RESEARCH ARTICLE

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The Predictive Model of Suboptimal Primary Debulking Surgery among Women with Ovarian Cancer Using Pre-Operative Computerized Tomography, Tumor Markers and Comparison with the Intraoperative Findings: An Experience in Tertiary Care Hospital of Pakistan

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Abstract

Objective: Ovarian cancer is reported to be one of the most morbid gynecological cancers, often diagnosed at advanced stages. Primary debulking surgery (PDS) along with chemotherapy is the treatment of choice; however, there is a high probability of suboptimal excision. Thus, each patient should be evaluated for the appropriate treatment modality and PDS should be deferred as the risk of surgical complications and delay in chemotherapy consequently impacts survival. It is imperative to formulate a predictive model to select patients for optimal debulking surgery.**Methods:** A prospective observational study was conducted on women with ovarian cancer who underwent PDS at Indus Hospital and Health Network (IHHN), Pakistan from March 1st, 2020 till June 30th, 2024. Data was analyzed using SPSS 20.0. Chi-Square test was used to find the association between the predictors of optimal and sub-optimal debulking surgery using pre-operative computed tomography (CT) scan findings, and serum tumor markers. The sensitivity and specificity of serum cancer antigen 125 (CA-125) levels were measured. **Results:** A total of 65 women with ovarian tumors were recruited in the study. Around 90.7% of patients had optimal PDS while 9.2% of patients underwent suboptimal PDS. Using pre-operative predictive scoring criteria, 48 (73.8%) patients scored 0-5 and all had optimal PDS while 11 (16.9%) patients scored 6-8, out of which 9 had suboptimal PDS (P value 0.00). A predictive score of 9 or more was reported in 6 (9.2%) patients, out of which 4 had suboptimal PDS. **Conclusion:** This study proposed a predictive model using pre-operative CT scan criteria and tumor marker serum CA-125 level which will help in scoring the patients with epithelial ovarian cancer. Subsequent treatment options should be decided either in the form of upfront debulking surgery or neoadjuvant chemotherapy. Further prospective studies are required to formulate a better applicable predictive model in all types of ovarian cancer including germ-cell ovarian tumors and sex cord-stromal tumors.

Keywords: Ovarian cancer- CT scan findings- CA-125

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Introduction

Ovarian cancer has been ranked as the most lethal form of gynecological cancer across the globe apart from being classified as the second gynecologic malignancy worldwide [1]. As per Globocan 2018, 4504 novel cases of ovarian cancer are being reported annually which constitutes 4.9 % of total cases. The surge of new cases contributes to the high mortality rate, i.e. 3326 (2.8 %) deaths per year [2]. Out of all the reported cases, 70% of the women with ovarian cancers present at advanced stages III C, and IV, as per ovarian cancer staging by the International Federation of Gynecology and Obstetrics (FIGO); while the remaining 30% present at an early stage [3]. Primary Debulking surgery (PDS) along with adjuvant chemotherapy is the ultimate treatment of choice for such cases [4]. For low-grade 1-2 disease, stage 1A epithelial ovarian cancer (EOC) including low-grade serous, endometrioid, mucinous, and clear-cell carcinoma, and non-epithelial ovarian cancer including sex cord-stromal and malignant germ-cell tumor, the guidelines of the European Society of Gynaecological Oncology (ESGO)

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recommends fertility-sparing surgery [5-6]. There is extensive literature available on ovarian cancer which has established the vast dependence of the prognosis of cancer on residual disease postoperatively [7]. An RCT conducted by S. Kehoe et al. has revealed that as long as progression-free survival and overall survival are concerned, neoadjuvant chemotherapy (NACT) has analogous and similar results with the PDS. He further testified regarding the lower morbidity and mortality rate associated with the NACT [8]. A significant impact on survival rates has been observed amid the risks of surgical complications and delay in chemotherapy, therefore, primary surgery should be deferred if suboptimal surgery is probable [9]. It is for that reason that a formulation of a predictive model to choose patients for optimal PDS is vital. However, when it comes to NACT, there is no absolute recommendation in the guideline [4]. The predictors for suboptimal PDS such as extensive omental involvement, porta-hepatis, intestinal, and liver parenchymal involvement, massive ascites, suprarenal lymphadenopathy, and diaphragmatic disease have been identified and discussed in various studies by using computer tomography (CT) scan findings [10]. While other studies also contend for pre-operative serum CA-125 (Cancer Antigen 125) level 420-500 IU/m1 as one of the independent yet strong predictors of suboptimal PDS [1, 11]. Surgical staging is also essential as CT scans have very low sensitivity when it comes to the detection of small-volume peritoneal diseases and has limited accuracy in staging early peritoneal dissemination [12].

