Correlation of Pattern of Spread and Outcomes in Advanced Epithelial Ovarian Cancers

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Abstract The purpose of this study was to correlate the pattern of spread with oncological outcomes in advanced ovarian cancer patients. This is a retrospective analysis of 55 consecutive patients who had advanced epithelial ovarian cancer or primary peritoneal carcinomatosis (stages 3C and 4) with primary surgical intervention as the initial modality of treatment. Based on the spread of disease, they were further classified into class A: disease confined to the pelvis (excluded); class B: disease extending to the lower abdomen and omentum; class C: diffuse small-bowel disease with or without A, B, or D; and class D: disease in the upper abdomen. There were 17 patients (30.9%) in class B, 17 (30.9%) in class C, and 21 (38.2%) in class D. The number of patients with suboptimal cytoreduction was highest in class C (six patients). At the end of follow-up (median 38.6 months), 16 patients had no evidence of disease and 26 patients were alive with disease. The 3-year overall survival rates in classes B, C, and D were 94.1, 52.5, and 93.3%, respectively. The 3-year progression-free survival rates were 55.8, 11.8, and 41.9%, respectively. The rates were lowest for class C. The differences in the overall survival rate ($p < 0.001$) and progression-free survival rate ($p = 0.001$) were statistically significant. In advanced ovarian cancer patients, the presence of disease in the small-bowel serosa and mesentery results in poorer outcomes in terms of overall and progression-free survival. The number of patients with suboptimal cytoreduction was also highest in this group.

Keywords Advanced ovarian cancer · Optimal cytoreduction · Pattern of spread · Survival · Epithelial ovarian cancers

Introduction

Ovarian cancers are the third most common gynaecological malignancies worldwide. They constitute the fourth commonest malignancy affecting Indian women. According to GLOBOCAN 2012, in India, the estimated incidence and mortality rates were 26,834 (5%) and 19,549 (6%), respectively [1]. The overall prognosis is poor, because 70% of the patients present with advanced disease, stages 3 and 4 [2]. Many studies have demonstrated that optimal surgical cytoreduction to less than 1 cm or no residual disease confers a definite survival benefit to these patients [3–7]. The surgical cytoreduction rates vary globally, from 22 to 98% [8, 9]. The reasons for suboptimal debulking include diffuse peritoneal carcinomatosis, metastatic deposits in difficult to access areas in the upper abdomen, and the requirement for resection of extensive areas of the bowel. It is not known whether it is the disease distribution which allows optimal cytoreduction or whether the ability to achieve optimal cytoreduction identifies a biologically more favourable patient subgroup or a combination of both. It was our observation that diffuse mesenteric and small-bowel disease probably had lower rates of optimal cytoreduction and therefore poorer survival benefits. However, there are not many studies on primary surgical debulking of diffuse disease over the mesentery and small bowel. A need was felt to analyse the anatomical pattern of spread and the oncological outcomes. The purpose of this study is to correlate the pattern of spread with oncological outcomes in advanced ovarian cancers.

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Methods

The study is a retrospective analysis conducted in a tertiary level cancer care centre during 5 years between January 2009 and December 2013. The institutional research board approval was obtained prior to the study. All patients included had advanced epithelial ovarian cancer or primary peritoneal carcinomatosis with primary surgical intervention as the initial modality of treatment. An assessment of the spread of disease at primary surgery was an essential inclusion criterion. This included patients who had initial exploration in the form of a mini laparotomy and biopsy in addition to those who underwent primary debulking surgery. Those who underwent neoadjuvant chemotherapy without an initial exploration followed by interval debulking were excluded from the analysis as neoadjuvant chemotherapy (NACT) alters the disease pattern which is observed at the time of surgery. Patients with early disease (stages 1–3B) were also excluded from the analysis as the survival rates would be altered in early disease. The study cohort included both low- and high-grade carcinoma stages 3C–4. The electronic medical records including clinical records and radiological, pathological, and operative details were studied. A preoperative CT/MRI scan was used to assess spread of the disease and resectability. The feasibility of primary cytoreduction is discussed in the multidisciplinary tumour board for all patients. Those patients in whom optimal cytoreduction is unlikely undergo neoadjuvant chemotherapy. Our policy was to offer NACT for patient with high-grade disease associated with diffuse carcinomatosis as assessed by clinical examination and imaging and also for patients with poor performance status. This centre employs standard surgical techniques to achieve complete cytoreduction. Complex surgical procedures are undertaken when indicated. Lymph node dissection is not done routinely in our centre. However, lymph nodes that are found to be palpable intraoperatively are dissected. A total of 307 patients with ovarian tumour were screened. Fifty-seven patients were treated with neoadjuvant chemotherapy without an initial surgical intervention and were therefore excluded from the study. Twenty-two had disease confined to the pelvis (early stage) and were excluded from the analysis. Fifty-five consecutive patients with advanced epithelial ovarian cancers (stages 3C and 4) who fit the inclusion criteria were identified (Fig. 1). The anatomical pattern of spread of the tumour in each patient was recorded in detail using an intraoperative mapping tool. Based on the intraoperative mapping of the disease, they were further classified into four classes:

