Original Article

The relationship between radial artery spasm and adropin levels in patients undergoing transradial coronary angiography

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Abstract

Introduction: Transradial coronary angiography (TRA) is associated with a lower incidence of bleeding rate and access site complications and is associated with better outcomes compared to transfemoral angiography. However, radial artery spasm (RAS) is an important limitation of TRA procedures. Little is known regarding the relationship of serum vasodilator and inflammatory markers with RAS. Therefore, the present study aimed to investigate the association between serum adropin level and RAS in patients undergoing TRA.

Methods: From February 2020 to January 2021, 39 consecutive patients who underwent elective daiagnostic TRA and experienced RAS during the procedure, and 42 age and sex matched controls who did not experience RAS were prospectively included into the study. The groups were compared regarding serum adropin levels and inflammatory markers.

Results: Although adropin levels were found to be lower in the RAS group, this difference was not statistically significant between the the patients with RAS and controls (14.9 vs. 16.1, $P=0.105$). However, inflammatory parameters monocyte count and MHR (monocyte/HDL cholesterol ratio) were found to be statistically significantly higher in the RAS group compared to controls ($P=0.001$ and $P=0.010$, respectively). Moreover, a significant positive correlation was found between the monocyte count and RAS (r:0.360, $P<0.001$), and between MHR and RAS (r:0.288, $P=0.009$). Furthermore, multivariate analysis demonstrated that monocyte count (OR:1.671, 95%CI:1.312-2.094, $P=0.001$) and MHR (OR:1.116, 95%CI:1.054-1.448, $P=0.022$) were found to be independent predictors of RAS.

Conclusion: Serum vasodilator and inflammatory markers may be useful in the prediction of RAS in patients undergoing TRA procedures.

Introduction

Coronary angiography (CAG) is the gold standard imaging method in the diagnosis and treatment of atherosclerotic coronary artery disease (CAD) and transradial coronary angiography (TRA) is associated with a lower incidence of complications, particularly bleeding and access site complications, and seems to be associated with better outcomes compared to transfemoral angiography.[1,2] However, radial artery spasm (RAS) is an important complication and limitation of TRA procedures, because the radial artery is more prone to spasm development, since it has a large muscular media, smaller calibration, and higher receptor-mediated vascular movement.[3] Importantly, it has been shown that RAS may be responsible for up to 38% of all TRA procedure failures.[4,5] RAS generally presents as severe forearm pain combined with difficult manipulation of the catheter or sheath. Clinical predictors of RAS include presence of radial artery anomalies, catheter changes, pain during radial cannulation, using large-diameter catheters, female gender, and small radial artery diameter.[6,7] However, little is known regarding the relationship of serum vasodilator and inflammatory markers with RAS.

Adropin is an endogenous polypeptide produced in heart, brain, liver and coronary endothelial cells and increases the secretion of nitric oxide (NO) by increasing the activity of endothelial nitric oxide synthetase (eNOS) and causes vasodilation in the vessel wall with an indirect effect and has a potential endothelial protective role.[8] Importantly, reduced circulating adropin level is associated with endothelial dysfunction.[9] Moreover, serum adropin level seems to be decreased in patients with atherosclerotic CAD and coronary slow flow.[9,10] However, the association of serume adropin level with RAS which is triggered by endothelial dysfunction remains unclear. Therefore, the present study aimed to investigate the association between serum adropin level and RAS in patients undergoing TRA. Additionally, the association of inflammatory markers

Materials and Methods

Study design

From February 2020 to January 2021, 39 consecutive patients who underwent elective daiagnostic TRA and experienced RAS during the procedure, and 42 age and sex matched controls who did not experience RAS were prospectively included into the study. Patients with acute coronary syndromes, failed TRA or insufficient visualization of coronary arteries were excluded at baseline. Serum adropin levels were measured for all study participants and groups were compared regarding clinical parameters, inflammatory markers, and serum adropin levels. Demographic characteristics of the patients were recorded at the admission. Biochemical markers were measured from blood samples obtained after 12 hours of fasting. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, and/or treatment with antihypertensive drugs. Diabetes was defined as at least two fasting blood glucose levels of ≥ 126 mg/dL, or two-hour blood glucose levels of ≥200 mg/dL, or HbA1C level ≥ 6.5, or treatment with antidiabetic medications. Smoking was defined as active smoking.

