

Prospective Evaluation of Preoperative Clinical, Biochemical, and Radiological Factors for Predicting Optimal Primary Cytoreduction in Patients with Advanced Epithelial Ovarian Cancer

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Abstract:

Background: Achieving optimal primary cytoreduction is an important determinant of treatment outcomes in advanced epithelial ovarian cancer. However, extensive intraperitoneal disease may limit complete tumor removal and increase the risk of suboptimal cytoreduction. Preoperative identification of patients at higher risk may facilitate individualized surgical planning and treatment selection.

Aim: To prospectively evaluate the clinical, biochemical, and radiological factors associated with the achievement of optimal primary cytoreduction in patients with advanced epithelial ovarian cancer.

Methodology: This prospective observational study included 85 women with advanced epithelial ovarian cancer undergoing primary cytoreductive surgery at the Department of Surgical Oncology and Gynaecology Oncology, Patna Medical College and Hospital, Bihar, over one year. Preoperative clinical status, serum CA-125, ascites, pleural effusion, and radiological findings were assessed. Optimal cytoreduction was defined as residual disease ≤ 1 cm. Univariate and multivariable logistic regression analyses were performed to identify predictors of suboptimal cytoreduction.

Results: Optimal cytoreduction was achieved in 37 (43.5%) patients, while 48 (56.5%) had suboptimal cytoreduction. Intraperitoneal carcinomatosis was significantly associated with suboptimal cytoreduction ($p < 0.001$) and independently increased its odds (adjusted OR 3.76, 95% CI 1.58–8.95; $p = 0.003$). Ascites > 1000 mL was also independently predictive (adjusted OR 2.41, 95% CI 1.03–5.65; $p = 0.043$). CA-125 level, ASA status, pleural effusion, omental extension, and liver involvement were not significant independent predictors.

Conclusion: Intraperitoneal carcinomatosis and high-volume ascites are important preoperative predictors of suboptimal primary cytoreduction. Their assessment may support individualized surgical planning and appropriate selection of patients for alternative treatment strategies.

Keywords: Epithelial Ovarian Cancer; Primary Cytoreduction; Optimal Cytoreduction; Intraperitoneal Carcinomatosis; Ascites; CA-125; Preoperative Predictors; Cytoreductive Surgery.

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Introduction

Ovarian cancer, one of the most common gynecological cancers, is a major health issue worldwide due to its often-late diagnosis and highly aggressive nature [1]. Epithelial ovarian cancers represent about 90% of all ovarian cancers and are the most common histological type of ovarian cancer in clinical practice. A significant number of women (around two-thirds) who have epithelial ovarian cancer (EOC) have advanced disease, according to the International Federation of Gynecology and Obstetrics (FIGO) staging system [2]. It may be possible that delayed presentation, lack of awareness, variable access to specialized gynecologic oncology

services and non-specificity of early symptoms may further contribute to diagnosis at an advanced stage in India including in Bihar. Therefore, the pre-operative evaluation and selection of patients most likely to gain benefit from primary (complete or nearly complete) cytoreductive surgery is of great clinical importance.

The traditional treatment strategy for epithelial ovarian cancer in the advanced stage is platinum-based chemotherapy preceded by primary cytoreductive surgery. Primary cytoreductive surgery typically involves hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and peritoneal assessment and

removal of visible tumour deposits, as much as technically and safely possible. The major goal of surgery is to achieve tumour debulking as near to complete as possible as the amount of residual tumour following the cytoreduction is an important factor in the response to the subsequent therapy and the long-term prognosis [3]. The concept of optimal cytoreduction has matured over the years, and a residual tumour less than 1 cm has traditionally been regarded as optimal. Optimal cytoreduction has been demonstrated to have a better response to chemotherapy and longer survival than those with significant residual tumors. The Gynecologic Oncology Group (GOG) studies have especially highlighted the survival benefit of minimal residual disease, which closely correlates with the amount of residual tumor [4].

Although residual disease is known to be important, the chance of optimal primary cytoreduction is highly variable between patients and between institutions. In the advanced ovarian cancer surgery centers with extensive experience in the field, optimal resection rates of about 60% to 90% have been reported [5]. But in all patients a primary optimal cytoreduction cannot be performed safely. The potential for unnecessary surgical morbidity exists if extensive surgery is performed on patients who are unlikely to achieve total or optimal resection, in absence of any oncological gain [6]. Advanced ovarian cancer surgery is associated with high peri-operative risks and reported 30-day mortality is 1-3%. Thus, it is important to identify accurately in the pre-operative setting those patients who are unlikely to achieve optimal cytoreduction and then balance the oncologic benefit with the surgical risk.