Therefore, determination of predictors of suboptimal PDS for better selection of patients for NACT and primary surgery using pre-operative CT, tumor markers, and intraoperative findings is the rationale of this study. Due to the dearth in literature regarding treatment of ovarian cancers, especially in settings of limited resources, this study is vitally important to investigate the predictors of suboptimal PDS.

Materials and Methods

Based on clinical examination, pre-operative CT scan of the chest abdomen, and pelvis, and tumor marker levels, the women diagnosed with ovarian cancer or suspicion of ovarian carcinoma or borderline epithelial tumors who underwent PDS at Indus Hospital and Health Network (IHHN), Karachi, Pakistan from March 1st, 2020 to June 30th, 2024 were included in the study. Informed consent from patients and prior approval of the Ethical Review Committee was taken for the study. Prospective data collection was done on structured Performa.

Inclusion Criteria

Women with pre-operative diagnosed ovarian cancer or intraoperative diagnosis of ovarian cancer or borderline ovarian tumor with micro invasion based on clinical examination, pre-operative CT scan of abdomen and pelvis, and tumor markers levels who underwent PDS at IHHN.

Exclusion Criteria

Women who had surgery for ovarian cancer recurrence

Women with ovarian cancer who received NACT.

Standard CT scanning protocol with oral and intravenous control was used and carried out at least 6 weeks before the surgery. Five CT scan parameters were selected as the best predictors and this criterion was based on the Bristow scoring on the prediction of suboptimal PDS for advanced-stage EOC [11]. These five parameters are delineated under:

1. Presence of ascites
2. Peritoneal thickening
3. Diaphragm, liver, and lung basis
4. Omentum
5. Pelvic and para-aortic lymph nodes

Apart from the afore-mentioned parameters, age, ECOG (Eastern Cooperative Oncology Group) performance status, and pre-operative tumor marker levels were also chosen as new parameters for formulating a predictor model (Table 1) [13]. Each parameter was allocated a score from 0 to 2 and a combined score of 0 to 16 was chosen to be compared with surgical findings. In order to measure the tumor markers, blood samples were taken in a span of four weeks prior to the surgery.

Treatment Modality

PDS was conducted by a trained gynecologic oncologist. Surgical procedures comprised of midline laparotomy including total abdominal hysterectomy, bilateral salpingoophorectomy, total omentectomy, pelvic and para-aortic lymphadenectomy, and resection of all visible tumor and appendectomy in mucinous ovarian cancer. Keeping the residual disease from 0 to < 1 cm was the ultimate goal of the procedure.

Outcome Measures

The intraoperative findings were then compared with the pre-operative scoring using CT Scan and tumor marker levels in order to predict suboptimal PDS defined as residual disease > 1 cm.

Statistical Analysis

SPSS 20.0 for Microsoft Windows was used to perform all the statistical analyses. The chi-square test was used to investigate the relationship among the predictors of optimal and sub-optimal PDS using pre-operative CT scan findings of ascites, omentum, peritoneal thickening, liver metastasis, retroperitoneal lymph nodes, diaphragm & lung base, and serum tumor marker levels. The sensitivity and specificity of serum CA-125 levels were measured. Continuous variables were expressed as mean and standard deviation while frequencies and percentages were calculated to describe categorical variables. A p-value of <0.05 was considered statistically significant.

