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Original article

Role of computed tomography (CT) in prediction of histological subtypes of epithelial ovarian carcinoma

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ABSTRACT

Introduction: *According to the 2018 Globocan Fact Sheet, 3.44 percent (36170) of all cancer cases in India's female population were attributable to ovarian cancer, making it the seventh most common cancer in females worldwide. Patients with type I ovarian carcinoma have a substantially longer overall survival duration than those with type II ovarian carcinoma. Type II epithelial ovarian carcinoma is a more aggressive form of the disease, which also progresses quickly and is associated with a lower likelihood of overall survival.*

Aims and Objectives: *To assess the role of CT in the prediction of different histological subtypes of epithelial ovarian carcinoma.*

Material and Methods: *The present prospective observational study was carried out in the Department of Radiodiagnosis, All India Institute of Medical Sciences (AIIMS) Patna from January 2022 and May 2023. This study investigated a group of 41 patients with ovarian carcinoma.*

Results: *Of the total 41 sample size, 28 patients (68%) were diagnosed with type II epithelial ovarian cancer, while 13 patients (32%) diagnosed with type I epithelial ovarian carcinoma. Patients diagnosed with type I epithelial ovarian cancers (EOCs) exhibit a higher likelihood of affecting younger individuals and demonstrate lower levels of the CA-125 biomarker in their serum. Type II epithelial ovarian cancers (EOCs) often have solid-cystic or mostly solid bilateral masses that are smaller in size and display mild enhancement on contrast-enhanced computed tomography (CECT) imaging, in contrast to type I EOCs. The presence of diffuse omentum involvement, peritoneal deposits, and metastatic lymphadenopathy was more frequently observed in type II epithelial ovarian cancer (EOC) in comparison to type I EOC. In comparison to type I epithelial ovarian cancer (EOC), type II EOC typically has irregular margins and is more frequently accompanied by pleural effusion.*

Conclusion: *Ovarian cancer of epithelial origin has diverse imaging characteristics that vary based on the level of differentiation and histological subtypes. In general, the study sheds light on CT imaging parameters that help differentiate histological subtypes of epithelial ovarian carcinoma into type I and type II which will guide clinicians in deciding appropriate treatment strategy as well as prognostication of patient. The findings of the present study contribute to a better understanding of the morphology, enhancement, laterality, size, and dissemination patterns of different subtypes of epithelial ovarian carcinoma. Present study recommends that a radiologist must be familiar with these specific patterns for better interpretation of images and to suggest adequate management for patients of ovarian carcinoma.*

Keywords: *Computed Tomography; Prediction; Histological Subtypes; Epithelial Ovarian Carcinoma*

INTRODUCTION

According to the 2018 Globocan Fact Sheet, 3.44 percent (36170) of all cancer cases in India's female population were attributable to ovarian cancer, making it the seventh most common cancer in females worldwide. From 2014 to 2016, Pandey et al. discovered that the incidence rate of ovarian cancer in Bihar (India) was 4.2%.[1] It also accounted for 3.34 percent (24015) of all cancer deaths in India in the same year, making it the leading cause of cancer death in Indian women. When detected in its earliest stages, ovarian cancer has a 94% 5-year survival rate, but only 15% of cases are discovered at early stage. 62% of diagnoses are made between Stages III and IV, when the 5-year survival rate is approximately 28%. Patients with advanced ovarian cancer have a dismal prognosis, and the disease has the highest case fatality ratio of all gynecological cancers worldwide.[2]

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Epithelial ovarian cancer (EOC), accounts for 90 to 95% of ovarian cancer cases. It is the leading cause of mortality resulting from gynecological cancers due to the absence of obvious initial symptoms and adequate screening methods. The World Health Organization published in 2014 its classification of cancers of female reproductive organs based on morphological, immunohistochemical, and molecular genetics research. Within the framework of this classification, EOC was split into two distinct types: Type I and Type II.[3] Low-grade serous carcinoma (LGSC), endometrioid carcinoma, clear cell carcinoma (CCC), mucinous carcinoma, and malignant Brenner tumors are all included in type I EOC. Type II EOC, on the other hand, encompasses high-grade serous carcinoma (HGSC), carcinosarcoma, and undifferentiated carcinoma. Both the mutation profiles and clinical courses between the two diseases are distinct. Mutations in KRAS, BRAF, ERBB2, CTNNB1, PTEN, and PIK3CA are found in type I early-onset ovarian malignancies that develop along an adenoma-carcinoma sequence, have a predominantly benign clinical course. They have a favorable prognosis when confined to the ovary and account for only 10% of ovarian cancer- related deaths. Eighty percent of high-grade serous ovarian cancers have TP53 mutations, andtype II epithelial ovarian cancers are rapidly growing tumors originating from ovarian surface epithelium or cortical inclusion cysts. Type II EOC are distinguished by BRCA1 or BRCA2 mutations and the absence of morphological precursors.[4] Over 90% of ovarian cancer deaths are caused by type II tumors because they are exceedingly aggressive, always have a high grade, and are discovered in advanced stages in about 75 percent of cases. In order to have a long, progression-free survival, patients with Type II would require more extensive surgery and more intensive treatment. Serous carcinoma, which is the most prevalent subtype of epithelial ovarian cancer (EOC), has a favorable response to chemotherapy but is associated with a poor prognosis. Conversely, certain subtypes of type I EOC, such as clear cell carcinoma and mucinous carcinoma, display resistance to treatment but are associated with a more favorable prognosis when compared to type II EOC. Therefore, to prevent overtreatment of patients with type I EOC, it is essential to accurately predict the histological subtype using appropriate imaging technique.[5]

After reviewing the available literature, we can say that, to the best of our knowledge, very few studies have been performed or give evidence in prediction of histological subtypes of epithelial ovarian carcinoma. Therefore, the purpose of the present study was to identify the variety of contrast-enhanced CT (CECT) imaging findings that can differentiate between type I and type II epithelial ovarian cancer. This study contributes to improved overall patient treatment and prognosis for patients with epithelial ovarian cancer.

