

KANSER HASTALARINDA KAS İSKELET SİSTEMİ AĞRILARINA YAKLAŞIM

Sevil OKAN¹

GİRİŞ

Kanserin erken teşhis ve tedavisindeki ilerlemeler sayesinde kanser hastalarında yaşam beklentisi artmıştır (1). Tedavi sürecinde veya tedavinin tamamlanmasından sonra ortaya çıkan uzun süren semptomlar, kanser hastalarını rehabilitasyon alanı için giderek daha önemli bir popülasyon haline getirmektedir(2). Kanser, vücutun günlük rutin aktiviteler sırasında ağırlık taşıma, hareket etme kabiliyetinin azalması ile ilişkilidir. Bunun sonucunda, ekstremiteler, omurga ve kaslar; özellikle hareket sırasında ağrı kaynağı haline gelir. Sağlam kas-iskelet sistemi yapılıları bile, kanser ve tedavisinin neden olduğu biyomekanik değişikliklerin sonucu olarak ağrılı hale gelebilir(3). Kas-iskelet sistemi ağrısı, mekanik, biyomekanik, psikolojik ve sosyal faktörlerin karmaşık etkileşiminden kaynaklanır(4). Kansere bağlı kas-iskelet sistemi ağrısı dört ana mekanizmadan kaynaklanmaktadır. Buna; doğrudan tümör invazyonu, kanser tedavisi veya lokal tümör etkileri ile induklenen değişiklikler, önceden var olan kas-iskelet sistemi ağrısının alevlenmesi ve yukarıdakilerden herhangi birine bağlı hipertonusite ve spazmdir(5).

Kanserli hastalarda en sık görülen, sürekli arzeden ve hastaların en çok korkutukları symptom ağrıdır; bu nedenle ağrı başlangıcını geciktirmek hastanın bakış açısından önemli bir tedavi başarısıdır. Ağrıyi hafif düzeyde tutmak, daha iyi fonksiyon ve yaşam kalitesi ile ilişkilendirilmiştir (6). Kas-iskelet sistemi ağrısının tedavisinde farmakolojik ajanlar, farmakolojik olmayan (fiziksel, psikolojik, sosyal / çevresel) müdahaleler, ve invaziv (cerrahi) yöntemler kullanılır(7).

¹ Uzm. Dr. Tokat Devlet Hastanesi, doctorsevil@yahoo.com

SONUÇ

Sonuç olarak kanser hastaları hem hastalığa, hem tedavisine bağlı çeşitli kas iskelet sistemi ağrısı ile karşımıza çıkabilir. Hastaların ağrısının şiddetli olması, sistematik tutulumlarının olması ve eş zamanlı kullanılan ilaçlar ağrı tedavisini zorlaştırmaktadır. Analjezik basamak tedavisi, fizik tedavi, minimal invaziv analjezik girişimler, radyoterapi, cerrahi ve psikolojik yöntemler gibi çeşitli tedaviler göz önünde bulundurulmalıdır. Hastalar multidisipliner yaklaşımla değerlendirilmeli ve ağrıyla yaşamaya mahkum edilmelidirler.

