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A multicenter assessment of the ability of preoperative computed tomography scan and CA-125 to predict gross residual disease at primary debulking for advanced epithelial ovarian cancer

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Abstract

Objective—To assess the ability of preoperative computed tomography scan and CA-125 to predict gross residual disease (RD) at primary cytoreduction in advanced ovarian cancer.

Methods—A prospective, non-randomized, multicenter trial of patients who underwent primary debulking for stage III–IV epithelial ovarian cancer previously identified 9 criteria associated with suboptimal (>1cm residual) cytoreduction. This is a secondary post-hoc analysis looking at the ability to predict any RD. Four clinical and 18 radiologic criteria were assessed, and a multivariate model predictive of RD was developed.

Results—From 7/2001–12/2012, 350 patients met eligibility criteria. The complete gross resection rate was 33%. On multivariate analysis, 3 clinical and 8 radiologic criteria were

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significantly associated with the presence of any RD: age ≥60 years (OR=1.5); CA-125 ≥600 U/ml (OR=1.3); ASA 3–4 (OR=1.6); lesions in the root of the superior mesenteric artery (OR=4.1), splenic hilum/ligaments (OR=1.4), lesser sac >1cm (OR=2.2), gastrohepatic ligament/porta hepatis (OR=1.4), gallbladder fossa/intersegmental fissure (OR=2); suprarenal retroperitoneal lymph nodes (OR=1.3); small bowel adhesions/thickening (OR=1.1); and moderate-severe ascites (OR=2.2). All ORs were significant with p<.01. A 'predictive score' was assigned to each criterion based on its multivariate OR, and the rate of having any RD for patients who had a total score of 0–2, 3–5, 6–8, and ≥9 was 45%, 68%, 87%, and 96%, respectively.

Conclusions—We identified 11 criteria associated with RD, and developed a predictive model in which the rate of having any RD was directly proportional to a predictive score. This model may be helpful in treatment planning.

Introduction

Epithelial ovarian cancer remains the leading cause of gynecologic cancer-related mortality in the United States, with an estimated 14,240 deaths in 2016 [1]. This is largely due to the majority of women presenting with advanced-stage (International Federation of Gynecology and Obstetrics [FIGO] III/IV) disease. Standard initial treatment for these patients consists of primary debulking surgery followed by platinum and taxane-based chemotherapy [2]. The goal of surgery is to remove as much tumor as possible given that the volume of residual disease is the most important predictor of overall survival [3].

It is well established that patients who undergo 'optimal' cytoreduction have a survival advantage over those who undergo 'suboptimal' debulking, with suboptimal defined as >1cm residual disease [4, 5]. Because a significant proportion of women will undergo a suboptimal cytoreductive procedure with its associated morbidity but without a commensurate improvement in survival, several attempts have been made to preoperatively predict cytoreductive outcome [6]. These studies have used imaging modalities, tumor markers, and laparoscopic scores, but were limited by their retrospective nature, small sample size, and broad inclusion criteria [6–10]. We have previously reported the results of a prospective trial assessing the ability of preoperative computed tomography (CT) scan and serum CA-125 to predict suboptimal debulking [11]. This trial was conducted at two high-volume ovarian cancer centers, and evaluated 350 patients who underwent primary debulking for stage III and IV epithelial ovarian cancer. In that study, three clinical and six radiologic criteria significantly associated with suboptimal debulking were identified. The three clinical criteria were: age ≥60 years, CA-125 ≥600 U/mL, and American Society of Anesthesiologists (ASA) class ≥3. The six CT criteria were: lesions in the splenic hilum/ligaments >1cm in size, retroperitoneal lymph nodes above the renal hilum (including supradiaphragmatic) >1cm, small bowel mesentery lesions >1cm, lesser sac lesions >1cm, diffuse small bowel adhesions/thickening, and lesions in the root of the superior mesenteric artery (SMA) >1cm. Using those criteria, a model predictive of suboptimal cytoreduction was developed.

The previous study enrolled patients continuously from 2001 to 2012. However, during that time, multiple analyses confirmed that women with complete gross resection of all visible

disease had the best survival outcomes in this population [12, 13]. Therefore, the objective of the current report was to assess the ability of preoperative CT scan and CA-125 to predict any gross residual disease (RD).