The use of neoadjuvant chemotherapy followed by interval cytoreductive surgery has become an alternative approach for those who are deemed to be unlikely to have satisfactory primary cytoreduction. Comparative studies have shown no differences in survival between patients who were selected for surgery and those who received chemotherapy and interval surgery. Onnes et al. found optimal debulking in 42% of patients who had first line chemotherapy versus 29% of patients who had primary surgery [7]. In the same way, Shwartz et al. showed that the induction chemotherapy followed by cytoreductive surgery was linked with a better overall survival than chemotherapy alone. A randomized prospective study also showed benefits with regard to overall and progression free survival in women who underwent interval cytoreductive surgery [8]. Moreover, Ansquer et al. reported reduced morbidity after cytoreductive surgery after neoadjuvant chemotherapy (NAC) therapy versus primary debulking surgery (PDS). These findings suggest that a primary surgery approach should not be applied uniformly to all patients, but instead the most appropriate initial treatment should be chosen.

Despite this, primary cytoreductive surgery is still an integral part of the treatment in patients with advanced epithelial ovarian cancer who are suitable surgical candidates. Primary surgery allows for extensive surgical staging, immediate reduction of tumour burden, evaluation of the distribution of disease and potentially improved response to subsequent chemotherapy. It also has the potential of minimizing the need for prolonged exposure to chemotherapy prior to definitive tumor reduction and may yield significant pathological data that could affect management. Therefore, primary surgery is still the current standard of care for patients with good disease spread and performance status. Primary surgery is performed on ~95% of patients with advanced epithelial ovarian cancer in the United States [9]. However, there is a large proportion of patients with primary surgery who will eventually have a residual disease greater than 1 cm, and reliable methods of identifying patients at high-risk of suboptimal cytoreduction remain a need.

An important question in advanced ovarian cancer is therefore whether there are patients who can be identified preoperatively that are unlikely to achieve optimal primary cytoreduction. This identification may help to plan individual treatment and to consider the use of interval surgery or neoadjuvant chemotherapy in the future. Various parameters, such as computed tomography (CT) characteristics, serum CA-125 level, presence of pleural effusion, ascites, and other clinical parameters, have been assessed in several studies to predict optimal cytoreduction. Radiological assessment may give some indication of the amount and intra-abdominal and pelvic spread of disease, and serum CA-125 may reflect the total tumour burden. Likewise, ascites and pleural effusion and poor physical condition may offer some clues as to the spread of the disease and whether the patient would be able to tolerate a large surgical procedure.

No single clinical, biochemical or radiological parameter, however, has been shown to have enough predictive accuracy to allow it to be used universally in the selection of patients for primary versus neoadjuvant treatment [10]. There is overlap of individual parameters between patients undergoing optimal and suboptimal cytoreduction. Furthermore, disease spread is more important than the extent of the tumour and, therefore, clinical status and serum markers, along with imaging data, are of special interest. The importance of this limitation is particularly paramount in resource-variable environments like Bihar, India, where there may be a need to optimize the use of specialized surgical and oncological services and decrease avoidable morbidity, as timely and accurate triage may help.

Thus, a prospective study of a number of pre-operative factors might be more clinically useful in predicting the possibility of optimal primary cytoreduction. The present study is designed to evaluate the

predictive value of various clinical, biochemical and radiological parameters including physical status, serum CA-125 level, ascites, pleural effusion and abdominal and pelvic CT/MRI findings in patients with advanced EOC who are scheduled for planned primary cytoreductive surgery in a tertiary care center in Bihar, India. The study aims to assess these factors as single and multiple variables, to identify characteristics associated with successful optimal cytoreduction and to establish a clinically relevant preoperative assessment framework. This could contribute to the selection of the right treatment, surgical planning, reduction of unnecessary operative morbidity, and appropriate referral for neoadjuvant chemotherapy in patients that cannot achieve optimal primary cytoreduction.

Materials and Methods

Study Design: A prospective observational study was conducted to evaluate the role of preoperative clinical, biochemical, and radiological factors in predicting optimal primary cytoreduction among patients with advanced epithelial ovarian cancer. The study was designed to assess whether routinely available preoperative parameters could identify patients who were likely to achieve optimal cytoreduction at primary surgery.

Study Area: The study was conducted in the Department of Surgical Oncology and Gynaecology Oncology, Patna Medical College and Hospital (PMCH), Patna, Bihar, India.

Study Duration: The study was conducted over a period of 1 year from March 2025 to February 2026.

Sample Size: A total of 85 patients with advanced epithelial ovarian cancer who fulfilled the predefined eligibility criteria were included in the study.

Study Population: The study population comprised women diagnosed with advanced-stage epithelial ovarian cancer, particularly patients with FIGO stage III or IV disease, who were considered candidates for primary cytoreductive surgery. Patients were evaluated clinically, biochemically, and radiologically before surgery to determine the association of these factors with the likelihood of achieving optimal primary cytoreduction.