Results

A total of 65 women diagnosed with ovarian cancer underwent PDS and were included in the analyses. Out of these, 59 patients (90.7%) had optimal PDS while 6

Table 1. Pre-operative Predictive Scoring Criteria

	Predictors variables	0	1	2
1	Age (yrs.)	< 40	40-60	> 60
2	ECOG performance status	0	1	2
3	Tumor marker levels			
	Epithelial ovarian cancer			
	- CA-125 (IU/ml)	< 35	>35 - <500	> 500
	Germ cell ovarian tumors			
	- AFP (ng/ml)	20	< 500	> 500
	- BHCG (mIU/ml)	25	26 - <500	> 500
	- LDH (U/L)	< 225	>225 - <500	> 500
4	Volume of ascites	No	Mild- moderate (<500 mi)	Massive (>500 mi)
5	Peritoneal involvement	No	Thickening	Nodular
6	Omentum	No	Nodularity	Caking
7	Retroperitoneal lymph nodes	No	< l cm	> l cm
8	Diaphragm, lung bases or liver parenchyma metastasis	No	< 2cm	> 2cm

[a] ECOG, Eastern Cooperative Oncology Group; CA-125, Cancer Antigen 125; BHCG, Beta-Human Chorionic Gonadotropin; AFP, Alpha-Fetoprotein; LDH, Lactate Dehydrogenase

patients (9.2%) had suboptimal PDS as delineated in Table 2. According to the FIGO classification, 38 patients (58.4%) had stage I disease, 2 patients (3%) had stage II, 21 patients (32.3%) had stage III and 4 patients (6.1%) had stage IV disease.

The patients with an age range between 20 to 30 years were 9 (13.8%), while only 1 was less than 20 years. A total of 10 patients (15.3%) ranged between 30-40 years while 45 patients (69.2%) were more than 40 years old. The majority of our patients (47.6%) had 5 or < 5 children, while 24 patients were found to be nulliparous (36.9%). According to the body mass index (BMI) classification, 20 (30.7%) patients had a BMI >30kg/m2. Meanwhile, 8 patients (12.3%) were found to have uncontrolled comorbidities, while 11 patients (16.9%) had no comorbidities. As per the American Society of Anesthesiologists Physical Status Classification System (ASA class), a majority of patients (87.7%) belonged to physical status classes 1 and 2. (Table 2)

On the basis of histological classification, 32 (49.2%) patients had grade 1 disease whereas 4 (6.1%) patients had grade 2 and 29 (44.6%) had grade 3 diseases. The results of this study revealed that the ratio of optimal PDS decreases as the FIGO stage of the disease increases from 100% for stage I to 76.5% for stage III. This association was found to be statically significant (P-value of 0.002) as shown in Table 2.

The involvement of the following areas was assessed by pre-operative CT scan: volume of ascites, pelvic and para-aortic lymph nodes, peritoneum, omentum, diaphragm, liver parenchyma, and bowel (Table 3). Similarly, table 4 presents a comparison of intraoperative findings with the advancement of the tumor with optimal and suboptimal resection. The results have shown that the chances of optimal PDS increase with the absence of disease in the aforementioned areas while chances of optimal resection decrease as the disease progresses. (Tables 3,4)

Analyses of tumor markers Alpha-Fetoprotein (AFP), Beta-Human Chorionic Gonadotropin (B-HCG), Lactate Dehydrogenase (LDH), and CA-125 were done pre-operatively, identifying them as useful predictive markers of ovarian cancers (Table 5). A total of 16 patients (24.6%) were reported to have pre-operative CA-125 levels of > 500 IU. Out of these, around 75% of patients had optimal PDS while 25% of patients had suboptimal PDS. This association is also statistically proven, showing a high sensitivity (79.6%) of CA-125 levels in the assessment of optimal resection of ovarian cancer (Table 6).

Our study population has shown a statistically significant P value of 0.00 for pre-operative predictive scoring criteria. The majority of the patients (73.8%) had score values between the range of 0-5 and all were reported to have optimal PDS. In total, 11 (16.9%) patients had score values between the range of 6-8, out of which 9 (13.8%) underwent suboptimal PDS. Only 6 patients (9.2%) in our study were reported to have a predictive score of 9 or more, out of which 4 patients (66.6%) had suboptimal PDS. Therefore, this study proves that the ratio of optimal PDS decreases with the increase in predictive score (P-value 0.00) (Table 7).

To conclude the optimal debulking ratio, intraoperative findings were compared with pre-operative tumor characteristics using a CT scan as an indicator and these findings have revealed comparable results (Table 8). CT scan has emerged as a reliable tool (modulator) in our study findings to predict pre-operative tumor characteristics and the possibility of optimal resection in patients with ovarian cancer.

