



KARDİYOEMBOLİK İNME TEDAVİSİNDE YENİ ORAL ANTİKOAGÜLANLARIN KULLANIMI

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GİRİŞ

Atrial fibrilasyon (AF), genel popülasyonda % 2 oranında görülürken yaşla birlikte prevalansı artar ve 80 yaş üzerindeki popülasyonda % 10-12 arasında görülen en sık ritim bozukluğudur. Küresel hastalık yüküne göre AF' nin tahmini prevalansı 33, 5 milyon kişidir. AF tüm kardiyak aritmilerin yarısından sorumludur. Görüldüğü üzere dünya genelinde bu durumdan muzdarip olan insan sayısının fazla olması bu alanda çok sayıda çalışma yapılmasını ve yeni tedavi seçeneklerinin ortaya çıkmasını sağlamıştır (1).

AF, sol atriumda staz yaparak burada trombüs oluşumunu kolaylaştırır ve sistemik tromboemboli riskini artırır. En sık emboli beyine olur. AF iskemik inme riskini yaklaşık 5 kat artırır. Bu hastalarda inme riskini azaltmak için profilaktik tedavide daha önce antiagregan ve antikoagülan ilaçların kullanıldığı bilinmektedir (2).

Yapılan bir çalışmada (ACTIVE W) yüksek inme riski olan AF hastalarından bir kısmına oral antikoagülan (OAK) (n:3371) verilirken diğer kısmına da aspirin artı klopidogrel (n:3335) verilerek yakın takibe alınmış. Yıllık inme riski OAK alan grupta % 3,93 iken ikili antiagregan alan grupta % 5.9 olarak belirlenmiş. Ayrıca bu çalışma ile AF hastalarında oral antikoagülasyon tedavisinin antiag-

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KAYNAKLAR

1. Sagris M, Vardas EP, Theofilis P, Antonopoulos AS, Oikonomou E, Tousoulis D. Atrial Fibrillation: Pathogenesis, Predisposing Factors, and Genetics. *Int J Mol Sci*. 2021 Dec 21;23(1):6. doi: 10.3390/ijms23010006.
2. Tsioufis C. Ischemic stroke in atrial fibrillation patients: don't put the blame always on heart. *Hellenic J Cardiol*. 2020 May-Jun;61(3):208-209. doi: 10.1016/j.hjc.2018.07.003. Epub 2018 Sep 19.
3. ACTIVE Writing Group of the ACTIVE Investigators, Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet*. 2006 Jun 10;367(9526):1903-12. doi: 10.1016/S0140-6736(06)68845-4.
4. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al. 2014 AHA/ACC/HRS guideline 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 Heart Rhythm Society. *Circulation*. 2014 Dec 2;130(23):2071-104. doi: 10.1161/CIR.0000000000000040. Epub 2014 Mar 28.
5. European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY, Schotten U, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010 Oct;31(19):2369-429. doi: 10.1093/eurheartj/ehq278. Epub 2010 Aug 29.
6. Chao TF, Lip GYH, Lin YJ, Chang SL, Lo LW, Hu YF, et al. Major bleeding and intracranial hemorrhage risk prediction in patients with atrial fibrillation: Attention to modifiable bleeding risk factors or use of a bleeding risk stratification score? A nationwide cohort study. *Int J Cardiol*. 2018 Mar 1;254:157-161. doi: 10.1016/j.ijcard.2017.11.025. Epub 2018 Jan 28.
7. Pisters R, Lane DA, Nieuwlaar R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010 Nov;138(5):1093-100. doi: 10.1378/chest.10-0134. Epub 2010 Mar 18.
8. Altiok E, Marx N. Oral Anticoagulation. *Dtsch Arztebl Int*. 2018 Nov 16;115(46):776-783. doi: 10.3238/arztebl.2018.0776.
9. Li J, Gao M, Zhang M, Liu D, Li Z, Du J, Hou Y. Treatment of atrial fibrillation: a comprehensive review and practice guide. *Cardiovasc J Afr*. 2020 May/ Jun 23;31(3):153-158. doi: 10.5830/CVJA-2019-064. Epub 2020 Mar 18.
10. Blair HA, Keating GM. Dabigatran Etxelilate: A Review in Nonvalvular Atrial Fibrillation. *Drugs*. 2017 Mar;77(3):331-344. doi: 10.1007/s40265-017-0699-z.
11. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009 Sep 17;361(12):1139-51. doi: 10.1056/NEJMoa0905561. Epub 2009 Aug 30.
12. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anti-coagulants in patients with atrial fibrillation. *Eur Heart J*. 2018 Apr 21;39(16):1330-1393. doi: 10.1093/eurheartj/ehy136
13. Pollack CV Jr, Reilly PA, van Ryn J, Eikelboom JW, Glund S, Bernstein RA, et al. Idarucizumab for Dabigatran Reversal - Full Cohort Analysis. *N Engl J Med*. 2017 Aug 3;377(5):431-441. doi: 10.1056/NEJMoa1707278. Epub 2017 Jul 11.
14. Acar BA, Akpınar ÇK, Alioğlu Z, Arlıer Z, Arsava EM, Aytaç E, et al. İnme klinik pratiğinde NOAK kullanımı: Türk Beyin Damar Hastalıkları Derneği Uzman Görüşü. *Türk Beyin Damar*

