



SEREBRAL VENÖZ TROMBOZDA ORAL ANTİKOAGULANLARIN YERİ

Elif GÜNEY¹

GİRİŞ

Serebral venöz tromboz (SVT), nadir görülen bir inme nedeni olup tüm inmelerin % 0.5-1' ini oluşturur. Genellikle doğurganlık çağındaki genç kadınlarda görülen bir hastalıktır (1). Hastaların çoğu fonksiyonel olarak bağımsız şekilde yaşamını sürdürebilmekte ancak % 10-15 hastada ciddi sekeller kalmakta veya hastalık ölümlü sonuçlanmaktadır (2). Bilgisayarlı Tomografi (BT) anjiyografi ve venografi gibi nörovasküler görüntüleme tekniklerinin kullanımının artmasıyla, SVT insidansı da artış göstermiştir (3).

SVT, pulmoner tromboemboli ve derin ven trombozunun aksine, genç kadınlarda daha sık görülmektedir. Bu durum, çoğunlukla gebelik, postpartum dönem ve kontrasepsiyon ile ilişkilendirilmektedir. SVT'nin etyolojisinde rol alan etkenler genetik ve genetik olmayan faktörler olarak ikiye ayrılmıştır (**Tablo 1**) (3,4).

Ayrıca son yıllarda SARS-Cov-2 enfeksiyonu ile ilişkili de çok sayıda olgu bildirilmiştir. Bu vakaların bir kısmı ağır enfeksiyonun geç komplikasyonu, bir kısmı ise izole başvuru semptomu şeklinde ortaya çıkmıştır (5).

¹ Uzm. Dr., Ordu Devlet Hastanesi, Nöroloji Kliniği, elifugur@windowslive.com

ilaçlar ve nonsteroid analjezik kullanımı, NOAK'lara karşı hipersensitivite gibi durumlarda kontrendikedir

Dabigatran ağır renal yetmezlikte (CrCL < 30 mL/dk) kontrendikedir. Rivaroksaban, apiksaban ve edoksaban CrCL < 15 mL/dk olan hastalarda önerilmez. Edoksaban, ilaç klirensi artması dolayısıyla iskemik inme riski arttığından, CrCL > 95 mL/dk olanlarda kontrendikedir; CrCL > 15–49 mL/dk olan hastalarda ise günlük 30 mg tek doz olarak kullanılmalıdır.

NOAK'lar, orta dereceli karaciğer yetmezliğinde doz ayarlaması yapılarak kullanılabilir. Ancak apiksaban ve rivaroksaban, koagülopatinin eşlik ettiği hepatik yetmezlikte kontrendikedir (42).