Discussion

Although the staging of ovarian carcinoma is surgical, pre-operative assessment via CT scan and tumor markers

Table 2. Demographics, Comorbidities, and Staging of Optimal and Suboptimal Debulking Surgery Patients

Demographics		Optimal debulking N (%)	Suboptimal debulking N(%)	Total number of cases N (%)	P Value
Total number of patients		59 (90.7%)	6 (9.2%)	65	
Age	<20	0	1 (1.5%)	1(1.5%)	0.017
	20-30	8 (12.3%)	1 (1.5%)	9 (13.8%)	
	30-40	9 (13.8%)	1 (1.5%)	10 (15.3%)	
	>40	42 (64.6%)	3 (4.6%)	45 (69.2%)	
Parity	Nulliparous	19 (29.2%)	5 (7.6%)	24 (36.9%)	0.08
	1-5	30 (46.1%)	1 (1.5%)	31 (47.6%)	
	>5	10 (15.3%)	0	10 (15.3%)	
Marital status	Single	10 (15.3%)	3 (4.6%)	13 (20%)	0.089
	Married	49 (75.3%)	3 (4.6%)	52 (80%)	
BMI	<20	9 (13.8%)	2 (3.07%)	11 (16.9%)	0.467
	20-30	32 (49.2%)	2 (3.07%)	34 (52.3%)	
	>30	18 (27.6%)	2 (3.07%)	20 (30.7%)	
Comorbidities	No	8 (12.3%)	3 (4.6%)	11 (16.9%)	0.058
	Controlled	44 (67.6%)	2 (3.07%)	46 (70.7%)	
	Uncontrolled	7 (10.7%)	1 (1.5%)	8 (12.3%)	
ECOG performance status	0	49 (75.3%)	6 (9.2%)	55 (84.6%)	0.75
	1	6 (9.2%)	0	6 (9.2%)	
	2	2 (3.07)	0	2 (3.1%)	
	3	2 (3.07)	0	2 (3.1%)	
FIGO Stage	I	38 (58.4%)	0	38 (58.4%)	0.002
	II	2 (3.07)	0	2 (3.1%)	
	III	17 (26.1%)	4 (6.15%)	21 (32.3%)	
	IV	2 (3.07%)	2 (3.07%)	4 (6.2%)	
Histological Grade	I	31 (47.6%)	1 (1.5%)	32 (49.2%)	0.236
	II	4 (6.15%)	0	4 (6.2%)	
	III	24 (36.9%)	5 (7.6%)	29 (44.6%)	
Histology subtype	Epithelial Ovarian Cancer	35 (53.8%)	5 (7.6%)	40 (61.5%)	0.28
	Germ Cell Ovarian Carcinoma	3 (4.6%)	1 (1.5%)	4 (6.2%)	
	Sex Cord Stromal Tumor	10 (15.38%)	0	10 (15.4%)	
	Epithelial Borderline Ovarian Tumor	11(16.9%)	0	11 (16.9%)	
ASA class	1	8 (12.3%)	2 (3.07%)	10 (15.4%)	0.117
	2	45 (69.2%)	2 (3.07%)	47 (72.3%)	
	3	6 (9.2%)	2 (3.07%)	8 (12.3%)	
	4	0	0	0	

[a] BMI, Body mass index; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; ASA class, American Society of Anesthesiologists Physical Status Classification System; [b] P-value of <0.05 considered statistically significant

is recommended [14]. The significant factors for selection criteria of NACT and PDS in ovarian cancers are: age, comorbidity, massive ascites, omental and peritoneal involvement, serum CA-125 levels, retroperitoneal lymph node involvement, diaphragmatic and hepatic metastasis.

The serum CA-125 is broadly used as a marker for the prognosis of EOC. Many research findings have confirmed and endorsed the significance of CA-125 level in the prediction of suboptimal PDS [1]. Janco et. al (2015) revealed that there is a significant correlation between suboptimal PDS and massive ascites [14]. Similarly, a strong association of serum CA-125 level with suboptimal PDS using a cut-off value of 500 IU/ml with a sensitivity of 68.9% and specificity of 63.2% has been shown in various other studies [15-16]. Our study has depicted similar findings (Figure 1) and revealed that the presence of massive ascites with a cut-off 500 IU/ml is correlated to suboptimal PDS with a sensitivity of 79.6% and specificity of 66.7% (P value: 0.029).