- Hastalıkları Dergisi 2020; 26(3): 190-235. doi: 10.5505/tbdhd.2020.26213
15. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med.* 2011 Sep 8;365(10):883-91. doi: 10.1056/NEJMoa1009638. Epub 2011 Aug 10.
 16. Mueck W, Stampfuss J, Kubitzka D, Becka M. Clinical pharmacokinetic and pharmacodynamic profile of rivaroxaban. *Clin Pharmacokinet.* 2014 Jan;53(1):1-16. doi: 10.1007/s40262-013-0100-7.
 17. Weir MR, Chen YW, He J, Bookhart B, Campbell A, Ashton V. Effectiveness and safety of rivaroxaban versus warfarin among nonvalvular atrial fibrillation patients with obesity and diabetes. *J Diabetes Complications.* 2021 Nov;35(11):108029. doi: 10.1016/j.jdiacomp.2021.108029. Epub 2021 Sep 4.
 18. Alberts MJ, He J, Kharat A, Ashton V. Effectiveness and Safety of Rivaroxaban versus Warfarin Among Nonvalvular Atrial Fibrillation Patients with Obesity and Polypharmacy. *Am J Cardiovasc Drugs.* 2022 Jul;22(4):425-436. doi: 10.1007/s40256-021-00520-7. Epub 2022 Jan 29.
 19. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2011 Sep 15;365(11):981-92. doi: 10.1056/NEJMoa1107039. Epub 2011 Aug 27.
 20. Byon W, Garonzik S, Boyd RA, Frost CE. Apixaban: A Clinical Pharmacokinetic and Pharmacodynamic Review. *Clin Pharmacokinet.* 2019 Oct;58(10):1265-1279. doi: 10.1007/s40262-019-00775-z.
 21. Hurst KV, O'Callaghan JM, Handa A. Quick reference guide to apixaban. *Vasc Health Risk Manag.* 2017 Jul 10;13:263-267. doi: 10.2147/VHRM.S121944. eCollection 2017.
 22. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, et al. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2013 Nov 28;369(22):2093-104. doi: 10.1056/NEJMoa1310907. Epub 2013 Nov 19.
 23. Lip GYH, Keshishian AV, Zhang Y, Kang A, Dhamane AD, Luo X, et al. Oral Anticoagulants for Nonvalvular Atrial Fibrillation in Patients With High Risk of Gastrointestinal Bleeding. *JAMA Netw Open.* 2021 Aug 2;4(8):e2120064. doi: 10.1001/jamanetworkopen.2021.20064.
 24. Cheung KS, Leung WK. Gastrointestinal bleeding in patients on novel oral anticoagulants: Risk, prevention and management. *World J Gastroenterol.* 2017 Mar 21;23(11):1954-1963. doi: 10.3748/wjg.v23.i11.1954.
 25. Polzin A, Dannenberg L, Wolff G, Helten C, Achilles A, Hohlfeld T, et al. Non-vitamin K oral anticoagulants (NOAC) and the risk of myocardial infarction: Differences between factor IIa and factor Xa inhibition? *Pharmacol Ther.* 2019 Mar;195:1-4. doi: 10.1016/j.pharmthera.2018.10.005. Epub 2018 Oct 12.
 26. Prisco D, Cenci C, Silvestri E, Ciucciarelli L, Di Minno G. Novel oral anticoagulants in atrial fibrillation: which novel oral anticoagulant for which patient? *J Cardiovasc Med (Hagerstown).* 2015 Jul;16(7):512-9. doi: 10.2459/JCM.0000000000000262.
 27. Yao X, Abraham NS, Sangaralingham LR, Bellolio MF, McBane RD, Shah ND, Noseworthy PA. Effectiveness and Safety of Dabigatran, Rivaroxaban, and Apixaban Versus Warfarin in Nonvalvular Atrial Fibrillation. *J Am Heart Assoc.* 2016 Jun 13;5(6):e003725. doi: 10.1161/JAHA.116.003725.
 28. Santarpia G, Curcio A, Sibilio G, Indolfi C. Clinical significance of non-vitamin K antagonist oral anticoagulants in the management of atrial fibrillation. *Circ J.* 2015;79(5):914-23. doi: 10.1253/circj.CJ-15-0319. Epub 2015 Apr 2.
 29. Chen S, Pürerfellner H, Meyer C, Sommer P, Kiuchi MG, Martinek M, et al. Anticoagulation in atrial fibrillation and liver disease: a pooled-analysis of >20 000 patients. *Eur Heart J Cardiovasc Pharmacother.* 2022 Jun 8;8(4):336-345. doi: 10.1093/ehjcvp/pvab032.
 30. Liakoni E, Rätz Bravo AE, Krähenbühl S. Hepatotoxicity of New Oral Anticoagulants (NOACs). *Drug Saf.* 2015 Aug;38(8):711-20. doi: 10.1007/s40264-015-0317-5.

31. Shah S, Norby FL, Datta YH, Lutsey PL, MacLehose RF, Chen LY, Alonso A. Comparative effectiveness of direct oral anticoagulants and warfarin in patients with cancer and atrial fibrillation. *Blood Adv.* 2018 Feb 13;2(3):200-209. doi: 10.1182/bloodadvances.2017010694.
32. Beyer-Westendorf J, Michalski F, Tittel L, Middeldorp S, Cohen H, Abdul Kadir R, Arachchilage DJ, Arya R, Ay C, Marten S. Pregnancy outcome in patients exposed to direct oral anticoagulants - and the challenge of event reporting. *Thromb Haemost.* 2016 Sep 27;116(4):651-8. doi: 10.1160/TH16-04-0305. Epub 2016 Jul 7.
33. Connolly G, Spyropoulos AC. Practical issues, limitations, and periprocedural management of the NOAC's. *J Thromb Thrombolysis.* 2013 Aug;36(2):212-22. doi: 10.1007/s11239-013-0911-2.