction, FBG: Fasting blood glucose, HDL-C: High-density lipoprotein cholesterol, HT: Hypertension, LDL-C: Low-density lipoprotein cholesterol, SBP: Systolic blood pressure, TC: Total cholesterol, TG: Triglycerides, WC: Waist circumference.

Table 2. Resistin levels, coronary angiographic characteristics and drugs of patients

	Ectasia group n= 42	Control group n= 39	p value
Resistin (ng/L)	703.5 ± 828.1 379.5 (40-4092)	313.5 ± 252.6 256 (30-1244)	0.001[a]
Distribution of ectasia			
LAD (n, %)	34 (81%)		
LCx (n, %)	24 (57%)		
RCA (n, %)	27 (64%)		
Number of involved vessels	2.02 ± 0.8		
One (n, %)	13 (31%)		
Two (n, %)	15 (36%)		
Three (n, %)	14 (33%)		
Beta blocker (n, %)	20 (48%)	11 (28%)	0.072[b]
ACE inhibitör/ARB (n, %)	24 (57%)	15 (38%)	0.093[b]
Calcium channel blocker (n, %)	14 (33%)	7 (18%)	0.114[b]
Statin (n, %)	7 (17%)	5 (13%)	0.626[b]
ASA (n, %)	23 (58%)	14 (36%)	0.089[b]

[a] Mann-Whitney U test, [b] Chi-square test.
ASA: Acetylsalicylic acid, ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, LAD: Left anterior descending coronary artery, LCx: Left circumflex coronary artery, RCA: Right coronary artery.

DISCUSSION

This study primarily demonstrated that subjects with CAE had significantly higher serum resistin levels compared with the control subjects who had normal coronary arteries on angiography.

CAE has a reported rate of 0.2% to 5.3% in different series[11-13]. Atherosclerosis is the primary factor leading to coronary artery ectasia and accounts for more than 50% of cases[1,14]. In addition, vasculitic syndromes, of which Kawasaki is the main disorder in children, collagenopathies, congenital malformations, infections, familial hypercholesterolemia and coronary artery revascularization procedures have been held responsible for the aetiology of this condition[15,16]. Histopathologically, ectasia and atherosclerosis have important common properties. Atheromatous plaque formation, degradation of medial elastic fibrils, disruption of elastic laminae and smooth muscle hyalinization are the main findings in both the conditions[4,17]. Histopathological findings suggest that ectasia represents a specific remodelling response as a result of local plaque formation in coronary arteries[18-20]. Previous studies have investigated the relationship between CAE and inflammatory factors, including adhesion molecules, C-reactive protein, vascular endothelial growth factor, leukotrienes and cytokinesand among adipokines and adiponectin[21-28]. However, there are no studies that have specifically sought out the relationship between CAE and serum resistin levels in adults.

Resistin is a cysteine-rich inflammatory protein in a polypeptide structure from the adipokine family, the role of which was first established in the emergence of insulin resistance and the development of diabetes mellitus[7]. Following the discovery of Reilly et al. that high resistin levels are associated with an increased coronary calcium score, the relationship of both the conditions has begun to attract attention[29]. Studies in literature have examined the role of resistin in stable angina pectoris, acute coronary syndrome (ACS) development and the prediction of myocardial ischaemia following an ACS[30-34]. On the other hand, Wang et al. reported that the resistin level increased in a stepwise fashion with the increasing number of coronary arteries stenosis to over 50% in patients with stable coronary artery disease[35]. Higher levels of resistin have been found to be linked to the occurrence of adverse events, such as cardiovascular death, myocardial infarction and restenosis in patients undergoing percutaneous coronary intervention[36,37]. Korah et al. reported that resistin levels significantly increased especially in ACS patients with type 2 diabetes mellitus and therefore it may be used as a diagnostic marker for diagnosing ACS[38]. Resistin impairs endothelial functions and causes the uptake of oxidized low density lipoprotein cholesterol and the formation of foam cells after being released by macrophages[39-41]. Resistin upregulates the release of adhesion molecules, increases the secretion of proinflammatory factors such as tumour necrosis factor-α, interleukin-6, interleukin-12, nitric oxide, endothelin-1 and matrix metalloproteinases and induces angiogenesis by increasing vascular epithelial growth factor[42-47]. It has also been reported that resistin exerts a prothrombotic effect by inducing the secretion of tissue factor[48]. Liu R et al., in a study investigating the relationship between adipokines and CAE in children with Kawasaki disease, found a significant relationship between the resistin level and inflammatory markers, and reported that levels of adiponectin, resistin and haemoglobin were significantly related to coronary artery aneurysm development in children with Kawasaki disease[49]. CAE has a clinical spectrum ranging from stable angina pectoris to acute coronary syndrome. In addition to atherosclerotic plaque formations accompanying ectatic segments, microembolism to the distal coronary bed, thrombotic occlusion of the ectatic arteries and slow flow phenomenon may be responsible from the clinical picture[50-52]. Canga et al. detected a significantly higher resistin level in subjects with a slow flow compared to those with a normal coronary blood flow[53]. Dagli et al. reported a significantly lower level of adiponectin, a cardioprotective adipokine, in patients with CAE compared to the control group in a study with 66 subjects. They also found a negative correlation between the diameter of the ectatic coronary artery and plasma adiponectin levels ($p= 0.03$, $r= -0.339$)[28]. We similarly found a higher resistin level, which is linked to atherosclerosis, in patients with coronary ectasia than those with normal coronaries.