Pre-operative CT scan can accurately predict surgical outcome in ovarian cancer having sensitivity of 85.7%, 100% and 73.6% to detect retroperitoneal lymphadenopathy, ascites, and omental caking respectively. Its sensitivity to detect peritoneal deposits

Table 3. Comparison of Tumor Characteristics of CT Scan between Optimal and Suboptimal Debulking Surgery Patients

Characteristics		Optimal debulking N (%)	Suboptimal debulking N (%)	Total number of cases N	P-Value
Volume of ascites	No	29 (44.6%)	0	29	0.009
	Mild to Moderate (< 500 ml)	27 (41.5%)	4 (6.15%)	31	
	Massive (>500 ml)	3 (4.6%)	2 (3.07%)	5	
Peritoneal involvement	No	46 (70.7%)	1 (1.5%)	47	0
	Thickening	10 (15.3%)	2 (3.07%)	12	
	Nodular	3 (4.6%)	3 (4.6%)	6	
Omentum	No	38 (58.4%)	1 (1.5%)	39	0.001
	Nodular	18 (27.6%)	2 (3.07%)	20	
	Caking	3 (4.6%)	3 (4.6%)	6	
Pelvic or paraaortic lymph nodes	No	50 (76.9%)	4 (6.15%)	54	0.002
	< 1 cms	8 (12.3%)	0	8	
	> 1cms	1 (1.5%)	2 (3.07%)	3	
Diaphragm or lung basis	No	59 (90.7%)	3 (4.6%)	62	0
	< 2 cm	0	1 (1.5%)	1	
	>2 cm	0	2 (3.07%)	2	
Liver parenchyma metastasis	No	59 (90.7%)	4 (6.15%)	63	0
	< 2 cm	0	1 (1.5%)	1	
	>2 cm	0	1 (1.5%)	1	
Bowel involvement	Yes	3 (4.6%)	0	3	0.744
	No	56 (86.15%)	6 (9.2%)	62	

[a] CT scan, Computed tomography scan; [b] Number of optimal debulking surgery patients: 59; number of suboptimal debulking surgery patients: 6 P-value of <0.05 considered statistically significant

Table 4. Comparison of Intraoperative Findings between Optimal and Suboptimal Debulking Surgery Patients

Characteristics		Optimal debulking N %	Suboptimal debulking N %	Total number of cases N	P-Value
Volume of ascites	No	18 (27.6%)	0	18	0.024
	Mild to Moderate (< 500 ml)	38 (58.4%)	4 (6.15%)	42	
	Massive (>500 ml)	3 (4.6%)	2 (3.07%)	5	
Peritoneal involvement	No	45 (69.2%)	0	45	0
	Thickening	10 (15.3%)	2 (3.07%)	12	
	Nodular	4 (6.15%)	4 (6.15%)	8	
Omentum	No	41 (63.07%)	0	41	0
	Nodular	12 (18.4%)	0	12	
	Caking	6 (9.2%)	6 (9.2%)	12	
Pelvic or paraaortic lymph nodes	No	41 (63.07%)	3 (4.6%)	44	0.1
	< 1 cms	14 (21.5%)	1 (1.5%)	15	
	> 1cms	4 (6.15%)	2 (3.07%)	6	
Diaphragm or lung basis	No	56 (86.15%)	3 (4.6%)	59	0
	< 2 cm	3 (4.6%)	1 (1.5%)	4	
	>2 cm	0	2 (3.07%)	2	
Liver parenchyma metastasis	No	59 (90.7%)	4 (6.15%)	63	0
	< 2 cm	0	1 (1.5%)	1	
	>2 cm	0	1 (1.5%)	1	
Bowel involvement	Yes	4 (6.15%)	0	4	0.672
	No	55 (84.6%)	6 (9.2%)	61	

[a] Number of optimal debulking surgery patients: 59; number of suboptimal debulking surgery patients: 6 P-value of <0.05 considered statistically significant

Table 5. Diagnostic Accuracy of Tumor Markers in Predicting Optimal Debulking Surgery

Levels of tumor markers		Optimal debulking N	Suboptimal debulking N	Total number of cases N	P-Value
CA-125	< 500	47 (96%)	2 (4%)	49	0.029
	> 500	12 (75%)	4 (25%)	16	
AFP	< 500	2 (100%)	0	2	0.006
	> 500	0	1 (100%)	1	
BHCG	< 500	1 (100%)	0	1	0.017
	> 500	1 (100%)	0	1	
LDH	< 500	0	0	0	0.256
	> 500	2 (66.7%)	1 (33.3%)	3	

