

Bölüm 16

EPİTELYAL OVER KANSERİNDE CERRAHİ YAKLAŞIM

Eda Adeviye ŞAHİN¹

GİRİŞ

Over kanseri, kadın üreme sisteminin en ölümcül patolojisidir. Kadınlarda tüm kanser vakalarının % 3'ünü temsil eder ve tüm kanser ölümlerinin % 5'ini oluşturur[1] Dünya çapında yılda yaklaşık 200.000 kadına over kanseri teşhisi konmaktadır[2]. Tanı alan kanserlerin neredeyse % 70'ine ileri evre hastalık teşhisi konulmaktadır[3]. Mevcut tedavi yöntemleriyle, 5 yıllık sağkalım oranı, organ sınırlı ya da erken evre hastalığı olanlarda (Uluslararası Jinekoloji ve Obstetrik Federasyonu (FIGO) evre I-II) %92 ; ilerlemiş hastalığı olan kadınlarda % 30 - 40 arasındadır(FIGO evre III-IV)[4]. Bu nedenle, over kanseri, zorlu ve karmaşık bir malignitedir. Yüksek mortalite oranı, etkili erken teşhis yöntemlerinin eksikliğinden ve non-spesifik semptomlardan kaynaklanır. Bu durum hastaların yaklaşık % 70'inin ileri evrede teşhis alması ile ilişkilidir. Vakaların yalnızca % 15-25'i erken evrede, tümörler pelvis içinde lokalize olduğunda teşhis edilir.

Over kanseri yönetiminde tedavi hemen hemen her zaman cerrahi ve kemoterapinin bir kombinasyonunu içerir. Over kanseri tedavisinde muazzam gelişmeler, son yirmi yılda yapılmış olup, ilerlemiş hastalığı olan birçok hasta çalışmasında medyan sağkalımı 6 yıldan fazladır. Bu başarı, daha yeni, aktif kemoterapötik ajanların keşfi ve sitoredüksiyon ile agresif cerrahi evrelemenin öneminin daha iyi anlaşılması ile ilgilidir. Günümüzde over kanseri tedavisinin sistematik bir şekilde yönetilmesi için başlangıç cerrahi tedavi aşağıdaki üç hedefi içermelidir: (1) evreleme, (2) sitoredüksiyon ve (3) kesin bir histolojik tanı koyma.

Sitoredüktif cerrahi başlangıç tedavinin temelini oluşturur. Veriler, over kanserinde, tümör yükünün azaltılmasının bu hastalığın tedavisinde önemli olduğu için diğer solid tümörlerden farklı olduğunu açıkça göstermektedir.

¹ Malatya Eğitim ve Araştırma Hastanesi Obstetri ve Jinekoloji Kliniği

bir hastalıkta etkiliyse ortaya çıkan bir sonraki soru, bu tekniğin primer ileri over kanseri olan hastalarda sonuçlarını iyileştirmek ve nüks oranı yaklaşık % 70 ile mücadele etmek için uygulanması makul olur mu? [56,57]. Klinik onkologların çoğu, neoadjuvan ve / veya adjuvan kemoterapisi ile kökleşmiş CS algoritmalarına dayanarak, aşırı ve gereksiz primer bir hastalık durumunda CS'ye HIPEC eklemeyi düşündüklerinden, kanıt eksikliği nedeniyle bu soru cevapsız kalmaktadır[58,59]. Ancak bu soru ciddi bir dikkate almayı hak ediyor.