In this study, it was anticipated that the CT imaging characteristics that distinguish type I from type II EOC will be identified. This will not only help in the right categorization of EOC patients for further treatment, but it will also help in the prognostication of EOC patients.

MATERIAL AND METHODS

The present prospective observational study was carried out in the Department of Radiodiagnosis, All India Institute of Medical Sciences (AIIMS) Patna from January 2022 and May 2023, after clearance from IRC and IEC . This study investigated a group of patients with ovarian carcinoma who were referred to the Department of Radiodiagnosis at AIIMS Patna for radiological examination by the surgical oncology and obstetrics and gynecology departments.

Inclusion criteria:

a. Patients with histopathological diagnosis of subtypes of epithelial ovarian carcinoma who underwent contrast enhanced computed tomography in the Department of Radiodiagnosis, AIIMS Patna.
b. Histopathological diagnosis made from resected specimen obtained by either primary debulking surgery, staging laparotomy or post NACT interval debulking surgery.

Exclusion criteria:

a) Recurrent ovarian mass after radical excision.
b) CT done after NACT.

All patients of ovarian carcinoma who fulfilled the inclusion criteria, referred to Department of Radiodiagnosis, AIIMS Patna for radiological evaluation during the study period.

Methodology

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All patients with features suspicious of ovarian carcinoma clinically or on USG, referred to the Department of Radiodiagnosis, AIIMS Patna for contrast CT abdomen were screened for eligibility based on inclusion and exclusion criteria as mentioned above. An informed written consent was obtained from all the patients. The patient's demographic details were documented. After initial evaluation, the patients were evaluated with CECT Abdomen and pelvis. Details of the procedure was explained to the patient. Then patients were followed up, and their histopathology reports were collected from the Department of Pathology and Lab Medicine, AIIMS PATNA, for confirmation of histological subtypes. Final histopathological diagnosis was obtained from resected specimen from the patient who underwent either primary cytoreductive surgery or post neoadjuvant chemotherapy (NACT) surgery. All the patients with histopathological diagnosis of epithelial ovarian cancer were included in the analysis while rest of the patients with diagnosis other than epithelial cancer were excluded from the study. Finally, 41 patients with histopathological diagnosis of epithelial ovarian carcinoma were included in study for analysis.

CECT:

After ruling out CT contraindications, all patients were instructed to fast for six hours prior to the CECT exam. Intravenous (IV) access was established with an 18G intravenous cannula. Vital signs of the patient were recorded. Every patient was tested for contrast sensitivity. Every individual underwent a kidney function test (KFT). Multiphasic CECT abdomen and pelvis was performed on a 256 slice MDCT Siemens Somatom Definition flash - CT scanner. The patient was instructed to consume 1.5 liters of water prior to the scan in order to distend bowel. Rectally, 350–500 ml of normal saline was administered to distend the rectum and large intestine.

Technique:

A non-contrast scan was taken first, followed by i.v. contrast-enhanced image acquisition. About 1-2 ml/kg body weight of non-ionic iodinated contrast agent (omnipaque 350mg/ml) was administered intravenously at a rate of 4 to 4.5 ml/sec using an 18G angiocath placed in the antecubital vein. The lower thorax, entire abdomen, and pelvis were covered in all phases. Late arterial phase was taken 25–30 sec after contrast injection. The venous phase was taken 80–90 sec after contrast injection. If necessary, a delayed phase of 10/15 minutes was taken.

CECT scan parameters - *Multiphasic Contrast enhanced computed tomography (CECT) scan parameters used whilea cquiring the study.*

CECT scan parameters	
Tube voltage setting	120 kVp
Tin filter	Yes
Slice collimation	5mm
Gantry rotation time	0.5sec
Pitch	0.6
Reconstruction slice thickness	0.6
Reconstruction increment	5mm
Reconstruction kernel	3of

Afterwards, the images were transmitted to a workstation (Syngo.via). In axial sections, all images were evaluated craniocaudally. In addition, the images were examined in coronal and sagittal sections using multiplanar reformation. For data collection, images were evaluated in non-contrast, delayed arterial, and venous phases. The following parameters were assessed by two radiologists:

1. **Size of the lesion** – The largest dimension was taken into consideration, and in the caseof bilateral lesions, the size of the larger lesion was considered.
2. **Laterality** – Unilateral/Bilateral.
3. **Morphology** - According to the percentage of the solid portion in the tumor, the morphology of masses was further divided into three categories: cystic or predominantly cystic tumor (Solid portion < 30 %), mixed tumor (solid portion (30% to 70%), and predominantly solid or purely solid tumor (solid portion > 70%).
4. **Mural nodule -** A mural nodule was deemed to be present when its diameter at maximum thickness exceeded 3 mm.
5. **Thickened septa** – When the thickness of septa was greater than 3 mm.
6. **Margins** – Distinct or indistinct/irregular.
7. **Presence of ascites.**
8. **Lymphadenopathy -** The presence of lymphadenopathy was determined when

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the diameter of a lymph node was greater than 10 mm.