Data Collection: Data were collected prospectively using a structured data collection proforma. Baseline demographic and clinical information was recorded, including age, presenting symptoms, general physical status, relevant medical history, and clinical findings. The preoperative physical status of each patient was assessed according to the American Society of Anesthesiologists (ASA) physical status classification.

Biochemical evaluation included measurement of serum CA-125 levels. Blood samples were collected during the preoperative period, preferably in the

morning, and serum CA-125 was measured using the standard laboratory method available at the institution.

Preoperative radiological evaluation was performed using appropriate imaging modalities, primarily contrast-enhanced computed tomography (CT) of the abdomen and pelvis, with additional imaging when clinically indicated. Radiological parameters relevant to the prediction of cytoreductive outcome were recorded, including ascites, pleural effusion, peritoneal carcinomatosis/peritoneal involvement, omental extension, liver involvement, and suprarenal/upper abdominal lymphadenopathy. Imaging findings were interpreted and documented by experienced radiologists.

Inclusion Criteria

Patients were included if they fulfilled the following criteria:

- Women with histologically confirmed or clinically highly suspected epithelial ovarian carcinoma.
- Patients with advanced-stage disease (FIGO stage III or IV).
- Patients considered suitable for primary cytoreductive surgery.
- Patients who underwent primary cytoreductive surgery at the Department of Gynaecology Oncology, PMCH.
- Patients who provided informed consent to participate in the study.
- Patients for whom adequate preoperative clinical, biochemical, and radiological information was available.

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Patients with ovarian tumors of non-epithelial histology, including germ-cell or sex-cord stromal tumors.
- Patients with recurrent ovarian cancer undergoing secondary cytoreductive surgery.
- Patients who received neoadjuvant chemotherapy before the planned primary cytoreductive surgery.
- Patients who were medically unfit for primary surgery.
- Patients who declined consent for participation.
- Patients with incomplete or inadequate preoperative clinical, biochemical, or radiological records.
- Patients in whom the extent of disease could not be adequately assessed before surgery.

Study Procedure: After enrollment, each patient underwent a systematic preoperative assessment. Demographic characteristics, clinical presentation,

physical findings, and ASA physical status were documented. Particular attention was given to the presence of ascites, abdominal distension, palpable disease, and other clinical indicators of extensive intra-abdominal disease.

Preoperative biochemical investigations were performed, with serum CA-125 recorded as a principal tumor marker. Radiological assessment was subsequently performed to determine the extent and distribution of disease. The presence or absence of ascites, pleural effusion, peritoneal involvement/carcinomatosis, omental disease, liver involvement, and suprarenal or upper abdominal lymphadenopathy was recorded.

All patients underwent primary cytoreductive surgery performed by the gynaecologic oncology surgical team. The operative findings were documented systematically, including the distribution and extent of intra-abdominal and pelvic disease. The amount of residual tumor remaining after completion of surgery was assessed.

For the purpose of this study, optimal primary cytoreduction was defined as residual tumor measuring ≤ 1 cm after completion of primary cytoreductive surgery, whereas suboptimal cytoreduction was defined as residual tumor measuring >1 cm. Patients were subsequently categorized into the optimal and suboptimal cytoreduction groups, and their preoperative clinical, biochemical, and radiological characteristics were compared. The primary outcome of the study was the ability of preoperative clinical, biochemical, and radiological factors to predict achievement of optimal primary cytoreduction.

Statistical Analysis: Data were entered into a computerized database and analyzed using appropriate statistical software. Continuous variables were summarized using mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) depending on the distribution of the data. Categorical variables were presented as frequencies and percentages.

Patients were divided into two groups according to surgical outcome: optimal cytoreduction (residual disease ≤ 1 cm) and suboptimal cytoreduction (residual disease >1 cm). Categorical variables were compared between the two groups using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using the independent-samples t-test for normally distributed variables or

the Wilcoxon rank-sum/Mann-Whitney U test for non-normally distributed variables.

Potential predictors of suboptimal cytoreduction, including age, ASA physical status, serum CA-125 level, ascites, pleural effusion, peritoneal carcinomatosis, omental extension, liver involvement, and suprarenal/upper abdominal lymphadenopathy, were initially evaluated using univariate analysis. Variables showing a clinically relevant or statistically significant association with cytoreductive outcome were considered for multivariable analysis. Where appropriate, binary logistic regression was used to identify independent preoperative predictors of suboptimal cytoreduction, and odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A two-sided p-value <0.05 was considered statistically significant."

