



BÖLÜM 22

KORONER ARTER HASTALIKLARININ TANISINDA GELİŞMELER

Fatih KOCA¹

GİRİŞ

Koroner arter hastalıkları (KAH) günümüzde dünya genelinde başta gelen ölüm sebebidir. Bu nedenle KAH'ın erken ve doğru teşhisi çok önemlidir. KAH'ın ana sebebi ateroskleroza bağlı gelişen koroner obstrüksiyon olmakla birlikte, uygun endikasyonla anjiyografi yapılan hastaların %50' sine yakınında obstrüktif olmayan KAH tespit edilmektedir (1). Bu hastalarda miyokardiyal iskemiyi belirleyen bir çok mekanizma sorumlu olabilir. Özellikle epikardiyal damarlar ve koroner mikrodolaşımındaki vazomotor koroner bozukluklar miyokardiyal iskeminin olası sebebi olarak tanımlanmaktadır (2,3). KAH obstrüktif, obstrüktif olmayan ve mikrovasküler disfonksiyon olmak üzere 3 grup olarak sınıflandırılabilir. Ayrıca KAH'ın sürekli değişkenlik gösteren doğası gereği değişik klinik prezantasyonlarla sonuçlanabildiğinden akut koroner sendromlar (AKS) ya da kronik koroner sendromlar (KKS) olarak iki gruba kategorize edilebilir (4).

KAH'ın teşhisinde bir çok biyokimyasal testler, elektrokardiyografi (EKG), stres testleri, invaziv olan ve olmayan görüntüleme yöntemleri kullanılmakta ve halen geliştirilmektedir. Avru-

pa Kardiyoloji Topluluğunun (ESC) 2019'da yımladığı KKS kılavuzunda temel testler, teşhis yöntemleri ve risk değerlendirmesi için yapılan majör öneriler tablo 1'de verilmiştir.

Hastanın anamnesi alındıktan sonra ilk seçenek olarak temel biyokimyasal testler, istirahat EKG'si, ambulatuvar EKG monitorizasyonu, istirahat ekokardiyografisi ve seçilmiş hastalarda aksesuar grafisi gibi testler kullanılır. Şimdi sırasıyla bu testleri özellikle yeni gelişmeler açısından ele alalım.

BIYOKİMYASAL TESTLER

Günümüzde aterosklerotik hastalıkların tespitiinde lipit profili, C-reaktif protein (CRP), *high-sensitive* troponin, *brain natriuretic peptide*

(BNP) ve lökosit sayısı gibi laboratuvar testleri halihazırda kullanılmaktadır (5). Fakat bu biyobelirteçler vücuttaki farklı vasküler alanlardaki aterosklerozun hem ilerleme miktarı ve hem de hızını göstermedeki bireysel farklılıklarından dolayı kullanımları sınırlıdır (6). Ayrıca bu belirteçler ateroskleroz sürecini ilerleten hücre içi süreçleri tam olarak gösteremeyebilir. Yine bu belirteçler gelecekteki kardiyovasküler komplikasyonları

¹ Başasistan, Sağlık Bilimleri Üniversitesi Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, drfatihkoca@gmail.com



olarak anjiyografik çalışmalardan gelen sonuçlar, AKS'nin darlık yüzdeleri ile direkt korele olmadığını ve tıkalıcı trombusun sık sık yüksek dereceli lezyonlara ikincil gelişmediğini göstermiştir (57). Bu bulgular önemli koroner aterosklerozun belirlenmesinde sadece klasik anjiyografi yapılmasının yetersiz olduğunu kanıtlar. Ateroma yükü darlık derecesinden bağımsız olup plaqın total miktarını gösterir (58). Glagov ve arkadaşları, plak yeniden şekillenme sürecinde plak tutulumu damar çevresinin % 40'ına ulaşıcaya kadar lümenin korunduğunu göstermişlerdir (59).

Sonuç olarak IVUS ve OKT anjiyografik olarak belirsiz lezyonları netleştirebilir, hassas plak morfolojisini gösterebilir ve revaskülarizasyon stratejisini değiştirebilir.

Koroner Anjiyoskopİ

KAS hastalarda vasküler lümen yüzeyinin direkt olarak görülebilmesini sağlayan tek tanışal yöntemdir. Canlı hastalarda makropatolojik muayenede rol alır. KAS; BT, MRG, IVUS ve OKT gibi görüntüleme yöntemleriyle yapılamayan gerçek zamanlı, tam renkli, üç boyutlu video görüntüsü sağlar.

KAS hem araştırmalarda hem de klinik uygulamalarda geniş bir role sahiptir. Koroner damarlarda plak rengini, yırtığını, erozyonunu ve trombusunu gösterebilir (60-64).