Limitations of the Study

Our study has several limitations. Its sample size was relatively small. This is mainly because CAE is a rare disorder when not accompanied by coronary stenosis. In addition, it has a heterogeneous etiologic spectrum, which makes it difficult to collect a sufficient number of cases to form homogenous groups. We were unable to investigate a third control group of subjects with coronary artery disease and without CAE. Our study did not employ intravascular ultrasonography to diagnose patients. This may have flawed our results since intravascular ultrasonography studies have shown that it, along with autopsy studies, may well show diffuse atherosclerotic formations in the vessel wall even when the coronary angiography is found to be normal.

CONCLUSION

CAE and atherosclerosis share common histopathological and clinical characteristics. Resistin, a polypeptide with a known role in the development and clinical presentation of atherosclerosis, may also mediate the formation of CAE. Future studies with a larger sample size are clearly needed to elucidate the effect of resistin on the development of CAE.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: All of authors
Analysis/Interpretation: MRS, MAÇ, İÖT
Data Acquisition: MRS, İA, TK, AÖ, SB
Writing: MRS, MAÇ
Critical Revision: All of authors
Final Approval: All of authors

REFERENCES

1. Hartnell GG, Parnell BM, Pridie RB. Coronary artery ectasia. Its prevalence and clinical significance in 4993 patients. Br Heart J 1985;54:392-5.
2. Mavrogeni S. Coronary artery ectasia: from diagnosis to treatment. Hellenic J Cardiol 2010;51:158-63.
3. Ozcan OU, Gulec S. Coronary artery ectasia. Cor et Vasa 2013;55: e242-e247.
4. Swanton RH, Thomas ML, Coltart DJ, Jenkins BS, Webb-Peploe MM, Williams BT. Coronary artery ectasia--a variant of occlusive coronary arteriosclerosis. Br Heart J 1978;40:393-400.
5. Collins MJ, Borges AJ, Singh G, Pillai JB, David TE, Leong SW, et al. A giant coronary artery aneurysm in the right coronary artery. Cardiovasc Pathol 2006;15:150-2.
6. Antoniadis AP, Chatzizisis YS, Giannoglou GD. Pathogenetic mechanisms of coronary ectasia. Int J Cardiol 2008;130:335-43.
7. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. Nature 2001;409:307-12.
8. Janke J, Engeli S, Gorzelniak K, Luft FC, Sharma AM. Resistin gene expression in human adipocytes is not related to insulin resistance. Obes Res 2002;10:1-5.
9. Fain JN, Cheema PS, Bahouth SW, Lloyd Hiler M. Resistin release by human adipose tissue explants in primary culture. Biochem Biophys Res Commun 2003;300:674-8.
10. Jamaluddin MS, Weakley SM, Yao Q, Chen C. Resistin: functional roles and therapeutic considerations for cardiovascular disease. Br J Pharmacol 2012;165:622-32.
11. Swaye PS, Fisher LD, Litwin P, Vignola PA, Judkins MP, Kemp HG, et al. Aneurysmal coronary artery disease. Circulation 1983;67:134-8.
12. Tunick PA, Slater J, Kronzon I, Glassman E. Discrete atherosclerotic coronary artery aneurysms: a study of 20 patients. J Am Coll Cardiol 1990;15:279-82.