KAYNAKÇA

1. Krok-Schoen JL, Fisher JL, Baltic RD, et al. White-Black differences in cancer incidence, stage at diagnosis, and survival among adults aged 85 years and older in the United States. *Cancer Epidemiol Biomarkers Prev.* 2016;25:1517–1523. Doi: 10.1158/1055-9965.EPI-16-0354
2. Harrington S, Gilchrist L, Sander A. Breast cancer EDGE task force outcomes: clinical measures of pain. *Rehabil Oncol.* 2014;32:13–21.
3. Jimenez-Andrade JM, Mantyh WG, Bloom AP, et al. Bone cancer pain. *Ann N Y Acad Sci* 2009;1198:173–181. Doi: 10.1111/j.1749-6632.2009.05429.x
4. Fetrow KO. The management of pain in orthopaedics. *Clin J Pain.* 1989;5(2):S26–32.
5. Cheville AL, Basford JR. Role of rehabilitation medicine and physical agents in the treatment of cancer-associated pain. *J Clin Oncol.* 2014;32:1691–1702. Doi:10.1200/JCO.2013.53.6680.
6. Cleeland CS, Body JJ, Stopeck A, et al. Pain outcomes in patients with advanced breast cancer and bone metastases: Results from a randomized, double-blind study of denosumab and zoledronic acid. *Cancer.*2013;119(4):832-838.Doi: 10.1002/cncr.27789.
7. Nicholas MK. Pain management in musculoskeletal conditions. *Best Pract Res Clin Rheumatol.*2008;22(3):451–70. Doi: 10.1016/j.berh.2007.11.008.
8. Jung BF, Ahrendt GM, Oaklander AL, et al. Neuropathic pain following breast cancer surgery: proposed classification and research update. *Pain.* 2003;104(1):1–13.
9. Marchettini P, Lacerenza M, Mauri E, et al. Painful peripheral neuropathies. *Curr Neuropharmacol.* 2006;4(3):175–181. doi: 10.2174/157015906778019536.
10. Hershman DL, Lacchetti C, Dworkin RH, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol.* 2014;32(18):1941–1967. Doi: 10.1200/JCO.2013.54.0914.
11. Pike CT, Birnbaum HG, Muehlenbein CE, et al. Healthcare costs and workloss burden of patients with chemotherapy-associated peripheral neuropathy in breast, ovarian, head and neck, and nonsmall cell lung cancer. *Cancer Ther Pract.* 2012;2012:913848. Doi:10.1155/2012/913848.
12. Staff NP, Grisold A, Grisold W, et al. Chemotherapy-induced peripheral neuropathy: A current review. *Annals of neurology.*2017;81(6): 772-781. Doi:0.1002/ana.24951
13. Park SB, Lin CS, Krishnan AV, et al. Oxaliplatin-induced neurotoxicity: changes in axonal excitability precede development of neuropathy. *Brain.* 2009;132(10):2712–23. Doi:10.1093/brain/awp219.
14. Freilich RJ, Balmaceda C, Seidman AD, et al. Motor neuropathy due to docetaxel and paclitaxel. *Neurology.* 1996;47(1):115–8.
15. Reeves BN, Dakhil SR, Sloan JA, et al. Further data supporting that paclitaxel-associated acute pain syndrome is associated with development of peripheral neuropathy. *Cancer.* 2012;118(20):5171–8. Doi:10.1002/cncr.27489.
16. Amato AA, Collins MP. Neuropathies associated with malignancy. *Semin Neurol.* 1998;18(1):125-144.

