

A Clinical and Computed Tomography Scan Correlation In Patients With Advanced Ovarian Carcinoma

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Abstract

Background: Epithelial ovarian carcinoma (EOC) is the most lethal malignant disease; especially due to its advanced stage of diagnosis. Computed tomography (CT) scan screening and cancer antigen 125 are tried in patients for early diagnosis but do not to have an impact on the survival. CT scan studies preoperatively are being used to identify predictability of optimal or suboptimal cytoreduction patients with EOC.

Materials and Methods: A retrospective study was conducted to correlate the CT scan findings and intra-operative findings of patients with advanced EOC of Stage III/IV undergoing cytoreduction. 42 patients undergoing surgical cytoreduction over a period of 9 years from a tertiary teaching hospital were included. Clinical data were obtained from earlier medical records. Pre-operative CT scan was done in all patients. Residual tumors identified measuring <1 cm were considered suboptimal cytoreduction.

Results: A total of 42 patients matching the inclusion criteria were included. On pre-operative CT scans, omental extension to the stomach or spleen and inguinal or pelvic lymph nodes >2 cm were predictors of suboptimal cytoreduction. Optimal cytoreduction <1 cm residual disease was achieved in 17 (40.47%) patients. Involvement of both omental extension and inguinal or pelvic lymph nodes had a positive predictive value of 85.29% in cytoreduction.

Conclusion: CT scan is the most valuable tool for the pre-operative prediction of successful resection of ovarian cancer during primary surgery. However, the CT-based pitfalls leading to suboptimal cytoreduction have to be identified with a larger study. The combination of omental extension to the stomach or spleen and involvement of inguinal or pelvic lymph nodes in pre-operative CT scans is considered predictive of suboptimal cytoreduction. These patients may be more appropriately treated with neoadjuvant chemotherapy followed by surgical cytoreduction.

Key words: Carcinoma, Computed tomography scan, Epithelial, Ovary, Peritoneal metastases

INTRODUCTION

Epithelial ovarian cancer is the most lethal of the gynecologic malignancies, largely due to the advanced stage at diagnosis in most patients. Screening strategies using ultrasound and the cancer antigen (CA) 125 tumor marker are currently under study and may lower stage at diagnosis but have not yet been shown to improve survival.

Women who have inherited a deleterious mutation in the BRCA1 or BRCA2 gene and those with the Lynch syndrome (hereditary nonpolyposis colorectal cancer) have the highest risk of developing ovarian cancer but account for only approximately 10% of those with the disease. Other less common and less well-defined genetic syndromes may increase the risk of ovarian cancer, but their contribution to genetic risk is small. A clear etiology for sporadic ovarian cancer has not been identified, but the risk is affected by reproductive and hormonal factors. Surgery has a unique role in ovarian cancer, as it is used not only for diagnosis and staging but also therapeutically, even in patients with widely disseminated, advanced disease. Ovarian cancer is highly sensitive to chemotherapy drugs, particularly the platinum agents, and most patients will attain a remission with initial treatment. Recent advances

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in the delivery of chemotherapy using the intraperitoneal route have further improved survival after initial therapy. Although the majority of ovarian cancer patients will respond to initial chemotherapy, most will ultimately develop disease recurrence. Chemotherapy for recurrent disease includes platinum-based, multiagent regimens for women whose disease recurs more than 6–12 months after the completion of initial therapy and sequential single agents for those whose disease recurs earlier. New targeted biologic agents, particularly those involved with the vascular endothelial growth factor pathway and those targeting the poly (ADP-ribose) polymerase enzyme, hold great promise for improving the outcome of ovarian cancer.

Ovarian neoplasms are classified according to the tissue of origin such as epithelium, stromal endocrine cells, and germ cells. Epithelial ovarian carcinoma (EOC) accounts for more than 90% of all ovarian malignancies. It is a disease of postmenopausal women, occurring most commonly in the sixth and seventh decades of life.^[1] In the USA it is second most common after carcinoma body of the uterus.^[1] The lifetime incidence for ovarian malignancies is 1 in 72 (1.39%) and the lifetime risk of death from ovarian cancer is 1 in 96 (1.04%) for women living in the United States. The median age at diagnosis is 63 years.^[2] One of the factors for greater mortality is its late diagnosis with more than 60 % of patients presenting already with metastatic spread beyond the pelvis.^[3] Hence, in spite of surgery or chemotherapy, the episodes of tumor recurrence will develop which needs to be monitored to enable early rescue.^[3] Computed tomography (CT) scan can provide staging information for pre-operative planning and determination of surgical resectability, demonstrate tumor response to therapy, and allow detection of persistent or recurrent disease.^[4] Review of literature shows extensive studies on the role of CT scan in the diagnosis of EOC. The reported pre-operative staging accuracy of CT is 70–90%.^[5-7] CT is more sensitive than ultrasonography (US) for detection of abnormalities in the para-aortic lymph nodes, omentum, mesentery, and sub-diaphragmatic regions.^[8] CT is a fast and widely available study, and it remains the most useful technique for pre-operative staging of ovarian cancer.^[5] The basis of management of EOC in advanced stage is primary cytoreductive surgery followed by platinum-based chemotherapy. The extent of residual disease after primary cytoreductive surgery is an important predictor of prognosis.^[9] However, the outcome of suboptimal cytoreduction is less evident.^[10] Such patients may incur significant surgical morbidity without an associated gain in survival.^[10] The present study was a review of medical records of patients who have undergone suboptimal cytoreduction for advanced stages of EOC and the role of CT scan in predicting the prognosis in a tertiary teaching hospital.