Materials and Methods

This is a secondary post-hoc analysis of the previously collected data. The original trial was a prospective, non-randomized, multicenter study that included patients aged ≥18 years with presumed advanced epithelial ovarian, fallopian tube, or peritoneal cancer. It was approved by the institutional review boards of each institution, and informed consent was obtained from all enrolled patients. A serum CA-125 and CT scan of the abdomen/pelvis were obtained within 14 and 35 days before surgery, respectively. Data collected included demographics, tumor characteristics, and cytoreductive outcome (defined as no gross RD, gross RD ≤1cm, and gross RD >1cm). Exclusion criteria and a CONSORT diagram detailing included and excluded patients were presented in the initial publication [11].

CT scans were performed after administration of intravenous and oral contrast. Images were analyzed and interpreted prior to surgery by five protocol radiologists, all experienced in body CT. The presence or absence and size of 18 radiologic criteria were prospectively recorded. The criteria included lesions in the lesser sac, root of the SMA, small bowel mesentery, omentum, gallbladder fossa/liver intersegmental fissure, gastrohepatic ligament/porta hepatis, spleen (hilum/ligaments and parenchyma individually), liver (perihepatic, subcapsular, and parenchyma individually), pulmonary bases, pleural bases, retroperitoneal lymph nodes above the renal hilum (including supradiaphragmatic), and diffuse small bowel adhesions/thickening. The latter was interpreted radiologically as angulated bowel loops in the presence of small bowel wall thickening (thickening was subjectively assessed with no specific measurement of bowel wall thickness used, as it was dependent on the caliber of the loop of bowel evaluated). Other criteria were presacral extraperitoneal disease, tumor invading the anterior abdominal wall, and the presence of ascites (categorized as mild, moderate, or severe). Quantitative bi-dimensional measurements were performed for all visualized lesions. In order to categorize the degree of radiologic certainty that a lesion identified on CT represented metastasis, qualitative analysis (QA) was done using the following five-point scale: 1=definitely normal; 2=probably normal; 3=indeterminate; 4=probably metastatic; and 5=definitely metastatic. There were no explicit criteria for assigning a QA score; scores were determined by the radiologists based on their experience, judgment, and each lesion's characteristics (i.e., well defined vs poorly defined, solid vs cystic). In addition to the CT criteria, the four clinical criteria that were previously assessed and considered as potential predictors of debulking outcome were: serum CA-125, age, FIGO stage, and ASA class as determined by anesthesiologists at the time of surgery.

Patients were categorized as having no RD or any gross RD (≤1cm and >1cm RD combined). All 18 radiologic and four clinical criteria were assessed for their association with the presence of any gross RD at cytoreduction. Radiologic criteria were considered present if lesions had a QA of 4 or 5 and absent if they had a QA of 1–3. The association between measurable radiologic criteria and debulking outcome was assessed both for lesions >1cm and for lesions of any size, and the most predictive cutoffs were used for each

individual criteria. Lesions of any size were more predictive in all cases with the exception of lesser sac lesions, for which 1cm was used. Due to the small number of patients with an ASA class of 1 or 4, patients with an ASA of 3 or 4 were combined and compared to those who had an ASA of 1 or 2. Receiver operating characteristic (ROC) curves were generated to determine the optimal cutoffs for age and CA-125. The cutoffs most predictive of RD were found to be 60 years and 600 U/mL, respectively. Associations between the criteria and cytoreductive outcome were tested using the Wilcoxon Rank-Sum test for continuous variables and Fisher's exact test for categorical variables. Generalized estimating equations were used to account for differences between the two institution-clusters, assuming independent covariance structure. Based on the univariate analysis results, backward selection was utilized to build a multivariate model predictive of any gross RD (outcome), for which an ROC curve was generated. The area under the curve (AUC) was used as a measure of predictive accuracy. The clinical and radiologic criteria found to be significant on multivariate analysis were then each assigned a 'predictive score' according to their multivariate odds ratios (ORs). The total predictive score of all patients in the cohort was subsequently calculated using each patient's radiologic and clinical characteristics, and the RD rate corresponding to each total score was determined. All statistical tests were two-sided, and a p value of <0.05 was considered significant. As the multivariate model was considered exploratory, no formal adjustment for multiple comparisons was made. Statistical analysis was performed using SAS statistical software 9.2 (SAS Institute, Cary, NC) and R (R development core team, 2015).