17. Kelly JJ, Karcher DS. Lymphoma and peripheral neuropathy: a clinical review. *Muscle Nerve*. 2005;31(3):301-313. Doi:10.1002/mus.20163.
18. Stubblefield MD. Cancer Rehabilitation. *Seminars in Oncology*.2011;38(3):386–393. doi:10.1053/j.seminoncol.2011.03.008
19. Stubblefield MD, Custodio CM. Upper-extremity pain disorders in breast cancer. *Arch Phys Med Rehabil*. 2006;87(3 Suppl 1):S96 –9. Doi: 10.1016/j.apmr.2005.12.017.
20. Kori SH, Foley KM, Posner JB. Brachial plexus lesions in patients with cancer: 100 cases. *Neurology* 1981;31:45-50. Doi: 10.1212/wnl.31.1.45.
21. Delanian S, Lefaix J-L, Pradat P-F. Radiation-induced neuropathy in cancer survivors. *Radiother Oncol*. 2012;105(3):273–82. Doi: 10.1016/j.radonc.2012.10.012.
22. Gärtner R, Jensen MB, Nielsen J, et al. Prevalence of and factors associated with persistent pain following breast cancer surgery. *Jama*.2009; 302(18):1985-1992. Doi:10.1001/jama.2009.1568.
23. Wallace MS, Wallace AM, Lee J, et al. Pain after breast surgery: a survey of 282 women. *Pain*. 1996;66(2-3):195–205.
24. Vadivelu N, Schreck M, Lopez J, et al. Pain after mastectomy and breast reconstruction. *Am Surg*. 2008;74(4):285–96.
25. Ebaugh D, Spinelli B, Schmitz KH. Shoulder impairments and their association with symptomatic rotator cuff disease in breast cancer survivors. *Med Hypotheses* 2011;77:481-487. Doi:10.1016/j.mehy.2011.06.015.
26. Ramesh, Shukla NK, Bhatnagar S. Phantom breast syndrome. *Ind J Palliat Care*. 2009;15:103-107.
27. Dijkstra PU, Rietman JS, Geertzen JH. Phantom breast sensations and phantom breast pain: A 2-year prospective study and a methodological analysis of literature. *Eur J Pain*. 2007;11(1):99-108
28. Wallace AM, Wallace MS. Postmastectomy and postthoracotomy pain. *Anesth Clin North Am*. 1997;15:353–370.
29. Macdonald DR. Neurologic complications of chemotherapy. *Neurologic Clinics* 1991;9:955-967.
30. Portlock CS, Boland P, Hays AP, et al. Nemaline myopathy: a possible late complication of Hodgkin's disease therapy. *Hum Pathol*. 2003;34:816 – 8.
31. Stone HB, Coleman CN, Anscher MS,e al. Effects of radiation on normal tissue: consequences and mechanisms. *Lancet Oncol*. 2003;4:529 –36.
32. Gottrup H, Andersen J, Arendt-Nielsen L,et al. Psychophysical examination in patients with post-mastectomy pain. *Pain*. 2000;87(3):275–284. Doi:10.1016/S0304-3959(00)00291-8.
33. Chaplin JM, Morton RP. A prospective, longitudinal study of pain in head and neck cancer patients. *Head & Neck*. 1999;21(6):531–537.
34. Han DW, Koo BN, Chung WY, et al. Preoperative greater occipital nerve block in total thyroidectomy patients can reduce postoperative occipital headache and posterior neck pain. *Thyroid*.2006;16(6):599–603. <https://doi.org/10.1089/thy.2006.16.599>
35. Park C, Choi JB, Lee YS, et al. The effect of intra-operative transcutaneous electrical nerve stimulation on posterior neck pain following thyroidectomy. *Anaesthesia*.2015;70(4):434–439. Doi:10.1111/anae.12933.
36. Rodriguez-Torres J, Lopez-López L, Cabrera-Martos I, et al. Musculoskeletal neck disorders in thyroid cancer patients after thyroidectomy. *Eur J Cancer Care*. 2019;e13053. Doi:10.1111/ecc.13053.
37. Caban ME, Yadav R. Rehabilitation of breast cancer-related functional deficits. *Critical Reviews in Physical and Rehabilitation Medicine* 2008;20(1):1-23.
38. Lacomba MT, Del Moral OM, Zazo JL et al.Incidence of myofascial pain syndrome in breast cancer surgery: a prospective study. *The Clinical journal of pain*.2010;26(4):320-325.
39. Latremoliere A,Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. *The journal of pain*.2009;10(9):895-926.Doi:10.1016/j.jpain.2009.06.012.
40. Falk S, Dickenson AH. Pain and nociception: mechanisms of cancer-induced bone pain. *J Clin Oncol*. 2014;32:1647–54. Doi:10.1200/JCO.2013.51.7219.