Period of Study

The study period was from March 2006 to February 2015 (9 years).

Institute of Study

This study was conducted at the Department of Radiology, Kannur Medical College, Anjarakandy, Kannur, Kerala.

MATERIALS AND METHODS

A retrospective study was undertaken by obtaining data from the medical records of the Department of Radiology about 42 patients who underwent cytoreduction surgery for advanced Sates III/IV stage of EOC. The demographic data were prepared using the records. Clinical features and pre-operative CT scan findings were noted.

Inclusion Criteria

1. Patients aged 45–90 years were included.
2. Patients with EOC of Stage III/IV were included.
3. Patients with CT scan done within 4 weeks of surgery only were included.

Exclusion Criteria

1. Patients aged below 50 and above 90 years were excluded.
2. Patients undergoing neoadjuvant chemotherapy were excluded.
3. Patients without CT scan reports were excluded.

CT scan findings included were large-volume ascites, pleural effusion, diffuse peritoneal thickening, omental cake, omental extension to the spleen or stomach, suprarenal lymph nodes larger than 1 cm, infrarenal or inguinal lymph nodes larger than 1 cm, and tumor implants larger than 2 cm on small and large bowel mesentery, peritoneum, diaphragm, liver, or porta hepatis. Patients undergoing cytoreduction were subjected to standard abdominal midline laparotomy, and extensive resection of the adnexa as per guidelines was done leaving no macroscopic residual tumor or <1 cm residual disease. Along with total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and appendectomy were done. Whenever necessary, multiple frozen sections were done. Additional surgeries when required were undertaken such as large bowel resections, small bowel resection, diaphragm stripping, splenectomy, and abdominopelvic peritoneal resection. Systematic pelvic and para-aortic lymphadenectomy were performed. The CT scan findings were correlated with intra-operative findings. Diffuse peritoneal thickening was defined as thickening ≤ 4 mm involving at least two of the five following areas: Lateral colic gutters, lateral conal fascia, anterior abdominal wall, diaphragm, and pelvic peritoneal reflections. Optimal

cytoreduction was defined as <1 cm residual disease. The clinical data also included age, CA-125 serum levels 4 weeks before surgery. Postoperatively, all patients received taxane/ platinum combination chemotherapy for six to eight cycles. Follow-up information was recorded until the date of last contact or death. Survival time was calculated from the date of last chemotherapy to the date of last contact or death.

RESULTS

Out of 42 patients, 2 (4.76%) were below 50 years, 6 were between 50 and 60 years, 13 (30.95%) were 60–70 years, 15 (35.71%) were between, and 5 (11.90%) were between 80 and 90 years old. The mean age of 8 (19.04%) was 65.30 ± 1.75 years. The serious type of EOC was observed in 27 patients, transitional cell type in 5 (11.90%), endometrioid type in 6 (14.28%), and mixed type in 4 (9.52%) patients. Optimal cytoreduction was undertaken in 11 (26.19%) patients and sub-optimal cytoreduction in 31 (73.80%) patients. The laboratory serum levels of CA-125 were <500 U/mL were observed in 16 (38.09%) and >500 <500 U/mL were observed in 26 patients (61.90%) [Table 1].

Cytoreduction was optimal in 17 (40.47%) patients and was suboptimal in 25 (59.52%) patients [Table 2].

There were no statistically significant differences in median age 68.45 ± 1.50 in optimal and 63.30 ± 1.65 in suboptimal groups. Similarly, there was no significance in CA-125 values of both the groups; the mean values in optimal group was 945 ± 5.60 and 1054 ± 6.10 in the suboptimal group; *P* value was more than 0.05 (*P* value taken significant at below 0.005) [Table 3].

CT scan findings were correlated with the intra-operative findings in relation to the anatomical sites involved with the disease. The different sites of involvement were tabulated [Table 4]. Out of 14 different anatomical sites, omental extension to stomach and spleen was present in 14/17 (82.35%) of optimal group, and 20/25 (80%) of suboptimal group with a total of 34/42 (80.95%) patients. Inguinal or pelvic lymph nodes were present in 15/17 (88.23%) of optimal group and 21/25 (84%) of the suboptimal group out of a total of 36/42 (85.71%) patients. All other sites were almost equally in both optimal and suboptimal groups. These two sites had a positive predictive value (PPV) of 85.29% in cytoreduction [Table 4].