[a] CA-125, Cancer Antigen 125; BHCG, Beta-Human Chorionic Gonadotropin; AFP, Alpha-Fetoprotein; LDH, Lactate Dehydrogenase; [b] P-value of <0.05 considered statistically significant

Table 6. Sensitivity and Specificity of CA-125 in Predicting Optimal Debulking Surgery

CA-125 level	Optimal debulking surgery (n)	Suboptimal debulking surgery (n)	Total	P-value
≤ 500	TP 47 (79.7%)	FP 2 (33.3%)	49	0.029
> 500	FN 12 (20.3%)	TN 4 (66.7%)	16	
Total	59	6	65	

[a] CA-125, Cancer Antigen 125; TP, True positive; TN, True negative; FP, False positive; FN, False negative; [b] Sensitivity, TP/TP+FN X 100 = 47/59X100 = 79.7% ; Specificity, TN/FP+TN X 100 = 4/6 X 100 = 66.7%; Positive predictive value, TP/TP+FP X 100 = 47/49X100 = 95.9%; Negative predictive value: TN/FN+TN X 100 = 4/16 X 100 = 25.0 %

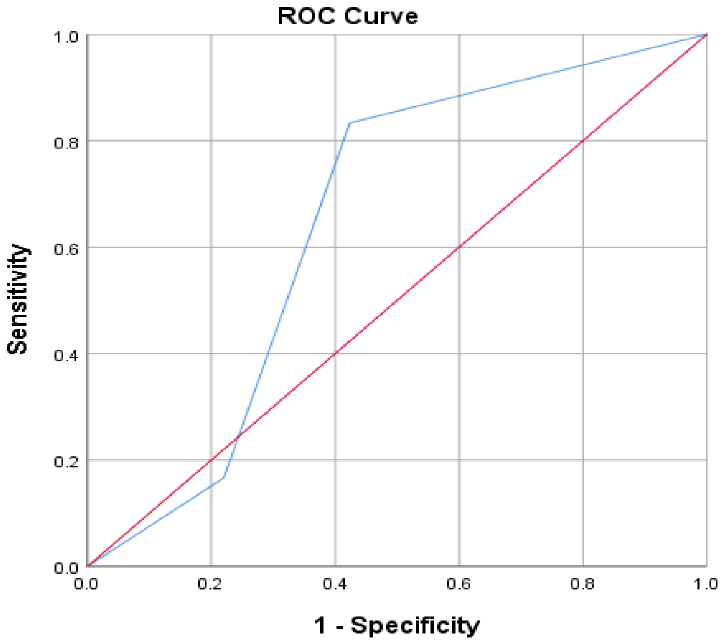

Figure 1. ROC Curve of Predicted Probability of Serum CA-125 for Suboptimal Debulking Surgerya CA-125: Cancer Antigen 125

Table 7. Predictive Score and Association with the Optimal Debulking Surgery

Total Predictive Score	Optimal debulking surgery N 9%)	Sub-Optimal debulking surgery N (%)	Total Patients N (%)	P-value
0-5	48 (100%)	0	48 (73.8%)	
6-8	9 (81.8%)	2 (18.18%)	11 (16.9%)	0
≥ 9	2 (33.3%)	4 (66.6%)	6 (9.2%)	

[a] Number of optimal debulking surgery patients, 59; number of suboptimal debulking surgery patients: 6; P-value of <0.05 considered statistically significant

Table 8. Comparison of Tumor Location According to CT Scan and Intraoperative Findings