Results

From July 2001 to December 2012, 350 patients met all eligibility criteria. Patient and tumor characteristics are shown in Table 1. The median age of our cohort was 61 years, the majority of women had FIGO stage IIIC disease, with most of serous histology, and the median CA-125 was 860 U/mL. The complete gross resection rate was 33% (n=117), and 67% (n=233) of the patients had gross RD at primary debulking.

On univariate analysis, all clinical and 13 radiologic criteria were significantly associated with gross RD at debulking surgery (Tables 2 and 3). Seventy-one percent (144/203) of patients with a CA-125 ≥600 U/mL had RD, compared to 61% (89/147) of those with a CA-125 <600 U/mL (OR 1.59, 95% CI 1.52 – 1.67). The presence of lesions in the root of the SMA was the radiologic criterion most predictive of RD: 92% (12/13) of patients with that finding had RD, compared to 66% (221/337) of those without it (OR 6.3, 95% CI 5.1 – 7.8).

On multivariate analysis, after backward selection, three clinical and eight radiologic criteria remained significantly associated with RD (Table 4). The clinical criteria were: age ≥60 years (OR 1.49), CA-125 ≥600 U/mL (OR 1.29), and ASA ≥3 (OR 1.6). The radiologic criteria were: lesions in the splenic hilum/ligaments (OR 1.36), retroperitoneal lymph nodes above the renal hilum (including supradiaphragmatic) (OR 1.31), gastrohepatic ligament/porta hepatis lesions (OR 1.44), diffuse small bowel adhesions/thickening (OR 1.12), lesions in the gallbladder fossa/liver intersegmental fissure (OR 2), moderate-severe abdominal ascites (OR 2.21), lesser sac lesions >1cm (OR 2.24), and lesions in the root of the SMA

(OR 4.06). All ORs were significant with p<.01. ROC curves were generated to compare different models' accuracy in predicting gross RD. The eight CT criteria combined showed an AUC of 0.694. An AUC of 0.704 was obtained when the CA-125 was added to the eight CT criteria. The highest AUC (0.72) was achieved when all eight CT and three clinical criteria were included (supplementary Figure S1).

In order to add clinical utility to these findings and develop a predictive model, a 'predictive score' was assigned to each of the 11 criteria significant on multivariate analysis, which was based on their multivariate ORs (Table 4). The total predictive score of all patients in our cohort was then calculated using their individual clinical and CT scan findings, and the rate of having any RD that corresponded to each total score was determined (Table 5). The rate was directly proportional to the predictive score. Among patients with a total score of 0–2, 45% had gross RD at primary debulking. The rate increased to 68% and 87% of patients with a total score of 3–5, and 6–8, respectively. Patients with a total score of 9 or more had the highest rate, 96%.

Discussion

In two tertiary care cancer centers, we identified three clinical and eight radiologic findings associated with gross RD. We also developed a predictive model in which the rate of having any gross RD increased progressively based on a predictive score. This model had an overall accuracy of 0.72.

Although many studies have evaluated the ability of CT scans and/or CA-125 to predict suboptimal debulking, there is a paucity of data and models predicting any RD [7–10, 14]. A recent systematic review of the literature identified only one study utilizing imaging to predict any RD [15]. In that study, Jung and colleagues retrospectively reviewed CT scans of 77 patients. Among nine imaging criteria assessed, upper abdominal ascites and diffuse subdiaphragmatic peritoneal nodularity were found to be associated with RD. The authors considered their analysis limited by the low number of patients included and subsequent low prevalence of positive imaging findings [16]. Petrillo et al. recently published a laparoscopy-based model predicting the presence of any RD, which evaluated six laparoscopic parameters. In that analysis, the authors recommended avoiding laparotomy at a cutoff score of 10 based on their model, due to a 0% likelihood of achieving complete gross resection. Women who had a score ≥10 comprised 6% of their cohort (n=14/234 patients) [17]. In another study of molecular biomarkers, Tucker et al. identified two genes (*FABP4* and *ADH1B*) whose high expression was associated with a higher risk of RD. Limitations of the use of genetic biomarkers include the need for a preoperative biopsy and the time required to perform the analysis, as well as the heterogeneity in gene expression rates between metastatic and primary tumor sites [18].