9. **Omental involvement** – Further divided as stranding, nodular or diffuse.
10. **Peritoneal deposits** – Further categorized as sporadic or diffuse based on number of sites involved. Sporadic – Few small peritoneal deposits. Diffuse – Multiple peritoneal deposits.
11. **Local invasion –** Infiltration of the adjacent pelvic organs.
12. **Calcifications** – Tumor calcifications were assessed in a non-contrast phase.
13. **Visceral/distant metastasis-** Metastasis was determined to exist when tumors resembling the primary tumor were discovered in other organs (e.g- Liver, Spleen) but were not connected to the primary tumor in three dimensions.
14. **Enhancement -** Tumor enhancement was compared to the myometrium of the uterus in the venous phase and further divided into three categories: hypoenhancement, hyperenhancement and isoenhancement.
15. **Others** – Pleural effusion and bowel involvement (either serosal deposits or direct infiltration) were considered in this category.

STATISTICAL ANALYSIS

SPSS version 22 software and STATA 17 were used for the analysis. Continuous variables were median and interquartile range values. All parameters were tested for normality using Shapiro-Wilk and Mann-Whitney. U-tests were used for continuous variables that were non-normally distributed, and student t-test used for normally distributed continuous variables. The chi-square test was used for categorical variables. Correlation was determined using Pearson and Spearman co-efficients. A ROC curve was made for those significant parameters to determine cut-off values. A univariate logistic regression was run to assess the association between various categories. Correlation coefficients were also calculated. Variables that had a higher correlation coefficient (>0.5), had a VIF of more than 5, or caused the Hosmer-Lemeshow test to become significant were dropped from the multivariable model. Multivariable logistic regression was run to assess the association between the factors and a favorable GOS outcome. OR (Odd's ratio) was reported with a 95% confidence interval (CI). A P value less than 0.05 was taken as significant. The logistic regression was performed in STATA 14.

OBSERVATIONS AND RESULTS

A total of 41 patients with histopathological subtype diagnosis of epithelial ovarian carcinoma were included in the present study.

Table 1: Descriptive statistics of continuous variables.

	AGE	CA-125	CEA	CA19.9	SIZE OF LESION (CM)
N	41	41	41	41	41
Mean	45.95	298.67	4.22	35.05	13.73
Std. Deviation	16.91	216.67	9.80	40.36	6.35
Minimum	11.00	5.20	0.26	0.40	2.80
Maximum	76.00	613.50	61.80	234.70	29.40
Percentiles	28.50	82.20	0.82	10.90	9.40
	49.00	294.20	1.67	27.80	11.80
	58.00	540.00	3.14	41.60	17.75

Table 1 depicts the mean, standard deviation, minimum, and maximum values of all the continuous variables of 41 cases analyzed in the present study. Among the 41 females who participated in the present study, 22 (53.7%) were post-menopausal and 19 (46.3%) were pre-menopausal. In the present study, Type II EOC was found in 28 (68%) of the total 41 cases, while type I EOC discovered in only 13 (32%) of the cases. As the sample size was less than 50, Shapiro-Wilk test was used to test the distribution of different continuous variables. It was found that CA-125, CEA, CA 19.9 and size of lesion were not normally distributed. Age was found to be normally distributed.

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Table 2: Comparison of demographic, biochemical and radiologicalparameters between type I and type II EOC.

Parameters	Type I	Type II	Statistics	p value
Age	37.31+/-21.98 (n=13)	49.96+/-12.51 (n=28)	t=1.936 df=15.72	0.071
CA-125	77.5(13.4-186.8) (n=13)	392.4(294.2-552.2) (n=28)	U=47 Z=3.78	0.001*
CEA	1.6(0.6-2.8) (n=13)	1.68(1.04-2.97) (n=28)	U=175 Z=0.196	0.844
CA 19.9	27.8(11.9-61) (n=13)	27.95(19.13-32.5) (n=28)	U=157.5 Z=0.686	0.492
Size of lesion	18.7(10.8-25.9) (n=13)	11.5(9.5-13.4) (n=28)	U=98 Z=2.354	0.019*

The mean age of the patients with type I and type II EOCs were 37.3 and 49.9 years respectively. However, this distribution was statistically insignificant. The median values of CA-125 was higher (392.4 IU) among the patients with type II EOCs than type I EOCs (77.5 IU). It was statistically significant (p=0.001). The median values of CEA and CA 19.9 were higher among the patients with type II EOCs than type I EOCs but it was not statistically significant. The type I EOCs had larger size of lesion (18.7 cm) than that of type II EOCs (11.5 cm) and this distribution was statistically significant (p=0.019).

Table 3: Correlation of the parameters with the grade of the tumor.

Parameters	Co-efficient	p value
Age	0.353	0.024*
CA-125	0.614	0.001*
CEA	0.118	0.461
CA 19.9	-0.198	0.214
Size of lesion	-0.473	0.002*

In the table 3, we have found that age and CA-125 are significantly and positively correlated with the grade of the tumor. It means that type II EOCs will be associated with increased age and higher value of CA-125 as compared to type I EOCs (p=0.024 and 0.001 respectively). Also, the size of lesion is significantly and negatively correlated with grade of tumor (p=0.002). It means that type II EOCs will be associated withsmaller size as compared to type I EOCs. The values of CEA and CA 19.9 are not significantly correlated with the grade of the tumor as p values are 0.461 and 0.214 respectively.