41. Ungard RG, Seidlitz EP, Singh G. Inhibition of breast cancer-cell glutamate release with sulfasalazine limits cancer-induced bone pain. *Pain.* 2014;155(1):28-36. Doi:10.1016/j.pain.2013.08.030.
42. Wedin R, Bauer HC, Skoog L, et al. Cytological diagnosis of skeletal lesions: fine-needle aspiration biopsy in 110 tumours. *J Bone Joint Surg Br.* 2000;82(5): 673-678.
43. Bauer HC. Controversies in the surgical management of skeletal metastases. *J Bone Joint Surg Br* 2005;87:608-617.
44. Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. *Clin Cancer Res* 2006;12:6243-6249. Doi: 10.1158/1078-0432.CCR-06-0931.
45. Ateş F, Baykal KV. Prostat, mesane ve böbrek tümörlerinin iskelet sistemi komplikasyonları ve bifosfonat tedavisi. *Turkish Journal of Urology.*2010;36(2):112-118.
46. Kransdorf MJ. Malignant soft-tissue tumors in a large referral population: distribution of diagnoses by age, sex, and location. *AJR Am J Roentgenol.*1995;164(1):129-134.
47. Muslimani AA, Spiro TP, Chaudhry AA, et al. Aromatase inhibitor-related musculoskeletal symptoms: is preventing osteoporosis the key to eliminating these symptoms? *Clin Breast Cancer.*2009; 9(1):34-38. Doi:10.3816/CBC.2009.n.006.
48. Mayadağlı A, Bulut G, Ekici, K. Metastatik kemik tümörlerine yaklaşım. *J Kartal TR* 2011;22(1):49-55. Doi:10.5505/jkartaltr.2011.82787.
49. Kim MJ, Ye YM, Park HS, et al. Chemotherapy-related arthropathy. *J Rheumatol.*2006; 33(7):1364-1368.
50. Coleman RE, Bolten WW, Lansdown M, et al. Aromatase inhibitor-induced arthralgia: clinical experience and treatment recommendations. *Cancer Treat Rev.* 2008;34(3):275-282. Doi:10.1016/j.ctrv.2007.10.004.
51. Burstein HJ, Lacchetti C, Anderson H et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American Society of Clinical Oncology Clinical Practice Guideline Update on Ovarian Suppression Summary. *J Oncol Pract.*2016;34(14):390-3. Doi:10.1200/JCO.2015.65.9573.
52. Robert K, Rickett K, Greer R, et al . Management of aromatase inhibitor induced musculoskeletal symptoms in postmenopausal early Breast cancer: A systematic review and meta-analysis. *Crit Rev Oncol Hematol.*2017;111: 66-80. Doi:10.1016/j.critrevonc.2017.01.010.
53. Robidoux A, Rich E, Bureau NJ, et al. A prospective pilot study investigating the musculoskeletal pain in postmenopausal breast cancer patients receiving aromatase inhibitor therapy. *Curr Oncol* 2011;18:285-294.
54. Selçuk B, Dalyan M, İnanır M et al. Meme cerrahisi ve aksiller diseksiyon uygulanan hastalarda üst ekstremite muskuloskeletal problemleri. *Turk Fiz Tip Rehab Derg.* 2001;47:38-46.
55. Panis C, Pavanelli WR. Cytokines as mediators of pain-related process in breast cancer. *Mediators Inflamm.* 2015;2015:129034. Doi:10.1155/2015/129034.
56. Straub JM, New J, Hamilton CD, et al. Radiation-induced fibrosis: mechanisms and implications for therapy. *J Cancer Res Clinical Oncol.* 2015;141(11):1985-1994.
57. De Sanctis V, Agolli L, Visco V, et al. Cytokines, fatigue, and cutaneous erythema in early stage breast cancer patients receiving adjuvant radiation therapy. *Biomed Res Int.* 2014;2014:523568. Doi:10.1155/2014/523568.
58. Janelins MC, Mustian KM, Palesh OG, et al. Differential expression of cytokines in breast cancer patients receiving different chemotherapies: implications for cognitive impairment research. *Support Care Cancer.* 2012;20(4):831-839. Doi:10.1007/s00520-011-1158-0.
59. Basbaum AI, Bautista DM, Scherrer G, et al. Cellular and molecular mechanisms of pain. *Cell.* 2009;139(2):267-284. Doi: 10.1016/j.cell.2009.09.028.
60. Bunker TD, Reilly J, Baird KS, et al. Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder. *J Bone Joint Surg Br.* 2000;82(5):768-773.
61. Mariette X, de Roquancourt A, d'Agay MF, et al. Monoarthritis revealing non- Hodgkin's T-cell lymphoma of the synovium. *Arthritis Rheum.*1988;31(4):571-572.

