



BÖLÜM 47

Atriyal Fibrilasyon Tedavisinde Antikoagülan Tedaviler

Hande OĞUL¹

GİRİŞ

Atriyal fibrilasyon (AF) toplumda en sık görülen ve tedavi gerektiren kardiyak aritmidir. AF' si olan çoğu hasta, iskemik inme ve diğer embolik olay riskini azaltmak amacıyla uzun süreli oral antikoagülan (OAK) tedavi almalıdır. Birçok hastada OAK tedavisi ile ilişkili kanama riski, tedaviden sağlanan faydadan daha fazla izlenmektedir. Bu nedenle OAK tedavi adayları olan tüm hastalar kanama riski ve OAK' a ilişkin olası kontraendikasyonlar açısından gözden geçirilmelidir.

ANTİKOAGÜLAN TEDAVİYE YAKLAŞIM:

AF' li her hasta, ilk AF atağından itibaren sistemik tromboemolik olayların engellenebilmesi için antikoagülan tedavi ihtiyacı açısından değerlendirilmelidir. Bu, inme için CHA₂DS₂-VASc skoru (tablo 1) adı verilen bir risk skorlama sistemi kullanılarak yapılır. Tromboemboli riski kanama riskinden fazla olan tüm AF hastaları uzun süreli antikoagülan tedavi adaydır.

ANTİKOAGÜLAN SEÇİMİ

AF' li hastalarda öncelikle OAK' ın endike olup olmadığı belirlenmelidir. Uzun süreli OAK alma-

sı gereken hastalar tespit edilmeli ve tedaviye başlanmadan önce olası kontraendikasyonlar gözden geçirilmelidir (tablo 2) (2).

Günümüzde OAK endikasyonu olan çoğu AF hastasında K vitamini antagonisti (VKA, örn. varfarin) yerine direkt oral antikoagülan (DOAK) tedaviler kullanılmaktadır. AF nedeniyle varfarin başlanmış olan hastalarda yıllık terapötik aralık %70 ve altında ise DOAK tedavisine geçilmesi önerilmektedir.

OAK endikasyonu olan AF' li hastalarda DOAK yerine varfarin tercih edilmesi gereken özel durumlar şunlardır:

- » DOAK' ların kullanılmadığı (örn. kalp kapak hastalıkları) ve VKA tedavisi ile yıllık terapötik aralığın \geq %70 olduğu hastalar
- » Herhangi bir tipte ve konumda mekanik kalp kapağı olan hastalar
- » Ciddi veya klinik olarak anlamlı (mitral kapak alanı \leq 1,5 cm²) romatizmal mitral darlığı olan hastalar
- » İlaç etkileşimleri nedeniyle DOAK kullanımının uygun olmadığı hastalar (tablo 3) (2).

¹ Uzm. Dr., Batman Eğitim ve Araştırma Hastanesi, Hematoloji Kliniği, handeogull@gmail.com, ORCID iD: 0000-0001-6715-2664

Tablo 4. HAS-BLED Kanama Risk Skoru (42)

		Puan
H	Hipertansiyon	1
A	Anormal böbrek ve karaciğer fonksiyonları (her biri için 1 puan)	1 veya 2
S	Stroke	1
B	Kanamaya yatkınlık	1
L	Labil INR (varfarin kullananlar için)	1
E	İleri yaş (65 yaş ve üzeri)	1
D	İlaçlar (eş zamanlı aspirin veya nonsteroid antiinflamatuar ilaç kullanımı) veya aşırı alkol alımı (her biri için 1 puan)	1 veya 2
		Maksimum 9 puan

SONUÇ

AF'nin olası komplikasyonlarını önlemek için OAK tedavisi hayati önem taşımaktadır. Hastalar OAK kullanımını başlangıcında kanama risklerinin artabileceğinin farkında olmalı, bu riski en aza indirecek stratejiler ve tıbbi yardım almaları gereken kanama belirti ve bulguları konusunda eğitilmelidir.

KAYNAKLAR

1. Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137:263.
2. Uptodate. Atrial fibrillation in adults: Use of oral anticoagulants. (Online) https://www.uptodate.com/contents/image?imageKey=HEME%2F107527&topicKey=CARD%2F1031&search=antikoag%C3%BClan%20tedaviler&rank=3~150&source=see_link (Accessed: 8 th July 2023)
3. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014; 383:955.
4. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009; 361:1139.
5. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011; 365:883.
6. Granger CB, Alexander JH, McMurray JJ, et al. Apix-

