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# Enhancing ovarian tumour evaluation with dynamic magnetic resonance imaging and diffusion weighted imaging

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**Abstract**
**Background and Aim:** Ovarian cancer has been a leading malignancy endangering women's health with high rate of worldwide prevalence. For the best possible outcome from treatment, the ovarian tumor must be accurately staged and characterized before surgery. To better characterize female pelvic masses, imaging techniques have developed significantly. This study aim is to evaluate the benefit of combining DCE MRI and DWI MRI with the conventional MRI in the ovarian cancers evaluation.
**Materials and Methods:** This prospective study was conducted at Tertiary Care Institute of India on 40 patients with ovarian cancers for the duration of 1 year. The use of a 1.5 Tesla MR scanner was used for MR imaging. The lesion morphological characteristics, such as its laterality, related size, and complexity, were assessed using standard MRI sequences. From quantitative data, maximum of all relative enhancements (MRE), Maximum enhancement (SImax), wash in rate (WIR) and wash out rate (WOR) were analyzed.
**Results:** The average size of the ovarian tumors according to conventional MRI was 10.40± 6.2 cm. The pathological tumor types (benign, malignant, and borderline) did not differ statistically significantly in terms of size, bilaterality of the lesion, or ancillary abnormalities on conventional MRI. The accuracy of predicting malignancy based on the ADC value and diffusion restriction is 90.9% and 81.8%, respectively. Between the three diagnostic techniques and the pathological diagnosis, there were statistically significant differences. However, compared to conventional based diagnosis, diffusion and perfusion-based diagnostic had greater AUC, sensitivity, specificity, and accuracy.
**Conclusion:** Ovarian neoplasia is one of the most common and lethal malignancy in female reproductive tract in older age group. The diagnostic accuracy of conventional MRI has significantly increased with the addition of DWI and DCE MR sequences. DCE MRI offers extra details on tumour vascularity.

**Keywords:** Maximum enhancement, maximum of all relative enhancements, MRI, Ovarian neoplasia

## Introduction
Ovarian tumors are common forms of neoplasia in women. These neoplasms have become increasingly important not only because of the large variety of neoplastic variants but more because they have gradually increased the mortality rate due to female genital cancers [1]. Ovarian neoplasms are common tumors in females encompassing 23% of all gynecologic tumors and are the most common gynecologic malignancy [2]. It is the 3rd commonest cause of death due to malignancies of the female genital tract in the western world [3].
Ovarian neoplasm is the most mysterious tumor in women concerning its histogenesis, clinical behavior, and malignant potentiality. Furthermore, no age group is immune to developing ovarian neoplasm and no age is exempted. Ovarian tumors show histological heterogenecity. The classification of ovarian tumors by World Health Organization is based on the histogenesis of ovary. They are largely divided in to epithelial cell tumors, germ cell tumors, and sex cord stromal cell tumors. In most of the population-based cancer registries in India, ovarian cancer is the third leading site of cancer among women trailing behind cervix and breast cancer. The age adjusted incidence rates of ovarian cancer vary between 5.4 and 8 per 100,000 populations in different parts of the country [4, 5].
Whether an ovarian tumor is benign, borderline, or malignant, the treatment plan will vary. Consequently, preoperative characterization is important. This is particularly important for young women who should be provided conservative surgery to protect their fertility. Despite the algorithmic existence that consider clinical symptoms, CA125 (cancer antigen) serum

determination and malignancy-related ultrasonographic indications. Preoperative characterization is still challenging, particularly for complicated lesions, and up to 25% of ovarian tumors are ultrasound-indeterminate and need further imaging. MRI is a powerful tool for problem-solving and can provide information on surgical planning without exposing users to radiation. Malignant ovarian tumors are diagnosed with MRI, which can locate huge solid masses. Previous research has shown that MRI technology can be used for preoperative diagnosis, accurately classifying ovarian tumors as benign or cancerous with a 91% accuracy rate. Dynamic contrast enhancement (DCE-MRI) offers superior functional imaging capabilities. It becomes a common diagnostic device for assessing the female pelvic. The tumor vasculature inside a tumor microenvironment is also described using multiparametric estimations of permeability and perfusion. Malignant tumors have a larger circulatory system than benign tumors, thus they contrast more quickly and have stronger signals [6-9].

DWI is an MRI sequence that enhances peritoneal implant detection and delineation both during initial staging and follow-up. Additionally, it aids in distinguishing benign from malignant lesions and enhances the contrast among lesions and surrounding tissues. Moreover, DWI offers quantitative data on tissue cellularity that can be used to distinguish between living tumors and changes brought on by treatment. Cancers have displayed decreased ADC (Apparent Diffusion Coefficient) values when DWI is applied in gynecologic applications. ADC levels rise in carcinomas that react to radiation therapy, making it a useful biomarker for treatment response and for assessing recurrence and multi-focal tumors [10, 11].

This study aim is to evaluate the benefit of combining DCE MRI and DWI MRI with the conventional MRI in the ovarian cancers evaluation.

