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Research Article

Comparative study of pre-operative CT scan and per-operative findings in carcinoma ovary

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ABSTRACT

Background: Initial therapy for ovarian carcinoma involves aggressive surgery to remove as much tumor as possible. However, this procedure is not beneficial for patients unless tumor is optimally debulked. This study was performed to compare the CT scan findings and per-operative findings and to determine whether CT can be used to predict the success of debulking surgery.
Methods: A retrospective and prospective study was conducted from 2011 to 2013 comparing pscan re operative CT findings and per operative findings of patients diagnosed with carcinoma ovary. 59patients met the inclusion criteria . Five radiographic features were analysed and a score of 0to 2was assigned to each .These scores were added and compared to the surgical results.
Results: We found that CT was highly sensitive in the diagnosis of retroperitoneal lymph node, ascites and omental involvement with sensitivity of 85.7%, 100% and 73.6% respectively. Sensitivity to detect peritoneal deposits and sub diaphragm deposits was 60% and 16.6% respectively. Specificity was uniformly greater than 85% for all parameters except ascites and retro peritoneal lymph nodes which was 71.4% and 54.8%. On a 10-point preoperative CT scoring system, a score of ≥3 identified patients whose tumors were not successfully debulked with a sensitivity of 79% and a specificity of 93%.
Conclusions: CT scan is highly sensitive and specific in identifying metastatic disease and can be used as a pre-operative tool in advanced carcinoma ovary to guide further management.

Keywords: Ovarian carcinoma, CT scan, Cytoreduction, Ca 125

INTRODUCTION

Worldwide, each year approximately 200,000 women are diagnosed with ovarian cancer. Ovarian cancer accounts for 5% of cancer-related death in women.[1] Epithelial ovarian cancers consist 90% of all ovarian cancers. Stage 3 and 4 (as defined by the staging classification of the International Federation of Gynecology and Obstetrics) consist about 2/3 of cases of epithelial ovarian cancer at the time of diagnosis.[2,3] Cytoreductive surgery and paclitaxel platinum chemotherapy are the cornerstone of treatment for advanced stage epithelial ovarian cancer. Maximal cytoreduction to no macroscopic residual tumor is the most important determinant of prognosis.[4-6] Patients with residual disease >1 cm after cytoreductive surgery are generally believed to have limited survival benefit from this extensive procedure and are probably candidates for an alternative treatment approach with neoadjuvant chemotherapy followed by interval cytoreduction.[7-10] Optimal cytoreduction rates range from 40-90%, with a higher rate of optimal cytoreduction in patients treated by gynecologic oncologists and when surgery is performed in high-volume institutions.[11] In order to prevent under treatment of a substantial number of patients, an accurate preoperative assessment on resectibility and operative risk is therefore essential to

guarantee proper decision making and management of these patients.[12,13]

Computed tomography (CT) scans have been used extensively as a diagnostic and surveillance tool in patients with ovarian carcinoma. Several investigators have attempted to identify preoperative radiologic criteria that would predict suboptimal debulking.[14,17,18] Accuracy of prediction using such parameters ranges between 71 and 93%.[14-16] However, discrepancies across the studies and reliability of the results are also conceivably related to the time frame, and duration of accrual as variations and/or improvements in the imaging techniques, equipment, and performances have occurred over time, and also diverge across different imaging centres.

Clinical examination and laboratory analyses, such as determination of CA-125 level, have not proved sufficiently accurate in making this decision.[19-20] Although CT is too insensitive to detect small metastatic foci for accurate staging of ovarian carcinoma; it may be useful in determining operability.[19,21] The purpose of this study is to make a sincere effort to compare the CT scan findings with per operative findings as this hospital has well established gynaecologic oncology, radiological imaging and medical oncology units. We also aimed to investigate the overall performance of CT in predicting the feasibility of primary optimal cytoreduction in advanced ovarian cancer patients over a period of 3 years.

METHODS

This is a retrospective and prospective observational study for predicting the success of debulking surgery in ovarian carcinoma based on CT scan findings. The study was done at Mazumdar Shaw Medical Centre, Narayana Health, Bangalore from September 2011- October 2014.Data was collected from medical records for retrospective analysis and case records for prospective study in the above period.

Inclusion criteria

Retrospective study of all patients who underwent primary surgery for ovarian carcinoma.

Prospective study of patients with suspicious Carcinoma ovary based on clinical examination, pre- operative CT scan of abdomen and pelvis and CA-125 levels who were also taken up for cytoreductive surgery.