- ban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011; 365:981.
7. Chatterjee S, Sardar P, Biondi-Zoccai G, Kumbhani DJ. New oral anticoagulants and the risk of intracranial hemorrhage: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. *JAMA Neurol* 2013; 70:1486.
8. Salazar CA, del Aguila D, Cordova EG. Direct thrombin inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in people with non-valvular atrial fibrillation. *Cochrane Database Syst Rev* 2014; :CD009893.
9. Bruins Slot KM, Berge E. Factor Xa inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in patients with atrial fibrillation. *Cochrane Database Syst Rev* 2018; 3:CD008980.
10. http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2014/022512Orig1s025ltr.pdf (Accessed on December 05, 2018).
11. Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013; 369:2093.
12. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Newly identified events in the RE-LY trial. *N Engl J Med* 2010; 363:1875.
13. Connolly SJ, Wallentin L, Ezekowitz MD, et al. The Long-Term Multicenter Observational Study of Dabigatran Treatment in Patients With Atrial Fibrillation (RELY-ABLE) Study. *Circulation* 2013; 128:237.
14. Okumura K, Akao M, Yoshida T, et al. Low-Dose Edoxaban in Very Elderly Patients with Atrial Fibrillation. *N Engl J Med* 2020; 383:1735.
15. Fuster V, Rydén LE, Asinger RW, et al. ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation) Developed in Collaboration With the North American Society of Pacing and Electrophysiology. *Circulation* 2001; 104:2118.
16. You JJ, Singer DE, Howard PA, et al. Antithrombotic therapy for atrial fibrillation: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141:e531S.
17. Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133:546S.
18. Hylek EM, Skates SJ, Sheehan MA, Singer DE. An analysis of the lowest effective intensity of prophylactic anticoagulation for patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1996; 335:540.
19. Hylek EM, Go AS, Chang Y, et al. Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. *N Engl J Med* 2003; 349:1019.

20. European Atrial Fibrillation Trial Study Group. Optimal oral anticoagulant therapy in patients with nonrheumatic atrial fibrillation and recent cerebral ischemia. *N Engl J Med* 1995; 333:5.
21. Singer DE, Chang Y, Fang MC, et al. Should patient characteristics influence target anticoagulation intensity for stroke prevention in nonvalvular atrial fibrillation?: the ATRIA study. *Circ Cardiovasc Qual Outcomes* 2009; 2:297.
22. Sherwood MW, Douketis JD, Patel MR, et al. Outcomes of temporary interruption of rivaroxaban compared with warfarin in patients with nonvalvular atrial fibrillation: results from the rivaroxaban once daily, oral, direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and embolism trial in atrial fibrillation (ROCKET AF). *Circulation* 2014; 129:1850.
23. Bernhardt P, Schmidt H, Hammerstingl C, et al. Patients with atrial fibrillation and dense spontaneous echo contrast at high risk a prospective and serial follow-up over 12 months with transesophageal echocardiography and cerebral magnetic resonance imaging. *J Am Coll Cardiol* 2005; 45:1807.
24. Tang RB, Dong JZ, Liu XP, et al. Is CHA2DS2-VASc score a predictor of left atrial thrombus in patients with paroxysmal atrial fibrillation? *Thromb Haemost* 2011; 105:1107.
25. Reynolds MW, Fahrback K, Hauch O, et al. Warfarin anticoagulation and outcomes in patients with atrial fibrillation: a systematic review and metaanalysis. *Chest* 2004; 126:1938.
26. Sadanaga T, Sadanaga M, Ogawa S. Evidence that D-dimer levels predict subsequent thromboembolic and cardiovascular events in patients with atrial fibrillation during oral anticoagulant therapy. *J Am Coll Cardiol* 2010; 55:2225.
27. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. *Chest* 2018; 154:1121.
28. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021; 143:e72.
29. Ha JT, Neuen BL, Cheng LP, et al. Benefits and Harms of Oral Anticoagulant Therapy in Chronic Kidney Disease: A Systematic Review and Meta-analysis. *Ann Intern Med* 2019; 171:181.
30. Siontis KC, Zhang X, Eckard A, et al. Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States. *Circulation* 2018; 138:1519.
31. Stanifer JW, Pokorney SD, Chertow GM, et al. Apixaban Versus Warfarin in Patients With Atrial Fibrillation and Advanced Chronic Kidney Disease. *Circulation* 2020; 141:1384.
32. Weir MR, Ashton V, Moore KT, et al. Rivaroxaban versus warfarin in patients with nonvalvular atrial fibrillation and stage IV-V chronic kidney disease. *Am Heart J* 2020; 223:3.
33. Su X, Yan B, Wang L, et al. Oral Anticoagulant Agents in Patients With Atrial Fibrillation and CKD: A Systematic Review and Pairwise Network Meta-analysis. *Am J Kidney Dis* 2021; 78:678.
34. <https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management> (Accessed: 2 nd October 2023)
35. Lip GYH, Keshishian AV, Zhang Y, et al. Oral Anticoagulants for Nonvalvular Atrial Fibrillation in Patients With High Risk of Gastrointestinal Bleeding. *JAMA Netw Open* 2021; 4:e2120064.
36. Paciaroni M, Agnelli G, Ageno W, Caso V. Timing of anticoagulation therapy in patients with acute ischemic stroke and atrial fibrillation. *Thromb Haemost* 2016; 116:410.
37. Smythe MA, Parker D, Garwood CL, et al. Timing of Initiation of Oral Anticoagulation after Acute Ischemic Stroke in Patients with Atrial Fibrillation. *Pharmacotherapy* 2020; 40:55.
38. Lansberg MG, O'Donnell MJ, Khatri P, et al. Antithrombotic and thrombolytic therapy for ischemic stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141:e601S.
39. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014; 45:2160.
40. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016; 37:2893.
41. Dunning J, Nagendran M, Alfieri OR, et al. Guideline for the surgical treatment of atrial fibrillation. *Eur J Cardiothorac Surg* 2013; 44:777.
42. Borre ED, Goode A, Raitz G, et al. Predicting Thromboembolic and Bleeding Event Risk in Patients with Non-Valvular Atrial Fibrillation: A Systematic Review. *Thromb Haemost* 2018; 118:2171.