Class A: disease confined to the pelvis (excluded from the study)

Class B: disease extending to the lower abdomen and omentum

Class C: diffuse small-bowel disease with or without A, B, or D

Class D: disease in the upper abdomen (liver, diaphragm, spleen, and pancreas)

The mean follow-up was for 38.6 months (range 6 to 81 months). Descriptive data analysis and Kaplan–Meier curves were used for statistical analysis.

Results

The mean age of the patients was 54.6 years, (range 30–87 years). Table 1 shows the demographics and disease characteristics. Table 2 shows the pattern of spread in different anatomical areas. There were 17 patients (30.9%) in class B, 17 patients (30.9%) in class C, and 21 patients (38.2%) in class D. Forty-eight patients underwent primary surgery followed by adjuvant chemotherapy. Seven patients had laparotomy and biopsy followed by neoadjuvant chemotherapy and debulking surgery. Table 3 shows the residual disease after cytoreductive surgery. Optimal cytoreduction to no residual disease was achieved in 36 patients (65.5%). Table 4 shows the correlation between the residual disease status and the classes of spread. The number of patients with suboptimal cytoreduction was highest in class C (six patients). Out of the 36 patients with optimal cytoreduction, 12 patients (33%) had grades 1 and 2 disease. Table 5 shows the outcome data in terms of recurrences and the status at the end of the follow-up. At the end of the follow-up (median 38.6 months), 16 patients had no evidence of disease and 26 patients were alive with disease. The 3-year overall survival rates in classes B, C, and D were 94.1, 52.5, and 93.3%, respectively. The 3-year progression-free survival rates for classes B, C, and D were 55.8, 11.8, and 41.9%, respectively. The rates were lowest for class C. Figures 2 and 3 show the Kaplan–Meier survival curves for overall survival and progression-free survival, comparing the classes of spread, respectively. The differences in the overall survival rate ($p < 0.001$) and progression-free survival rate ($p = 0.001$) were statistically significant.

Discussion

Ovarian cancer metastasises by direct extension from the ovarian/fallopian tumour. The exfoliated cells are transported throughout the peritoneum by physiological peritoneal fluid. Patients usually present with locally advanced disease with contiguous extension to or encasement of the reproductive organs and sigmoid colon. The omentum is almost always transformed by the tumour. The tumour stays within the peritoneal cavity and only invades the mesothelium-lined surfaces [10, 11]. This study analyses whether the anatomical location

Fig. 1 Flow diagram of the study cohort. Class B- Disease extending to the lower abdomen and omentum, Class C- Diffuse small bowel disease with or without a,b,d, Class D- Disease in the upper abdomen

of the tumour within the peritoneal cavity has any bearing on the outcome of the disease.

The results of the present study showed that, in patients with advanced ovarian cancer, disease on the small-bowel serosa and mesentery was associated with poorer outcomes in terms of overall and progression-free survival. A search of literature showed some related studies about the disease pattern at surgery. In a retrospective analysis of 417 stage 3 patients, cytoreduced to microscopic disease, Hamilton et al. [12] classified the disease into (a) minimal disease, (b) abdominal peritoneal disease, and (c) upper abdominal disease. On multivariate analysis, the upper abdominal disease group had a worse prognosis than the minimal disease and abdominal peritoneal disease groups both individually and combined. This study used a type of classification different from that used in our study. Also, diffuse mesenteric disease was not included in their data. In our study, patients who underwent neoadjuvant chemotherapy without an initial surgical exploration were excluded from the analysis. This was done as chemotherapy alters the disease pattern [13, 14]. Also, disease confined to the pelvis was excluded in our study, as the survival rates would be affected by the earlier stage of the disease [15].