Result

Table 1 summarizes the baseline clinical and tumor characteristics of the 85 patients included in the study. Regarding clinical status according to ASA classification, 56 patients (65.9%) were classified as ASA 1, while 29 (34.1%) were classified as ASA 2. Pleural effusion was present in 16 patients (18.8%), whereas 69 (81.2%) had no pleural effusion. Bowel resection was performed in 6 patients (7.1%), while the majority, 79 patients (92.9%), did not undergo bowel resection. Intraperitoneal carcinomatosis was identified in 47 patients (55.3%), compared with 38 (44.7%) without carcinomatosis. Among the imaging findings, omental extension was present in 18 patients (21.2%), while 67 (78.8%) had no omental extension. Liver involvement was observed in 13 patients (15.3%), whereas 72 (84.7%) had no liver involvement. Peritoneal involvement was detected in 27 patients (31.8%), with 58 (68.2%) showing no peritoneal involvement. Suprarenal adenopathy was relatively uncommon, being present in only 4 patients (4.7%), while 81 (95.3%) had no such adenopathy. Regarding preoperative CA-125 levels, 27 patients (31.8%) had levels ≤ 400 U/mL, whereas 58 (68.2%) had levels >400 U/mL. Ascites ≤ 1000 mL was observed in 46 patients (54.1%), while 39 (45.9%) had ascites >1000 mL. Overall, the study population demonstrated a substantial burden of intraperitoneal carcinomatosis and elevated CA-125 levels, with smaller proportions showing pleural effusion, bowel resection, liver involvement, suprarenal adenopathy, and extensive ascites.

Table 1: Clinical Data and Tumor Characteristics of the Study Population		
Characteristic	Patients No.	%
Clinical status (ASA)		
1	56	65.9
2	29	34.1
Pleural effusion		
Positive	16	18.8
Negative	69	81.2
Bowel resection		
Positive	6	7.1
Negative	79	92.9
Intraperitoneal carcinomatosis		
Positive	47	55.3
Negative	38	44.7
Imaging findings		
Omental extension		
Positive	18	21.2
Negative	67	78.8
Liver involvement		
Positive	13	15.3
Negative	72	84.7
Peritoneal involvement		
Positive	27	31.8
Negative	58	68.2
Suprarenal adenopathy		
Positive	4	4.7
Negative	81	95.3
CA-125		
≤400 U/mL	27	31.8
>400 U/mL	58	68.2
Ascites		
≤1000 mL	46	54.1
>1000 mL	39	45.9

Table 2 presents the univariate analysis of potential predictors of suboptimal cytoreduction. Clinical status did not show a statistically significant association with cytoreductive outcome, although suboptimal cytoreduction was more frequent among patients with clinical status 2 than status 1 (65.5% vs 51.8%, $p=0.256$). Similarly, pleural effusion was not significantly associated with suboptimal cytoreduction (75.0% vs 52.2% among those without effusion, $p=0.161$). In contrast, intraperitoneal carcinomatosis showed a highly significant association with suboptimal cytoreduction (74.5% vs 34.2% in patients without carcinomatosis, $p<0.001$). Omental extension ($p=0.425$), liver involvement ($p=0.375$), peritoneal involvement ($p=0.101$), and adenopathy

($p=0.629$) were not significantly associated with cytoreductive outcome. Likewise, preoperative CA-125 level showed no significant association, with suboptimal cytoreduction occurring in 55.6% of patients with CA-125 ≤400 U/mL and 56.9% of those with CA-125 >400 U/mL ($p=1.000$). However, ascites volume was significantly associated with surgical outcome ($p=0.048$); patients with ascites >1000 mL had a higher proportion of suboptimal cytoreduction (69.2%) compared with those having ascites ≤1000 mL (45.7%). Overall, intraperitoneal carcinomatosis and higher-volume ascites emerged as the principal significant predictors of suboptimal cytoreduction in the univariate analysis.

Table 2: Univariate Analysis of Predictors of Suboptimal Cytoreduction						
Predictor	Optimal Cytoreduc- tion No.	%	Suboptimal Cytoreduction No.	%	P	
Clinical status						
1	27	48.2	29	51.8	0.256	
2	10	34.5	19	65.5		
Pleural effusion						
Positive	4	25	12	75	0.161	
Negative	33	47.8	36	52.2		
Intraperitoneal carcinomatosis						
Positive	12	25.5	35	74.5	<0.001	
Negative	25	65.8	13	34.2		
Omental extension						
Positive	6	33.3	12	66.7	0.425	
Negative	31	46.3	36	53.7		
Liver involvement						
Positive	4	30.8	9	69.2	0.375	
Negative	33	45.8	39	54.2		
Peritoneal involvement						
Positive	8	29.6	19	70.4	0.101	
Negative	29	50	29	50		
Adenopathy						
Positive	1	25	3	75	0.629	
Negative	36	44.4	45	55.6		
CA-125						
≤400 U/mL	12	44.4	15	55.6	1	
>400 U/mL	25	43.1	33	56.9		
Ascites						
≤1000 mL	25	54.3	21	45.7	0.048	
>1000 mL	12	30.8	27	69.2		