Table 4: ROC curve analysis of the parameters predicting the grade of thetumor

Parameters	Predicting grade	AUC	p Value
Age	Type II EOC	0.703(0.473-0.933)	0.038*
CA-125	Type II EOC	0.871 (0.758-0.984)	0.001*
CEA	Type II EOC	0.519 (0.334-0.704)	0.845
CA 19.9	Type I EOC	0.567 (0.377-0.758)	0.492
Size of lesion	Type I EOC	0.731 (0.548-0.914)	0.019*

We have found in ROC curve that Age, CA-125 and size of the lesion were found to be statistically significant with p-values 0.038, 0.001 and 0.019 respectively. The AUC for age and CA-125 predicting the type II tumor was 0.703 and 0.871 respectively. The AUC for the size of the lesion predicting type I tumor was found to be 0.731.

Figure 1: ROC curve analysis of the age predicting type II EOC.

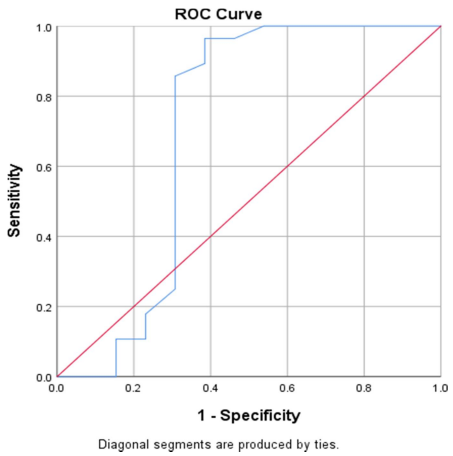


Figure 2: ROC curve analysis of the CA-125 predicting type II EOC.

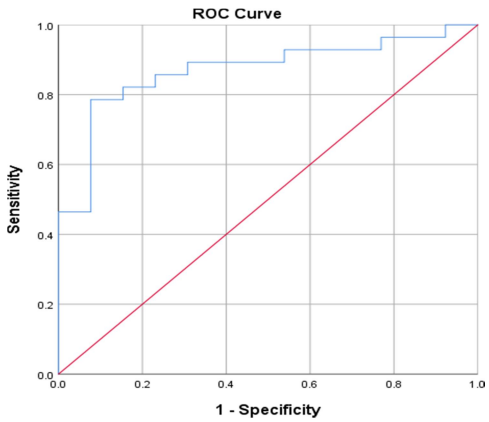


Figure 3: ROC curve analysis of the CEA predicting type II EOC.

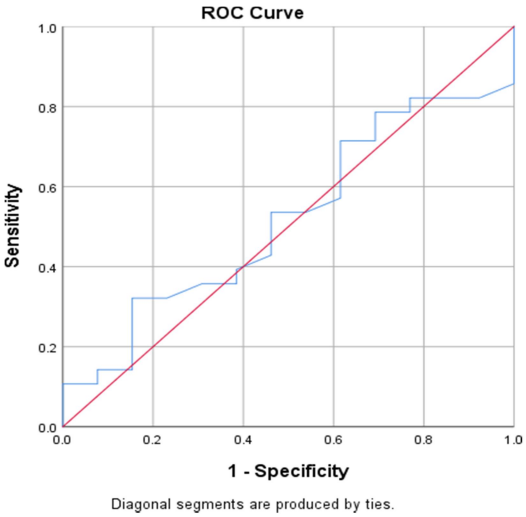
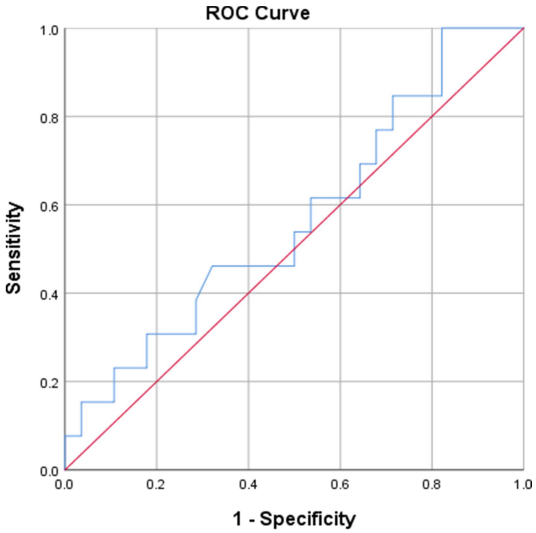


Figure 4: ROC curve analysis of the CA 19.9 predicting type II



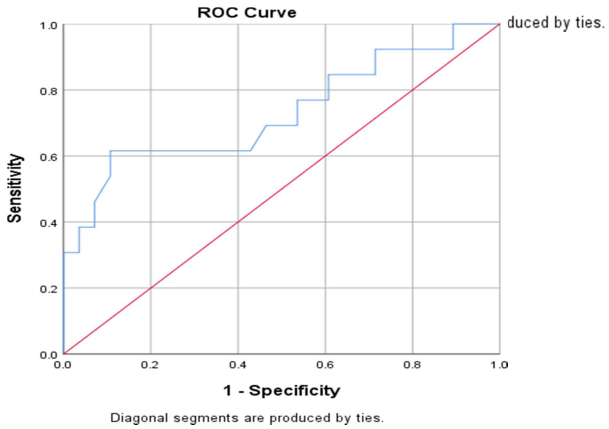


Figure 5: ROC curve analysis of the size predicting type I EOC.