Zivanovic et al. conducted a retrospective study of 526 patients with International Federation of Gynecology and Obstetrics (FIGO) stage 3C disease who underwent primary cytoreduction [16]. The study group was classified into three, based on the presence and size of disease, cephalad to the greater omentum at the beginning of the operative procedure. On multivariate analysis, patients with bulky upper abdominal disease who underwent optimal cytoreduction had decreased risk of relapse compared to patients who underwent suboptimal cytoreduction. The median progression-free survival of patients who had no visible or palpable upper abdominal disease on exploration was superior to that of patients who had more extensive upper abdominal disease. The outcome of this study is similar to that conducted by Hamilton et al.

Elene et al., in a study of 79 consecutive epithelial ovarian cancer patients who underwent both primary and secondary cytoreduction over a 10-year period, used a validated documentation tool for intraoperative mapping [17]. It was found that secondary cytoreduction is associated with significantly lower optimal tumour debulking rates compared to primary surgery. This is because the disease tends to recur in patterns less accessible to complete resection such as the

Table 1 Demographics and disease characteristics

		Number	Percentage
Parity	Nulliparous	7	12.7
	Para 1 or 2	32	55.2
	Multiparous	9	15.5
	Not available	9	15.5
Menopausal status	Post meno	28	50.9
	Pre meno	20	36.4
	Not available	7	12.7
Type	Ovary	44	80.0
	PPC	11	20.0
Histopathology	Serous	27	47.3
	Adenocarcinoma (NOS)	13	23.6
	Mucinous	4	7.3
	Endometrioid	4	7.3
	Clear cell	3	5.5
	Mixed epithelial	3	5.5
	Undifferentiated	2	3.6
Grade	1	2	3.6
	2	18	32.7
	3	18	32.7
	Not available	17	31.0

NOS not otherwise specified

Table 2 Pattern of disease spread

Site	Number	Percentage
Right hemidiaphragm	34	61.8
Left hemidiaphragm	16	29.0
Porta hepatis	4	7.2
Lesser sac	3	5.4
Omentum	44	80.0
Right paracolic space	23	41.8
Left paracolic space	19	34.5
Small-bowel serosa	14	25.4
Small-bowel mesentery	19	34.5
Cecum	6	10.9
Large-bowel serosa	12	21.8
Large-bowel mesentery	6	10.9
Sigmoid	37	67.2
Uterus	9	16.3
Tubes	4	7.3
Bladder peritoneum	33	60.0
Rectovaginal pouch	42	76.3
Liver	13	23.6
Spleen	8	14.5
Parietal peritoneum	10	18.2
Ascites	41	74.5
Nodes	12	21.8

Table 3 Residual disease after cytoreductive surgery

Residual disease status	Number	Percentage
No residual disease	36	65.5
Disease <1 cm	8	14.5
Disease >1 cm	7	12.7
Not mentioned	4	7.3

gastrointestinal serosa, mesentery, and upper abdomen. No other predictors of surgical outcome or tumour pattern such as peritoneal carcinomatosis, intestinal tumour involvement, or positive lymph nodes could be identified. This study shares our observation that disease on the gastrointestinal serosa and the mesentery is less amenable to optimal cytoreduction. However, this pattern of spread did not predict surgical outcome. Fotopoulou et al. used a validated intraoperative documentation tool for the study of 360 consecutive epithelial ovarian cancer patients with FIGO stages 3 and 4 who underwent primary surgery [18]. The intra-abdominal tumour dissemination pattern, maximal tumour load, tumour residuals, and operative morbidity were evaluated. It was found that tumour expansion in multiple (>4) abdominal quadrants was the major negative predictor for complete tumour resection. The middle abdomen (including the mesentery and splenic or left colic flexure) and the upper abdomen in the region of the porta hepatis had the highest risk of incomplete tumour resection. This study echoes our findings that disease in the middle abdomen including the small-bowel mesentery has unfavourable outcomes. Chereau et al. compared peritoneal carcinomatosis scoring methods in predicting resectability and found that Fagotti-modified score outperformed other scores [19].