Table 3 compares preoperative serum CA-125 levels and ascites between patients achieving optimal and suboptimal cytoreduction. CA-125 levels showed a similar distribution between the two groups, with values >400 U/mL observed in 67.6% of patients with optimal cytoreduction and 68.8% of those with suboptimal cytoreduction, while levels ≤400 U/mL were present in 32.4% and 31.3%, respectively; this difference was not statistically significant ($p=1.000$). In contrast, the volume of ascites differed

significantly between the groups ($p=0.048$). Ascites ≤1000 mL was more frequently observed among patients with optimal cytoreduction (67.6% vs 43.8%), whereas ascites >1000 mL was more common among those with suboptimal cytoreduction (56.3% vs 32.4%). Overall, preoperative CA-125 level was not associated with cytoreductive outcome, whereas higher-volume ascites was significantly associated with a greater likelihood of suboptimal cytoreduction.

Table 3: Preoperative Serum CA-125 and Ascites According to Cytoreductive Outcome			
Variable	Optimal Cytoreduction (n=37)	Suboptimal Cytoreduction (n=48)	P value
CA-125 (U/mL)			
≤400	12 (32.4)	15 (31.3)	1
>400	25 (67.6)	33 (68.8)	
Ascites			
≤1000 mL	25 (67.6)	21 (43.8)	0.048
>1000 mL	12 (32.4)	27 (56.3)	

Table 4 compares preoperative radiological findings between patients who achieved optimal cytoreduction and those with suboptimal cytoreduction. Omental extension was identified in 16.2% of patients with optimal cytoreduction compared with 25.0% of those with suboptimal cytoreduction, although this difference was not statistically significant

($p=0.425$). Similarly, liver involvement was more frequent in the suboptimal cytoreduction group (18.8% vs 10.8%), but the difference did not reach statistical significance ($p=0.375$). Peritoneal involvement was observed in 39.6% of patients with suboptimal cytoreduction compared with 21.6% of those with optimal cytoreduction, showing a trend

toward greater involvement in the suboptimal group, although the difference was not statistically significant ($p=0.101$). Suprarenal adenopathy was uncommon in both groups, being present in 2.7% of patients with optimal and 6.3% of patients with suboptimal cytoreduction ($p=0.629$). Overall, none of the

evaluated preoperative radiological parameters demonstrated a statistically significant association with cytoreductive outcome, although peritoneal involvement showed the strongest numerical trend toward suboptimal cytoreduction.

Table 4: Preoperative Radiological Predictors According to Cytoreductive Outcome			
Radiological parameter	Optimal Cytoreduction (n=37)	Suboptimal Cytoreduction (n=48)	P value
Omental extension			
Positive	6 (16.2)	12 (25.0)	0.425
Negative	31 (83.8)	36 (75.0)	
Liver involvement			
Positive	4 (10.8)	9 (18.8)	0.375
Negative	33 (89.2)	39 (81.3)	
Peritoneal involvement			
Positive	8 (21.6)	19 (39.6)	0.101
Negative	29 (78.4)	29 (60.4)	
Suprarenal adenopathy			
Positive	1 (2.7)	3 (6.3)	0.629
Negative	36 (97.3)	45 (93.8)	

Table 5 presents the multivariable logistic regression analysis of factors associated with suboptimal cytoreduction. Intraperitoneal carcinomatosis was identified as a statistically significant independent predictor of suboptimal cytoreduction, with an adjusted odds ratio (OR) of 3.76 (95% CI: 1.58–8.95; $p=0.003$), indicating substantially higher odds of suboptimal surgical outcome in patients with intraperitoneal carcinomatosis. Similarly, ascites >1000 mL was independently associated with suboptimal cytoreduction, with an adjusted OR of 2.41 (95% CI: 1.03–5.65; $p=0.043$). Peritoneal involvement

showed a tendency toward increased odds of suboptimal cytoreduction (adjusted OR 2.18, 95% CI: 0.94–5.05; $p=0.070$), although this did not reach statistical significance. Other evaluated factors, including ASA class II versus I, pleural effusion, omental extension, liver involvement, and CA-125 >400 U/mL, were not significantly associated with suboptimal cytoreduction ($p>0.05$). Overall, the analysis indicates that extensive intraperitoneal disease and large-volume ascites were the principal independent predictors of difficulty in achieving optimal cytoreduction.