The study was conducted in full accordance with the Declaration of Helsinki and approved by the local ethics committee. An informed consent was obtained from all study participants.

Adropin level measurement

Blood samples taken from the patients were centrifuged immediately and the plasmas of the centrifuged blood samples were placed in eppendorf tubes and stored at -80 ˚C until the day of analysis. Plasma samples were gradually thawed and homogenized on the day of the study. The plasmas were processed by keeping them at room temperature on the day of the study. Adropin levels were measured with the FineTest brand Human ENHO (Adropin) ELISA Kit (Wuhan, Fine Biotech Co., Wuhan, Hubei, China) with the ELISA method Sandwich principle. Human ENHO (Adropin) ELISA Kit's intra-assay CV < 8%, inter-assay CV < It is specified as 10% and its sensitivity is 9.375pg/ml.

Transradial angiography

TRA was performed according to its standard procedure. A 5cc (200 mcg glyceryl trinitrate and 3 cc prilocaine) local anesthesia was applied into the radial artery area. The radial artery was punctured with a 3.8 cm seldinger needle. Subsequently, a 6F radial sheath (7cm) was placed into the radial artery. After the sheath placement, intravenous 5000 units of heparin and 200 mcg of glyceryl trinitrate were routinely administered to all patients. A 0.035 inch hydrophilic or 0.032-inch teflon coated guide wires were used in the procedures to advance the angiography catheters (5F terumo radial catheter or 5F right and left diagnostic/guiding catheters). At the end of the TRA procedure, the sheath was removed, and the radial artery was compressed by the arm cuff. RAS was defined as acute onset pain in the patients' forearm or arm, and inability to advance the catheter or difficulty in the manipulation of the catheter.

Statistical analysis

Statistical analyses were performed using SPSS software version 22.0. Normality distribution of continuous variables was tested with Kolmogorov-Smirnov or Shapiro-Wilk tests. Descriptive variables were presented using medians and interquartile range for non-normally distributed variables. Since the continuous variables were not normally distributed, the Mann-Whitney U test was conducted to compare these parameters. Categorical data were compared using chi-square test or Fisher's exact test. Spearman correlation analysis was performed to demonstrate the correlation between RAS and laboratory parameters. Multivariate logistic regression analysis was performed to demonstrate the independent predictors of RAS. A p-value less than 0.05 was considered to indicate statistical significance.

Results

The median age of the study participants was 63 years with 59.3% being female. The frequency of hypertension, diabetes and smoking in the study population was 64.2%, 44.4% and 19.8%, respectively. Importantly, there was no statistically significant difference between the patients with RAS and control group regarding cardiovascular risk factors. When comparing the groups regarding adropin levels, although adropin levels were found to be lower in the RAS group, this difference was not statistically significant between the the patients with RAS and controls (14.9 vs. 16.1, p = 0.105). However, in the laboratory analysis, inflammatory parameters monocyte count and MHR (monocyte/HDL cholesterol ratio) were found to be statistically significantly higher in the RAS group compared to controls (p = 0.001 and p = 0.010, respectively). Table 1 demonstrates the clinical and laboratory characteristics of the patient groups. In the gender basis analysis, no statistically significant difference was observed between male and female patients regarding adropin levels (15.9 vs. 15.8, p = 0.475). Importantly, there was a trend toward lower adropin levels in patients with RAS compared to controls in female patients; however, this difference was not statistically significant (14.8 vs. 16.6, p = 0.053). Conversely, adropin levels were found to be numerically higher in patients with RAS compared to controls in male patients; however, this difference was not also statistically significant (16.0 vs 14.4, p = 0.797). Table 2 shows the adropin levesl of female and male patients.

