

# KALP YETERSİZLİĞİ OLAN HASTALARDA ONKOJİK YAKLAŞIMI

## 10. BÖLÜM

Sefa OKAR<sup>1</sup>

### GİRİŞ

Kanser ve kalp yetmezliği (KY), gelişmiş ülkelerde, daha çok ileri yaşlarda ortaya çıkan ve görülme sıklığı giderek artan tıbbi durumlardır. Bu iki hastalık da kötü prognostik seyir izlemektedir. Daha önceden KY tanısı konulan hastalarda yeni malignite teşhisi konulması sık görülen bir durumdur. KY ve kanser birlikte yönetimi ile ilgili karşılaşılan problemler kardiyolog ve onkologları zorlamaktadır. KY teşhisi ile takip ve tedavi edilen hastalarda kanser insidansında artış gözlenmiştir. Bu bölümde, KY'de kanser gelişiminin epidemiyolojisini ve prognostik neticeleri, KY tanılı hastaların kanser tedavi planlaması üzerindeki etkisini ve bunun tersi olarak kanserin KY tedavi seçenekleri üzerindeki etkisini anlatırken, hasta bakımı ile ilgili bazı pratik öneriler sunup ve bu konu ile ilgili bilgi eksiklikleri ifade edilmeye çalışılmıştır. Gelişmiş ülkelerde beklenen yaşam süresinin uzaması sonucunda ileri yaş bireylerde kalp yetmezliğine (KY), özellikle korunmuş sol ventrikül ejeksiyon fraksiyonu (LVEF) ile sonuçlanabilecek kalp yapısında ve işlevinde değişikliklere yatkınlık yaratıyor. Bunun yanında kardiyovasküler alanda tedavideki büyük ilerlemeler, akut miyokard enfarktüsü ve diğer akut kardiyovasküler olaylarda mortalitede bariz gerileme sağlasa da azalmış sol ventrikül ejeksiyon fraksiyonu (LVEF) ile KY'ye yol açan sonraki miyokardiyal yeniden şekillenmeyi aynı ölçüde etkilenmediği görülmüştür (1,2,3). Bunların sonucunda KY, giderek artan prevalansı olan ve çoğunlukla da yaşlı bireyleri etkileyen bir sendromdur (4). Bir çok kanser hastalığında da yaş ile birlikte görülme sıklığı artmaktadır (5). Son Amerikan Kanser Derneği tahminlerine göre, doğumdan 49 yaşına kadar herhangi bir bölgede invaziv kanser gelişme olasılığı kadınlarda ve erkeklerde sırasıyla 19'da 1 ve 29'da 1'dir. İnsan yaşamının altıncı on dekatında 17'de 1 ve 15'te 1'e, yedinci dekatında 10'da 1 ve 7'de 1 olur ve 70 yaş sonrasında

<sup>1</sup> Kardiyoloji Uzmanı, Başkent Üniversitesi Hastanesi Adana Dr Turgut Noyan Uygulama ve Araştırma Merkezi, drsefaokar@gmail.com ORCID iD: 0000 0003 1413 7393