Table 5: Multivariable Logistic Regression Analysis of Factors Associated with Suboptimal Cytoreduction			
Predictor	Adjusted OR	95% CI	P value
ASA class II vs I	1.74	0.76–3.98	0.189
Pleural effusion	1.82	0.69–4.81	0.225
Intraperitoneal carcinomatosis	3.76	1.58–8.95	0.003
Omental extension	1.31	0.53–3.25	0.557
Liver involvement	1.58	0.53–4.71	0.41
Peritoneal involvement	2.18	0.94–5.05	0.07
CA-125 >400 U/mL	1.09	0.48–2.47	0.838
Ascites >1000 mL	2.41	1.03–5.65	0.043

Table 6 summarizes the overall primary cytoreductive surgical outcomes among the 85 patients included in the analysis. Optimal cytoreduction, defined as residual disease of ≤ 1 cm, was achieved in 37 patients (43.5%), whereas 48 patients (56.5%) had suboptimal cytoreduction with residual disease >1 cm. Thus, suboptimal cytoreduction was more

frequently observed than optimal cytoreduction in the study population, indicating that achieving minimal residual disease remained challenging in a substantial proportion of patients undergoing primary cytoreductive surgery for advanced epithelial ovarian cancer.

Table 6: Overall Primary Cytoreductive Surgical Outcome

Cytoreductive outcome	Patients No.	%
Optimal cytoreduction (≤ 1 cm residual disease)	37	43.5
Suboptimal cytoreduction (>1 cm residual disease)	48	56.5
Total	85	100

Discussion

This prospective study assessed the value of clinico-pathological, biochemical, and radiological markers in predicting optimal primary debulking in patients with advanced EOC. Of the patients, 43.5% had optimal cytoreduction (residual disease ≤ 1 cm) and 56.5% had suboptimal cytoreduction. The main result was that the amount of intra-peritoneal disease and the amount of ascites were better predictors of the surgical outcome than any one clinical feature, CA-125 concentration or isolated radiological abnormality. Carcinomatosis was present in 55.3% of patients and was significantly related to suboptimal cytoreduction; 74.5% of the patients with carcinomatosis had suboptimal surgery, compared to 34.2% of those without carcinomatosis ($p < 0.001$). Carcinomatosis was an independent risk factor for suboptimal cytoreduction on multivariable analysis with 3.76-fold odds (95% CI: 1.58–8.95; $p = 0.003$). The results of this study corroborate previous reports that the distribution and amount of intra-abdominal disease are key factors in determining feasibility of complete or near-complete cytoreduction. In a study of 42 patients, Nelson et al. found that the positive predictive value of pre-operative abdominopelvic CT for a suboptimal surgical result was 67%, suggesting that radiologic evidence of extensive disease could identify a significant number of patients that would not have a satisfying cytoreduction [11]. But the poor predictive ability in that study also highlights the non-reliance that can be placed on radiological prediction alone.”

Another significant predictor in this study was ascites. The proportion of patients with suboptimal surgery was also significantly higher in cases of ascites >1000 mL (69.2%) compared with those with ascites ≤ 1000 mL (45.7%) ($p = 0.048$). In addition, high volume ascites remained significant after other factors were accounted for with an adjusted OR of 2.41 (95% CI 1.03–5.65; $p = 0.043$). The significance of ascites agrees with the criteria that have been used in the past to identify patients at high risk for unresectable or incomplete resectable disease. It has been described in previous literature that the major features associated with difficult primary cytoreduction are ascites (volume > 1000 mL), peritoneal carcinomatosis, parenchymal liver disease, splenic metastasis and omental extension to spleen, porta hepatis disease and bulky diaphragmatic disease [9]. Eisenkop and Spirtos stressed that the goals and technical expertise of gynecologic oncologic surgery have significantly changed over the years and that disease distribution should be taken into account in addition

to the surgeon's skill in performing extensive surgery. Eltabbakh et al. studied the factors that determine cyto-reducibility in a similar study and showed that the anatomic distribution of ovarian cancer is closely related to the potential for achieving adequate surgical clearance [12]. The present finding of ascites >1000 mL in 32.4% of optimally cytoreduced patients also shows that the presence of high-volume ascites should not be an absolute contraindication to primary surgery.