We proposed a cut off for those parameters found to be significant in ROC curve analysis. If the age of the patient was more than or equal to 42 years, we could say that the patient would have type II EOC with 71.4% sensitivity and 69.2% specificity. If CA-125 of the patient was more or equal to 197.4 IU, we could say that the patient would have type II EOC with 82.1% sensitivity and 84.6% specificity. If the size of the lesion in the patient was greater than or equal to 12.7 cm, we could say that the patient would have type I EOC with 61.5% sensitivity and

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60.7% specificity. In the present study, majority (9) of pre-menopausal women had type I tumors (69.2%), while the majority (18) of post-menopausal women had type II tumors (64.3%). The p value for this distribution was found to be 0.09, which indicates that it is statistically insignificant. Majority 22 (78.6%) of bilateral tumors are type II EOCs, while the majority 9 (69.2 %) of unilateral tumors are type I EOCs. The p value for this distribution was found to be 0.005, which indicates that it is statistically significant. Majority of type I EOCs are cystic (53.8%) and solid-cystic (38.5 %), while the majority of type II EOCs are solid-cystic (60.7 %) and solid(32.1%). The p value for this distribution was found to be 0.003, which indicates that it is statistically significant. 50 % of Type II EOCs have irregular margins, while all patients of Type I EOCs have regular margins. p-value = 0.001 which indicated statistical significance. 14.3% of type II tumors have pelvis lymphadenopathy and 39.3% type II tumors have pelvic lymphadenopathy with retroperitoneal extension. However, no lymphadenopathy is seen in type I tumors. P- value of 0.004 indicates statistical significance. Nodular and diffuse omental involvement was seen in 42.9 % and 25 % type II EOCs respectively. Majority of type I EOCs (84.6%) showed no omental involvement. P-value of 0.005 indicates statistical significance. Sporadic and diffuse peritoneal involvement was seen in 10.7 % and 60.7 % of type II EOCs respectively. Majority (84.6 %) of type I EOCs showed no peritoneal involvement. However, few (15.4 %) type I EOCs showed diffuse peritoneal involvement. P-value of 0.003 indicates statistical significance. Majority (60.7 %) of type II EOCs showed hypoenhancement and majority (53.8 %) of type I tumors showed hyperenhancement. Also, 30.8 % of type I EOCs and 14.3% of type II EOCs showed isoenhancement. A p-value of 0.026 indicates its statistical significance. 32.1% of type II EOCs showed evidence of pleural effusion. However, no type I tumor showed evidence of pleural effusion. A p-value of 0.038 indicates statistical significance. Multiple mural nodules were seen in 38 % of type Itumors, which was higher as compared to type II tumors (21.4%). However, this was not found to be statistically significant. Thickened septa are seen in 53.8 % of type I tumors is slightly higher as compared to type II tumors (39.3%). However, this was not found statistically significant. Majority of Type II tumors have small or large ascites (39.3 % and 46.4 % respectively), while majority of Type I tumors have small(53.8 %) or no ascites (30.8 %). p-value of 0.135 indicated its statistical insignificance. In 32.1 % of type II tumors, local invasion was observed, as shown in the table above. However, only 7.7 % type I tumors exhibited evidence of local invasion. A p-value of 0.129 indicates its statistical insignificance. We can observe from the above table that 14.3 % of type II tumors showed visceral or distant metastasis. No type I tumor showed distant/visceral metastasis. However, this was not found to be statistically significant. The above table shows that 15.4 % of type I tumors exhibited calcifications, while only 7.1% of type II tumors exhibited calcifications. A p-value of 0.408 indicated statistical insignificance. We can observe from the table above that 17.9 % of type II tumors showed evidence of bowel involvement. However, no type I tumor showed evidence of bowel involvement. A p-value of 0.104 indicates it is statistically insignificant.

Table 5: Univariate analysis of parameters predicting type II EOC.

Parameters	Odd's ratio (CI=95%)	p value
Age	1.05(0.99-1.11)	0.099
Menopausal status (post)		
Pre-menopausal	0.24(0.06-1.03)	0.05
CA-125	1.01(1-1.02)	**0.003***
CEA	1.37(0.97-1.94)	0.074
CA 19.9	0.99 (0.98-1.01)	0.367
Size of lesion (cm)	0.85(0.76-0.95)	**0.006***
Laterality (U/L)		**0.006***
B/L	8.25(1.84-37.06)	
Morphology (cystic)Solid-		
cystic	11.9(1.8-78.31)	**0.01***
Solid	31.5(2.28-436.14)	**0.01***
Mural Nodule (no)		
Single	1	0.98
Multiple	0.48(0.11-2.07)	0.325
Thickened septa (yes)		
No	1.8(0.49-6.92)	0.86
Margins (regular)		0.97
Irregular	1	

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Ascites (no)		
Within pelvis	1.57 (0.3-8.6)	0.52
Beyond pelvis	6.5(0.83-50.96)	0.075
Lymphadenopathy (no)		
Pelvic		
Pelvic with	1	0.95
	1	098
retroperitoneal		
Omental involvement (no)		
Stranding	1	0.98
Nodular	18.86 (1.93-184.13)	**0.012***
	11(1.07-113.02)	**0.044***
Diffuse		
Peritoneal deposit (no)		
Sporadic	1	0.89
Diffuse	11.69 (2.03-67.14)	**0.006***
Local invasion (no)		
Yes	5.69(0.615-52.12)	0.124
Visceral/ Distant metastasis(no)		
Yes	1	0.88
Enhancement (hypo)		
Isoenhancement	0.12 (0.01-0.91)	**0.04***
Hyperenhancement	0.12 (0.02-0.72)	**0.021***
Calcification (no)		0.42
Yes	0.42(0.05-3.48)	
Pleural effusion (no)	1	0.89
Yes		
Bowel involvement (no)	1	0.85
Yes		