In the correlation analysis, a significant positive

Table 1. Clinical and laboratory characteristics of study participants

Variables	All patients (n=81)	RAS (n=39)	No RAS (n=42)	P
Age; median (IQR)	63.0 (55.0; 67.0)	63 (54.5; 66.0)	61.5 (55.0; 67.0)	0.943
Females; n (%)	48 (59.3%)	24 (61.5%)	24 (57.1%)	0.687
Diabetes n (%)	36 (44.4%)	20 (51.3%)	16 (38.1%)	0.233
Hypertension n (%)	52 (64.2%)	27 (69.2%)	25 (59.5%)	0.363
Previous CAD; n (%)	16 (19.8%)	6 (15.4%)	10 (23.8%)	0.341
Smoking; n (%)	16 (19.8%)	8 (20.5%)	8 (19.0%)	0.869
Ad-hoc PCI n (%)	28 (34.6%)	13 (33.3%)	15 (35.7%)	0.822
Adropin (ng/ml) median (IQR)	15.9 (11.9; 18.2)	14.9 (6.6; 17.5)	16.1 (12.1; 18.6)	0.105
Creatinine (mg/dl) median (IQR)	0.79 (0.69; 0.95)	0.80 (0.69; 0.95)	0.77 (0.63; 0.95)	0.640
BMI (kg/m²)	29.4 (25.9; 32.1)	30.1 (27.0; 32.8)	27.9 (25.6; 31.2)	0.204
AST(U/L)	18.3 (14.7; 23.0)	18.3 (14.6; 22.3)	18.3 (15.1; 23.1)	0.813
WBC (10³ /mL)	7.2 (6.0; 8.6)	7.8 (6.8; 8.7)	6.9 (6.0; 8.0)	0.070
HGB (gr/dl)	13.1 (12.2; 14.5)	12.8 (12.0; 14.9)	13.3 (12.6; 14.2)	0.561
PLT (10³ /uL)	265 (217;313)	248 (212; 304)	269 (223; 323)	0.182
TSH	1.39 (0.85; 1.99)	1.56 (0.82; 2.09)	1.27 (0.87; 1.89)	0.319
Total Cholesterol (mg/dl)	177 (147; 198)	182 (152; 201)	169 (137; 196)	0.123
LDL-Cholesterol (mg/dl)	120 (91; 142)	124 (103; 141)	112 (81; 140)	0.151
HDL-Cholesterol (mg/dl)	41.2 (36.5; 47.9)	41.4 (35.9; 47.5)	41.1 (36.6; 48.2)	0.777
Triglyceride (mg/dl)	142 (112; 222)	165 (119; 232)	128 (109; 210)	0.183
Neutrophil (10³ /uL)	4.27 (3.53; 5.30)	4.50 (3.95; 5.46)	3.90 (3.17; 5.10)	0.072
Lymphocyte (10³ /uL)	2.12 (1.73; 2.52)	2.02 (1.71; 2.54)	2.13 (1.75; 2.48)	0.839
NLR	1.85 (1.50; 2.78)	2.17 (1.58; 2.84)	1.63 (1.46; 2.49)	0.127
PLR	125 (93; 161)	120 (94; 151)	126 (96; 161)	0.593
Monocytes (10³ /uL)	0.52 (0.40; 0.66)	0.58 (0.45; 0.73)	0.44 (0.34; 0.56)	**0.001**
MHR	12.5 (9.2; 17.4)	13.4 (10.9; 18.1)	10.6 (7.4; 15.4)	**0.010**

Abbreviations: RAS, radial artery spasm; IQR, interquartile range; CAD, coronary arter disease; BMI, body-mass index; AST, aspartate aminotransferase; WBC, white blood cell; HGB, hemoglobin; PLT, Platelet; TSH; thyroid stimulating hormone; LDL-cholesterol, low density lipoprotein cholesterol; HDL-cholesterol, high density lipoprotein cholesterol; NLR, Neutrophil/Lymphocyte ratio; PLR, Platelet/lymphocyte ratio; MHR, Monocytes/high density lipoprotein cholesterol ratio

correlation was found between the monocyte count and RAS (r:0.360, p<0.001), and between MHR and RAS (r:0.288, p = 0.009). Furthermore, multivariate analysis demonstrated that monocyte count (OR:1.671, 95%CI:1.312-2.094, p = 0.001) and MHR (OR:1.116, 95%CI:1.054-1.448, p = 0.022) were found to be independent predictors of RAS in patients undergoing TRA. Table 3 shows independent predictors of RAS in multivariate analysis

Discussion

The present study demonstrated that serum adropin level was not associated with RAS occurrence in patients undergoing TRA. However, the relationship of adropin level with RAS was inverse in male and female patients. Moreover, inflammatory markers monocyte count and MHR were found to be significantly associated with RAS emergence, and both parameters were found to be independent predictors of RAS in patients undergoing TRA. To the best of our knowledge, this the the first study that investigated the clinical usefulness of adropin

in patients undergoing TRA. Furthermore, our results revaled that inflammatory parameters may be useful in