Exclusion criteria

Patients with poor performance status (ECOG score 3 and 4).

Stage 4 and Stage 3 diseases involving liver parenchyma, base of small bowel mesentery, stomach, lesser sac and paraaortic lymph nodes above renal vessels on CT scans. These patients are sent for neoadjuvant chemotherapy.

Method of study

Pre-operative assessments

Standard preoperative work-up of the patients consisted of patient history, physical examination, CA 125, transvaginal sonography (TVS) and abdominopelvic CT scan.

All CT scans were carried out within 4 weeks prior to surgery. A standard CT scanning protocol was used. With oral and intravenous contrast, images with a 5 mm collimation area through the abdomen and pelvis were obtained. We selected a set of earlier reported predictors for suboptimal cytoreduction. From previously published CT scan studies on prediction of suboptimal cytoreduction for advanced stage EOC, five CT scan parameters with the best predictive performance were chosen:

(1) Peritoneal thickening
(2) Omentum
(3) Pelvic and para aortic lymph nodes
(4) Diaphragm and lung bases
(5) Volume of ascites

A score of 0 to 2 was assigned to each. These scores were added together for a score of 0 to 10 which was compared to the surgical results.[14-16,22,23]

Table 1: Pre-operative CT scoring criteria.

Region	0	1	2
Volume of ascitis	No disease	Mild/moderate	Large
Peritoneal involvement	No disease	thickening	nodular
omentum	No disease	nodularity	caking
Retroperitoneal lymph nodes	No disease	<2 cm	>2cm
Diaphragm and lung bases	No disease	<2cm	>2cm

Blood samples for measurement of CA125, within four weeks prior to surgery. CA125 was assessed by enzyme immunoassay (Roche E170) using a sandwich method with chemoluminescence.

Treatment regimen

Primary cytoreductive surgery was performed by a gynecologic oncologist using an abdominal midline incision and included total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, retroperitoneal lymph node dissection and resection of all visible and palpable bulky tumors. Retro peritoneal lymph nodes dissection included common, external and internal iliac group of nodes, omental nodes and visible enlarged para aortic lymph nodes. The aim of this procedure was to

resect all macroscopic tumor, a sincere effort was made to reduce the lesions ultimately to a size <1 cm. Appendicectomy, splenectomy and diaphragmatic scraping and bowel resection were performed if warranted to achieve an optimal cytoreduction, defined as residual disease ≤1 cm.

Study parameters and outcome measures

Pre-operative CT scan parameters were compared with per operative findings thereby predicting suboptimal cytoreduction, defined as residual tumor <1 cm.

Statistical methods

The Statistical analysis was performed by STATA11.1 (College Station TX USA). Sensitivity, Specificity, Positive and negative predicted values were calculated between the CT and Per operative findings for ASCITIS, Omentum, Peritoneal thickening, retroperitoneal lymph node and Diaphragm & lung bases. Demographic variables of age and gender will be analyzed. Chi Square test were used to find the association between the optimal and Sub optimal with Ascitis, Omentum, peritoneal thickening, retro perineal lymph node, diaphragm & lung bases, CA125 and total score. Categorical variables will be described as frequency and percentage. P <0.05 Considered as statistically significance.

RESULTS

In Table 4 categorises accuracy, sensitivity, specificity, positive predictive value, negative predictive value respectively in (%). Preoperative CA 125 of all patients was available and ranged from 8.6 IU/ml to 3711 IU/ml. 34% patients had CA 125 > 500 IU/ml. Of these, 70% had optimal and 30% had sub optimal cytoreduction. Amongst 66% patients with CA125 <500, 74.3% had optimal and 25.6% had sub optimal cytoreduction. P-value of this system was 0.721 which is statistically insignificant.

Table 4 categorises the results of CT detection of tumour at specific sites. CT was highly sensitive in the diagnosis of retroperitoneal lymph node, presence of ascites and omental involvement with sensitivity of 85.7%, 100% and 73.6% respectively. Sensitivity to detect peritoneal deposits and sub diaphragm deposits was very low, 60% and 16.6% respectively.

In the present study, 59 patients met the inclusion criteria. Demographic criteria are described in Table 1. 72.8% of patients underwent optimal cytoreduction i.e., <1cm of residual disease.

Specificity was uniformly greater than 85% for all parameters except ascites and retro peritoneal lymph nodes which was 71.4% and 54.8%.