13. Boztosun B, Gunes Y, Kırma C. Koroner arter ektazisi-Coronary artery ectasia. Türk Kardiyol Dern Arş-Arch Turk Soc Cardiol 2005;33:356-9.
14. Syed M, Lesch M. Coronary artery aneurysm: a review. ProgCardiovasc Dis 1997;40:77-84.
15. Yetkin E, Waltenberger J. Novel insights into an old controversy: is coronary artery ectasia a variant of coronary atherosclerosis? Clin Res Cardiol 2007;96:331-9.
16. Manginas A, Cokkinos DV. Coronary artery ectasias: imaging, functional assessment and clinical implications. Eur Heart J 2006;27:1026-31.
17. Markis JE, Joffe CD, Cohn PF, Feen DJ, Herman MV, Gorlin R. Clinical significance of coronary arterial ectasia. Am J Cardiol 1976;37:217-22.
18. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316:1371-5.
19. Zarins CK, Weisenberg E, Kolettis G, Stankunavicius R, Glagov S. Differential enlargement of artery segments in response to enlarging atherosclerotic plaques. J Vasc Surg 1988;7:386-94.
20. Bentzon JF, Pasterkamp G, Falk E. Expansive remodeling is a response of the plaque-related vessel wall in aortic roots of apoE-deficient mice: an experiment of nature. Arterioscler Thromb Vasc Biol 2003;23:257-62.
21. Yilmaz H, Tayyareci G, Sayar N, Gurkan U, Tangurek B, Asilturk R, et al. Plasma soluble adhesion molecule levels in coronary artery ectasia. Cardiology 2006;105:176-81.
22. Turhan H, Erbay AR, Yasar AS, Aksoy Y, Bicer A, Yetkin G, et al. Plasma soluble adhesion molecules; intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin levels in patients with isolated coronary artery ectasia. Coron Artery Dis 2005;16:45-50.
23. Turhan H, Erbay AR, Yasar AS, Balci M, Bicer A, Yetkin E. Comparison of C-reactive protein levels in patients with coronary artery ectasia versus patients with obstructive coronary artery disease. Am J Cardiol 2004;94:1303-6.
24. Savino M, Parisi Q, Biondi-Zoccai GG, Pristipino C, Cianflone D, Crea F. New insights into molecular mechanisms of diffuse coronary ectasiae: a possible role for VEGF. Int J Cardiol 2006;106:307-12.
25. Zhao L, Moos MP, Gräbner R, Pédrono F, Fan J, Kaiser B, et al. The 5-lipoxygenase pathway promotes pathogenesis of hyperlipidemia-dependent aortic aneurysm. Nat Med 2004;10:966-73.
26. Brunetti ND, Salvemini G, Cuculo A, Ruggiero A, De Gennaro L, Gaglione A, et al. Coronary artery ectasia is related to coronary slow flow and inflammatory activation. Atherosclerosis 2014;233:636-40.
27. Aydin M, Tekin IO, Dogan SM, Yildirim N, Arasli M, Sayin MR, et al. The levels of tumor necrosis factor-alpha and interleukin-6 in patients with isolated coronary artery ectasia. Mediators Inflamm 2009:106145. doi: 10.1155/2009/106145.
28. Dagli N, Ozturk U, Karaca I, Yavuzkir M, Koca S, Akbulut H, et al. Adiponectin levels in coronary artery ectasia. Heart Vessels 2009;24:84-9.
29. Reilly MP, Lehrke M, Wolfe ML, Rohatgi A, Lazar MA, Rader DJ. Resistin is an inflammatory marker of atherosclerosis in humans. Circulation 2005;111:932-9.
30. Ohmori R, Momiyama Y, Kato R, Taniguchi H, Ogura M, Ayaori M, et al. Associations between serum resistin levels and insulin resistance, inflammation, and coronary artery disease. J Am Coll Cardiol 2005;46:379-80.