Table 2. Adropin levels of gender subgroups

Variables	Adropin (median, IQR)	P
Males (n=33) Females (n=48)	15.9 (9.3, 18.2) 15.8 (12.4, 18.2)	0.475
Females (n=48);		
RAS (n=24)	14.8 (6.8, 17.5)	0.053
No RAS (n=24)	16.6 (14.6, 18.5)	
Males (n=33);		
RAS (n=15)	16.0 (8.7, 17.3)	0.797
No RAS (n=18)	14.4 (9.6, 18.6)	

Abbreviations: IQR, interquartile range; RAS, radial artery spasm

Table 3. Independent predictors of radial artery spasm in multivariate analysis

Variables	Odds Ratio	95% Confidence interval	P
MHR	1.116	1.054-1.448	**0.022**
Monocyte count	1.671	1.312-2.094	**0.001**

Abbreviations: MHR, Monocytes/ High density lipoprotein cholesterol ratio

the prediction of RAS in patients undergoing TRA.

TRA is the recommended method for patients undergoing CAG and is associated with reduced bleeding rates and better outcomes compared to transfemoral angiography.[1,2] Also, TRA is associated with early mobilization, improved patient comfort, reduced access site and cardiovascular complications and reduced hospital stay.[11] RAS is an important complication that may occur during TRA procedures. Radial artery is prone to spasm due its small caliber, large muscular media and a higher receptor-mediated vascular movement.[3,12] Importantly, RAS is more common in women, and its frequency rises when the number of catheters used, and manipulation increases.[6,7] Moreover, a decrease in the NO levels, which is a vasoactive substance produced from the endothelium and plays an important role in vascular tonus, seems to be associated with RAS occurrence in patients undergoing TRA procedures.[13] Adropin increases the release of NO by increasing eNOS activity, causes vasodilation in the vessel wall with an indirect effect and has a potential endothelial protective role. Adropin plays a protective role against endothelial dysfunction by regulating eNOS expression through various growth factors and proteins.[14] Importantly, it has been demonstrated that decreased serum adropin level is significantly associated with CAD.[9,15,16] Therefore, decreased adropin level may lead endothelial dysfunction that may cause vascular damage and increased vascular tonus. In the present study, there was a trend toward lower adropin levels in patients with RAS compared to controls. However, this difference was not statistically significant. The small number of patients may be the main reason in the lack of statistical significance of this difference. Since the adropin has an endhotelial protective role and causes vasodilation, larger studies may be useful in the defining the association of adropin with RAS emergence in patients undergoing TRA procedures.

Another important finding of our study is that a significant association of inflammatory markers monocyte count and MHR with RAS was demonstrated. Inflammation plays an important role in the pathophysiology of endothelial dysfunction and atherosclerosis and has a significant effect on vascular tonus.[17] However, little is known regarding the the relationship of inflammatory markers with RAS in patients undergoing TRA procedures. Monocytes are a source of various cytokines and molecules that interact with endothelial cells and are one of the most important cells in the inflammation. Also, monocytes play an important role in the vascular inflammation and atherosclerosis.[18] Previous studies have shown that the number of circulating monocytes is increased in people with atherosclerotic disease, and increased monocyte count can independently predict cardiovascular events.[19,20] Additionally, increased monocyte count seems to be associated with deterioration in the vascular structure.[21] MHR is also an important inflammatory marker, and it is associated with major cardiovascular adverse events in

patients with CAD.[22,23] MHR seems to be associated with increased oxidative stress and inflammatory status in patients with CAD, and is a predictor of severe and complex coronary atherosclerosis.[24,25] Also, increased MHR is a sign of endothelial dysfunction, and is significantly associated with abnormal vascular structure and functions.[26-28] Therefore, current evidence suggest that monocyte count and MHR seem to be associated with inflammation and endothelial dysfunction in patients with CAD. Our results revealed that both inflammatory markers were independently associated with RAS emergence and may be useful in clinical practice to distinguish the high-risk patients for RAS in patients undergoing TRA procedures.

The present study has some limitations. First, low sample volume and study power is the major limitation. However, it should be considered that the study was conducted during the covid-19 pandemic. Larger studies are necessary to demonstrate the association between adropin level and RAS. Second, since the radial artery angiography was not routinely performed during TRA procedures, radial artery diameter could not be measured. In this study, RAS was defined according to clinical findings and new onset symptoms, like previous studies.