When comparing the model in this manuscript to our initial model predicting suboptimal cytoreduction (>1cm residual), many of the criteria are common. Among the clinical factors, age ≥60 years and ASA ≥3 were significant in both models, with the main difference being a CA-125 cutoff of ≥600 U/mL in the current model and ≥500 U/mL in the initial one. CT criteria that were significant in both models were lesions in the lesser sac, splenic hilum/

ligaments, root of the SMA, and diffuse small bowel adhesions/thickening, and suprarenal retroperitoneal lymph nodes (including supradiaphragmatic). The observation that many findings are common makes intuitive sense. One would expect that if preoperative criteria predict that a gross residual of ≤1cm cannot be achieved, then the same findings would imply that debulking to no RD is unlikely. Factors that were additionally significant in the current model were lesions in the gastrohepatic ligament/porta hepatis, gallbladder fossa/ liver intersegmental fissure, and moderate-severe ascites. The first two criteria reflect extensive disease in the right upper abdomen that is technically challenging to resect and may preclude a complete gross resection in certain patients. Moderate-severe ascites on the other hand, while easily drained and having no bearing on debulking outcome, may be a surrogate for advanced disease in multiple anatomic locations. Notably, the finding most predictive of having RD in our model was the presence of root of the SMA lesions, with a multivariate OR of 4.06 and a predictive score of 4. Although only 13 patients had that finding (4% of our cohort), 92% of those women had RD at debulking. The median total predictive score of those 13 patients was 10, with a range of 6 – 14. Disease in this area is not only very challenging to surgically resect, but the high associated total predictive score in those patients also suggests that it is a marker for very high tumor burden. A radiology checklist combining the criteria from both models (with detailed definitions) is provided in Table 6 for clinical use by the readership.

Although the goal of primary debulking should always be a complete gross resection when feasible, predicting and debulking to ≤1cm residual remains an important clinical endpoint. Studies have shown that patients with 0.1–1cm residual have improved survival compared to those with >1cm residual [19]. This is reflected in recent guidelines on the primary management of ovarian cancer published by a joint Society of Gynecologic Oncology and American Society of Clinical Oncology expert panel [20]. The guidelines state that in women with stage IIIC and IV ovarian cancer, “primary cytoreductive surgery is preferred to neoadjuvant chemotherapy if there is a high likelihood of achieving cytoreduction to ≤1cm (ideally to no visible disease) with acceptable morbidity.” Therefore, although we believe that the new model predicting any RD is clinically useful and important, our intent is not to supplant the previous model predicting >1cm residual or dissuade from its use. We consider that both models have a role in the preoperative management of ovarian cancer, and it is up to each surgeon and center to use them as they deem appropriate to their practice.

The main strengths of our study include its large sample size, its multicentricity, and the fact that the data was collected prospectively. We included 350 women, all with advanced-stage cancer, and those patients were enrolled at two institutions, which increases the generalizability of our analysis. The CT images were all evaluated prior to surgery by a dedicated group of radiologists who were highly experienced in body CT, minimizing bias and assuring their blinding to debulking status and findings at laparotomy. As with our initial model, we were able to incorporate both imaging modalities and clinical factors into the current one, which we consider to be a strength. Although a patient’s disease burden may render her amenable to a complete gross resection, the majority of gynecologic oncologists consider age and medical status when making a decision to proceed with primary debulking or neoadjuvant chemotherapy. As such, we consider that including age and ASA helps account for the fact that some patients who are older and/or have multiple comorbidities may

be less able to tolerate an extensive cytoreductive surgery and therefore less likely to be left with no RD. To illustrate how our model would be used, a theoretical patient who is 70 years old (predictive score = 1), has a CA-125 of 800 U/mL (score = 1), an ASA of 2 (score = 0), lesions in the splenic hilum (score = 1), liver intersegmental fissure (score = 2), and root of the SMA (score = 4), would have a total predictive score of 9 (Table 4). Based on our model and on that total score, that patient would have a 96% chance of having RD at primary debulking (Table 5). In other words, she would only have a 4% chance of undergoing a complete gross resection.

Our study has several limitations. First, it is a secondary post-hoc analysis of the previously collected data, and the original trial was designed to predict >1cm residual. That trial had a long time for accrual, and surgical practice may have changed over time. Indeed, the complete gross resection rate is currently higher at both institutions than the one reported in this study. CT imaging technology has also likely improved since the initial patients were enrolled, allowing better identification and characterization of metastatic lesions in current practice. As each individual CT scan was evaluated by one study radiologist, the inter-observer variability and reproducibility of the imaging findings were not assessed. Our scoring model has also not been validated in another population at this time.

