



ONKOLOJİK TEDAVİYE BAĞLI TROMBOEMBOLİK HASTALIKLARDA TANI VE TEDAVİ YAKLAŞIMLARI

Özge GÜZELBURÇ¹

GİRİŞ

Günümüzde kanser önemli sağlık sorunlarından biri haline gelmiştir. Tedavi seçeneklerinin artması ile kanser hastalarının sağ kalımında iyileşme sağlanmıştır. Bu iyileşmeyi sağlarken kullanılmak zorunda olunan ilaçların yan etkileri ise halen ciddi morbidite ve mortalite nedenidir. Bu yan etkilerin en sık görülenlerinden birisi kardiyovasküler hastalıklardır. Kardiyovasküler hastalıklar arasında tromboembolik hastalıklar önemli yer tutmakta; tanı ve tedavide dikkatli bir yaklaşım ihtiyacı oluşturmaktadır.

Tromboembolik hastalıklar arteriyel veya venöz tromboz ve venöz tromboemboli (VTE) olarak kendini gösterebilir. Arteriyel tromboz nadir olmakla birlikte (insidansı yaklaşık %1), çoğunlukla antrasiklinler ve taksan ve platin içeren kemoterapi ajanları ile tedavi edilen metastatik meme, pankreas, akciğer ve kolorektal kanser hastalarında görülmektedir (1).

Kanser tanısı ile hastanede yatan hastaların %20'sinde venöz tromboz ve VTE görülmektedir (2). Kanser hastalarında VTE gelişme riski kanser olmayanlara göre 4-7 kat fazladır (3, 4). Son yıllarda kullanılan yeni kemoterapi ajanlarının trombojenik potansiyelinin yüksek olması VTE insidansını arttırmaktadır (5). Kanser ilişkili VTE risk faktörleri arasında tedavi ilişkili faktörler mevcuttur. Bunlar arasında majör cerrahi, hospitalizasyon, kemoterapi ve anti-anjiyojenik ajanlar, hormonal tedavi, transfüzyon ve santral venöz kateterler sayılabilir (5). VTE pulmoner emboli (PE) ve derin ven trombozu (DVT) olarak prezente olabilir.

¹ Uzm. Dr., SBÜ Dr. Siyami Ersek Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği
ozgeguzelburc@hotmail.com

İKS ve 1 ay İATT'nin ilaç kaplı olmayan stente göre daha daha güvenli ve etkili olduğu saptanmıştır (49).

Kanser hastalarında endotel fonksiyonlarının korunması için bazı önlemler alınması önem arz eder. Bunlar arasında egzersiz, statinler ve anjiyotensin dönüştürücü enzim inhibitörleri sayılabilir (50).

SONUÇ

Kanser hastalarında etkin tedaviler uygulanmakta ancak tedavilerin neden olduğu vasküler toksisite önemli bir morbidite ve mortalite nedeni olmaktadır. Kanser tedavisi gören hastalarda ayrıntılı bir klinik değerlendirme ve görüntüleme teknikleri ile tromboembolik hastalıkların tanısı konulmalı ve güncel kılavuzlar ışığında tedaviye başlanmalıdır.

KAYNAKLAR

1. DiNisio M, Ferrante N, Feragalli B, et al. Arterial thrombosis in ambulatory cancer patients treated with chemotherapy. *Thromb Res.*2011;127:382 –383
2. Lecumberri R, Marques M, Panizo E, et al. High incidence of venous thromboembolism despite electronic alerts for thromboprophylaxis in hospitalised cancer patients. *Thromb Haemost.* 2013;110:184-190.
3. Timp JF, Braekkan SK, Versteeg HH, et al. Epidemiology of cancer-associated venous thrombosis. *Blood.* 2013;122:1712-23.
4. Blom JW. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. *JAMA.*2005;293:715.
5. Khorana AA, Francis CW, Culakova E, et al. Frequency, risk factors, and trends for venous thromboembolism among hospitalized cancer patients. *Cancer.* 2007;110:233-46.
6. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the Simplified D-dimer. *Thromb Haemost.* 2000;83:416-420
7. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med.*2006;144:165-171.
8. Klok FA, Mos IC, Nijkeuter M, et al. Simplification of the revised Geneva score for assessing clinical probability of pulmonary embolism. *Arch Intern Med.*2008;168:2131-2136.
9. Barco S, Ende-Verhaar YM, Becattini C, et al. Differential impact of syncope on the prognosis of patients with acute pulmonary embolism: a systematic review and meta-analysis. *Eur Heart J.* 2018;39:4186-4195.
10. Shopp JD, Stewart LK, Emmett TW, et al. Findings from 12-lead electrocardiography that predict circulatory shock from pulmonary embolism: systematic review and meta-analysis. *Acad Emerg Med.*2015;22:1127-1137.
11. Stein PD, Hull RD, Patel KC, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism. *Ann Intern Med.* 2004; 140: 589-602.
12. DiNisio M, Sohne M, Kamphuisen PW, et al. D-Dimer test in cancer patients with suspected acute pulmonary embolism. *J Thromb Haemost.*2005; 3: 1239-42.
13. Konstantinides SV, Meyer G, Becattini C, et al; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J.* 2020 Jan 21;41(4):543-603. doi: 10.1093/eurheartj/ehz405.