KAYNAKLAR

- Patel MR, Peterson ED, Dai D. Low diagnostic yield of elective coronary angiography. *N Engl J Med.* 2010;362(10):886-895. doi: 10.1056/NEJMoa0907272.
- Lanza GA, Careri G, Crea F. Mechanisms of coronary artery spasm. *Circulation.* 2011; 124(16):1774-1782. doi:10.1161/CIRCULATION-AHA.111.037283.
- Mohri M, Koyanagi M, Egashira K, et al. Angina pectoris caused by coronary microvascular spasm. *Lancet,* 1998;351(9110):1165-1169. doi:10.1016/S0140- 6736(97)07329.
- Knuuti J, Wijns W, Saraste A, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2019. <https://doi.org/10.1093/eurheartj/ehz425>.
- Lobbes MB, Kooi ME, Lutgens E, et al. Leukocyte counts, myeloperoxidase, and pregnancy-associated plasma protein a as biomarkers for cardiovascular disease: towards a multi-biomarker approach. *Int J Vasc Med.* 2010;2010:726207.
- Chaturvedi N, Coady E, Mayet J, et al. Indian Asian men have less peripheral arterial disease than European men for equivalent levels of coronary disease. *Atherosclerosis,* 2007;193(1):204 -12.
- Kozomara A, Griffiths-Jones S, Griffiths-Jones S. miRBase: annotating high confidence microRNAs using deep sequencing data. *Nucleic Acids Res.* 2014;42:D68-73.
- Valadi H, Ekström K, Bossios A, et al. Exosome-mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells. *Nat Cell Biol.* 2007;9:654-659.
- Weber JA, Baxter DH, Zhang S, et al. The microRNA spectrum in 12 body fluids. *Clin Chem.* 2010;56:1733-1741.
- Villarroya-Beltri C, Gutierrez-Vazquez C, Sanchez-Cabo F, et al. Sumoylated hnRNPA2B1 controls the sorting of miRNAs into exosomes through binding to specific motifs. *Nat Commun.* 2013;4:2980.
- Knuuti J, Ballo H, Juarez-Orozco LE, et al. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. *Eur Heart J.* 2018;39:33223330.
- Shaw LJ, Mieres JH, Hendel RH, et al. WOMEN Trial Investigators. Comparative effectiveness of exercise electrocardiography with or without myocardial perfusion single photon emission computed tomography in women with suspected coronary artery disease: results from the What Is the Optimal Method for Ischemia Evaluation in Women (WOMEN) trial. *Circulation,* 2011;124:1239124.
- Benfari G, Rossi A, Geremia G, et al. Optimizing the role of transthoracic echocardiography to improve the cardiovascular risk stratification: the dream of subclinical coronary artery disease detection. *Minerva Med.* 2018;109:31-40.
- Shimony S, Gendelman G, Ayzenberg O, et al. Differential effects of coronary artery stenosis on my-