Table 2: Demographic characters (n=59).

	No of cases	percentage
Age distribution (in yrs)		
<50	14	24%
50-59	27	46%
60-69	16	27%
70-79	2	3%
Menopausal status		
Post-Menopausal	45	76.2%
Pre-Menopausal	14	23.7%
FIGO staging of tumour on staging laparotomy		
Stage I	14	23.7%
Stage II	2	1.7%
Stage III	36	62.7%
Stage IV	7	11.8%
Grading of Tumour		
Grade I	9	15%
Grade II	10	17%
Grade III	40	68%
Histopathology of tumor		
Serous	42	71.2%
Mucinous	6	10.1%
Endometrioid	4	6.8%
Clear cell	3	5.08%
Others	4	6.77%
Preoperative CA 125 values		
≤500	39	66%
>500	20	34%

Table 3: CA 125 and surgical outcome.

CA 125	Optimal	Sub Optimal	Total	P-Value
>500	14(70%)	6 (30%)	20 (34%)	0.721
≤500	29(74.3%)	10(25.6%)	39 (66%)	
Total	43	16	59	

Table 4: Results of pre-operative CT scan.

CT Parameter					
Volume of ascites	79.6	100	71.4	58.6	100
Peritoneal involvement	77.9	60	88.8	77.7	78
Retroperitoneal lymph nodes	69.5	85.7	54.8	63.2	81
Omentum	83	73	100	100	67.7
Diaphragm and lung bases	74.5	16.6	100	100	73.2

Table 5: CT findings and surgical outcome.

	Optimal	Sub Optimal	Total	P-Value
Ascites				
Present	16	13	29	0.003
Absent	27	3	30	
Omentum				
Present	14	14	28	0.001
Absent	29	2	31	
Peritoneal Thickening				
Present	5	13	18	0.001
Absent	38	3	41	
Retroperitoneal Lymph node				
Present	23	15	38	0.004
Absent	20	1	21	
Diaphragm and Lung Bases				
Present	0	3	3	*
Absent	43	13	56	

*chi square test approximately invalid as one cell contains value < 1.

Table 5 denotes the optimal cytoreduction with each parameter. P value was significant for ascites, retroperitoneal lymph node, omental deposits (nodularity and caking), peritoneal thickening and sub diaphragm deposits > 2cm and lung bases deposits.

We assigned a CT score of 0 to 2 for each parameter under study. Table 5 represents the total score and the surgical outcome. It was observed that as the total score increased, the number of patients who underwent sub optimal cytoreduction also increased. 33 out of 34 cases (97%) with a total score of 0, 1 and 2 underwent optimal cytoreduction. Amongst 15 patients with score of 4, 5, 6 and 7, 12 (80%) underwent sub optimal cytoreduction. Out of the 9 patients with a total score of 3, 6 had optimal and 3 had sub optimal surgery.

Table 6: Pre-operative total CT scan score comparison with optimal and suboptimal debulking.

Total Score	Optimal	Sub Optimal	Total
0	13	0	13
1	8	0	8
2	13	1	14
3	6	3	9
4	2	5	7
5	1	2	3
6		4	4
7		1	1
Total	43(72.8%)	16(27.1%)	59

Table 7: Total pre-operative CT score and surgical outcome.

Total Score	Optimal	Sub Optimal	Total	P-Value
<3	34	1	35	<0.001
≥3	9	15	24	
Total	43	16	59	

Table 7 demonstrates the surgical outcome when the total score of 3 or higher was used to classify a tumour as unlikely to be optimally debulked with surgery. The sensitivity of this system was 79% and specificity was 93%. P value was found to be <0.001 which is statistically significant. Higher the pre-operative CT score, the result of study shows, less number of optimal debulking.

DISCUSSION

We conducted a comparative study evaluating utility of preoperative CT scan and correlation of per operative findings in 59 patients of carcinoma ovary. The surgical outcome was compared with the pre-operative CT scanning, the potential of pre-operative CT scanning and its value was used as a factor to predict the outcome of cytoreductive surgery.