KAYNAKLAR

1. Bousser M-G, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol.* 2007;6:162–70.
2. Canhão P, Ferro JM, Lindgren AG, Bousser M-G, Stam J, Barinagarrementeria F, et al. Causes and predictors of death in cerebral venous thrombosis. *Stroke.* 2005;36:1720–5.
3. Green M, Styles T, Russell T, Sada C, Jallow E, Stewart J, et al. Non-genetic and genetic risk factors for adult cerebral venous thrombosis. *Thromb Res.* 2018;169:15–22. Comprehensive meta-analysis of case-control studies examining risk factors for CVT.
4. Cerebral venous thrombosis. (2018). Accessed: September 29, 2022; <https://emedicine.medscape.com/article/1162804-overview#a5>.
5. Alimohammadi A, Kim D.J, Field T.S. Updates in Cerebral Venous Thrombosis. *Stroke, Current Cardiology Reports* (2022) 24:43–50.
6. Piazza G: Cerebral venous thrombosis. *AHA Journals.* 2012, 125:1704-1709.
7. Sidhom Y, Mansour M, Messelmani M, Derbali H, Fekih-Mrissa N, Zaouali J, Mrissa R: Cerebral venous thrombosis: clinical features, risk factors, and long-term outcome in a Tunisian cohort. *J Stroke Cerebrovasc Dis.* 2014, 23:1291-5. 10.1016/j.jstrokecerebrovasdis.2013.10.025
8. Ferro JM, Bousser MG, Canhão P, Coutinho JM, Crassard I, Dentali F, et al; European Stroke Organization. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis— endorsed by the European Academy of Neurology. *Eur J Neurol.* 2017;24:1203–1213. doi: 10.1111/ene.13381.
9. Saposnik G, Barinagarrementeria F, Brown RD Jr, Bushnell CD, Cucchiara B, Cushman M, et al; American Heart Association Stroke Council and the Council on Epidemiology and Prevention. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2011;42:1158–1192. doi: 10.1161/STR.0b013e31820a8364
10. Girot M, Ferro JM, Canhão P, Stam J, Bousser M-G, Barinagarrementeria F, et al. Predictors of outcome in patients with cerebral venous thrombosis and intracerebral hemorrhage. *Stroke.* 2007;38:337–42.
11. Ortega-Gutierrez S, Holcombe A, Aksan N, Dai B, Shaban A, Lazarre L, et al. Association of admission clinical predictors and functional outcome in patients with cerebral venous and dural sinus thrombosis. *Clin Neurol Neurosurg.* 2020;188:105563.
12. Busch MA, Hofmann O, Einhüpl KM, Masuhr F. Outcome of heparin-treated patients with acute cerebral venous sinus thrombosis: influence of the temporal pattern of intracerebral haemorrhage. *Eur J Neurol.* 2016;23:1387–92.

13. Field TS, Camden M-C, Al-Shimemeri S, Lui G, Lee AY. Oflabel use of novel anticoagulants for treatment of cerebral venous thrombosis: a Canadian survey. *Int J Stroke*. 2017;12:NP16–8.
14. Bose G, Graveline J, Yogendrakumar V, Shorr R, Fergusson DA, Le Gal G, et al. Direct oral anticoagulants in treatment of cerebral venous thrombosis: a systematic review. *BMJ Open*. 2021;11:e040212. Systematic review examining use of DOACs in CVT.
15. Mekaj Y.H, Mekaj A.Y, Duci S.B, Miftari E.I. New oral anticoagulants: their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events. *Ther Clin Risk Manag*. 2015 Jun 24;11:967-77. doi: 10.2147/TCRM.S84210. eCollection 2015.
16. Ruf CT, Giugliano RP, Braunwald E, Hofman EB, Deenadayalu N, Ezekowitz MD, 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;383:955–62.
17. Ferro JM, Coutinho JM, Dentali F, Kobayashi A, Alasheev A, Canhão P, et al. Safety and efficacy of dabigatran etexilate vs dose-adjusted warfarin in patients with cerebral venous thrombosis: a randomized clinical trial. *JAMA Neurol*. 2019. [https:// doi.org/10.1001/jamaneurol.2019.2764](https://doi.org/10.1001/jamaneurol.2019.2764). Randomized clinical trial of dabigatran versus standard care in CVT.
18. Yaghi S, Shu L, Bakradze E, et al. Direct Oral Anticoagulants Versus Warfarin in the Treatment of Cerebral Venous Thrombosis (ACTION-CVT): A Multicenter International Study. *Stroke*, Volume 53-3, March 2022; 728-738. <https://doi.org/10.1161/STROKEAHA.121.037541>
19. Pengo V, Denas G, Zoppellaro G, Jose SP, Hoxha A, Rufatti A, et al. Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome. *Blood*. 2018;132:1365–71. Randomized clinical trial of rivaroxaban versus warfarin in highrisk APLAS
20. Holy EW, Beer JH. Update on the status of new oral anticoagulants for stroke prevention in patients with atrial fibrillation. *Cardiovasc Med*. 2013;16:103–114.
21. Büller HR, Prins MH, Lensin AW, Decousus H, Jacobson BF, Minar E, et al; EINSTEIN–PE Investigators. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. *N Engl J Med*. 2012;366:1287–1297. doi:10.1056/NEJMoa1113572
22. Schulman S, Kearon C, Kakkar AK, Mismetti P, Schellong S, Eriksson H, et al; RE-COVER Study Group. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med*. 2009;361:2342–2352. doi: 10.1056/NEJMoa0906598
23. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, et al; ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2013;369:2093–2104. doi: 10.1056/NEJMoa1310907
24. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361:1139–1151. doi: 10.1056/NEJMoa0905561
25. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2011;365:981–992. doi: 10.1056/NEJMoa1107039
26. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365:883–891. doi:10.1056/NEJMoa1009638
27. Campbell HA, Roberts WL, Smith WK, Link KP. Studies of the hemorrhagic sweet clover disease. I. The preparation of hemorrhagic concentrates. *J Biol Chem*. 1940;136:47–55.
28. Hirsh J, Dalen JE, Anderson DR, et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. *Chest*. 1998;114:445S–469S.
29. Acar B.A, Akpınar Ç.K ve ark. İNME KLİNİK PRATİĞİNDE NOAK KULLANIMI: TÜRK BEYİN DAMAR HASTALIKLARI DERNEĞİ UZMAN GÖRÜŞÜ. *Türk Beyin Damar Hastalıkları Dergisi* 2020; 26(3): 190-235. doi: 10.5505/tbdhd.2020.26213
30. Wieland E, Shipkova M. Pharmacokinetic and Pharmacodynamic Drug Monitoring of Dire-