In the table above, odds ratios greater than 1 indicate a positive association with a high grade,while odds ratios less than 1 indicate a negative association. The p-values indicate the statistical significance of the associations, with values less than 0.05 (indicated by *) considered statistically significant. From the above table, we can say that with each unit increase in CA-125, there are 1.01 times higher odds of developing type II EOCs, or else we can say that there is a 1% higher risk of developing type II EOCs. Similarly, for each 1 unit increase in size, there is a 0.85-fold decrease in the likelihood of type II EOCs. (P value = 0.003). Similarly, with each unit increase in size (1 cm), there are 0.85 times lower odds of developing type II EOCs. (p value=0.006) Patients with bilateral tumors had 8.25 times the odds of developing type II EOCs as compared to patients with unilateral tumors or we can say that patients with bilateral tumors were 8.25 times more likely to develop type II tumors than those with unilateral tumors. (p value = 0.006). Patients with solid-cystic tumors had 11.9 times the odds of developing type II EOCs as compared to patients with cystic tumors or we can say that patients with solid-cystic tumors were 11.9 times more likely to develop type II EOCs as compared to those with cystic tumors. (p value = 0.01). Patients with solid tumors had 31.5 times the odds of developing type II EOCs as compared to patients with cystic tumors or we can say that patients with solid tumors were 31.5 times more likely to develop type II EOCs as compared to those with cystic tumors. (p value = 0.01). When compared to patients without omental involvement, those with nodular omental involvement were 18.6 times more likely to acquire type II EOCs. (p value = 0.012). When compared to patients without omental involvement, those with diffuse omental involvement were 11 times more likely to acquire type II EOCs. (p value = 0.044). When compared to patients without peritoneal deposits, those with diffuse peritoneal deposits were 11.69 times more likely to acquire type II EOCs. (p value = 0.006). Patients with hyperenhancing tumors had a 0.12-fold decrease in the odds of developing type II EOCs compared to those with hypoenhancing tumors. In other words, patients with hyperenhancing tumors were 0.12 times less likely to develop type II EOCs than those with hypoenhancing tumors. (p value = 0.021). Patients with isoenhancing tumors had a 0.12-fold decrease in the odds of developing type II EOCs compared to those with hypoenhancing tumors. In other words, patients with isoenhancing tumors were

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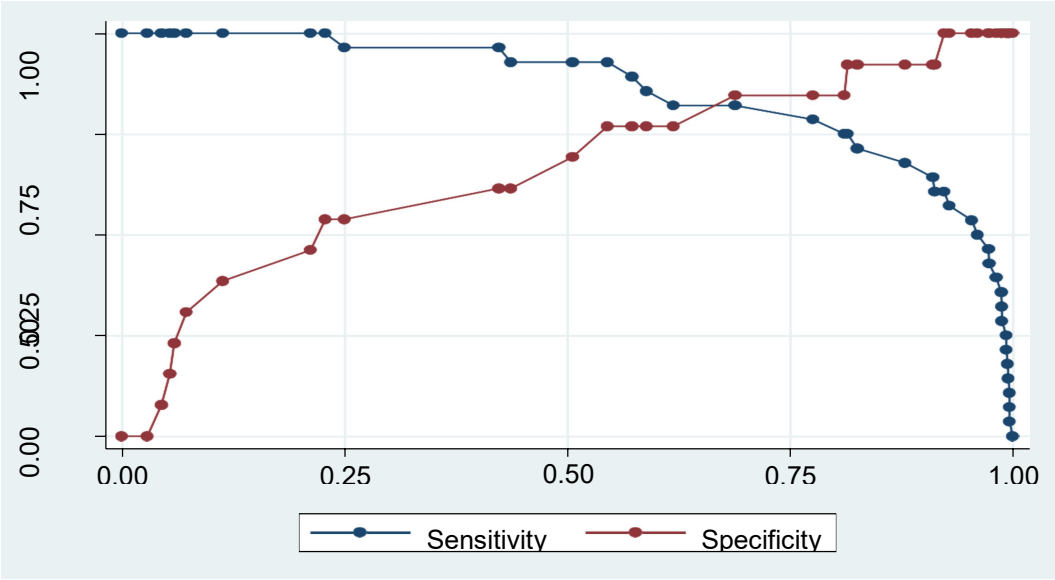
0.12 times less likely to develop type II EOCs than those with hypoenhancing tumors. (p value = 0.04).

Table 6: Multivariate analysis to predict type II EOC (Pseudo R square =0.55, P value = 0.001)

Parameters	Odd's ratio	p value
CA-125	1.007(1.001-1.014)	0.018*
Laterality	1.26(0.7-23.71)	0.876
Morphology		
Solid-cystic	2.16(0.07-71.02)	0.666
Solid	3.92(0.13-122.87)	0.437
Enhancement		
Isoenhancement	0.32(0.01-8.9)	0.503
Hyperenhancement	0.21(0.02-2.43)	0.212

Variable that showed most statistical significance in univariant logistic regression analysis were included in the multivariate logistic regression model. The overall multivariate model was found to be statistically significant with a p value of 0.005, and the pseudo-R square value was found to be 0.55. However, as far as the individual parameters were concerned, the CA-125 was found to be statistically significant. The odd's ratio for that parameter was found to be 1.007, which meant that for every one unit increase in the value of CA-125, there are 1.007 times the odds of getting a high-grade tumor, or in other words, there are 0.7% higherchances of developing a high-grade tumor. No CT imaging parameter was found to be statistically significant in multivariate logistic regression model.

Figure-6: Sensitivity and Specificity plot of the multivariate model.



From the above figure 6, we found that if we take the cut off of probabilities getting from themodel to be around 70%, we could have said that the patient will have type II EOC with nearly 70% sensitivity and 70% specificity.