In conclusion, we developed a multivariate model that predicts gross RD at primary debulking for epithelial ovarian cancer. This adds to our previously developed model predicting suboptimal cytoreduction, and may be helpful in treatment planning and counseling. We do not advocate the use of one model over the other, and also do not recommend a specific cutoff in the current model above which patients should receive neoadjuvant chemotherapy. We feel it is appropriate for each institution and provider to determine which model and cutoffs to use, based on their own individual outcomes, practice, and treatment philosophy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016; 66:7–30. [PubMed: 26742998]
2. Bristow RE, Chang J, Ziogas A, Anton-Culver H. Adherence to treatment guidelines for ovarian cancer as a measure of quality care. Obstet Gynecol. 2013; 121:1226–34. [PubMed: 23812456]
3. Winter WE, Maxwell GL, Tian C, Carlson JW, Ozols RF, Rose PG, et al. Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007; 25:3621–7. [PubMed: 17704411]
4. Ozols RF, Bundy BN, Greer BE, Fowler JM, Clarke-Pearson D, Burger RA, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected

stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2003; 21:3194–200. [PubMed: 12860964]

5. Chi DS, Franklin CC, Levine DA, Akselrod F, Sabbatini P, Jarnagin WR, et al. Improved optimal cytoreduction rates for stages IIIC and IV epithelial ovarian, fallopian tube, and primary peritoneal cancer: a change in surgical approach. Gynecol Oncol. 2004; 94:650–4. [PubMed: 15350354]
6. Fagotti A, Ferrandina G, Fanfani F, Ercoli A, Lorusso D, Rossi M, et al. A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: a pilot study. Ann Surg Oncol. 2006; 13:1156–61. [PubMed: 16791447]
7. Bristow RE, Duska LR, Lambrou NC, Fishman EK, O'Neill MJ, Trimble EL, et al. A model for predicting surgical outcome in patients with advanced ovarian carcinoma using computed tomography. Cancer. 2000; 89:1532–40. [PubMed: 11013368]
8. Axtell AE, Lee MH, Bristow RE, Dowdy SC, Cliby Wa, Raman S, et al. Multi-institutional reciprocal validation study of computed tomography predictors of suboptimal primary cytoreduction in patients with advanced ovarian cancer. J Clin Oncol. 2007; 25:384–9. [PubMed: 17264334]
9. Chi DS, Zivanovic O, Palayekar MJ, Eisenhauer EL, Abu-Rustum NR, Sonoda Y, et al. 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. 2009; 112:6–10. [PubMed: 19100916]
10. Vorgias G, Iavazzo C, Savvopoulos P, Myriokefalitaki E, Katsoulis M, Kalinoglou N, et al. Can the preoperative Ca-125 level predict optimal cytoreduction in patients with advanced ovarian carcinoma? A single institution cohort study. Gynecol Oncol. 2009; 112:11–5. [PubMed: 19119502]
11. Suidan RS, Ramirez PT, Sarasohn DM, Teitcher JB, Mironov S, Iyer RB, et al. 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. 2014; 134:455–61. [PubMed: 25019568]
12. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med. 2006; 354:34–43. [PubMed: 16394300]
13. Chang S-J, Hodeib M, Chang J, Bristow RE. Survival impact of complete cytoreduction to no gross residual disease for advanced-stage ovarian cancer: a meta-analysis. Gynecol Oncol. 2013; 130:493–8. [PubMed: 23747291]
14. Dowdy SC, Mullany SA, Brandt KR, Huppert BJ, Cliby WA. The utility of computed tomography scans in predicting suboptimal cytoreductive surgery in women with advanced ovarian carcinoma. Cancer. 2004; 101:346–52. [PubMed: 15241833]
15. Rutten MJ, van de Vrie R, Bruining A, Spijkerboer AM, Mol BW, Kenter GG, et al. Predicting surgical outcome in patients with International Federation of Gynecology and Obstetrics stage III or IV ovarian cancer using computed tomography: a systematic review of prediction models. Int J Gynecol Cancer. 2015; 25:407–15. [PubMed: 25695545]
16. Jung DC, Kang S, Kim MJ, Park SY, Kim HB. Multidetector CT predictors of incomplete resection in primary cytoreduction of patients with advanced ovarian cancer. Eur Radiol. 2010; 20:100–7. [PubMed: 19657649]
17. Petrillo M, Vizzielli G, Fanfani F, Gallotta V, Cosentino F, Chiantera V, et al. Definition of a dynamic laparoscopic model for the prediction of incomplete cytoreduction in advanced epithelial ovarian cancer: proof of a concept. Gynecol Oncol. 2015; 139:5–9. [PubMed: 26196319]
18. Tucker SL, Gharpure K, Herbrich SM, Unruh AK, Nick AM, Crane EK, et al. Molecular biomarkers of residual disease after surgical debulking of high-grade serous ovarian cancer. Clin Cancer Res. 2014; 20:3280–8. [PubMed: 24756370]
19. Chi DS, Eisenhauer EL, Lang J, Huh J, Haddad L, Abu-Rustum NR, et al. What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? Gynecol Oncol. 2006; 103:559–64. [PubMed: 16714056]
20. Wright AA, Bohlke K, Armstrong DK, Bookman MA, Cliby WA, Coleman RL, et al. Neoadjuvant Chemotherapy for Newly Diagnosed, Advanced Ovarian Cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2016; 34:3460–73. [PubMed: 27502591]