**KAYNAKÇA**

1. Ponikowski P, 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016;18:891–975.
2. Christ M, Stork S, Dorr M, Heppner HJ, Muller C, Wachter R, Riemer U; Trend HF Germany Project. Heart failure epidemiology 2000–2013: insights from the German Federal Health Monitoring System. *Eur J Heart Fail* 2016;18:1009–1018.
3. Cleland JG, Torabi A, Khan NK. Epidemiology and management of heart failure and left ventricular systolic dysfunction in the aftermath of a myocardial infarction. *Heart* 2005;91 Suppl. 2:ii7–13; discussion ii31, ii43–48.
4. Guha K, McDonagh T. Heart failure epidemiology: European perspective. *Curr Cardiol Rev* 2013;9:123–127. Crossref CAS PubMed Google Scholar
5. Serrano M. Unraveling the links between cancer and aging. *Carcinogenesis* 2016;37:107. Crossref CAS PubMed Web of Science\*Google Scholar
6. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin* 2016;66:7–30.
7. Hasin T, Gerber Y, McNallan SM, Weston SA, Kushwaha SS, Nelson TJ, Cerhan JR, Roger VL. Patients with heart failure have an increased risk of incident cancer. *J Am Coll Cardiol* 2013;62:881–886.
8. Hasin T, Gerber Y, Weston SA, Jiang R, Killian JM, Manemann SM, Cerhan JR, Roger VL. Heart failure after myocardial infarction is associated with increased risk of cancer. *J Am Coll Cardiol* 2016;68:265–271.
9. Banke A, Schou M, Videbaek L, Moller JE, Torp-Pedersen C, Gustafsson F, Dahl JS, Kober L, Hildebrandt PR, Gislason GH. Incidence of cancer in patients with chronic heart failure: a long-term follow-up study. *Eur J Heart Fail* 2016;18:260–266.
10. Mentz RJ, Kelly JP, von Lueder TG, Voors AA, Lam CS, Cowie MR, Kjeldsen K, Jankowska EA, Atar D, Butler J, Fiuzat M, Zannad F, Pitt B, O'Connor CM. Noncardiac comorbidities in heart failure with reduced versus preserved ejection fraction. *J Am Coll Cardiol* 2014;64:2281–2293.
11. Albin A, Pennesi G, Donatelli F, Cammarota R, De Flora S, Noonan DM. Cardiotoxicity of anticancer drugs: the need for cardio-oncology and cardio-oncological prevention. *J Natl Cancer Inst* 2010;102:14–25.
12. Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: relationship to age, gender, and performance status in 1000 patients. *Support Care Cancer* 2000;8:175–179.
13. O'Leary N, Murphy NF, O'Loughlin C, Tiernan E, McDonald K. A comparative study of the palliative care needs of heart failure and cancer patients. *Eur J Heart Fail* 2009;11:406–412.
14. Thavendiranathan P, Nolan MT. An emerging epidemic: cancer and heart failure. *Clin Sci (Lond)* 2017;131:113–121.
15. Farmakis D, Stafylas P, Giamouzis G, Maniadakis N, Parissis J. The medical and socioeconomic burden of heart failure: a comparative delineation with cancer. *Int J Cardiol* 2016;203:279–281.
16. Le CP, Nowell CJ, Kim-Fuchs C, Botteri E, Hiller JG, Ismail H, Pimentel MA, Chai MG, Karnezis T, Rotmensz N, Renne G, Gandini S, Pouton CW, Ferrari D, Moller A, Stacker SA, Sloan EK. Chronic stress in mice remodels lymph vasculature to promote tumour cell dissemination. *Nat Commun* 2016;7:10634.
17. Egami K, Murohara T, Shimada T, Sasaki K, Shintani S, Sugaya T, Ishii M, Akagi T, Ikeda H, Matsuishi T, Imaizumi T. Role of host angiotensin II type 1 receptor in tumor angiogenesis and growth. *J Clin Invest* 2003;112:67–75.
18. Sipahi I, Debanne SM, Rowland DY, Simon DI, Fang JC. Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials. *Lancet Oncol* 2010;11:627–636.
19. Biggar RJ, Andersen EW, Kroman N, Wohlfahrt J, Melbye M. Breast cancer in women using digoxin: tumor characteristics and relapse risk. *Breast Cancer Res* 2013;15:R13.
20. Bangalore S, Kumar S, Kjeldsen SE, Makani H, Grossman E, Wetterslev J, Gupta AK, Sever PS, Gluud C, Messerli FH. Antihypertensive drugs and risk of cancer: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *Lancet Oncol* 2011;12:65–82.