Conclusion

The present study demonstrated that serum adropin level was found to be lower in patients experienced RAS compared to the controls, however, this difference was not statistically significant. The relationship of adropin with RAS needs to be investigated in larger studies. Moreover, a significant association between inflammatory markers and RAS was found. Monocyte count and MHR were found to be independent predictors of RAS in patients undergoing TRA procedures. Since the endothelial dysfunction and inflammation seem to be associated with occurrence of RAS, endothelial biomarkers and inflammatory parameters may be useful in clincal practice to define the patients at high-risk for emergence of RAS during TRA procedures.

Competing interest
The authors declare that they have no conflicts of interest.

References
1. Jolly SS, Yusuf S, Cairns J, Niemelä K, Xavier D, Widimsky P, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. **Lancet**. 2011;377(9775):1409-1420. doi:10.1016/s0140-6736(11)60404-2
2. Andò G, Capodanno D. Radial access reduces mortality

in patients with acute coronary syndromes: results from an updated trial sequential analysis of randomized trials. **JACC Cardiovasc Interv**. 2016;9(7):660-670. doi:10.1016/j.jcin.2015.12.008

3. He GW, Yang CQ. Radial artery has higher receptor-mediated contractility but similar endothelial function compared with mammary artery. **Ann Thorac Surg**. 1997;63(5):1346-1352. doi:10.1016/s0003-4975(97)00106-9

4. Chugh SK, Chugh Y, Chugh S. How to tackle complications in radial procedures: tip and tricks. **Indian Heart J**. 2015;67(3):275-281. doi:10.1016/j.ihj.2015.05.016

5. Ball WT, Sharieff W, Jolly SS, Hong T, Kutryk MJ, Graham JJ, et al. Characterization of operator learning curve for transradial coronary interventions. **Circ Cardiovasc Interv**. 2011;4(4):336-341. doi:10.1161/circinterventions.110.960864

6. Ruiz-Salmerón RJ, Mora R, Masotti M, Betriu A. Assessment of the efficacy of phentolamine to prevent radial artery spasm during cardiac catheterization procedures: a randomized study comparing phentolamine vs. verapamil. **Catheter Cardiovasc Interv**. 2005;66(2):192-198. doi:10.1002/ccd.20434

7. Varenne O, Jégou A, Cohen R, Empana JP, Salengro E, Ohanessian A, et al. Prevention of arterial spasm during percutaneous coronary interventions through radial artery: the SPASM study. **Catheter Cardiovasc Interv**. 2006;68(2):231-235. doi:10.1002/ccd.20812

8. Lovren F, Pan Y, Quan A, Singh KK, Shukla PC, Gupta M, et al. Adropin is a novel regulator of endothelial function. **Circulation**. 2010;122(11 Suppl):S185-192. doi:10.1161/circulationaha.109.931782

9. Zheng J, Liu M, Chen L, Yin F, Zhu X, Gou J, et al. Association between serum adropin level and coronary artery disease: a systematic review and meta-analysis. **Cardiovasc Diagn Ther**. 2019;9(1):1-7. doi:10.21037/cdt.2018.07.09

10. Zhao ZW, Ren YG, Liu J. Low serum adropin levels are associated with coronary slow flow phenomenon. **Acta Cardiol Sin**. 2018;34(4):307-312. doi:10.6515/acs.201807_34(4).20180306b

11. Feldman DN, Swaminathan RV, Kaltenbach LA, Baklanov DV, Kim LK, Wong SC, et al. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: an updated report from the national cardiovascular data registry (2007-2012). **Circulation**. 2013;127(23):2295-2306. doi:10.1161/circulationaha.112.000536

12. He GW, Yang CQ. Characteristics of adrenoceptors in the human radial artery: clinical implications. **J Thorac Cardiovasc Surg**. 1998;115(5):1136-1141. doi:10.1016/s0022-5223(98)70414-3

13. Kocayigit I, Cakar MA, Kahyaoğlu B, Aksoy MNM, Tatli E, Akdemir R. The relationship between serum asymmetric dimethylarginine levels and radial artery spasm. **Anatol J Cardiol**. 2020;23(4):228-232. doi:10.14744/AnatolJCardiol.2020.93213