- ocardial function: the value of myocardial strain analysis for the detection of coronary artery disease. *J Am Soc Echocardiogr.* 2011;24:748–57.
15. Motoyama S, Ito H, Sarai M, et al. Ultra-high-resolution computed tomography angiography for assessment of coronary artery stenosis. *Circ J.* 2018;82:1844–1851. doi: 10.1253/circj.CJ-17-1281.
 16. Leschka S, Seitun S, Dettmer M, et al. Ex vivo evaluation of coronary atherosclerotic plaques: characterization with dual-source CT in comparison with histopathology. *J Cardiovasc Comput Tomogr.* 2010;4:301–308.
 17. Hoffmann U, Ferencik M, Udelson JE, et al. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the PROMISE trial (prospective multicenter imaging study for evaluation of chest pain). *Circulation.* 2017;135:2320–2332.
 18. Min JK, Shaw LJ, Devereux RB, et al. Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. *J Am Coll Cardiol.* 2007;50:1161–1170.
 19. Schulman-Marcus J, o Hartaigh B, Gransar H, et al. Sex-specific associations between coronary artery plaque extent and risk of major adverse cardiovascular events: the CONFIRM long-term registry. *JACC Cardiovasc Imaging.* 2016;9:364–372.
 20. Chang HJ, Lin FY, Lee SE, et al. Coronary atherosclerotic precursors of acute coronary syndromes. *J Am Coll Cardiol.* 2018;71:2511–2522.
 21. Williams MC, Moss AJ, Dweck M, et al. Coronary artery plaque characteristics associated with adverse outcomes in the SCOT-heart study. *J Am Coll Cardiol.* 2019;73:291–301.
 22. Ferencik M, Mayrhofer T, Bittner DO, et al. Use of high-risk coronary atherosclerotic plaque detection for risk stratification of patients with stable chest pain: a secondary analysis of the promise randomized clinical trial. *JAMA Cardiol.* 2018;3:144–152.
 23. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve: scientific basis. *J Am Coll Cardiol.* 2013;61:2233–2241.
 24. Mathew RC, Gottbrecht M, Salerno M. Computed tomography fractional flow reserve to guide coronary angiography and intervention. *IntervCardiolClin.* 2018;7:345–54. doi: 10.1016/j.iccl.2018.03.008.
 25. Pijls NH, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenosis. *N Engl J Med.* 1996;334:1703–8.
 26. Koo BK, Erglis A, Jh Doh, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. *J Am Coll Cardiol.* 2011;58:1989–97.
 27. Nakazato R, Park HB, Berman DS, et al. Noninvasive fractional flow reserve derived from computed tomography angiography for coronary lesions of intermediate stenosis severity: results from the DeFACTO study. *Circ Cardiovasc Imaging.* 2013;6:881–9.
 28. Nørgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). *J Am Coll Cardiol.* 2014;63:1145–55.
 29. Kato S, Kitagawa K, Ishida N, et al. Assessment of coronary artery disease using magnetic resonance coronary angiography: a national multicenter trial, *J Am Coll Cardiol.* 56 (12) (2010) 983–991.
 30. François C J, Tuite D, Deshpande V, et al. Unenhanced MR angiography of the thoracic aorta: initial clinical evaluation, *Am J Roentgenol.* 2008;190 (4): 902–906.
 31. Greil GF, Stuber M, Botnar RM, et al. Coronary magnetic resonance angiography in adolescents and young adults with Kawasaki disease, *Circulation.* 2002;105 (8) (Feb 26):908–911.
 32. Greil GF, Seeger A, Miller S, et al. Coronary magnetic resonance angiography and vessel wall imaging in children with Kawasaki disease, *Pediatr Radiol.* 2007 Jul; 37 (7):666–673.
 33. Prakken NH, Cramer MJ, Olimulder MA, et al. Screening for proximal coronary artery anomalies with 3-dimensional MR coronary angiography, *Int J. Cardiovasc. Imag.* 2010;26:701–710.
 34. Greenwood JP, Maredia N, Younger JF, et al. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. *Lancet.* 2012;379(9814):453–60.
 35. Greenwood JP, Maredia N, Radjenovic A, et al. Clinical evaluation of magnetic resonance imaging in coronary heart disease: the CE-MARC study Trials, 2009;10:62.