DISCUSSION

Patients with type I ovarian carcinoma have a substantially longer overall survival duration than those with type II ovarian carcinoma. Type II epithelial ovarian carcinoma is a more aggressive form of the disease, which also progresses quickly and is associated with a lower likelihood of overall survival. Historically, patients with type I and type II epithelial ovarian carcinoma received similar surgical and chemotherapy treatment. Patients with type I epithelial ovarian carcinoma, however, responded less favorably to conventional platinum-based

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chemotherapy than those with type II carcinoma. To avoid overtreatment, patients with type I ovarian carcinoma require a more individualized approach to care. This is, to the best of our knowledge, one of the few studies correlating CT findings with types of epithelial ovarian cancer.

Present study correlated the radiological data of 41 patients with the histopathological diagnosis of their surgical specimens. Our results distinguished between types I and II of epithelial ovarian cancer based on clinical data, biochemical data, and imaging findings. Among 41 patients, 13 (32%) cases were type I EOC, and 28 (68%) were type II EOC. The median age of patients with type II tumors was 49.9 years, higher than the median age of patients with type I tumors, which was 37.2 years. However, this was not found to be statistically significant. Also, patients with type II demonstrated higher levels of CA-125 as compared to type I EOC with statistically significant difference (p value = 0.001). Based on ROC analysis, we concluded that a CA-125 value greater than or equal to 197.4 indicates a patient has a type II tumor with a sensitivity of 82.1% and a specificity of 84.6%. The AUC for CA-125 predicting the type II tumor was 0.87. Ca-125 was one of four variables that showed the highest statistical significance in the univariable logistic regression study and included in multivariate logistic regression. Since it was included in the multivariable logistic regression model, Ca-125 was one of the variables that showed the most statistical significance in multivariate logistic regression model (p value=0.018). Similar results were also reported in a study by Liu et al., where patients with type I EOC showed lower CA-125 levels as compared to type II EOCs (p value = 0.016).[3] A separate ultrasonography investigation, Alcaraz et al came to the conclusion in a retrospective study that type I EOCs are more frequently seen in younger females who have lower amounts of CA-125.[6]

In present study, we could not find any link between CA 19.9 and the histological grade of the tumor (p value= 0.492). Tanaka et al who conducted the study to classify epithelial ovarian carcinoma subtypes by imaging and clinical criteria.[7] CA 19.9 levels were found to be considerably higher in mucinous carcinoma, which falls under the category of type I epithelial ovarian cancer (p value = 0.009). It's possible that the low number of mucinous carcinoma cases in our research is the reason for this disparity in findings. There was no significant correlation seen between the levels of CEA and the gradeof the tumor.

There was a statistically significant size disparity between type I and type II tumors, with the majority of type I tumors being larger in size than type II tumors (p value = 0.019). Also, on univariate analysis showed, for each 1 unit increase in size (cm), there is a 0.85-fold decrease in the likelihood of type II EOCs. (P value = 0.003). We proposed a cut off for thoseparameters found to be significant in ROC curve analysis. If the size of the lesion in the patient was greater than or equal to 12.7 cm, we could say that the patient would have type I EOC with 61.5% sensitivity and 60.7% specificity. The AUC for the size of the lesion predicting type I tumor was found to be 0.731. Liu et al., found in their study that most of the type I tumors were larger than type II tumors (p value = 0.016).[3] Qian et al., also concluded from their study that type II EOC are smaller in size as compared to type I EOC.[8] Both of these studies support the conclusions of our investigation.

In the present study, we found that in the majority of postmenopausal women (64.3%), type II tumors were seen, while in the majority of premenopausal women (69.2%), type I tumors were seen. However, this was not found to be statistically significant (p value=0.09). Similarly, Liu et al. discovered no statistical significance between post-menopausal status andtumor grade in their study.[3]

In the present study, we observed that majority (78.6 %) of bilateral tumors are type II, while majority (69.2 %) of unilateral tumors are type I EOCs. Jang et al., conducted research on 124 EOC patients with CT and discovered that poorly differentiated epithelial ovarian carcinomas were more likely to involve both ovaries (42%).[9] This study backs up what we found in our research. On the other hand, this result hints to how difficult it can be to distinguish primary ovarian carcinoma from metastatic ovarian cancer. Also, in univariate logistic regression analysis, the odds ratio for bilateral tumors in predicting high grade came to 8.25, which indicated patients with bilateral tumors were 8.25 times more likely to develop type II tumors than those with unilateral tumors. However, in multivariate analysis, predicting the type II EOC laterality of the lesion was not found to be statistically significant.

In the present study, type II EOC exhibited predominantly solid (32.1%) or solid-cystic (60.7%) morphology, whereas type I EOC exhibited predominantly cystic (53.8%) morphology (P value =0.003). Also, in univariate logistic regression analysis, Patients with solid-cystic tumors had 11.9 times the odds of developing type II EOCs as compared to patients with cystic tumors (p value = 0.01). Furthermore, Patients with solid tumors had 31.5 times the odds of developing type II EOCs as compared to patients with cystic tumors (p value = 0.01). In a separate MRI study, Qian et al. discovered that type II EOC typically exhibits a solid morphology, whereas type I EOC exhibits a predominantly cystic morphology.[8] Jang et al discovered in a CT study that solid nature of tumor was more common in poorly differentiated carcinoma as compared to well differentiated EOC.[9] Liu et al. also concluded in a combined MRI and CT investigation that type II EOC are frequently associated with solid morphology (38.6%).[3] All of these investigations provide support for our conclusions.