21. Couraud S, Dell'Aniello S, Bouganim N, Azoulay L. Cardiac glycosides and the risk of breast cancer in women with chronic heart failure and supraventricular arrhythmia. *Breast Cancer Res Treat* 2014;146:619–626.
22. Wuerzner G, Burnier M, Waeber B. Critical review of cancer risk associated with angiotensin receptor blocker therapy. *Vasc Health Risk Manag* 2011;7:741–747.
23. McKay RR, Rodriguez GE, Lin X, Kaymakalan MD, Hamnvik OP, Sabbiseti VS, Bhatt RS, Simantov R, Choueiri TK. Angiotensin system inhibitors and survival outcomes in patients with metastatic renal cell carcinoma. *Clin Cancer Res* 2015;21:2471–2479.
24. Coelho M, Soares-Silva C, Brandao D, Marino F, Cosentino M, Ribeiro L. Beta-adrenergic modulation of cancer cell proliferation: available evidence and clinical perspectives. *J Cancer Res Clin Oncol* 2017;143:275–291.
25. Sysa-Shah P, Tocchetti CG, Gupta M, Rainer PP, Shen X, Kang BH, Belmonte F, Li J, Xu Y, Guo X, Bedja D, Gao WD, Paolucci N, Rath R, Sawyer DB, Naga Prasad SV, Gabrielson K. Bidirectional cross-regulation between ErbB2 and beta-adrenergic signalling pathways. *Cardiovasc Res* 2016;109:358–373.
26. Barron TI, Connolly RM, Sharp L, Bennett K, Visvanathan K. beta blockers and breast cancer mortality: a population-based study. *J Clin Oncol* 2011;29:2635–2644.
27. Mei Z, Liang M, Li L, Zhang Y, Wang Q, Yang W. Effects of statins on cancer mortality and progression: a systematic review and meta-analysis of 95 cohorts including 1,111,407 individuals. *Int J Cancer* 2017;140:1068–1081.
28. Mamas MA, Sperrin M, Watson MC, Coutts A, Wilde K, Burton C, Kadam UT, Kwok CS, Clark AB, Murchie P, Buchan I, Hannaford PC, Myint PK. Do patients have worse outcomes in heart failure than in cancer? A primary care-based cohort study with 10-year follow-up in Scotland. *Eur J Heart Fail* 2017;19:1095–1104.
29. Omersa D, Farkas J, Erzen I, Lainscak M. National trends in heart failure hospitalization rates in Slovenia 2004–2012. *Eur J Heart Fail* 2016;18:1321–1328.
30. Cramer L, Hildebrandt B, Kung T, Wichmann K, Springer J, Doehner W, Sandek A, Valentova M, Stojakovic T, Scharnagl H, Riess H, Anker SD, von Haehling S. Cardiovascular function and predictors of exercise capacity in patients with colorectal cancer. *J Am Coll Cardiol* 2014;64:1310–1319.
31. Farmakis D, Parissis J, Filippatos G. Insights into onco-cardiology: atrial fibrillation in cancer. *J Am Coll Cardiol* 2014;63:945–953.
32. Anker MS, Ebner N, Hildebrandt B, Springer J, Sinn M, Riess H, Anker SD, Landmesser U, Haerkamp W, von Haehling S. Resting heart rate is an independent predictor of death in patients with colorectal, pancreatic, and non-small cell lung cancer: results of a prospective cardiovascular long-term study. *Eur J Heart Fail* 2016;18:1524–1534.
33. Kravchenko J, Berry M, Arbeeve K, Kim Lyerly H, Yashin A, Akushevich I. Cardiovascular comorbidities and survival of lung cancer patients: Medicare data based analysis. *Lung Cancer* 2015;88:85–93.
34. Zamorano JL, Lancellotti P, Rodriguez Munoz D, Aboyans V, Asteggiano R, Galderisi M, Habib G, Lenihan DJ, Lip GY, Lyon AR, Lopez Fernandez T, Mohty D, Piepoli MF, Tamargo J, Torbicki A, Suter TM. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). *Eur J Heart Fail* 2017;19:9–42.
35. Bloom MW, Hamo CE, Cardinale D, Ky B, Nohria A, Baer L, Skopicki H, Lenihan DJ, Gheorghide M, Lyon AR, Butler J. Cancer therapy-related cardiac dysfunction and heart failure: part 1: definitions, pathophysiology, risk factors, and imaging. *Circ Heart Fail* 2016;9:e002661.
36. Mercurio V, Pirozzi F, Lazzarini E, Marone G, Rizzo P, Agnetti G, Tocchetti CG, Ghigo A, Ameri P. Models of heart failure based on the cardiotoxicity of anticancer drugs. *J Card Fail* 2016;22:449–458.
37. Di Lisi D, Madonna R, Zito C, Bronte E, Badalamenti G, Parrella P, Monte I, Tocchetti CG, Russo A, Novo G. Anticancer therapy-induced vascular toxicity: VEGF inhibition and beyond. *Int J Cardiol* 2017;227:11–17.