KAYNAKLAR

1. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, Alteri R, Robbins AS, Jemal A (2014) Cancer treatment and survivorship statistics, 2014. *CA Cancer J Clin* 64 (4):252-271. doi:10.3322/caac.21235
2. Siegel R, DeSantis C, Virgo K, Stein K, Mariotto A, Smith T, Cooper D, Gansler T, Lerro C, Fedewa S, Lin C, Leach C, Cannady RS, Cho H, Scoppa S, Hachey M, Kirch R, Jemal A, Ward E (2012) Cancer treatment and survivorship statistics, 2012. *CA Cancer J Clin* 62 (4):220-241. doi:10.3322/caac.21149
3. Hacker NF, Rao A (2017) Surgery for advanced epithelial ovarian cancer. *Best Pract Res Clin Obstet Gynaecol* 41:71-87. doi:10.1016/j.bpobgyn.2016.10.007
4. Noone AM, Cronin KA, Altekruse SF, Howlader N, Lewis DR, Petkov VI, Penberthy L (2017) Cancer Incidence and Survival Trends by Subtype Using Data from the Surveillance Epidemiology and End Results Program, 1992-2013. *Cancer Epidemiol Biomarkers Prev* 26 (4):632-641. doi:10.1158/1055-9965.EPI-16-0520
5. Stuart GC, Kitchener H, Bacon M, duBois A, Friedlander M, Ledermann J, Marth C, Thigpen T, Trimble E, participants of 4th Ovarian Cancer Consensus C, Gynecologic Cancer I (2011) 2010 Gynecologic Cancer InterGroup (GCI) consensus statement on clinical trials in ovarian cancer: report from the Fourth Ovarian Cancer Consensus Conference. *Int J Gynecol Cancer* 21 (4):750-755. doi:10.1097/IGC.0b013e31821b2568
6. Hengeveld EM, Zusterzeel PLM, Lajer H, Hogdall CK, Rosendahl M (2019) The value of surgical staging in patients with apparent early stage epithelial ovarian carcinoma. *Gynecol Oncol*. doi:10.1016/j.ygyno.2019.06.006
7. Zuna RE, Behrens A (1996) Peritoneal washing cytology in gynecologic cancers: long-term follow-up of 355 patients. *J Natl Cancer Inst* 88 (14):980-987. doi:10.1093/jnci/88.14.980
8. Powless CA, Bakkum-Gamez JN, Aletti GD, Cliby WA (2009) Random peritoneal biopsies have limited value in staging of apparent early stage epithelial ovarian cancer after thorough exploration. *Gynecol Oncol* 115 (1):86-89. doi:10.1016/j.ygyno.2009.06.037
9. Young RC, Decker DG, Wharton JT, Piver MS, Sindelar WF, Edwards BK, Smith JP (1983) Staging laparotomy in early ovarian cancer. *JAMA* 250 (22):3072-3076
10. Zeppernick F, Meinhold-Heerlein I (2014) The new FIGO staging system for ovarian, fallopian tube, and primary peritoneal cancer. *Arch Gynecol Obstet* 290 (5):839-842. doi:10.1007/s00404-014-3364-8
11. Angioli R, Plotti F, Palaia I, Calcagno M, Montera R, Cafa EV, Sereni MI, Panici PB (2008) Update on lymphadenectomy in early and advanced ovarian cancer. *Curr Opin Obstet Gynecol* 20 (1):34-39. doi:10.1097/GCO.0b013e3282f2fd68
12. Panici PB, Maggioni A, Hacker N, Landoni F, Ackermann S, Campagnutta E, Tamussino K, Winter R, Pellegrino A, Greggi S, Angioli R, Mancini N, Scambia G, Dell'Anna T, Fossati R, Floriani I, Rossi RS, Grassi R, Favalli G, Raspagliesi F, Giannarelli D, Martella L, Mangioni C (2005) Systematic aortic and pelvic lymphadenectomy versus resection of bulky nodes only in optimally debulked advanced ovarian cancer: a randomized clinical trial. *J Natl Cancer Inst* 97 (8):560-566. doi:10.1093/jnci/dji102