DISCUSSION

In this retrospective study, an attempt is made to select 42 patients with Stage III/IV EOC disease and correlate the pre-operative CT scan findings to observe the

Table 1: Age, staging of EOC, histologic type and CA levels in the study group (n=42)

Observation	n (%)
Age (years)	
<50	02 (4.76)
50–60	06 (14.28)
60–70	13 (30.95)
70–80	15 (35.71)
80–90	05 (11.90)
Staging	
III A/B	05 (11.90)
III C	29 (69.04)
IV	08 (19.04)
Histologic subtype	
Serous	27 (64.28)
Transitional	05 (11.90)
Endometrioid	06 (14.28)
Mixed	04 (9.52)
Optimal cytoreduction	11 (26.19)
Suboptimal cytoreduction	31 (73.80)
CA-125 levels (U/mL)	
<500	16 (38.09)
>500	26 (61.90)

EOC: Epithelial ovarian carcinoma, CA-125: Cancer antigen-125

Table 2: The grading of cytoreduction in the study (n=42)

Cytoreduction	n (%)
Optimal	17 (40.47)
Suboptimal	25 (59.52)

Table 3: The mean values and their significance in optimal and suboptimal groups (n=42)

Mean values of observations	Optimal group	Suboptimal group	<i>P</i>
Age	68.45±1.50	63.30±1.65	0.072
CA-125 levels	945±5.60	1054±6.10	0.086

CA-125: Cancer antigen 125, SD: Standard deviation

anatomical sites involved with the actual involvement during surgery. The patients are divided into optimal and suboptimal groups depending on the cytoreduction achieved after surgery. The role of CT scan in predicting the suboptimal cytoreduction in future patients was mad. Even though such pretreatment evaluation of ovarian cancer is controversial because both staging and tumor debulking are undertaken at the time of exploratory laparotomy; however, cross-sectional imaging can provide staging information that may help in pre-operative planning.^[11] Pre-operative neoadjuvant chemotherapy has been used recently in patients with Stage III/ IV disease,^[12] and CT scans can help identify those patients who may benefit from pre-operative neoadjuvant chemotherapy.^[11] The reported pre-operative staging accuracy of CT is 70%–90%.^[13,14] In this study, CT scan showed PPV of 85.29%. CT scan was commented as more

Table 4: Univariate analysis of CT scan findings of optimal and suboptimal groups (n=42)

CT scan findings	Optimal group-17		Suboptimal group- 25		Total	
	Present	Absent	Present	Absent	Present	Absent
Diaphragm disease >2 cm	8	9	12	13	20	25
Liver implants	8	9	14	11	22	20
Porta hepatis or gallbladder fossa disease	07	10	15	10	22	20
Diffuse peritoneal thickening	10	07	14	11	25	21
Peritoneal implants >2 cm	9	8	13	12	22	20
Large-volume ascites	11	6b	14	11	25	17
Large bowel mesentery implants >2 cm	05	12	11	14	16	26
Small bowel mesentery implants >2 cm	4	13	11	14	15	27
Omental extension to stomach or spleen	14	3	20	5	34	8
Omental cake	5	12	09	16	14	28
Suprarenal lymph nodes >1 cm	9	8	11	14	20	22
Infra-renal lymph nodes >1 cm	07	09	15	11	22	20
Inguinal or pelvic lymph nodes >2 cm	15	02	21	04	36	06
Pleural effusion	08	09	07	18	15	27

CT: Computed tomography

sensitive than the US for detection of abnormalities in the para-aortic lymph nodes, omentum, mesentery, and sub-diaphragmatic regions.^[8] CT scan is also useful in detecting persistent or recurrent ovarian cancer and demonstrates tumor response to subsequent therapy.^[15] In one study, sensitivity and specificity of CT scan performed before second-look surgery was 59%–83% and 83%–88%, respectively.^[16,17] A major limitation of both CT and magnetic resonance imaging is relatively poor sensitivity for detection of small tumor implants, especially on the small intestine or mesentery;^[18] this limitation is related to the natural history of metastatic ovarian cancer. If CT shows evidence of residual or recurrent tumor, unnecessary second-look laparotomy can be avoided in over 20% of patients subjected to second-look surgery with current restaging methods.^[8,19] As there is improvement in CT scan techniques including spiral CT the detection of small peritoneal implants also has improved; recent studies show that CT allows detection of 50% of peritoneal implants as small as 5 mm in diameter located in the sub-phrenic regions or profiled by ascites^[18] and 28% of implants smaller than 5 mm in diameter.^[20] There were some limitations to this study. First, this was a retrospective analysis of a single-center cohort of patients with advanced EOC. The most important predictors vary between institutions depending on surgical practice and cytoreduction rates, so present study results may not be applicable to other institutions and surgeons.

CONCLUSIONS

CT scan is the most valuable tool for the pre-operative prediction of successful resection of ovarian cancer during primary surgery. However, the CT scan based pitfalls leading to suboptimal cytoreduction have to be identified with a larger study. The combination of omental extension to the

stomach or spleen and involvement of inguinal or pelvic lymph nodes in pre-operative CT scans can be considered predictive of suboptimal cytoreduction. These patients may be more appropriately treated with neoadjuvant chemotherapy followed by surgical cytoreduction.

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