- ct-Acting Oral Anticoagulants: Where Do We Stand? *Ther Drug Monit* 2019; 41(2): 180-191.
31. Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J* 2018; 39(16): 1330-1393.
 32. Da Silva RM. Novel oral anticoagulants in non-valvular atrial fibrillation. *Cardiovasc Hematol Agents Med Chem*. 2014;12(1):3-8.
 33. Graham DJ, Reichman ME, Wernecke M, et al. Cardiovascular, bleeding, and mortality risk in elderly Medicare patients treated with dabigatran or warfarin for nonvalvular atrial fibrillation. *Circulation*. 2015;131(2):157-164.
 34. Schulman S, Kakkar AK, Goldhaber SZ, et al. RE-COVER II Trial Investigators. Treatment of acute venous thromboembolism with dabigatran or warfarin and pooled analysis. *Circulation*. 2014;129(7):764-772.
 35. Little JW. New oral anticoagulants: will they replace warfarin? *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;113(5):570-580.
 36. Gulseth MP, Michaud J, Nutescu EA. Rivaroxaban: an oral direct inhibitor of factor Xa. *Am J Health Syst Pharm*. 2008;65(16):1520-1529.
 37. EINSTEIN Investigators. Oral rivaroxaban for symptomatic venous thromboembolism. *N Engl J Med*. 2010;363(26):2499-2510.
 38. Eikelboom JW, Weitz JI. New anticoagulants. *Circulation*. 2010; 121(13):1523-1532.
 39. Hokusai-VTE Investigators, Büller HR, Décousus H, Grosso MA, et al. Edoxapan versus warfarin for the treatment of symptomatic venous thromboembolism. *N Engl J Med*. 2013;369(15):1406-1415.
 40. Rognoni C, Marchetti M, Quaglini S, Liberato NL. Edoxaban versus warfarin for stroke prevention in non-valvular atrial fibrillation: a cost-effectiveness analysis. *J Thromb Thrombolysis*. 2015;39(2):149-154.
 41. Leung LLK. Direct oral anticoagulants (DOACs) and parenteral direct-acting anticoagulants: Dosing and adverse effects. *UpToDate* 2020; Waltham, MA(UpToDate Inc).
 42. Heidbuchel H, Verhamme P, Alings M, et al. European Heart Rhythm Association Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation. *Europace*. 2013;15(5):625-651.