In their review of GOG protocol 52, Hoskins et al. showed that the volume of initial extrapelvic disease remained a significant predictor of decreased survival [20]. But this study did not address if further cytoreduction to no gross visible disease could overcome these factors important in predicting survival. 40.5% of patients in the small-volume group had complete gross resection vs 17.1% in the large-volume group. Eisenkop et al. demonstrated that though the total extent of

Table 4 Correlation between the residual disease status and the classes of spread ($n = 51$, residual disease status of four patients was not available)

Class of spread	Residual disease			Total
	Nil	<1 cm	>1 cm	
B	13	1	0	14
C	5	5	6	16
D	18	2	1	21
Total	36	8	7	51

Table 5 Outcome in terms of recurrences and the status at the end of the follow-up

	Number	Percentage
Any recurrence or progressive disease	40	72.7
Site of first recurrence		
Pelvic	12	
Nodal	3	
Liver	3	
Multiple	6	
Mesentery	1	
Distant	3	
Not available	12	
Status at the last follow-up		
No evidence of disease	16	29.1
Alive with disease	26	47.3
Died of other cause	1	1.8
Died of disease	12	21.8

intra-abdominal tumour burden did independently influence survival, complete surgical resection to microscopic residual had a more significant independent influence on survival [21].

Preoperative identification of patients at high risk of incomplete cytoreduction may allow triaging them into an alternate management-like neoadjuvant chemotherapy. In our study, out of the 112 patients registered as advanced ovarian cancer, 75 patients (68%) actually would have benefitted from primary chemotherapy than primary surgery. Data from the present study suggests that a preoperative identification of diffuse mesenteric/small-bowel involvement by imaging could avoid unnecessary surgery. However, the usefulness of CT/MRI in

identification of miliary mesenteric deposits is questionable. Seung et al. [22] constructed a nomogram for predicting incomplete cytoreduction in advanced ovarian cancers. This was done by studying 343 consecutive ovarian cancer patients who underwent PET CT before primary surgery. Both PET CT features and surgical aggressiveness index of individual surgeons were used in constructing the nomogram. However, the use of PET scan for routine imaging before surgery is not an accepted evidence-based practice. Mesenteric tumour implants as depicted on CT and MRI and tumour involvement of the porta hepatis, the lesser sac, or the root of the small-bowel mesentery have broadly been identified as markers of unresectability in primary EOC [23]. Potential predictors of cytoreducibility might include tumour location and size and mesenteric disease [24]. Suidan et al. in their prospective, multicentre trial of 350 patients who underwent primary cytoreduction of stages 3–4 ovarian cancers assessed preoperative CT scans and CA 125 values. They identified nine criteria associated with suboptimal cytoreduction and developed a model to predict suboptimal debulking [25]. Out of the 36 patients in whom optimal cytoreduction to no residual disease was achieved in our series, 12 patients (33%) had grades 1 and 2 disease. It is known that low-grade type 1 ovarian cancers, typically present in young women, respond better to surgery and have a relatively good prognosis, despite being resistant to chemotherapy. They also have high prevalence of KRAS and BRAF mutations [26]. ER/PR receptor status was not checked in our series. Receptor-positive patients may benefit from regimes like letrozole or tamoxifen especially in young patients with grades 1 and 2 disease. Our institute does

Fig. 2 Kaplan–Meier curve showing overall survival difference between the classes. b- Disease extending to the lower abdomen and omentum, c- Diffuse small bowel disease with or without a,b,d, d- Disease in the upper abdomen

Fig. 3 Kaplan–Meier curve showing progression-free survival difference between the classes. b- Disease extending to the lower abdomen and omentum, c- Diffuse small bowel disease with or without a,b,d- Disease in the upper abdomen

not use intraperitoneal chemotherapy routinely for advanced ovarian cancer. However, it has been tried in selected cases. Intraperitoneal therapy enhanced survival of those with gross residual disease according to Tewari et al. [27]. Survival improved with increasing number of IP cycles.

The other implication of this study is in the use of molecular markers to predict optimal cytoreduction. For instance, P-cadherin expression is more in suboptimally resected tumours. Receptor-type tyrosine phosphatase F was also differentially expressed in association with optimal cytoreductive surgery [28]. Data from similar studies could be used to validate the use of molecular markers in predicting optimal cytoreduction.

The strength of this study is that it is a single-institution analysis with a short inclusion period. Therefore, it reduces bias caused by change of treatment. A limitation is the retrospective and non-randomized design and the short follow-up of 36 months. This study is an audit of practice of the surgical management of advanced ovarian cancers in our institute. An attempt has been made to find out the resectability and oncological outcomes when there is diffuse disease on the small-bowel mucosa and mesentery. However, a definitive conclusion about the PFS and OS in this group requires a larger number of patients to be recruited for the study.