13. Chan JK, Munro EG, Cheung MK, Husain A, Teng NN, Berek JS, Osann K (2007) Association of lymphadenectomy and survival in stage I ovarian cancer patients. *Obstet Gynecol* 109 (1):12-19. doi:10.1097/01.AOG.0000249610.95885.ef
14. Harter P, Sehouli J, Lorusso D, Reuss A, Vergote I, Marth C, Kim JW, Raspagliesi F, Lampe B, Aletti G, Meier W, Cibula D, Mustea A, Mahner S, Runnebaum IB, Schmalfeldt B, Burges A, Kimmig R, Scambia G, Greggi S, Hilpert F, Hasenburg A, Hillemanns P, Giorda G, von Leffern I, Schade-Brittinger C, Wagner U, du Bois A (2019) A Randomized Trial of Lymphadenectomy in Patients with Advanced Ovarian Neoplasms. *N Engl J Med* 380 (9):822-832. doi:10.1056/NEJMoa1808424
15. Bogani G, Borghi C, Leone Roberti Maggiore U, Ditto A, Signorelli M, Martinelli F, Chiappa V, Lopez C, Sabatucci I, Scaffa C, Indini A, Ferrero S, Lorusso D, Raspagliesi F (2017) Minimally Invasive Surgical Staging in Early-stage Ovarian Carcinoma: A Systematic Review and Meta-analysis. *J Minim Invasive Gynecol* 24 (4):552-562. doi:10.1016/j.jmig.2017.02.013
16. Falcetta FS, Lawrie TA, Medeiros LR, da Rosa MI, Edelweiss MI, Stein AT, Zelmanowicz A, Moraes AB, Zanini RR, Rosa DD (2016) Laparoscopy versus laparotomy for FIGO stage I ovarian cancer. *Cochrane Database Syst Rev* 10:CD005344. doi:10.1002/14651858.CD005344.pub4
17. Nezhat FR, Ezzati M, Chuang L, Shamsirsaz AA, Rahaman J, Gretz H (2009) Laparoscopic management of early ovarian and fallopian tube cancers: surgical and survival outcome. *Am J Obstet Gynecol* 200 (1):83 e81-86. doi:10.1016/j.ajog.2008.08.013
18. Chi DS, Abu-Rustum NR, Sonoda Y, Ivy J, Rhee E, Moore K, Levine DA, Barakat RR (2005) The safety and efficacy of laparoscopic surgical staging of apparent stage I ovarian and fallopian tube cancers. *Am J Obstet Gynecol* 192 (5):1614-1619. doi:10.1016/j.ajog.2004.11.018
19. Salani R, Bristow RE (2012) Surgical management of epithelial ovarian cancer. *Clin Obstet Gynecol* 55 (1):75-95. doi:10.1097/GRF.0b013e31824b4629
20. Tozzi R, Schneider A (2005) Laparoscopic treatment of early ovarian cancer. *Curr Opin Obstet Gynecol* 17 (4):354-358
21. Magrina JF, Zanagnolo V, Noble BN, Kho RM, Magtibay P (2011) Robotic approach for ovarian cancer: perioperative and survival results and comparison with laparoscopy and laparotomy. *Gynecol Oncol* 121 (1):100-105. doi:10.1016/j.ygyno.2010.11.045
22. Baldwin LA, Huang B, Miller RW, Tucker T, Goodrich ST, Podzielinski I, DeSimone CP, Ueland FR, van Nagell JR, Seamon LG (2012) Ten-year relative survival for epithelial ovarian cancer. *Obstet Gynecol* 120 (3):612-618. doi:10.1097/AOG.0b013e318264f794
23. Griffiths CT (1975) Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma. *Natl Cancer Inst Monogr* 42:101-104
24. Hoskins WJ, Bundy BN, Thigpen JT, Omura GA (1992) The influence of cytoreductive surgery on recurrence-free interval and survival in small-volume stage III epithelial ovarian cancer: a Gynecologic Oncology Group study. *Gynecol Oncol* 47 (2):159-166
25. Farias-Eisner R, Teng F, Oliveira M, Leuchter R, Karlan B, Lagasse LD, Berek JS (1994) The influence of tumor grade, distribution, and extent of carcinomatosis in minimal residual stage III epithelial ovarian cancer after optimal primary cytoreductive surgery. *Gynecol Oncol* 55 (1):108-110. doi:10.1006/gyno.1994.1257
26. Chiva LM, Castellanos T, Alonso S, Gonzalez-Martin A (2016) Minimal Macroscopic Residual Disease (0.1-1 cm). Is It Still a Surgical Goal in Advanced Ovarian Cancer? *Int J Gynecol Cancer* 26 (5):906-911. doi:10.1097/IGC.0000000000000690
27. Onda T, Yoshikawa H, Yasugi T, Yamada M, Matsumoto K, Taketani Y (2005) Secondary cytoreductive surgery for recurrent epithelial ovarian carcinoma: proposal for patients selection. *Br J Cancer* 92 (6):1026-1032. doi:10.1038/sj.bjc.6602466
28. Thigpen T (2012) A rational approach to the management of recurrent or persistent ovarian carcinoma. *Clin Obstet Gynecol* 55 (1):114-130. doi:10.1097/GRF.0b013e31824b9bc5
29. Nicklin JL, Copeland LJ, O'Toole RV, Lewandowski GS, Vaccarello L, Havenar LP (1995) Splenectomy as part of cytoreductive surgery for ovarian carcinoma. *Gynecol Oncol* 58 (2):244-247. doi:10.1006/gyno.1995.1218