Role of imaging in ovarian cancer is to detect and characterize adnexal masses, recognize unusual findings that may suggest atypical or alternative diagnosis, demonstrate metastasis in order to prevent surgical under staging and detect specific sites of the disease that may be unresectable.[24] Ultrasonography is usually the first imaging modality in evaluation of patients suspected to have adnexal mass. Transvaginal sonography and doppler studies in combination with clinical and laboratory findings (tumor markers) are fairly satisfactory for characterization of adnexal masses. Sonography is unsuitable for evaluation of peritoneal spread of the ovarian cancer. Ultrasonography lacks objectivity in evaluating the global extent of the disease. CT is a superior imaging modality for evaluation of ovarian cancer. The staging of ovarian cancer is surgical. In standard surgical procedure both staging as well as therapeutic resection of tumor is combined.

Although the staging is completely surgical, pre-operative CT is recommended. Demonstration of GIT and urinary tract involvement helps to modify the surgical plan. Preoperative CT can accurately predict the surgical outcome and hence has important role in deciding the management of ovarian cancer.[18] Non resectable disease such as those with large deposits at root of mesentery, diaphragm and retro peritoneum can be spared of surgery and put on neoadjuvant chemotherapy, as optimal debulking of the disease is unlikely to be achieved in these patients.[18,25] Involvement of uterus, rectum, colon

and small bowel by the tumor is well demonstrated. CT can also detect deposits on peritoneum, liver or bowel surfaces. Three most common sites to have peritoneal deposits are right sub diaphragmatic space, greater omentum and pouch of douglas. The sensitivity of CT in this regard is moderate, conventional CT scanners can detect only up to 50% of peritoneal deposits that are 5mm or less in size. The helical and multi detector CT scanners have improved sensitivity in detection of small peritoneal deposits, especially in upper abdomen.[26,27] Detailed analysis of volumetric data of multiple detector computed tomography (MDCT) in multiple planes allows better detection of subtle lesions.

The morphological features of ovarian cancer on MRI are similar to those seen on sonography or CT, but because of excellent soft tissue contrast, the details are better demonstrated. MRI is better than other modalities in determining the origin of a pelvic mass. It is also accurate in demonstration of direct involvement of other pelvic structures by the ovarian tumour. The peritoneal and lymph nodal spread detection by MRI is comparable to the CT.[28] Long imaging time required for MRI evaluation of entire abdomen and pelvis makes it less suitable. Lack of universal availability, high cost of examination makes this modality impractical for routine study in ovarian cancer. For pre-operative staging MRI is used predominantly as a problem solving modality at present.[29] Evolving technology with faster scan time and wider availability will make MRI examination method of choice.

The median age of patients presenting with carcinoma ovary in our study was 54.6years. Age of patients ranged from 40 to 74years. This was in accordance with studies done by G Ferrandina et al[30] where the median age was 59 years (range: 31–85) and Gerestein C et al[35] where the median age of patients was 62.4 years (range 15.9-83.6 years). On staging laparotomy, we observed that 74.5% patients presented to us at an advanced stage (Stage III and IV).[2,3] All the patients underwent primary debulking surgery done by an experienced gynaecology oncosurgeon. 72.8% of patients underwent optimal debulking i.e., residual disease <1cm which was quite high as compared to other studies. Gerestein C et al and Mausavi A et al observed optimal cytoreduction in 45% and 41% cases respectively.[31,32] These studies included only stage III and IV cases. We included patients at all stages of cancer and therefore the high optimal cytoreduction rate can also be attributed to 25.5% cases belonging to FIGO stage I and II which usually undergo optimal cytoreduction. Residual disease in the patients who underwent sub optimal cytoreduction was mesentery of bowel in 6 cases, splenic hilum was involved in 3 cases along with porta hepatis in 2 cases, liver parenchyma in 1 case, sub diaphragmatic deposits >2 cm were present in 6 cases wherein liver was plastered to sub diaphragm in 4 cases. In 6 cases, sub centimetre sub diaphragmatic seedlings were present which was considered optimal. Appendicectomy was done in all patients with intra operative and CT findings of mucinous neoplasm.