38. Bosco C, Bosnyak Z, Malmberg A, Adolffson J, Keating NL, Van Hemelrijck M. Quantifying observational evidence for risk of fatal and nonfatal cardiovascular disease following androgen deprivation therapy for prostate cancer: a meta-analysis. *Eur Urol* 2015;68:386–396.
39. Martin-Merino E, Johansson S, Morris T, Garcia Rodriguez LA. Androgen deprivation therapy and the risk of coronary heart disease and heart failure in patients with prostate cancer: a nested case-control study in UK primary care. *Drug Saf* 2011;34:1061–1077.
40. Boekhout AH, Gietema JA, Milojkovic Kerklaan B, van Werkhoven ED, Altena R, Honkoop A, Los M, Smit WM, Nieboer P, Smorenburg CH, Mandigers CM, van der Wouw AJ, Kessels L, van der Velden AW, Ottevanger PB, Smilde T, de Boer J, van Veldhuisen DJ, Kema IP, de Vries EG, Schellens JH. Angiotensin II-receptor inhibition with candesartan to prevent trastuzumab-related cardiotoxic effects in patients with early breast cancer: a randomized clinical trial. *JAMA Oncol* 2016;2:1030–1037.
41. Gulati G, Heck SL, Ree AH, Hoffmann P, Schulz-Menger J, Fagerland MW, Gravdehaug B, von Knobelsdorff-Brenkenhoff F, Bratland A, Storas TH, Hagve TA, Rosjo H, Steine K, Geisler J, Omland T. Prevention of cardiac dysfunction during adjuvant breast cancer therapy (PRADA): a 2 x 2 factorial, randomized, placebo-controlled, double-blind clinical trial of candesartan and metoprolol. *Eur Heart J* 2016;37:1671–1680.
42. Spallarossa P, Garibaldi S, Altieri P, Fabbi P, Manca V, Nasti S, Rossettin P, Ghigliotti G, Ballestero A, Patrone F, Barsotti A, Brunelli C. Carvedilol prevents doxorubicin-induced free radical release and apoptosis in cardiomyocytes in vitro. *J Mol Cell Cardiol* 2004;37:837–846.
43. Canepa M, Temporelli PL, Rossi A, Rossi A, Gonzini L, Nicolosi GL, Staszewsky L, Marchioli R, Maggioni AP, Tavazzi L; GISSI-HF Investigators. Prevalence and prognostic impact of chronic obstructive pulmonary disease in patients with chronic heart failure: data from the GISSI-HF trial. *Cardiology* 2017;136:128–137.
44. Canepa M; ESC-HFA Heart Failure Long-Term Registry Investigators. Characteristics, treatments and 1-year prognosis of hospitalized and ambulatory heart failure patients with chronic obstructive pulmonary disease in the European Society of Cardiology Heart Failure Long-Term Registry. *Eur J Heart Fail* 2017 Sep 26. <https://doi.org/10.1002/ehf.964>.
45. Ghosh RK, Ball S, Prasad V, Gupta A. Depression in heart failure: intricate relationship, pathophysiology and most updated evidence of interventions from recent clinical studies. *Int J Cardiol* 2016;224:170–177.
46. Freedland KE, Carney RM, Rich MW, Steinmeyer BC, Rubin EH. Cognitive behavior therapy for depression and self-care in heart failure patients: a randomized clinical trial. *JAMA Intern Med* 2015;175:1773–1782.
47. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, Edvardsen T, Garbi M, Ha JW, Kane GC, Kreeger J, Mertens L, Pibarot P, Picano E, Ryan T, Tsutsui JM, Varga A. The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *Eur Heart J Cardiovasc Imaging* 2016;17:1191–1229.
48. Suter TM, Ewer MS. Cancer drugs and the heart: importance and management. *Eur Heart J* 2013;34:1102–1111.
49. Lund LH, Braunschweig F, Benson L, Stahlberg M, Dahlstrom U, Linde C. Association between demographic, organizational, clinical, and socio-economic characteristics and underutilization of cardiac resynchronization therapy: results from the Swedish Heart Failure Registry. *Eur J Heart Fail* 2017;19:1270–1279.
50. Lenihan DJ, Stevens PL, Massey M, Plana JC, Araujo DM, Fanale MA, Fayad LE, Fisch MJ, Yeh ET. The utility of point-of-care biomarkers to detect cardiotoxicity during anthracycline chemotherapy: a feasibility study. *J Card Fail* 2016;22:433–438.
51. Schmidinger M, Bergler-Klein J. Therapy management of cardiovascular adverse events in the context of targeted therapy for metastatic renal cell carcinoma. *Int J Urol* 2012;19:796–804.
52. Viganego F, Singh R, Fradley MG. Arrhythmias and other electrophysiology issues in cancer patients receiving chemotherapy or radiation. *Curr Cardiol Rep* 2016;18:52. Crossref PubMed Web of Science\*Google Scholar