Conclusion

In advanced ovarian cancer patients, the presence of disease on the small-bowel serosa and mesentery may be associated with poor oncological outcomes. The number of patients with

suboptimal cytoreduction is high in this group. However, larger studies are required for reaching a definitive conclusion. We must continue to develop techniques whereby diffuse disease on the small-bowel serosa and mesentery is better predicted preoperatively by imaging. Laparoscopic Fagotti scoring could predict incomplete cytoreduction associated with small-bowel disease. This subgroup may benefit from NACT rather than a primary surgery with gross residual disease. Further prospective studies could throw light on whether diffuse small-bowel disease and mesenteric disease can be predicted preoperatively by imaging or molecular markers.

Compliance with Ethical Standards

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References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 1(5):136
2. Heintz AP, Odicino F, Maisonneuve P, Quinn MA, Benedet JL, Creasman WT, Ngan HY, Pecorelli S, Beller U (2006) Carcinoma of the ovary. FIGO 26th annual report on the results of treatment in gynecological cancer. *Int J Gynaecol Obstet* 95(Suppl 1):S161–S192
3. Elattar A, Bryant A, Winter-Roach BA, Hatem M, Naik R (2011) Optimal primary surgical treatment for advanced epithelial ovarian cancer. *Cochrane Database Syst Rev*. 10;(8)
4. 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
5. Eisenkop SM, Spirtos NM, Lin WC (2006) Optimal cytoreduction for advanced epithelial ovarian cancer: a commentary. *Gynecol Oncol* 103(1):329–335
 6. Morgan RJ Jr, Alvarez RD, Armstrong DK, Burger RA, Chen LM, Copeland L, Crispens MA, Gershenson DM, Gray HJ, Hakam A, Havrilesky LJ, Johnston C, Lele S, Martin L, Matulonis UA, O'Malley DM, Penson RT, Powell MA, Remmenga SW, Sabbatini P, Santoso JT, Schink JC, Teng N, Werner TL, Dwyer MA, Hughes M; National comprehensive cancer networks. Ovarian cancer, version 2.2013. *J Natl Compr Cancer Netw* 2013;11(10): 1199–1209.
 7. Aletti GD, Dowdy SC, Gostout BS, Jones MB, Stanhope CR, Wilson TO, Podratz KC, Cliby WA (2006) Aggressive surgical effort and improved survival in advanced-stage ovarian cancer. *Obstet Gynecol* 107(1):77–85
 8. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ (2002) Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* 20(5):1248–1259
 9. Eisenkop SM, Friedman RL, Wang HJ (1998) Complete cytoreductive surgery is feasible and maximizes survival in patients with advanced epithelial ovarian cancer: a prospective study. *Gynecol Oncol* 69(2):103–108
 10. Lengyel E (2010) Ovarian cancer development and metastasis. *Am J Pathol* 177(3):1053–1064
 11. Karst AM, Drapkin R (2010) Ovarian cancer pathogenesis: a model in evolution. *J Oncol* 2010:932371
 12. Hamilton CA, Miller A, Miller C, Krivak TC, Farley JH, Chernofsky MR, Stany MP, Rose GS, Markman M, Ozols RF, Armstrong DK, Maxwell GL (2011) The impact of disease distribution on survival in patients with stage III epithelial ovarian cancer cytoreduced to microscopic residual: a gynecologic oncology group study. *Gynecol Oncol* 122(3):521–526
 13. Vergote I, Tropé CG, Amant F, Kristensen GB, Ehlen T, Johnson N, Verheijen RH, van der Burg ME, Lacave AJ, Panici PB, Kenter GG, Casado A, Mendiola C, Coens C, Verleye L, Stuart GC, Pecorelli S, Reed NS; European Organization for Research and Treatment of Cancer-Gynaecological Cancer Group; NCIC Clinical Trials Group. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med* 2010;363(10):943–953.