36. Knott KD, Seraphim A, Augusto JB, et al. The prognostic significance of quantitative myocardial perfusion: An artificial intelligence-based approach using perfusion mapping. *Circulation*, 2020;141:1282–1291.
37. Klocke FJ, Baird MG, Lorell BH, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging—executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (ACC/AHA/ASNC Committee to revise the 1995 guidelines for the clinical use of cardiac radionuclide imaging). *J Am Coll Cardiol*. 2003;42(7):1318–33.
38. Fiechter M, Ghadri JR, Gebhard C, et al. Diagnostic value of ¹³N-ammonia myocardial perfusion PET: added value of myocardial flow reserve. *J Nucl Med*. 2012;53(8):1230–4.
39. Mc Ardle BA, Dowsley TF, deKemp RA, et al. Does rubidium-82 PET have superior accuracy to SPECT perfusion imaging for the diagnosis of obstructive coronary disease?: A systematic review and meta-analysis. *J Am Coll Cardiol*. 2012;60:1828–37.
40. Parker MW, Iskandar A, Limone B, et al. Diagnostic accuracy of cardiac positron emission tomography versus single photon emission computed tomography for coronary artery disease: a bivariate meta-analysis. *Circ Cardiovasc Imaging*, 2012;5(6):700–7.
41. Bateman TM, Heller GV, McGhie AI, et al. Diagnostic accuracy of rest/stress ECGgated Rb-82 myocardial perfusion PET: comparison with ECG-gated Tc-99m sestamibi SPECT. *J Nucl Cardiol*. 2006;13(1):24–33.
42. Bateman TM. Advantages and disadvantages of PET and SPECT in a busy clinical practice. *J Nucl Cardiol*. 2012;19(Suppl 1):S3–11.
43. Taqueti VR, Di Carli MF. Clinical significance of noninvasive coronary flow reserve assessment in patients with ischemic heart disease. *Curr Opin Cardiol*. 2016;31(6):662–9.
44. Murthy VL, Bateman TM, Beanlands RS, et al. Clinical quantification of myocardial blood flow using PET: joint position paper of the SNMMI cardiovascular council and the ASNC. *J Nucl Med*. 2018;59(2): 273–93.
45. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2019;40:87165.
46. Escaned J, Echavarria-Pinto M, Garcia-Garcia et al. ADVISE II Study Group. Prospective assessment of the diagnostic accuracy of instantaneous wave-free ratio to assess coronary stenosis relevance: results of ADVISE II international, multi-center study (ADenosine Vasodilator Independent Stenosis Evaluation II). *JACC Cardiovasc Interv*. 2015;8:824833.
47. Toth G, Hamilos M, Pyxaras S, et al. Evolving concepts of angiogram: fractional flow reserve discordances in 4000 coronary stenoses. *Eur Heart J*. 2014;35:28312838.
48. Jeremias A, Maehara A, Genereux P, et al. Multi-center core laboratory comparison of the instantaneous wave-free ratio and resting Pd/Pa with fractional flow reserve: the RESOLVE study. *J Am Coll Cardiol*. 2014;63:1253.
49. Mason PJ, Shah B, Tamis-Holland JE, et al. American Heart Association Interventional Cardiovascular Care Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; Council on Genomic and Precision Medicine. An update on radial artery access and best practices for transradial coronary angiography and intervention in acute coronary syndrome: a scientific statement from the American Heart Association. *Circ Cardiovasc Interv*. 2018;11:e000035.
50. Mintz GS, Guagliumi G. Intravascular imaging in coronary artery disease. *Lancet*, 2017;390:793–809.
51. Koskinas KC, Ughi GJ, Windecker S, et al. Intra-coronary imaging of coronary atherosclerosis: validation for diagnosis, prognosis and treatment. *Eur Heart J*. 2016;37:524–535.
52. Stone GW, Maehara A, Lansky AJ, et al. PROSPECT Investigators. A prospective natural-history study of coronary atherosclerosis. *N Engl J Med*. 2011;364:226–235.
53. Calvert PA, Obaid DR, O'Sullivan M, et al. Association between IVUS findings and adverse outcomes in patients with coronary artery disease: the VIVA (VH-IVUS in Vulnerable Atherosclerosis) Study. *JACC Cardiovasc Imaging*, 2011;4:894–901.
54. Yun KH, Mintz GS, Farhat N, et al. Relation between angiographic lesion severity, vulnerable plaque morphology and future adverse cardiac events (from the Providing Regional Observations to Study Predictors of Events in the Coronary Tree study). *Am J Cardiol*. 2012;110:471–477.



55. Cheng JM, Garcia-Garcia HM, de Boer SP, et al. In vivo detection of high-risk coronary plaques by radiofrequency intravascular ultrasound and cardiovascular outcome: results of the ATHEROREMO-IVUS study. *Eur Heart J.* 2014;35:639–647.
56. Bezerra HG, Costa MA, Guagliumi G, et al. Intracoronary optical coherence tomography: a comprehensive review clinical and research applications. *JACC Cardiovasc Interv.* 2009;2:1035–1046.
57. Ambrose JA, Tannenbaum MA, Alexopoulos D, et al. Angiographic progression of coronary artery disease and the development of myocardial infarction. *J Am Coll Cardiol.* 1988;12:56–62.
58. Virmani R, Burke AP, Farb A, et al. Pathology of the vulnerable plaque. *J Am Coll Cardiol.* 2006;47(suppl 8):C13–C18.
59. Glagov S, Weisenberg E, Zarins CK, et al. Compensatory enlargement of human atherosclerotic coronary arteries. *N Engl J Med.* 1987;316:1371–1375.
60. Mizuno K, Miyamoto A, Satomura K, et al. Angioscopic coronary macromorphology in patients with acute coronary disorders. *Lancet.* 1991;337:809–12.
61. Falk E. Plaque rupture with severe pre-existing stenosis precipitating coronary thrombosis. Characteristics of coronary atherosclerotic plaques underlying fatal occlusive thrombi. *Br Heart J.* 1983;50:127–34.
62. Mizuno K, Satomura K, Miyamoto A, et al. Angioscopic evaluation of coronary-artery thrombi in acute coronary syndromes. *N Engl J Med.* 1992;326:287–91.
63. Muller JE, Abela GS, Nesto RW, et al. Triggers, acute risk factors and vulnerable plaques: the lexicon of a new frontier. *J Am Coll Cardiol.* 1994;23:809–13.
64. Mizuno K, Miyamoto A, Isojima K, et al. A serial observation of coronary thrombi in vivo by a new percutaneous transluminal coronary angioscope. *Angiology,* 1992;43:91–9.