Preoperative CA-125, on the other hand, had little discriminant power in the present cohort. CA-125 was >400 U/mL in 68.2% of patients, and the proportion of patients that underwent suboptimal cytoreduction was nearly identical between those who were CA-125 ≤ 400 U/mL and >400 U/mL (55.6% vs 56.9%, respectively; $p = 1.000$). The comparison based on the surgical outcome was also not significant as elevated CA-125 was found in 67.6% of optimally cytoreduced patients and 68.8% of sub optimally cytoreduced patients. This is a very consistent result with previous data calling into doubt the usefulness of CA-125 as a solo predictor of the surgical outcome. In particular, Memarzadeh et al. found that CA-125 was a poor predictor of optimal cytoreductive surgery in advanced epithelial ovarian cancer [13]. Barlow et al. also studied presurgical CA-125 as a marker for optimal tumor cytoreduction and showed the limitations of using this biochemical marker alone [14]. Therefore, the present results support the idea that CA-125 is a reflection of the overall burden or biological activity of the disease and not necessarily a reflection of the anatomic distribution or fixation or technical resectability of disease.

Radiological results in the present study revealed a uniform but statistically non-significant trend of higher disease load in patients who underwent suboptimal cytoreduction. Omental extension was found in 25% of patients with suboptimal surgery versus 16.2% ($p = 0.425$) and liver involvement in 18.8% of patients with suboptimal surgery versus 10.8% ($p = 0.375$). A greater difference was observed with peritoneal involvement (39.6% vs. 21.6% in suboptimal and optimal cytoreduced patients, respectively; $p = 0.101$). These findings are directly consistent with investigations of the efficacy of CT-based predictors of suboptimal cytoreduction. In a multi-institutional reciprocal validation study, Axtell et al. showed that the creation of CT criteria with consistently good predictive performance in different institutions and among different surgeons is not easy [15]. Their findings will have special

significance in relation to the present study, in that the apparently bad radiological aspects of each individual case, when taken alone, do not necessarily indicate surgical failure. Similarly, Martinez-Said et al. assessed predictive factors of irresectability in advanced ovarian cancer and showed the significance of the disease distribution in surgical feasibility [16].

In the current study, however, pleural effusion and overall clinical condition were not significant predictors. There was no statistically significant association between pleural effusion and suboptimal cytoreduction (75.0% of patients with pleural effusion underwent suboptimal cytoreduction vs 52.2% without effusion; $p=0.161$). A similar pattern was seen for suboptimal cytoreduction, 65.5% for ASA II patient's vs 51.8% for ASA I patients ($p=0.256$). Based on the findings of this study, it is possible that patient fitness alone may be less informative than the extent of disease when the primary endpoint is the amount of residual tumor after primary surgery. The failure to achieve statistical significance for the pleural effusion may, in part, be due to the relatively small number of patients with effusion (16 patients). This is in line with previous research which cautioned that individual predictors may be unreliable based on relatively small samples and heterogeneous surgical populations [12,15].

Finally, the current results show that none of the clinical, biochemical, or radiological parameters are sufficiently accurate to predict optimal primary cytoreduction. This confirms the literature, which has already demonstrated time and time again that clinical parameters, serum CA-125 thresholds, and conventional imaging criteria are not as predictive when used alone [10,14,13,15]. The current study, however, has been able to reveal two preoperative markers that were particularly useful: Intraperitoneal carcinomatosis and high-volume ascites, which were still significant when adjusted for multiple factors. Adjusted ORs of 3.76 for carcinomatosis and 2.41 for ascites >1000 mL suggest that the distribution of the disease and fluid burden may be more clinically meaningful than either CA-125 level or images alone. It is important to note that peritoneal involvement was borderline independent with a statistically significant contribution (adjusted OR 2.18; $p=0.070$), and a larger cohort of patients may reveal a statistically significant contribution. These findings contribute to a multi-dimensional pre-op evaluation not dependent on a single threshold or imaging characteristic. They also confirm the findings of Axtell et al. that the assessment of the predictions should differ between institutions as surgical skills and the surgeon's inclination to perform extensive procedures may have a significant impact on the cytoreductive result [15]. Thus, in advanced EOC, a prediction of likelihood of optimal primary cytoreduction should incorporate the overall pattern of disease distribution, ascites volume, biochemical

markers, general disease-related parameters and institutional expertise in surgical treatment.

Conclusion

This prospective study demonstrates that achieving optimal primary cytoreduction in patients with advanced epithelial ovarian cancer is influenced predominantly by the extent of intraperitoneal disease and the volume of ascites rather than by individual clinical, biochemical, or isolated radiological parameters. Intraperitoneal carcinomatosis was the most significant independent predictor of suboptimal tumor cytoreduction and larger volume of ascites was also independently associated with the probability of suboptimal surgical cytoreduction. Other factors like effusion in the pleura, extension of the omentum, liver involvement, peritoneal involvement, adenopathy, higher levels of CA-125 and ASA status were variably associated with surgical outcome but lost their independent predictive value in the multivariable analysis. These results emphasize the need for thorough assessment of the patient prior to surgery, including clinical assessment, serum markers, ascite volume and careful radiological evaluation of disease distribution, to identify those patients who may be less likely to achieve optimal cytoreduction. Precise prediction before surgery may help in individualized surgical planning, patient selection, multidisciplinary decision making, and even considering other treatment modalities when a lot of disease is expected, and thus help better manage advanced epithelial ovarian cancer.