14. van der Hulle T, Cheung WY, Kooij S, et al, Years Study Group. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. *Lancet*.2017;390:289-297.
15. Righini M, Goehring C, Bounameaux H, et al. Effects of age on the performance of common diagnostic tests for pulmonary embolism. *Am J Med*. 2000;109:357-361.
16. Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cut-off levels to rule out pulmonary embolism: the ADJUST-PE study. *JAMA*.2014;311:1117-1124.
17. Becattini C, Vedovati MC, Agnelli G. Prognostic value of troponins in acute pulmonary embolism: a meta-analysis. *Circulation*. 2007;116:427-433.
18. Lankeit M, Friesen D, Aschoff J, et al. Highly sensitive troponin T assay in normotensive patients with acute pulmonary embolism. *Eur Heart J*. 2010;31:18361-844.
19. Klok FA, Mos IC, Huisman MV. Brain-type natriuretic peptide levels in the prediction of adverse outcome in patients with pulmonary embolism: a systematic review and meta-analysis. *Am J Respir Crit Care Med*. 2008;178:425-430.
20. Ageroef MJ, Schutgens RE, Snijder RJ, et al. Out of hospital treatment of acute pulmonary embolism in patients with a low NT-proBNP level. *J Thromb Haemost*. 2010;8:1235-1241.
21. Vanni S, Nazerian P, Bova C, et al. Comparison of clinical scores for identification of patients with pulmonary embolism at intermediate-high risk of adverse clinical outcome: the prognostic role of plasma lactate. *Intern Emerg Med*. 2017;12:657-665.
22. Kostrubiec M, Plywaczewska M, Jime'nez D, et al. The prognostic value of renal function in acute pulmonary embolism a multi-centre cohort study. *Thromb Haemost*. 2019;119:140-148
23. Zhou XY, Chen HL, Ni SS. Hyponatremia and short-term prognosis of patients with acute pulmonary embolism: a meta-analysis. *Int J Cardiol*.2017;227:251-256.
24. Kostrubiec M, Labyk A, Pedowska-Wloszek J, et al. Neutrophil gelatinase-associated lipocalin, cystatin C and Egfr indicate acute kidney injury and predict prognosis of patients with acute pulmonary embolism. *Heart*. 2012;98:1221-1228
25. Vuilleumier N, Simona A, Mean M, et al. Comparison of cardiac and non-cardiac biomarkers for risk stratification in elderly patients with non-massive pulmonary embolism. *PLoS One*. 2016;11:e0155973.
26. Rodger MA, Carrier M, Jones GN, et al. Diagnostic value of arterial blood gas measurement in suspected pulmonary embolism. *Am J Respir Crit Care Med*. 2000;162:2105-2108.
27. Stein PD, Fowler SE, Goodman LR, et al; PIOPED II Investigators. Multidetector computed tomography for acute pulmonary embolism. *N Engl J Med*. 2006;354:2317-2327.
28. Glaser JE, Chamrathy M, Haramati LB, et al. Successful and safe implementation of a trinary interpretation and reporting strategy for V/Q lung scintigraphy. *J Nucl Med*. 2011;52:1508-1512.
29. Stein PD, Athanasoulis C, Alavi A, et al. Complications and validity of pulmonary angiography in acute pulmonary embolism. *Circulation*. 1992;85:462-468.
30. Kurnicka K, Lichodziejewska B, Goliszek S, et al. Echocardiographic pattern of acute pulmonary embolism: analysis of 511 consecutive patients. *J Am Soc Echocardiogr*.2016;29:907-913.
31. Roy PM, Colombet I, Durieux P, et al. Systematic review and meta-analysis of strategies for the diagnosis of suspected pulmonary embolism. *BMJ*. 2005;331:259.
32. Kurzyna M, Torbicki A, Pruszczyk P, et al. Disturbed right ventricular ejection pattern as a new Doppler echocardiographic sign of acute pulmonary embolism. *Am J Cardiol*. 2002;90:507-511.
33. Casazza F, Becattini C, Guglielmelli E, et al. Prognostic significance of free-floating right heart thromboemboli in acute pulmonary embolism: results from the Italian Pulmonary Embolism Registry. *Thromb Haemost*.2014;111:5357.
34. Casazza F, Bongarzone A, Centonze F, et al. Prevalence and prognostic significance of right-sided cardiac mobile thrombi in acute massive pulmonary embolism. *Am J Cardiol*.1997;79:1433-1435.