14. Kumar KG, Trevaskis JL, Lam DD, Sutton GM, Koza RA, Chouljenko VN, et al. Identification of adropin as a secreted factor linking dietary macronutrient intake with energy homeostasis and lipid metabolism. **Cell Metab**. 2008;8(6):468-481. doi:10.1016/j.cmet.2008.10.011

15. Küçükosmanoğlu M, Kaplan M, Yavuz F. Serum Adropin Level in Patients with Isolated Coronary Artery Ectasia. **Eur J Ther**. 2020;26(3):178-82. doi:10.5152/eurjther.2020.19119

16. Yosaee S, Soltani S, Sekhavati E, Jazayeri S. Adropin- a novel biomarker of heart disease: a systematic review article. **Iran J Public Health**. 2016;45(12):1568-1576.

17. Raggi P, Genest J, Giles JT, Rayner KJ, Dwivedi G, Beanlands RS, et al. Role of inflammation in the pathogenesis of atherosclerosis and therapeutic interventions. **Atherosclerosis**. 2018;276:98-108. doi:10.1016/j.atherosclerosis.2018.07.014

18. Ozaki Y, Imanishi T, Taruya A, Aoki H, Masuno T, Shiono Y, et al. Circulating CD14+CD16+ monocyte subsets as biomarkers of the severity of coronary artery disease in patients with stable angina pectoris. **Circ J**. 2012;76(10):2412-2418. doi:10.1253/circj.cj-12-0412

19. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood cell subtypes predict increased cardiovascular risk? **J Am Coll Cardiol**. 2005;45(10):1638-1643. doi:10.1016/j.jacc.2005.02.054

20. Olivares R, Ducimetière P, Claude JR. Monocyte count: a risk factor for coronary heart disease? **Am J Epidemiol**. 1993;137(1):49-53. doi:10.1093/oxfordjournals.aje.a116601

21. Demir M, Demir C, Keceoglu S. The relationship between blood monocyte count and coronary artery ectasia. **Cardiol Res**. 2014;5(5):151-154. doi:10.14740/cr315w

22. Canpolat U, Çetin EH, Cetin S, Aydin S, Akboga MK, Yayla C, et al. Association of monocyte-to-HDL cholesterol ratio with slow coronary flow is linked to systemic inflammation. **Clin Appl Thromb Hemost**. 2016;22(5):476-482. doi:10.1177/1076029615594002

23. Cetin EH, Cetin MS, Canpolat U, Aydin S, Topaloglu S, Aras D, et al. Monocyte/HDL-cholesterol ratio predicts the definite stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. **Biomark Med**. 2015;9(10):967-977. doi:10.2217/bmm.15.74

24. Kundi H, Kiziltunc E, Cetin M, Cicekcioglu H, Cetin ZG, Cicek G, et al. Association of monocyte/HDL-C ratio with SYNTAX scores in patients with stable coronary artery disease. **Herz**. 2016;41(6):523-529. doi:10.1007/s00059-015-4393-1

25. Akboga MK, Balci KG, Maden O, Ertem AG, Kirbas O, Yayla C, et al. Usefulness of monocyte to HDL-cholesterol ratio to predict high SYNTAX score in patients with stable coronary artery disease. **Biomark Med**. 2016;10(4):375-383. doi:10.2217/bmm-2015-0050

26. Acikgoz N, Kurtoğlu E, Yagmur J, Kapicioglu Y, Cansel M, Ermis N. Elevated monocyte to high-density lipoprotein cholesterol ratio and endothelial dysfunction in Behçet disease. **Angiology**. 2018;69(1):65-70. doi:10.1177/0003319717704748

27. Cagli K, Tok D, Turak O, Gunertem E, Yayla C, Lafci G, et al. Monocyte count-to-high-density lipoprotein-cholesterol ratio is associated with abdominal aortic aneurysm size. **Biomark Med**. 2016;10(10):1039-1047. doi:10.2217/bmm-2016-0157

28. Kundi H, Gok M, Kiziltunc E, Cetin M, Cicekcioglu H, Cetin ZG, et al. Relation between monocyte to high-density lipoprotein cholesterol ratio with presence and severity of isolated coronary artery ectasia. **Am J Cardiol**. 2015;116(11):1685-1689. doi:10.1016/j.amjcard.2015.08.036