30. Bilgin T, Ozerkan K, Ozan H (2005) Splenectomy in cytoreductive surgery for advanced ovarian cancer. *Arch Gynecol Obstet* 271 (4):329-331. doi:10.1007/s00404-004-0612-3
31. Weber AM, Kennedy AW (1994) The role of bowel resection in the primary surgical debulking of carcinoma of the ovary. *J Am Coll Surg* 179 (4):465-470
32. Chang SJ, Bristow RE, Ryu HS (2012) Prognostic significance of systematic lymphadenectomy as part of primary debulking surgery in patients with advanced ovarian cancer. *Gynecol Oncol* 126 (3):381-386. doi:10.1016/j.ygyno.2012.05.014
33. du Bois A, Reuss A, Harter P, Pujade-Lauraine E, Ray-Coquard I, Pfisterer J, Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe O, Groupe d'Investigateurs Nationaux pour l'Etude des Cancers O (2010) Potential role of lymphadenectomy in advanced ovarian cancer: a combined exploratory analysis of three prospectively randomized phase III multicenter trials. *J Clin Oncol* 28 (10):1733-1739. doi:10.1200/JCO.2009.25.3617
34. Rouzier R, Bergzoll C, Brun JL, Dubernard G, Selle F, Uzan S, Pomel C, Darai E (2010) The role of lymph node resection in ovarian cancer: analysis of the Surveillance, Epidemiology, and End Results (SEER) database. *BJOG* 117 (12):1451-1458. doi:10.1111/j.1471-0528.2010.02633.x
35. Scarabelli C, Gallo A, Zarrelli A, Visentin C, Campagnutta E (1995) Systematic pelvic and para-aortic lymphadenectomy during cytoreductive surgery in advanced ovarian cancer: potential benefit on survival. *Gynecol Oncol* 56 (3):328-337. doi:10.1006/gyno.1995.1059
36. Zhou J, Zhang WW, Zhang QH, He ZY, Sun JY, Chen QH, Wu SG (2018) The effect of lymphadenectomy in advanced ovarian cancer according to residual tumor status: A population-based study. *Int J Surg* 52:11-15. doi:10.1016/j.ijsu.2018.02.006
37. Vergote I, De Wever I, Tjalma W, Van Gramberen M, Decloedt J, van Dam P (1998) Neoadjuvant chemotherapy or primary debulking surgery in advanced ovarian carcinoma: a retrospective analysis of 285 patients. *Gynecol Oncol* 71 (3):431-436. doi:10.1006/gyno.1998.5213
38. Schwartz PE, Rutherford TJ, Chambers JT, Kohorn EL, Thiel RP (1999) Neoadjuvant chemotherapy for advanced ovarian cancer: long-term survival. *Gynecol Oncol* 72 (1):93-99. doi:10.1006/gyno.1998.5236
39. du Bois A, Reuss A, Pujade-Lauraine E, Harter P, Ray-Coquard I, Pfisterer J (2009) Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). *Cancer* 115 (6):1234-1244. doi:10.1002/cncr.24149
40. Winter WE, 3rd, Maxwell GL, Tian C, Carlson JW, Ozols RF, Rose PG, Markman M, Armstrong DK, Muggia F, McGuire WP, Gynecologic Oncology Group S (2007) Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group Study. *J Clin Oncol* 25 (24):3621-3627. doi:10.1200/JCO.2006.10.2517
41. Eisenkop SM, Spirtos NM, Friedman RL, Lin WC, Pisani AL, Peticucci S (2003) Relative influences of tumor volume before surgery and the cytoreductive outcome on survival for patients with advanced ovarian cancer: a prospective study. *Gynecol Oncol* 90 (2):390-396
42. Chi DS, Eisenhauer EL, Lang J, Huh J, Haddad L, Abu-Rustum NR, Sonoda Y, Levine DA, Hensley M, Barakat RR (2006) What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? *Gynecol Oncol* 103 (2):559-564. doi:10.1016/j.ygyno.2006.03.051
43. Pecorelli S, Odicino F, Favalli G (2002) Interval debulking surgery in advanced epithelial ovarian cancer. *Best Pract Res Clin Obstet Gynaecol* 16 (4):573-583
44. Vergote IB, De Wever I, Decloedt J, Tjalma W, Van Gramberen M, van Dam P (2000) Neoadjuvant chemotherapy versus primary debulking surgery in advanced ovarian cancer. *Semin Oncol* 27 (3 Suppl 7):31-36
45. Hegazy MA, Hegazi RA, Elshafei MA, Setit AE, Elshamy MR, Eltatoongy M, Halim AA (2005) Neoadjuvant chemotherapy versus primary surgery in advanced ovarian carcinoma. *World J Surg Oncol* 3:57. doi:10.1186/1477-7819-3-57