62. Gridley G, McLaughlin JK, Ekbom A, et al. Incidence of cancer among patients with rheumatoid arthritis. *J Natl Cancer Inst.* 1993;85(4):307-311.
63. Gheita TA, Ezzat , Sayed S, et al. Musculoskeletal manifestations in patients with malignant disease. *Clinical rheumatology.* 2010;29(2):181. Doi:10.1007/s10067-009-1310-0.
64. Calabro JJ. Cancer and arthritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology.* 1967;10(6):553-567.
65. Zuther JE, Norton S. (2012). *Lymphedema management: The Comprehensive Guide for Practitioners.* New York: Thieme.
66. Johansson K, Holmström H, Nilsson I, et al. Breast cancer patients' experiences of lymphoedema. *Scand j Caring Sci.* 2003;17(1):35-42.
67. Shahpar H, Atieh A, Maryam A, et al. Risk factors of lymph edema in breast cancer patients. *International journal of breast cancer.* 2013;641818:7. Doi:10.1155/2013/641818.
68. Herrera JE, Stubblefield MD. Rotator cuff tendonitis in lymphedema: a retrospective case series. *Arch Phys Med Rehabil.* 2004;85(12):1939-1942.
69. Gürsoy AA. Meme kanseri tedavisine bağlı lenfödem ve hemşirelik bakımı. *C.U. Hemşirelik Yüksekokulu Dergisi.* 2005;9(2):18-25.
70. WHO (1996). WHO's cancer pain ladder for adults. <https://www.who.int/cancer/palliative/painladder/en/>. (Erişim Tarihi: 4 Temmuz 2019).
71. Kurita GP, Sjögren P. Pain management in cancer survivorship. *Acta Oncol.* 2015;54(5):629-634. Doi:10.3109/0284186X.2014.99666.2
72. Glare PA, Davies PS, Finlay E, et al. Pain in cancer survivors. *J Clin Oncol.* 2014;32(16):1739-1747. Doi:10.1200/JCO.2013.52.4629.
73. Levick S, Jacobs C, Loukas DF, et al. Naproxen sodium in treatment of bone pain due to metastatic cancer. *Pain.* 1988;35:253-8.
74. Paice JA, Portenoy R, Lacchetti C, et al. Management of chronic pain in survivors of adult cancers: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol.* 2016;34(27):3325-3345. Doi:10.1200/JCO.2016.68.5206.
75. Jaxox A, Carr DB, Payne R. New Clinical-Practice Guidelines for the management of pain in patients with cancer. *N Engl J Med.* 1994;330(9):651-655.
76. Gaillard S, Stearns V. Aromatase inhibitor-associated bone and musculoskeletal effects: New evidence defining etiology and strategies for management. *Breast Cancer Res.* 2011;13:205. Doi: 10.1186/bcr2818.
77. Sánchez C, Hyttel J. Comparison of the effects of antidepressants and their metabolites on the reuptake of biogenic amines and on receptor binding. *Cell Mol Neurobiol.* 1999;19(4):467-489.
78. Smith EM, Pang H, Cirrincione C, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. *Alliance for Clinical Trials in Oncology. JAMA.* 2013;309(13):1359-67. Doi:10.1001/jama.2013.2813.
79. Henry NL, Unger JM, Schott AF, et al. Randomized, Multicenter, Placebo-Controlled Clinical Trial of Duloxetine Versus Placebo for Aromatase Inhibitor-Associated Arthralgias in Early-Stage Breast Cancer: SWOG S1202. *J Clin Oncol.* 2018;36:326-332. Doi:10.1200/JCO.2017.74.6651.
80. Jordan RI, Mulvey MR, Bennett MI. A critical appraisal of gabapentinoids for pain in cancer patients. *Curr opin support palliat care.* 2018;12(2):108-117. Doi: 0.1097/SPC.0000000000000337.
81. Caraceni A, Zecca E, Bonezzi C, et al. Gabapentin for neuropathic cancer pain: a randomized, controlled trial from the gabapentin cancer pain study group. *J Clin Oncol.* 2004;22(14):2909-2917.
82. Vadalouca A, Raptis E, Moutzouri A, et al. (2010). Pregabalin for the management of neuropathic cancer pain: preliminary results. *Third International Congress on Neuropathic Pain, May 27-30 2010, Athens, Greece,* 73.
83. Koyyalagunta D, Simmonds MJ, Novy DM. (2019). General Pain Management Concepts. Ed. **Gulati A, Puttanniah V, Bruel BM, Rosenberg W, Hung JC.** In *Essentials of Interventional Cancer Pain Management* (47-54). Switzerland, Springer.