Tumor Location		CT scan findings N (%)	Intraoperative findings N (%)	P-Value
Volume of ascites	No	18 (27.69%)	29 (44.6%)	0
	Mild to Moderate (< 500 ml)	42 (64.6%)	31 (47.6%)	
	Massive (>500 ml)	5 (7.6%)	5 (7.6%)	
Peritoneal involvement	No	45 (69.2%)	47 (72.3%)	0
	Thickening	12 (18.4%)	12 (18.4%)	
	Nodular	8 (12.3%)	6 (9.2%)	
Omentum	No	41 (63.07%)	39 (60%)	0
	Nodular	12 (18.4%)	20 (30.7%)	
	Caking	12 (18.4%)	6 (9.2%)	
Pelvic or paraaortic lymph nodes	No	44 (67.6%)	54 (83.07%)	0
	< 1 cms	15 (23.07%)	8 (12.3%)	
	> 1cms	6 (9.2%)	3 (4.6%)	
Diaphragm or lung basis	No	59 (90.7%)	62 (95.3%)	0
	< 2 cm	4 (6.15%)	1 (1.5%)	
	> 2 cm	2 (3.07%)	2 (3.07%)	
Liver parenchyma metastasis	No	63 (96.9%)	63 (96.9%)	0
	< 2 cm	1 (1.5%)	1(1.5%)	
	> 2 cm	1 (1.5%)	1 (1.5%)	
Bowel involvement	Yes	4 (6.15%)	3 (4.6%)	0
	No	61 (93.8%)	62 (95.3%)	

[a] CT scan, Computed tomography scan; b P-value of <0.05 considered statistically significant

is 60% and that of subdiaphragmatic deposits is 16.6% with overall specificity of 85% [17].

The women within the age range from less than 20 years to more than 40 years were recruited for this study. The majority of the women (69.2%) in our study were found to be over 40 years of age and this was in following with the previously conducted studies. As per surgical staging, 21 women presented at stage III while 4 women presented at stage IV of ovarian carcinoma. All of the women underwent PDS by a trained gynecology oncologist. In the majority of the cases (90.76%) optimal PDS was achieved whereas the remaining 9.2% of the patients had suboptimal PDS. The results of this study are in contrast with the other studies as they show higher rates of optimum debulking surgery [17-18].

All stages of ovarian cancer were included in our study and higher optimal PDS was achieved in early-stage (I and II) disease. The residual disease in patients who underwent suboptimal PDS was found to be liver parenchyma, diaphragm, and bowel serosal deposits. Appendectomy was performed in all cases of mucinous ovarian carcinoma. Previous literature on ovarian cancer has established a correlation between CT scans and intraoperative findings [17, 19]. The results of this study are comparable with the previous studies in regards to the association between pre-operative CT scan and intra-operative findings (P-value < 0.005) showing the involvement of peritoneum, omentum, pelvic and para-aortic lymph nodes, diaphragm, lung, liver parenchyma, bowel, and the volume of ascites (Table 8).

In the current study, we found that hepatic metastasis in pre-operative CT scans is associated with an increased risk of suboptimal PDS (P-value < 0.05). Several other studies have also proven a similar correlation and used hepatic metastasis as one of the major selection criteria for NACT due to its significance [14].

Previous studies conducted on a similar topic have formulated and validated multivariate models to predict the suboptimal PDS. The studies' corresponding findings have reported that the age of > 60 years, serum CA-125 levels (600 IU/ml), ASA 3-4, lesions in the root of superior mesentery artery, splenic hilum, lesser sac, porta hepatis, suprarenal lymphadenopathy, small bowel thickening, and massive ascites are significantly associated with residual disease after debulking surgery [10, 20]. Our study presented that the risk of suboptimal PDS with all types of ovarian cancer increases due to factors such as age, comorbidity, massive ascites, omental and peritoneal involvement, pelvic and para-aortic lymphadenopathy, diaphragm and lung basis and liver involvement (P-value < 0.005). Furthermore, the chances of residual disease in EOC and Endometrioid borderline ovarian tumors (EBOT) also increase with serum CA-125 level > 500 IU/ml (P-value < 0.029). Around half of the cases (40%) in our study were EOC, whereas germ-cell ovarian tumor, sex cord-stromal tumor, and EBOT were found to be 4%, 10%, and 11% respectively. The accuracy of tumor markers such as AFP, B-HCG, and LDH for germ-cell ovarian tumors and inhibin for granulosa cell ovarian tumors could not be predicted due to the smaller number of cases of gem cell and sex cord-stromal tumors in our study.