46. Eltabbakh GH, Mount SL, Beatty B, Simmons-Arnold L, Cooper K, Morgan A (2004) Factors associated with cytoreducibility among women with ovarian carcinoma. *Gynecol Oncol* 95 (2):377-383. doi:10.1016/j.ygyno.2004.07.045
47. Nelson BE, Rosenfield AT, Schwartz PE (1993) Preoperative abdominopelvic computed tomographic prediction of optimal cytoreduction in epithelial ovarian carcinoma. *J Clin Oncol* 11 (1):166-172. doi:10.1200/JCO.1993.11.1.166
48. Bristow RE, Santillan A, Diaz-Montes TP, Gardner GJ, Giuntoli RL, 2nd, Meisner BC, Frick KD, Armstrong DK (2007) Centralization of care for patients with advanced-stage ovarian cancer: a cost-effectiveness analysis. *Cancer* 109 (8):1513-1522. doi:10.1002/cncr.22561
49. Fagotti A, Ferrandina G, Fanfani F, Ercoli A, Lorusso D, Rossi M, Scambia G (2006) A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: a pilot study. *Ann Surg Oncol* 13 (8):1156-1161. doi:10.1245/ASO.2006.08.021
50. Kireeva GS, Gafton GI, Guseynov KD, Senchik KY, Belyaeva OA, Bespalov VG, Panchenko AV, Maydin MA, Belyaev AM (2018) HIPEC in patients with primary advanced ovarian cancer: Is there a role? A systematic review of short- and long-term outcomes. *Surg Oncol* 27 (2):251-258. doi:10.1016/j.suronc.2018.05.006
51. Neuwirth MG, Alexander HR, Karakousis GC (2016) Then and now: cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC), a historical perspective. *J Gastrointest Oncol* 7 (1):18-28. doi:10.3978/j.issn.2078-6891.2015.106
52. International Collaborative Ovarian Neoplasm G (2002) Paclitaxel plus carboplatin versus standard chemotherapy with either single-agent carboplatin or cyclophosphamide, doxorubicin, and cisplatin in women with ovarian cancer: the ICON3 randomised trial. *Lancet* 360 (9332):505-515. doi:10.1016/S0140-6736(02)09738-6
53. Bakrin N, Cotte E, Golfier F, Gilly FN, Freyer G, Helm W, Glehen O, Bereder JM (2012) Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for persistent and recurrent advanced ovarian carcinoma: a multicenter, prospective study of 246 patients. *Ann Surg Oncol* 19 (13):4052-4058. doi:10.1245/s10434-012-2510-4
54. Bakrin N, Bereder JM, Decullier E, Classe JM, Msika S, Lorimier G, Abboud K, Meeus P, Ferron G, Quenet F, Marchal F, Gouy S, Morice P, Pomel C, Pocard M, Guyon F, Porcheron J, Glehen O, Group F (2013) Peritoneal carcinomatosis treated with cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for advanced ovarian carcinoma: a French multicentre retrospective cohort study of 566 patients. *Eur J Surg Oncol* 39 (12):1435-1443. doi:10.1016/j.ejso.2013.09.030
55. Mulier S, Claes JP, Dierieck V, Amiel JO, Pahaut JP, Marcelis L, Bastin F, Vanderbeeken D, Finet C, Cran S, Velu T (2012) Survival benefit of adding Hyperthermic IntraPERitoneal Chemotherapy (HIPEC) at the different time-points of treatment of ovarian cancer: review of evidence. *Curr Pharm Des* 18 (25):3793-3803
56. Leitao MM, Jr., Chi DS (2009) Surgical management of recurrent ovarian cancer. *Semin Oncol* 36 (2):106-111. doi:10.1053/j.seminoncol.2008.12.002
57. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, Copeland LJ, Walker JL, Burger RA, Gynecologic Oncology G (2006) Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med* 354 (1):34-43. doi:10.1056/NEJMoa052985
58. Goff BA (2013) Advanced ovarian cancer: what should be the standard of care? *J Gynecol Oncol* 24 (1):83-91. doi:10.3802/jgo.2013.24.1.83
59. Markman M (2009) Response to: "Establishing evidence for change in ovarian cancer surgery - Proposing clinical trials of cytoreductive surgery and hyperthermic chemotherapy (HIPEC) in ovarian cancer peritoneal carcinomatosis (Chua TC, et al.)". *Gynecol Oncol* 115 (1):168. doi:10.1016/j.ygyno.2009.06.024