In the present study, we found that 50% of type II tumors presented with irregular margins, and all type I tumors presented with regular margins. This was found to be statistically significant. (p value=0.001). Liu et al., in their study, evaluated margins of tumors on both CT and MRI andfound no statistically significant difference in tumor margins among type I and type II

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EOC.[3]

According to the majority of available literature, high-grade epithelial ovarian carcinoma, which has a greater propensity to spread early and are more likely to give lymph node metastasis as compared to the low grade epithelial ovarian carcinoma. Our research came to the same conclusions as the previous ones. 14.3% of type II tumors presented with pelvic lymphadenopathy, while 39.3% of type II tumors presented with pelvic lymphadenopathy along with retroperitoneal and abdominal extension. This was found to be statistically significant (p value=0.004).

According to the findings of our research, 25% of type II tumors displayed diffuse omental involvement, whereas 42.9% of type II tumors displayed nodular omental involvement. In contrast, majority of the type I tumors 84.6 %) demonstrated no involvement of the omentum. The p value for this finding was found to be 0.005, indicating that it is statistically significant. Similarly, 60.7 % of type II tumors showed multifocal diffuse peritoneal involvement and majority (84.6%) of type I tumors showed no peritoneal deposits. This was found to be statistically significant (p value=0.003). On univariate analysis, we can say that when compared to patients without omental involvement, those with nodular omental involvement were 18.6 times more likely to acquire type II EOCs. (p value = 0.012). Compared to patients without omental involvement, those with diffuse omental involvement had an 11-fold increased risk of developing type II EOCs (p value = 0.044).

When compared to patients without peritoneal deposits, those with diffuse peritoneal deposits were 11.69 times more likely to acquire type II EOCs. (P value = 0.006). Jang et al., came to a similar conclusion in their study, where they found poorly differentiated epithelial ovarian carcinomas showed early and extensive tumor seeding into the peritoneal cavity.[9]

Type II epithelial ovarian tumors, because of their high grade, develop necrosis in the solid portion early and extensively as compared to type I tumors. This accounts for the fact that they tend to be hypoenhancing as compared to type I tumors. Also, the enhancement of tumors depends on multiple factors like microvascular density, permeability, the size of extracellular space, and the integrity of the vessel basement membrane. The frequency of Type II EOCs showing wash-out time density/intensity curves on DCE CT/MRI scans was higher than that of Type I EOCs. This can be explained by the factors that were discussed before. As a result, they would ordinarily exhibit a less pronounced enhancement than Type IEOCs would during the delayed enhancement.

In the present study, we observed that the majority (60.7%) of type II tumors showed hypoenhancement as compared to uterine myometrium on the venous phase, and 53.8% of type I tumors showed hyperenhancement. This was found to be statistically significant (p value = 0.026). On univariate analysis, we can say that Patients with isoenhancing tumors hada 0.12-fold decrease in the odds of developing type II EOCs compared to those with hypoenhancing tumors (p value=0.04). Similarly, Patients with hyperenhancing tumors had a 0.12-fold decrease in the odds of developing type II EOCs compared to those with hypoenhancing tumors (p value=0.021). Liu et al., also came to a similar conclusion in their study, where they evaluated enhancement of epithelial ovarian carcinoma using both CT and dynamic MRI.[3] The majority of type I tumors were moderately to avidly enhanced as compared to uterine myometrium.

The type II epithelial ovarian cancer is characterized by the presence of high-grade lesions, which have an early propensity to spread. Other results, such as involvement of the intestine and pleural effusion, were investigated in this study of ours. Observations of pleural effusion were made in 32% of type II EOC patients. On the other hand, no type I tumor was found to be related with a pleural effusion. Its statistical significance was shown by its P-value, whichwas 0.038. This is also a reflection of the fact that type II tumors almost always present at a more advanced stage than type I tumors.

On Chi-square analysis, the results showed that there was no statistically significant link between the presence of ascites, bowel involvement, thickened septa, mural nodule, calcifications, visceral metastasis, or local invasion and the histological grade of epithelial ovarian cancer. However, bowel involvement, visceral metastasis and local invasion frequency was higher among type II tumors as compared to type I tumors. Only CA-125 was statistically significant in the multivariate logistic regression model among the four most significant parameters we included (CA-125, Laterality, Enhancement and morphology). In the multivariable logistic regression model, no CT imaging parameter was found to be statistically significant. The overall multivariate model was found to be statistically significant with a p value of 0.005, and the pseudo-R square value was found to be 0.55. However, as far as the individual parameters were concerned, the CA-125 was foundto be statistically significant.

CONCLUSION

In conclusion, ovarian cancer is a form of malignancy that is quite worrisome and is associated with a dismal prognosis. The vast majority of patients are diagnosed at a more advanced stage, making it impossible to perform surgery that could cure them. Additionally, various histological subtypes of epithelial ovarian cancer react differently to treatment depending on the type of carcinoma. While type II EOC tumors better respond to treatment than type I EOC tumors, the former are more dangerous. Therefore, preoperative diagnosis of the subtype is required in order to prevent unnecessary treatment Imaging with MDCT has developed as a trustworthy technique for the early diagnosis of disease, for staging the disease, and for planning curative or palliative interventions that are appropriate. It is interesting to note that our research has uncovered differences in a number of

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CT imaging characteristics, and these differences aid in classifying histological subtypes of epithelial ovarian carcinoma into one of two overarching groups: type I and type II epithelial ovarian cancer. Ca-125 levels, tumor enhancement pattern, margins, laterality, morphology of tumor, size, extent of lymphadenopathy, pleural effusion, omental and peritoneal involvement pattern are all factors that can help to differentiate between the various histological subtypes of epithelial ovarian carcinoma. So, we can say that the combination of clinical and imaging markers allows for a likely accurate preoperative diagnosis of the EOC subtype, which holds significance in terms of patient prognosis and the development of a treatment plan.

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