35. Perrier A, Bounameaux H. Ultrasonography of leg veins in patients suspected of having pulmonary embolism. *Ann Intern Med.* 1998;128:243-253.
36. Prandoni P, Siragusa S, Girolami B, et al; BELZONI Investigators Group. The incidence of heparin-induced thrombocytopenia in medical patients treated with low-molecular-weight heparin: a prospective cohort study. *Blood.* 2005;106:3049-3054.
37. Young AM, Marshall A, Thirlwall J, et al. Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized Trial (SELECT-D). *J Clin Oncol.* 2018;36:2017-23.
38. GE, van Es N, Verhamme P. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med.* 2018;378:615-24.
39. Hakoum MB, Kahale LA, Tsolakian IG, et al. Anticoagulation for the initial treatment of venous thromboembolism in people with cancer. *Cochrane Database Syst Rev.* 2018;1:CD006649.
40. Posch F, Königsbrugge O, Zielinski C, et al. Treatment of venous thromboembolism in patients with cancer: a network meta-analysis comparing efficacy and safety of anticoagulants. *Thromb Res* 2015;136:582-589.
41. Vedovati MC, Germini F, Agnelli G. Direct oral anticoagulants in patients with VTE and cancer: a systematic review and meta-analysis. *Chest.* 2015;147:475-83.
42. Raskob GE, van Es N, Verhamme P, et al; Hokusai VTE Cancer Investigators. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med.* 2018;378:615-624.
43. Jara-Palomares L, Solier-Lopez A, Elias-Hernandez T, et al. Tinzaparin in cancer associated thrombosis beyond 6 months: TiCAT study. *Thromb Res.* 2017;157:90-96.
44. Francis CW, Kessler CM, Goldhaber SZ, et al. Treatment of venous thromboembolism in cancer patients with dalteparin for up to 12 months: the DALTECAN study. *J Thromb Haemost.* 2015;13: 1028-1035.
45. Napolitano M, Saccullo G, Malato A, et al. Optimal duration of low molecular weight heparin for the treatment of cancer-related deep vein thrombosis: the Cancer-DACUS Study. *J Clin Oncol.* 2014;32:3607-3612.
46. Rafii H, Frère C, Benzidia I, et al. Management of cancer-related thrombosis in the era of direct oral anticoagulants: A comprehensive review of the 2019 ITAC-CME clinical practice guidelines. On behalf of the Groupe Francophone Thrombose et Cancer (GFTC). *J Med Vasc.* 2020 Feb;45(1):28-40.doi: 10.1016/j.jdmv.2019.12.004.
47. Iliescu C. A, Girnes CL, Herrman J, et al. SCAI Expert Consensus Statement: evaluation, management, and special considerations of cardio-oncology patients in the cardiac catheterization laboratory (endorsed by the Cardiological Society of India, and Sociedad Latino Americana de Cardiología Intervencionista). *Catheter Cardiovasc Interv.* 87, E202-E223 (2016).
48. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*, 40, 87-165 (2019).
49. Urban P, Meredith IT, Abizaid A, et al. Polymer-free drug-coated coronary stents in patients at high bleeding risk. *N Engl J Med*, 373, 2038-2047 (2015)
50. Touyz RM, Herrmann SMS, Herrmann J. Vascular toxicities with VEGF inhibitor therapies-focus on hypertension and arterial thrombotic events. *J Am Soc Hypertens*, 12, 409-425 (2018)