84. Cherny NI. The pharmacologic management of cancer pain. *Oncology*.2004; 18(12): 1499-1515.
85. Uzunoğlu S, Çiçin I. Kanser hastalarında ağrıya yaklaşım. *Klinik Gelişim*, 2011;24(1):14-20.
86. Trescot AM, Datta S, Lee M, et al. Opioid pharmacology. *Pain physician*. 2008;11(2):133-53.
87. Mercadante S,Vellucci R, Cuomo A, et al. Long-term efficacy and tolerability of intranasal fentanyl in the treatment of breakthrough cancer pain. *Support Care Cancer*.2015;23(5):1349-1354.
88. Hadley G, Derry S, Moore RA, et al. Transdermal fentanyl for cancer pain. *Cochrane Database Syst Rev*. 2013;10:CD010270.Doi: 10.1002/14651858.CD010270.
89. FDA. (2019). Extended-release (ER) and long-acting (LA) opioid analgesics Risk Evaluation and Mitigation Strategy (REMS).www.fda.gov/downloads/drugs/drugsafety/postmarketdrug safetyinformationforpatientsandproviders/ucm311290.pdf. (Erişim Tarihi: 3 Temmuz 2019).
90. PaulsenØ, N Aass, S Kaasa, et al. Do corticosteroids provide analgesic effects in cancer patients? A systematic literature review *J Pain Symptom Manage*.2013;46:96-105.
91. Colvin L, Forbes K, Fallon M. Difficult pain. *BMJ*. 2006;332(7549):1081-1083.
92. Hans GH, Robert DN, Van Maldeghem KN. Treatment of an acute severe central neuropathic pain syndrome by topical application of lidocaine 5% patch: a case report. *Spinal Cord*. 2008;46(4):311-313.
93. Söderberg Löfdal KC, Andersson ML, Gustafsson LL. Cytochrome P450-mediated changes in oxycodone pharmacokinetics/pharmacodynamics and their clinical implications. *Dru-gs*.2013;73:533-543. Doi:10.1007/s40265-013-0036-0.
94. Samer CF, Daali Y, Wagner M, et al. The effects of CYP2D6 and CYP3A activities on the pharmacokinetics of immediate release oxycodone. *Br J Pharmacol*. 2010;160:907-918.
95. Kapur BM, Hutson JR, Chibber T, et al. Methadone: A review of drug-drug and pathophysiological interactions. *Crit Rev Clin Lab Sci*.2011;48:171-195.
96. Diamond TH, Bucci J, Kersley JH, et al. Osteoporosis and spinal fractures in men with prostate cancer: risk factors and effects of androgen deprivation therapy. *J Urol*. 2004;172:529-32.
97. Boissier S, Magnetto S, Frappart L, et al. Bisphosphonates inhibit prostate and breast carcinoma cell adhesion to unmineralized and mineralized bone extracellular matrices. *Cancer Res*. 1997;57:3890-4.
98. Boissier S, Ferreras M, Peyruchaud O,et al. Bisphosphonates inhibit breast and prostate carcinoma cell invasion, an early event in the formation of bone metastases. *Cancer Res*..2000;60:2949-54.
99. Rosen LS, Gordon D, Kaminski M, et al. Zoledronic acid versus pamidronate in the treatment of skeletal metastases in patients with breast cancer or osteolytic lesions of multiple myeloma: a phase III, double-blind, comparative trial. *Cancer J*. 2001;7:377-387.
100. Rosen LS, Gordon D, Tchekmedyan NS, et al. Long-term efficacy and safety of zoledronic acid in the treatment of skeletal metastases in patients with nonsmall cell lung carcinoma and other solidtumors: a randomized, phase III, double-blind, placebo-controlled trial. *Cancer*. 2004;100:2613-2621.
101. Robb KA, Williams JE, Duvivier V, et al. A pain management program for chronic cancer-treatment-related pain: a preliminary study. *J. Pain*.2006;7(2):82-90.
102. Cheville AL, Kollasch J, Vandenberg J, et al. A home-based exercise program to improve function, fatigue, and sleep quality in patients with stage IV lung and colorectal cancer: A randomized controlled trial. *J Pain Symptom Manage*. 2013;45:811-821. Doi: 10.1016/j.jpainsym-man.2012.05.006.
103. Iyer S, Kim HJ. Cervical radiculopathy. *Curr Rev Musculoskeletal Med*.2016;9(3):272-280. Doi: doi: 10.1007/s12178-016-9349-4.
104. Nijs J, Kosek E, Van Oosterwijck J, et al. Dysfunctional endogenous analgesia during exercise in patients with chronic pain: to exercise or not to exercise? *Pain Physician*. 2012;15:ES205-ES213.
105. Irwin ML, Cartmel B, Gross CP, et al. Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer survivors. *J Clin Oncol*. 2015;33:1104-1111.Doi: 10.1200/JCO.2014.57.1547.