Histopathological correlation was done after staging laparotomy. The ability of CT to predict reliably optimal cytoreduction is dependent on the precision of CT in identifying disease at various metastatic sites. Several studies have reported accuracy of CT by disease site in patients at initial diagnosis. Glaser G et al recently reported on CT and surgical findings correlation in 46 patients.[33] Nelson et al, Bristow et al and Meyer et al conducted studies on 41, 28 and 42 patients respectively.[14,17,18] They compared preoperative CT criteria with laparotomy findings thereby predicting optimal cytoreduction. The accuracy of CT at individual sites is comparable to that reported in the literature. We observed that sensitivity and specificity of CT to detect ascites was 100% and 71.4% respectively. This was comparable to study done by Nelson et al, who found the sensitivity to be 85% and specificity >90%.[18]

The accuracy of CT to identify peritoneal involvement in our study was 77.9%. This was similar to studies done by Bristow et al and G Ferrandina et al where accuracy was 80.5% and 78.5% respectively.[14,30] The sensitivity and specificity were also comparable – 60% and 88.8% in our study to 71.4% and 90% (Bristow et al).[14] The sensitivity and specificity to detect omental metastasis was 73.6% and 100% in our study. Similar results were found in studies done by Glaser G et al, Nelson et al and Meyer et al[17] with a sensitivity and specificity of 72%/65%, 83.3%/83.3% and 80%/100% respectively.[18,33] Enlarged retroperitoneal lymph nodes was detected with an accuracy , sensitivity and specificity of 69.5%,85.7% and 54.8%, respectively in our study which corresponded to results of studies done by G Ferrandina et al where accuracy was 81.9% and specificity was 91.8% and Meyer et al where sensitivity was 60% and specificity100%.[17,30]

Diaphragm and base of lung are difficult to differentiate so they were taken together. It was found that CT scan could detect metastasis to this region with accuracy, sensitivity and specificity of 74.5%, 16.6% and 100% respectively. This is similar to studies done by Glaser G et al, Nelson et al, Bristow et al and Meyer et al.[14,17,18,33] The sensitivity and specificity in their studies were 48%/100%, 79.2%/90%, 42%/75% and 54%/87%, respectively. Sensitivity of CT scan to detect sub diaphragm, lung bases and peritoneal deposits was low. This may be because CT scan could not detect sub diaphragm deposits <1cm, but the specificity for detection of both the parameters was high i.e., 100% and 88.8% respectively.

Table 4 demonstrates P value of each variable for predicting optimal and sub optimal debulking. We observed that presence of ascites, omental caking, peritoneal deposits and enlarged retroperitoneal lymph-nodes on pre-operative CT scan was associated with sub

optimal cytoreduction. Previous investigators assessing the utility of preoperative CT scan in this setting have retrospectively identified different radiologic predictors.[14-18] Axtell et al.'s analysis of 65 patients showed diaphragm disease and large bowel mesentery implants to be significant factors.[15] Dowdy et al.'s review of 89 patients found diffuse peritoneal thickening to be the only variable significantly associated with suboptimal debulking which is comparable to our study.[16]

Pre-operative CA125 levels were obtained for all patients within a month prior to cytoreductive surgery.4 patients had CA125 values <35 IU/ml which is the accepted cut off. Of these, 2 were found to have mucinous and 2 were serous cystadenocarcinoma stage 1. A recent meta-analysis concluded that although a CA-125 > 500 U/mL was a strong risk factor for suboptimal debulking, it lacked the accuracy to independently predict surgical outcome.[34-38] In our study, it was found that almost equal number of patients (around 70 and 74.9%%) underwent optimal cytoreduction in both groups i.e., <500IU/ml and >500IU/ml. The value of CA125 did not correlate with optimal cytoreduction with P value – 0.721 which is statistically not significant. We consequently feel that the preoperative CA-125 level should be used in combination with the other criteria to guide clinical management. We observed that the score of 3 or higher as indicative of noncytoreducibility would have spared over half such patients from surgery while excluding none whose tumors could be optimally reduced. A score of 3 or higher indicates that disease was detected in at least two regions. In our study, only one patient with score <3 i.e., score 2 underwent suboptimal cytoreductive surgery. It was found to be primary appendiceal neoplasm (mucinous) where whole bowel, stomach and spleen were also involved.

CONCLUSIONS

CT scanning has proven useful in monitoring the course of women with epithelial ovarian carcinoma. In this study, common sites of sub optimally resected tumor were proposed and the ability of CT scan to identify these inoperable lesions was investigated .Although preoperative abdominopelvic CT is not sufficiently accurate to stage patients with epithelial ovarian carcinoma , our results suggest that, staging laparotomy may not result in optimal debulking in these patients. The use of a CT scoring system emphasizing multiple potential disease locations appears to improve accuracy. Hence CT scan may help select patients who might be more appropriately managed by neoadjuvant chemotherapy. This study has sincerely attempted to reduce the uncertainty as to which patient should be initially subjected to neoadjuvant chemotherapy and which patients can be directly taken up for primary debulking surgery.

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