 14. Steed H, Oza AM, Murphy J, Laframboise S, Lockwood G, DE Petrillo D, Sturgeon J, Rosen B (2006) A retrospective analysis of neoadjuvant platinum-based chemotherapy versus up-front surgery in advanced ovarian cancer. *Int J Gynecol Cancer* 16(Suppl 1):47–53
 15. Wahner Hendrickson AE, Hawthorne KM, Goode EL, Kalli KR, Goergen KM, Bakkum-Gamez JN, Cliby WA, Keeney GL, Visscher DW, Tarabishy Y, Oberg AL, Hartmann LC, Maurer MJ 2015. Assessment of published models and prognostic variables in epithelial ovarian cancer at Mayo Clinic. *Gynecol Oncol*. 22.
 16. Zivanovic O, Sima CS, Iasonos A, Hoskins WJ, Pingle PR, Leitao MM Jr, Sonoda Y, Abu-Rustum NR, Barakat RR, Chi DS (2010) The effect of primary cytoreduction on outcomes of patients with FIGO stage IIIC ovarian cancer stratified by the initial tumor burden in the upper abdomen cephalad to the greater omentum. *Gynecol Oncol* 116(3):351–357
 17. Braicu EI, Sehouli J, Richter R, Pietzner K, Lichtenegger W, Fotopoulou C (2012) Primary versus secondary cytoreduction for epithelial ovarian cancer: a paired analysis of tumour pattern and surgical outcome. *Eur J Cancer* 48(5):687–694
 18. Fotopoulou C, Richter R, Braicu EI, Schmidt SC, Lichtenegger W, Sehouli J (2010) Can complete tumor resection be predicted in advanced primary epithelial ovarian cancer? A systematic evaluation of 360 consecutive patients. *Eur J Surg Oncol* 36(12):1202–1210
 19. Chéreau E, Ballester M, Selle F, Cortez A, Daraï E, Rouzier R (2010) Comparison of peritoneal carcinomatosis scoring methods in predicting resectability and prognosis in advanced ovarian cancer. *Am J Obstet Gynecol* 202(2):178.e1–178.e10
 20. 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
 21. 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
 22. Shim SH, Lee SJ, Kim SO, Kim SN, Kim DY, Lee JJ, Kim JH, Kim YM, Kim YT, Nam JH (2015) Nomogram for predicting incomplete cytoreduction in advanced ovarian cancer patients. *Gynecol Oncol* 136(1):30–36
 23. Brockbank EC, Ind TE, Barton DP, Shepherd JH, Gore ME, A'Hern R, Bridges JE (2004) Preoperative predictors of suboptimal primary surgical cytoreduction in women with clinical evidence of advanced primary epithelial ovarian cancer. *Int J Gynecol Cancer* 14(1):42–50
 24. Chi DS, Zivanovic O, Palayekar MJ, Eisenhauer EL, Abu-Rustum NR, Sonoda Y, Levine DA, Leitao MM, Brown CL, Barakat RR (2009) A contemporary analysis of the ability of preoperative serum CA-125 to predict primary cytoreductive outcome in patients with advanced ovarian, tubal and peritoneal carcinoma. *Gynecol Oncol* 112(1):6–10
 25. Suidan RS, Ramirez PT, Sarasohn DM, Teitcher JB, Mironov S, Iyer RB, Zhou Q, Iasonos A, Paul H, Hosaka M, Aghajanian CA, Leitao MM Jr, Gardner GJ, Abu-Rustum NR, Sonoda Y, Levine DA, Hricak H, Chi DS (2014) A multicenter prospective trial evaluating the ability of preoperative computed tomography scan and serum CA-125 to predict suboptimal cytoreduction at primary debulking surgery for advanced ovarian, fallopian tube, and peritoneal cancer. *Gynecol Oncol* 134(3):455–461
 26. Kaldawy A, Segev Y, Lavie O, Auslender R, Sopic V, Narod SA (2016) Low-grade serous ovarian cancer: a review. *Gynecol Oncol* 143(2):433–438. doi:10.1016/j.ygyno.2016.08.320
 27. Tewari D, Java JJ, Salani R, Armstrong DK, Markman M, Herzog T, Monk BJ, Chan JK. Long-term survival advantage and prognostic factors associated with intraperitoneal chemotherapy treatment in advanced ovarian cancer: a gynecologic oncology group study. *J Clin Oncol*, doi: 10.1200/JCO. 2014. 55.9898
 28. K Fuh, T.K. Kiet, L Chen, R A Brooks, A E Sherman, D S Kapp, J K Chan The use of molecular markers to predict for optimal cytoreduction in ovarian cancer.