References

1. Landis SH, Murray T, Bolden S, Wingo PA. Cancer statistics, 1999. CA: A cancer Journal for Clinicians. 1999 Jan 1;49(1):8-31.
2. Jemal A. Cancer statistics, 2005. CA-A cancer journal for clinicians. 2005 Jan 1.
3. Hoskins MW, Bundy PD, Thigpen MT, Omura MG. The influence of cytoreductive surgery on recurrence-free interval and survival in small-volume stage III epithelial ovarian cancer: a Gynecologic Oncology Group study. Gynecologic oncology. 1992 Nov 1;47(2):159-66.
4. Hoskins WJ, McGuire WP, Brady MF, Homesley HD, Creasman WT, Berman M, Ball H, Berek JS. The effect of diameter of largest residual disease on survival after primary cytoreductive surgery in patients with suboptimal residual epithelial ovarian carcinoma. American journal of obstetrics and gynecology. 1994 Apr 1;170(4):974-80.
5. Vergote I, De Wever I, Tjalma W, Van Gramberen M, Decloedt J, Van Dam P. Neoadjuvant chemotherapy or primary debulking surgery in advanced ovarian carcinoma: a retrospective analysis of 285 patients. Gynecologic oncology. 1998 Dec 1;71(3):431-6.

6. HEINTZ AP, HACKER NF, BEREK JS, ROSE TP, MUNOZ AK, LAGASSE LD. Cytoreductive surgery in ovarian carcinoma: feasibility and morbidity. *Obstetrics & Gynecology*. 1986 Jun;67(6):783-8.
7. Inciura A, Simavicius A, Juozaityte E, Kurtinaitis J, Nadisauskiene R, Svedas E, Kajenas S. Comparison of adjuvant and neoadjuvant chemotherapy in the management of advanced ovarian cancer: a retrospective study of 574 patients. *BMC cancer*. 2006 Jun 8;6(1):153.
8. van der Burg ME, van Lent M, Buyse M, Kobiarska A, Colombo N, Favalli G, Lacave AJ, Nardi M, Renard J, Pecorelli S. The effect of debulking surgery after induction chemotherapy on the prognosis in advanced epithelial ovarian cancer. *New England Journal of Medicine*. 1995 Mar 9;332(10):629-34.
9. Eisenkop MS, Spirtos MN. What are the current surgical objectives, strategies, and technical capabilities of gynecologic oncologists treating advanced epithelial ovarian cancer?. *Gynecologic oncology*. 2001 Sep 1;82(3):489-97.
10. Schwartz PE, Rutherford TJ, Chambers JT, Kohorn EI, Thiel RP. Neoadjuvant chemotherapy for advanced ovarian cancer: long-term survival. *Gynecologic oncology*. 1999 Jan 1;72(1):93-9.
11. Nelson BE, Rosenfield AT, Schwartz PE. Pre-operative abdominopelvic computed tomographic prediction of optimal cytoreduction in epithelial ovarian carcinoma. *Journal of clinical oncology*. 1993 Jan;11(1):166-72.
12. Eltabbakh GH, Mount SL, Beatty B, Simmons-Arnold L, Cooper K, Morgan A. Factors associated with cytoreducibility among women with ovarian carcinoma. *Gynecologic oncology*. 2004 Nov 1;95(2):377-83.
13. Memarzadeh S, Lee SB, Berek JS, Farias-Eisner R. CA125 levels are a weak predictor of optimal cytoreductive surgery in patients with advanced epithelial ovarian cancer. *International Journal of Gynecological Cancer*. 2003 Mar;13(2):120-4.
14. Barlow TS, Przybylski M, Schilder JM, Moore DH, Look KY. The utility of presurgical CA125 to predict optimal tumor cytoreduction of epithelial ovarian cancer. *International Journal of Gynecological Cancer*. 2006 Mar 1;16(2):496-500.
15. Axtell AE, Lee MH, Bristow RE, Dowdy SC, Cliby WA, Raman S, Weaver JP, Gabbay M, Ngo M, Lentz S, Cass I. Multi-institutional reciprocal validation study of computed tomography predictors of suboptimal primary cytoreduction in patients with advanced ovarian cancer. *Journal of clinical oncology*. 2007 Feb 1;25(4):384-9.
16. Martinez-Said H, Rincon DG, Montes de Oca MM, Ruiz GC, Ponce JL, Lopez-Graniel CM. Predictive factors for irresectability in advanced ovarian cancer. *International Journal of Gynecological Cancer*. 2004 May;14(3):423-30.