Highlights

- 3 clinical and 8 CT criteria associated with residual disease (RD) were identified
- A model predictive of surgical outcome at primary debulking was developed
- In this model, the rate of having any RD was proportional to a predictive score

Table 1

Patient and tumor characteristics (N = 350)

Variable	n (%)
Age	
Median (range)	61 years (34 – 86)
Stage	
III A/B	8 (2%)
IIIC	248 (71%)
IV	94 (27%)
Histology	
Serous	314 (90%)
Endometrioid/Clear cell	2 (0.6%)
Mixed/Other	34 (10%)
Tumor grade*	
1/2	19 (5%)
3	328 (95%)
Primary tumor site	
Ovary	264 (75%)
Fallopian tube	42 (12%)
Peritoneal	44 (13%)
ASA class	
1	10 (3%)
2	158 (45%)
3	179 (51%)
4	3 (1%)
Preoperative CA-125	
Median (range)	860 U/mL (9 – 38,100)

ASA, American Society of Anesthesiologists

*Data missing for 3 patients.

Table 2

Clinical criteria – univariate analysis

Criteria	Rate of having gross residual disease	OR	95% CI	p
Age				
≥ 60 years	132/187 (71%)	1.47	1.36 – 1.59	<.001
< 60 years	101/163 (62%)			
CA-125				
≥ 600 U/mL	144/203 (71%)	1.59	1.52 – 1.67	<.001
< 600 U/mL	89/147 (61%)			
ASA				
≥ 3	130/182 (72%)	1.58	1.4 – 1.78	<.001
≤ 2	103/168 (61%)			
Stage				
IV	67/94 (71%)	1.35	1.14 – 1.59	<.001
III	166/256 (65%)			

ASA, American Society of Anesthesiologists

Table 3

Radiologic criteria – univariate analysis

Criteria	Rate of having gross residual disease		OR	95% CI	p
	Criteria present	Criteria absent			
Perihepatic lesion	88/121 (73%)	145/229 (63%)	1.54	1.5 – 1.6	<.001
Subcapsular liver lesion	35/52 (67%)	198/298 (66%)	1.04	0.6 – 1.8	.89
Liver intraparenchymal lesion	8/11 (73%)	225/339 (66%)	1.35	1.1 – 1.7	.007
Spleen intraparenchymal lesion	6/9 (67%)	227/341 (67%)	1	0.99 – 1.02	.58
Lesion in splenic hilum/ligaments	56/70 (80%)	177/280 (63%)	2.33	2.1 – 2.6	<.001
Lesser sac lesion >1 cm	31/35 (89%)	202/315 (64%)	4.34	3.3 – 5.7	<.001
Gastrohepatic ligament/Porta hepatis lesion	71/88 (81%)	162/262 (62%)	2.58	2 – 3.3	<.001
Gallbladder fossa/Liver intersegmental fissure lesion	69/85 (81%)	164/265 (62%)	2.66	1.9 – 3.7	<.001
Omental lesion	142/220 (65%)	91/130 (70%)	0.78	0.5 – 1.3	.33
Root of the superior mesenteric artery lesion	12/13 (92%)	221/337 (66%)	6.3	5.1 – 7.8	<.001
Small bowel mesentery lesion	49/67 (73%)	184/283 (65%)	1.46	1.3 – 1.7	<.001
Retroperitoneal lymph nodes above the renal hilum (including supradiaphragmatic)	71/94 (76%)	162/256 (63%)	1.79	1.7 – 1.9	<.001
Pulmonary metastasis (lung bases)	9/13 (69%)	224/337 (66%)	1.14	0.98 – 1.3	.08
Pleural metastasis (lung bases)	9/17 (53%)	224/333 (67%)	0.55	0.3 – 0.9	.02
Tumor invading anterior abdominal wall	12/16 (75%)	221/334 (66%)	1.53	1.5 – 1.6	<.001
Presacral extraperitoneal disease	3/4 (75%)	230/346 (67%)	1.51	0.9 – 2.5	.09
Diffuse small bowel adhesions/thickening	18/24 (75%)	215/326 (66%)	1.55	1.5 – 1.6	<.001
Abdominal ascites (moderate-severe)	120/154 (78%)	113/196 (58%)	2.59	2.3 – 3	<.001