106. Cheville AL, Tchou J. Barriers to rehabilitation following surgery for primary breast cancer. *J Surg Oncol.* 2007;95:409-418. Doi: 10.1002/jso.20782.
107. McNeely ML, Parliament MB, Seikaly H, et al: Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: A randomized controlled trial. *Cancer.*2008;113:214 222.Doi: 10.1002/cnrc.23536.
108. Peppone LJ, Janelsins MC, Kamen C et al. The effect of YOCASyoga for musculoskeletal symptoms among breast cancer survivors on hormonal therapy. *Breast Cancer Res Treat.* 2015;150(3): 597–604. Doi:10.1007/s10549-015-3351-1.
109. Knols R, Aaronson NK, Uebelhart D,et al. Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. *J Clin Oncol.*2005;23(16):3830–3842. Doi:10.1200/JCO.2005.02.148.
110. Beurskens CHG, van Uden CJT, Strobbe LJA, et al. The efficacy of physiotherapy upon shoulder function following axillary dissection in breast cancer, a randomized controlled study. *BMC Cancer.*2007;7(1):166. Doi:10.1186/1471-2407-7-166.
111. Wijayasinghe N, Andersen KG, Kehlet H. Neural blockade for persistent pain after breast cancer surgery. *Reg Anesth Pain Med.* 2014;39(4):272–278. Doi:10.1097/AAP.0000000000000101.
112. Moseley AL, Carati CJ, Piller NB. A systematic review of common conservative therapies for arm lymphoedema secondary to breast cancer treatment. *Ann Oncol.* 2007;18:639–646. Doi:10.1093/annonc/mdl182.
113. Korpan MI, Crevenna R, Fialka-Moser V. Lymphedema: a therapeutic approach in the treatment and rehabilitation of cancer patients. *Am J Phys Med Rehabil.* 2011;90(5):69–75. Doi:10.1097/PHM.0b013e31820be160.
114. Özcan DS, Aras M. Kompleks Dekonjestif Terapi-Ana Hatlar. *Turkiye Klinikleri Physical Medicine Rehabilitation-Special Topics.*2016;9(4):38-44.
115. Goodman CC, Fuller KS. (2008). Pathology: implications for the physical therapist. (3. Edition).Philadelphia:Saunders Co.
116. Földi M, Ströbenreuther R. (2005). Foundations of manual lymph drainage. (3. Edition). Germany: Elsevier Mosby.
117. Chang CJ,Cormier JN. Lymphedema interventions: exercise, surgery, and compression devices. *Semin Oncol Nurs.* 2013;29(1):28-40. Doi: 10.1016/j.soncn.2012.11.005.
118. Shao Y, Qi K, Zhou QH, et al. Intermittent pneumatic compression pump for breast cancer-related lymphedema:a systematic review and meta-analysis of randomized controlled trials. *Oncol Res Treat.* 2014;37(4):170–4. Doi:10.1159/000360786.
119. Hurlow A, Bennett MI, Robb KA, et al. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst Rev.* 2012;(3):CD006276. Doi:10.1002/14651858. CD006276. pub3.
120. Maxwell L. Therapeutic ultrasound and tumour metastasis. *Physiotherapy.* 1995;81:272–5. Doi:10.1016/S0031-9406(05)66822-8.
121. Napoli A, Anzidei M, Marincola BC, et al. Primary pain palliation and local tumor control in bone metastases treated with magnetic resonance-guided focused ultrasound. *Investig Radiol.* 2013;48(6):351–358. Doi:10.1097/RLI.0b013e318285bbab.
122. Stubblefield MD, Levine A, Custodio CM et al. The role of botulinum toxin type A in the radiation fibrosis syndrome: a preliminary report. *Arch Phys Med Rehabil.* 2008;89(3):417–21. Doi: 10.1016/j.apmr.2007.11.022.
123. Wallace AN, Robinson CG, Meyer J, et al. The metastatic spine disease multidisciplinary working group algorithms. *Oncologist.* 2015;20(10):1205–15. Doi:10.1634/theoncologist.2015-0085.
124. Greenwood TJ, Wallace A, Friedman MV, et al. Combined ablation and radiation therapy of spinal metastases: a novel multimodality treatment approach. *Pain Physician.* 2015;18(6):573–81.
125. Westhoff PG, Verdam MGE, Oort FJ, et al. Course of Quality of Life After Radiation Therapy for Painful Bone Metastases: A Detailed Analysis From the Dutch Bone Metastasis Study. *Int J Radiat Oncol Biol Phys.* 2016;95(5):1391-1398. Doi:10.1016/j.ijrobp.2016.03.032.