31. Pischon T, Bamberger CM, Kratzsch J, Zyriax BC, Algenstaedt P, Boeing H, et al. Association of plasma resistin levels with coronary heart disease in women. Obes Res 2005;13:1764-71.
32. Weikert C, Westphal S, Berger K, Dierkes J, Möhlig M, Spranger J, et al. Plasma resistin levels and risk of myocardial infarction and ischemic stroke. J Clin Endocrinol Metab 2008;93:2647-53.
33. Lubos E, Messow CM, Schnabel R, Rupprecht HJ, Espinola-Klein C, Bickel C, et al. Resistin, acute coronary syndrome and prognosis results from the Athero Gene study. Atherosclerosis 2007;193:121-8.
34. Chu S, Ding W, Li K, Pang Y, Tang C. Plasma resistin associated with myocardium injury in patients with acute coronary syndrome. Circ J 2008;72:1249-53.
35. Wang H, Chen DY, Cao J, He ZY, Zhu BP, Long M. High serum resistin level may be an indicator of the severity of coronary disease in acute coronary syndrome. Chin Med Sci J 2009;24:161-6.
36. Kreçki R, Krzemińska-Pakuła M, Peruga JZ, Szcześniak P, Lipiec P, Wierzbowska-Drabik K, et al. Elevated resistin opposed to adiponectin or angiogenin plasma levels as a strong, independent predictive factor for the occurrence of major adverse cardiac and cerebrovascular events in patients with stable multivessel coronary artery disease over 1-year follow-up. Med Sci Monit 2011;17:CR26-32.
37. Momiyama Y, Ohmori R, Uto-Kondo H, Tanaka N, Kato R, Taniguchi H, et al. Serum resistin levels and cardiovascular events in patients undergoing percutaneous coronary intervention. J Atheroscler Thromb 2011;18:108-14.
38. Korah TE, Ibrahim HH, Badr EA, ElShafie MK. Serum resistin in acute myocardial infarction patients with and without diabetes mellitus. Postgrad Med J 2011;87:463-7.
39. Burnett MS, Lee CW, Kinnaird TD, Stabile E, Durrani S, Dullum MK, et al.The potential role of resistin in atherogenesis. Atherosclerosis 2005;182:241-8.
40. Xu W, Yu L, Zhou W, Luo M. Resistin increases lipid accumulation and CD36 expression in human macrophages. Biochem Biophys Res Commun 2006;351:376-82.
41. Lee TS, Lin CY, Tsai JY, Wu YL, Su KH, Lu KY, et al. Resistin increases lipid accumulation by affecting class A scavenger receptor, CD36 and ATP-binding cassette transporter-A1 in macrophages. Life Sci 2009;84:97-104.
42. Jung HS, Park KH, Cho YM, Chung SS, Cho HJ, Cho SY, et al. Resistin is secreted from macrophages in atheromas and promotes atherosclerosis. Cardiovasc Res 2006;69:76-85.
43. Cosmacini P, Veronesi P, Zurrida S, Sacchini V, Ferranti C, Galimberti V, et al. [Nonpalpable breast lesions. General considerations and a review of the literature in the light of the authors' own experience with 344 cases located preoperatively]. [Article in Italian] Radiol Med 1992;83:383-9.
44. Chen C, Jiang J, Lü JM, Chai H, Wang X, Lin PH, et al. Resistin decreases expression of endothelial nitric oxide synthase through oxidative stress in human coronary artery endothelial cells. Am J Physiol Heart Circ Physiol 2010;299:H193-201.
45. Verma S, Li SH, Wang CH, Fedak PW, Li RK, Weisel RD, et al. Resistin promotes endothelial cell activation: further evidence of adipokine-endothelial interaction. Circulation 2003;108:736-40.
46. Ding Q, Chai H, Mahmood N, Tsao J, Mochly-Rosen D, Zhou W. Matrix metalloproteinases modulated by protein kinase Cε mediate resistin-induced migration of human coronary artery smooth muscle cells. J Vasc Surg 2011;53:1044-51.
47. Mu H, Ohashi R, Yan S, Chai H, Yang H, Lin P, et al. Adipokineresistin promotes in vitro angiogenesis of human endothelial cells. Cardiovasc Res 2006;70:146-57.
48. Calabrò P, Cirillo P, Limongelli G, Maddaloni V, Riegler L, Palmieri R, et al. Tissue factor is induced by resistin in human coronary artery endothelial cells by the NF-κB-dependent pathway. J Vasc Res 2011;48:59-66.
49. Liu R, He B, Gao F, Liu Q, Yi Q. Relationship between adipokines and coronary artery aneurysm in children with Kawasaki disease. Transl Res 2012;160:131-6.
50. al-Harthi SS, Nouh MS, Arafa M, al-Nozha M. Aneurysmal dilatation of the coronary arteries: diagnostic patterns and clinical significance. Int J Cardiol 1991;30:191-4.
51. Rab ST, Smith DW, Alimurung BN, Rab R, King SB 3rd. Thrombolytic therapy in coronary ectasia and acute myocardial infarction. Am Heart J 1990;119:955-7.
52. Papadakis MC, Manginas A, Cotileas P, Demopoulos V, Voudris V, Pavlides G, et al. Documentation of slow coronary flow by the TIMI frame count in patients with coronary ectasia. Am J Cardiol 2001;88:1030-2.
53. Canga A, Cetin M, Kocaman SA, Durakoğlugil ME, Kırbaş A, Erdoğan T, et al. Increased serum resistin levels in patients with coronary slow-flow phenomenon. Herz 2013;38:773-8.