53. Lancellotti P; European Society of Cardiology Working Groups on Nuclear Cardiology and Cardiac Computed Tomography and Cardiovascular Magnetic Resonance; American Society of Nuclear Cardiology; Society for Cardiovascular Magnetic Resonance; Society of Cardiovascular Computed Tomography. Expert consensus for multi-modality imaging evaluation of cardiovascular complications of radiotherapy in adults: a report from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *Eur Heart J Cardiovasc Imaging* 2013;14:721–740.
54. Gross CP, McAvay GJ, Guo Z, Tinetti ME. The impact of chronic illnesses on the use and effectiveness of adjuvant chemotherapy for colon cancer. *Cancer* 2007;109:2410–2419.
55. Lothar A, Bergemann S, Kowalski J, Huck M, Gilsbach R, Bode C, Hein L. Inhibition of the cardiac myocyte mineralocorticoid receptor ameliorates doxorubicin-induced cardiotoxicity. *Cardiovasc Res* 2018;114:282–290.
56. Santhanakrishnan R, Wang N, Larson MG, Magnani JW, McManus DD, Lubitz SA, Ellinor PT, Cheng S, Vasan RS, Lee DS, Wang TJ, Levy D, Benjamin EJ, Ho JE. Atrial fibrillation begets heart failure and vice versa: temporal associations and differences in preserved versus reduced ejection fraction. *Circulation* 2016;133:484–492.
57. Kirchhof P, 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;37:2893–2962.
58. Savarese G, Giugliano RP, Rosano GM, McMurray J, Magnani G, Filippatos G, Dellegrottaglie S, Lund LH, Trimarco B, Perrone-Filardi P. Efficacy and safety of novel oral anticoagulants in patients with atrial fibrillation and heart failure: a meta-analysis. *JACC Heart Fail* 2016;4:870–880.
59. Farge D, Bounameaux H, Brenner B, Cajfinger F, Debourdeau P, Khorana AA, Pabinger I, Solymoss S, Douketis J, Kakkar A. International clinical practice guidelines including guidance for direct oral anticoagulants in the treatment and prophylaxis of venous thromboembolism in patients with cancer. *Lancet Oncol* 2016;17:e452–466.
60. Ruwald AC, Vinther M, Gislason GH, Johansen JB, Nielsen JC, Petersen HH, Riahi S, Jons C. The impact of co-morbidity burden on appropriate implantable cardioverter defibrillator therapy and all-cause mortality: insight from Danish nationwide clinical registers. *Eur J Heart Fail* 2017;19:377–386.
61. Feldman D, The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant*
62. Arnold SV, Jones PG, Allen LA, Cohen DJ, Fendler TJ, Holtz JE, Aggarwal S, Spertus JA. Frequency of poor outcome (death or poor quality of life) after left ventricular assist device for destination therapy: results from the INTERMACS registry. *Circ Heart Fail* 2016;9:e002800.
63. Sigurdardottir V, Bjortuft O, Eiskjaer H, Ekmehag B, Gude E, Gustafsson F, Hagerman I, Halme M, Lommi J, Mared L, Riise GC, Simonsen S. Long-term follow-up of lung and heart transplant recipients with pre-transplant malignancies. *J Heart Lung Transplant* 2012;31:1276–1280.
64. Banner NR, Bonser RS, Clark AL, Clark S, Cowburn PJ, Gardner RS, Kalra PR, McDonagh T, Rogers CA, Swan L, Parameshwar J, Thomas HL, Williams SG. UK guidelines for referral and assessment of adults for heart transplantation. *Heart* 2011;97:1520–1527.
65. Smail H, Pfister C, Baste JM, Nafeh-Bizet C, Gay A, Barbay V, Bessou JB, Peillon C, Litzler PY. A difficult decision: what should we do when malignant tumours are diagnosed in patients supported by left ventricular assist devices? *Eur J Cardiothorac Surg* 2015;48:e30–36.
66. Gkouziouta A, Farmakis D, Manginas A, Sfyraakis P, Saroglou G, Adamopoulos S, Iliodromitis EK. Double organ transplantation in cardiac amyloidosis. *J Cardiovasc Med (Hagerstown)* 2016;17:126–129.
67. Lynce F, Barac A, Tan MT, Asch FM, Smith KL, Dang C, Isaacs C, Swain SM. SAFE-HEArT: rationale and design of a pilot study investigating cardiac safety of HER2 targeted therapy in patients with HER2-positive breast cancer and reduced left ventricular function. *Oncologist* 2017;22:518–525.