Table 4

Multivariate model of significant clinical and radiologic criteria predictive of gross residual disease

Criteria	OR	95% CI	p	Predictive Score
Age ≥60 years	1.49	1.14 – 1.93	.003	1
CA-125 ≥600 U/mL	1.29	1.15 – 1.43	<.001	1
ASA ≥3	1.6	1.55 – 1.66	<.001	1
Lesion in splenic hilum/ligaments	1.36	1.13 – 1.64	.001	1
Gastrohepatic ligament/Porta hepatis lesion	1.44	1.24 – 1.67	<.001	1
Retroperitoneal lymph nodes above the renal hilum (including supradiaphragmatic)	1.31	1.11 – 1.55	.002	1
Diffuse small bowel adhesions/thickening	1.12	1.1 – 1.14	<.001	1
Abdominal ascites (moderate-severe)	2.21	1.72 – 2.83	<.001	2
Gallbladder fossa/Liver intersegmental fissure lesion	2	1.72 – 2.33	<.001	2
Lesser sac lesion >1 cm	2.24	1.51 – 3.31	<.001	2
Root of the superior mesenteric artery lesion	4.06	3.12 – 5.29	<.001	4

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Table 5

Predictive score and gross residual disease (N = 350)

Total predictive score	Total patients n (%)	No residual disease (n)	Gross residual disease (n)	Rate of having gross residual disease
0 – 2	107/350 (31%)	59	48	45%
3 – 5	151/350 (43%)	48	103	68%
6 – 8	68/350 (19%)	9	59	87%
≥ 9	24/350 (7%)	1	23	96%

Table 6

Radiology checklist combining significant radiologic criteria from models predicting any residual disease and >1cm residual

Radiologic Criteria	Yes (QA=4,5) any size	Yes (QA=4,5) >1cm	No (QA=1,2,3)
Perisplenic lesion(s): Splenic hilum (splenic vessel entry) **or splenic ligaments** (gastrocolic, splenocolic, and splenorenal) **lesion(s)**			
Lesser sac lesion(s)			
Gastrohepatic ligament or porta hepatis lesion(s) (implants or nodes) >1 cm in SA (or ≤1 cm in SA but rounded, heterogeneous, or irregular borders). If portocaval node(s) then >1.5 cm in SA or (≤1.5 cm in SA but loss of oblong shape and/or heterogeneity)			
Gallbladder fossa or left inter-segmental fissure lesion(s) (fissure for the ligamentum venosum)			
Root of the SMA lesion(s) (fat immediately around SMA origin down to 1st jejunal branch)			
Small bowel mesentery lesion(s) (anywhere in SB mesentery except for root of SMA)			
Diffuse SB adhesions/thickening (Angulated bowel loops in the presence of SB wall thickening [No specific measurement of bowel wall thickness used as dependent on caliber of that loop of bowel]. Alternatively defined as SB tethering and/or angulation without measurable lesion(s))		N/A	
Ascites (moderate to large volume)		N/A	
Retroperitoneal lymph node(s) above the renal hilum >1 cm in SA (or ≤1 cm in SA but rounded, heterogeneous, or irregular borders) **or Supra-diaphragmatic lymph node(s)** (>0.5 cm in SA)			

SMA, Superior mesenteric artery; SB, Small bowel; SA, Short axis

QA (qualitative analysis) scale: QA=5: Definitely metastatic, QA=4: Probably metastatic, QA=3: Indeterminate, QA=2: Probably normal, QA=1: Definitely normal