126. Choi JY. Treatment of Bone Metastasis with Bone-Targeting Radiopharmaceuticals. *Nucl Med Mol Imaging.* 2018;52(3):200-207. Doi:10.1007/s13139-017-0509-2.
127. Malviya A, Gerrard C. Evidence for orthopaedic surgery in the treatment of metastatic bone disease of the extremities: a review article. *Palliative medicine.* 2012;26(6):788-796. Doi:10.1177/0269216311419882.
128. Skovlund Sorensen M, Hindsø K, Frederik Horstmann P et al. Incidence of surgical interventions for metastatic bone disease in the extremities: a population-based cohort study. *Acta Oncol.* 2019;58(4): 456-462. Doi:10.1080/0284186X.2018.1549368.
129. Sutcliffe P, Connock M, Shyangdan D, et al. A systematic review of evidence on malignant spinal metastases: natural history and technologies for identifying patients at high risk of vertebral fracture and spinal cord compression. *Health Technol Assess.* 2013;17(42):1-274. Doi:10.3310/hta17420.
130. van Geel AN, Lans TE, Haen R, e al. Partial mastectomy and m. latissimus dorsi reconstruction for radiation-induced fibrosis after breast-conserving cancer therapy. *World J Surg.* 2011;35(3):568-72. Doi:10.1007/s00268-010-0911-8.
131. Chaudhury S, Gwilym SE, Moser J, et al. Surgical options for patients with shoulder pain. *Nat Rev Rheumatol.* 2010;6:217-226. Doi: 10.1038/nrrheum.2010.25.
132. Nguyen JT, Buchanan IA, Patel PP, et al. Intercostal neuroma as a source of pain after aesthetic and reconstructive breast implant surgery. *Br J Plast Surg.* 2012;65(9):1199-1203. Doi:10.1016/j.bjps.2012.04.003.
133. Smith HS, Wu S-X. Persistent pain after breast cancer treatment. *Ann Palliat Med.* 2012;1(3):182-94. Doi:10.3978/j.issn.2224-5820.2012.10.13.
134. Syrjala KL, Jensen MP, Mendoza ME, et al. Psychological and behavioral approaches to cancer pain management. *Journal of Clinical Oncology.* 2014;32(16):1703-1711. Doi:10.1200/JCO.2013.54.4825.
135. Thomas EM, Weiss SM. Nonpharmacological interventions with chronic cancer pain in adults. *Cancer Control.* 2000;7:157-64. Doi:10.1177/107327480000700206