As per existing literature, the significant predictors of suboptimal PDS were diffuse peritoneal thickening, mesenteric disease, suprarenal lymph nodes, a large volume of ascites, carcinomatosis on the diaphragm, and liver involvement [7, 21]. To identify the peritoneal carcinomatosis index (PCI) marker, Llueca A et. al, formulated a model for the prediction of incomplete cytoreduction using pre-operative CT scan findings, laparoscopy, and laparotomy. The PCI of 20 or more and bowel obstruction were found to be significant factors for prognosis and suboptimal PDS [22]. A systematic review has determined that nine imaging criteria using pre-operative CT scans comprise upper abdominal ascites, diffuse sub-diaphragmatic, and peritoneal nodularity, and is found to be associated with incomplete cytoreduction [7].

In our hospital setting, we aimed to determine the rate of suboptimal PDS in women with ovarian cancer. We gathered that out of 65 patients, 59 (90.76%) underwent optimal PDS with no residual disease, while 6 patients (9.2%) had suboptimal resection. These patients had all presented with advanced disease (FIGO Stage III and IV). These findings were consistent with various other studies [21, 23-24].

The predictive model of our study was similar to another recent study conducted by Suidan RS et al., with analogous parameters like age, ASA, and the FIGO staging but there was a difference in CA-125 levels. Serum CA-125 cut-off level of 600 IU/ml was used in their study while we used the cut-off level of 500 IU/ml. According to both studies, significant CT scan criteria included bowel involvement, pelvic and para-aortic lymphadenopathy, and diaphragm involvement [10].

The aim of PDS encompasses complete gross resection and residual disease 0.1-1cm as it significantly improves survival when compared with suboptimal resection with residual disease > 1cm [3, 10]. In our formulated predictive model, we incorporated both pre-operative CT scan imaging and serum CA-125 levels along with clinical factors such as age, ECOG performance status, and disease burden in different regions. All these factors play a vital role in deciding whether to proceed with PDS or NACT.

Patients with high-risk comorbidities are unable to tolerate extensive staging procedures, therefore, the risk of residual disease remains. In an attempt to describe the usage of our predictive model, let's consider a theoretical patient who is 65 years old (predictive score 2), having CA-125 levels of 600 IU/ml (score 2), ECOG status 1 (score 1), massive ascites (score 2), peritoneal nodularity (score 2), omental caking (score 2), retroperitoneal lymph nodes >1 cm (score 2), diaphragm and liver metastasis < 2 cm (score 1), comprising of a total predictive score of 14 (i.e. >9). (see table 1). Based on our predictive model, this patient has a high chance of residual disease in PDS and would be better suitable for NACT. Correspondingly, in our study, 6 patients had predictive scores of 9 or more, out of which 4 underwent suboptimal PDS (P-value < 0.005).

In conclusion, this study proposed a useful predictive model that will aid in scoring the patients with epithelial ovarian cancer for subsequent management either in the form of upfront debulking surgery or subject to NACT. This can be an important tool to formulate local guidelines, especially in hospitals with limited resources to treat patients with epithelial ovarian cancer. The strengths of our study included the prospective data collection and interdepartmental collaboration between gynecology oncology and radiology. All patients with ovarian cancer were operated on by a trained gynecology oncologist; similarly, the CT scan images were evaluated pre-operatively by a dedicated experienced radiologist. The limitations of our study included a small sample size, a low prevalence of positive imaging findings, and a single institution-based study.

Further prospective studies are required to formulate a better and applicable predictive model in all types of ovarian cancer including germ-cell ovarian tumors and sex cord-stromal tumors.

Author Contribution Statement

Dr. Ayesha Saba proposed the idea of research and was the principal investigator, and critically reviewed the manuscript. Dr. Muhammad Saqib Qamar Ishaqi contributed to the radiological findings of the study. Dr. Muhammad Shadab Khan contributed to the research findings and data interpretation and helped to formulate the predictive model. Dr. Anita Manzoor collected the data for the study and analyzed and interpreted the data. Dr. Shajeea Arshad Ali drafted and prepared the manuscript. All authors are equally accountable for all aspects of this research study. No secondary data or outsourcing was done for this research study.

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Approval

This work was done with the code of ethics approved and issued by the institutional Ethics Committee IHHN-IRB Number: IRD_IRB_2020_11_002/ IHHN_IRB_2020_11_002, titled: "Predictive model of suboptimal primary debulking surgery among women with ovarian cancer using pre-operative computerized tomography, tumor markers and comparison with the intraoperative findings: An experience in Tertiary care hospital of Pakistan".

Conflict of interest

The authors declare that there is no conflict of interest.

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