## Material and Methods

This prospective study was conducted at Tertiary Care Institute of India on 40 patients with ovarian cancers for the duration of 1 year. All participants in this study were given their signed consent after our institution's ethical committee gave its approval. In the current study, patients with complicated ovarian related lesions, cystic lesions with solid vegetations, thick septa, or components of soft tissue, solid ovarian lesions, two adnexal lesions either suspicious or solid lesions were all considered. While we rolled out patients with 1) uncomplicated cystic ovarian lesions or 2) just fatty ovarian lesions. Individuals with impaired renal function, general MRI contraindications such as the presence of pacemakers or mechanical clips, or patients with claustrophobia were also excluded from the study. Every patient has through a thorough history taking process, pelvic ultrasonography (trans-abdominal and/or transvaginal), MRI evaluation, and histopathological evaluation.

### MRI protocol

The use of a 1.5 Tesla MR scanner was used for MR imaging. All patients underwent a pelvic phased array coil scan while they were lying flat. Three common MRI sequences, axial, sagittal, and coronal T2WIs, were run on the female pelvis. Before administering the contrast agent, DWI was captured in the axial plane using a single shot echo-planar imaging sequence with the following parameters: b values (0, 800, 1000), TR/TE (2871/78), Slice thickness (5 mm), Gap (1.5 mm), FOV (RL 375 mm, AP 312 mm, FH 161 mm), and reconstruction matrix. High resolution isotropic volumetric examination was used for MR perfusion. Most frequently, an axial plane was selected, and the procedure was carried out on the appropriate plane that showed both the lesion and the myometrium on the same image.

Gadolinium chelate was administered at a dose of 0.2 ml per kilogramme of body weight using a power injector at a rate of 2 ml/sec. Next, 20 milliliters of normal saline were injected into the tubing to flush it. Images were captured one after the other every 14 seconds for a total of 420 seconds, start 14 seconds (first phase) before the bolus injection. 40 consecutive slices of 2 mm thickness were collected.

### Interpretation of images

The captured images were transformed.

### Conventional sequences analysis

The lesion morphological characteristics, such as its laterality, related size, and complexity, were assessed using standard MRI sequences.

### Analysis of DWI

#### Qualitative analysis

While most malignant masses have high intensity of signal on DWI and low signal in the related ADC maps, the majority of benign masses have low intensity of signal on DWI and high signal in the associated ADC maps (facilitated diffusion) (limited diffusion).

### Quantitative analysis

The ROI was manually selected on the solid and cystic parts of the tumors after the ADC map was created, and the workstation then automatically computed the ROI to get the ADC calculated values.

### Dynamic contrast enhancement (DCE) analysis

On the DCE MR sequence, two areas of interest were set on the exterior myometrium and the ovarian mass's solid tissue that showed the greatest contrast. Using a colored workstation-generated map with the highest level of improvement, the most enhanced solid part was identified. The classification of the solid tissue augmentation was categorized using a previously defined time-signal intensity curve:

1. A type 1 curve was defined as a steady rise in the intensity of the solid tissue signal without a distinctly marked shoulder.
2. A type 2 curve was known as an early, modest rise in the signal strength of solid tissue in comparison to the myometrium, succeeded by a plateau.
3. A type 3 curve was characterized by an early elevation in the solid tissue related signal intensity that was steeper than the myometrium's

From quantitative data, maximum of all relative enhancements (MRE), Maximum enhancement (SImax), wash in rate (WIR) and wash out rate (WOR) were analyzed.

### Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2019) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

## Results

The median age was 40.25± 16.10 years, with a range of 10 to 70. 26 patients (65%) were premenopausal, compared to 14 patients (35%) who were post-menopausal. Pelvic pain was the primary presenting symptom in 25 instances.

### Conventional MRI analysis

The average size of the ovarian tumors according to conventional MRI was 10.40± 6.2 cm. Out of the 40 instances, 3 cases (7.5%) only revealed bilateral disease, whereas the remaining 37 cases (92.5%) revealed unilateral pathology. The pathological tumor types (benign, malignant, and borderline) did not differ statistically significantly in terms of size, bilaterality of the lesion, or ancillary abnormalities on conventional MRI.

### Diffusion weight images MRI analysis

DWI MRI revealed diffusion restriction in 32 instances (80%) and facilitated diffusion in 8 cases (20%). the ADC value range with a mean of 1.2±0.5. Regarding diffusion limitation and ADC value, there was a difference that was statistically highly significant among the pathogenic forms of tumors. ($p \leq 0.05$)

The ROC curve involved area under the curve (AUC) is used to predict malignancy based on DWI was higher for the ADC value than for diffusion restriction (Table 1). The accuracy of predicting malignancy based on the ADC value and diffusion restriction is 90.9% and 81.8%, respectively.

### Dynamic contrast enhanced MRI analysis

From the 40 cases, type 1 curves were present in 13 (32%.5) cases, type 2 curves in 12 (30%) cases, and type 3 curves in 15 (37.5%) cases. On histological diagnosis, type 1 curve cases all presented benign instances. The pathogenic types of the tumors and the curve type differed statistically significantly. Curve types 2 and 3 accurately predict the chance of malignancy with 95.6% accuracies, 89% sensitivity, and 92.5% specificity. For curves 2 or 3, the negative predictive value is 100%. (Table 2). Regarding MRE%, there was a difference of no statistical significance found among the pathological diagnoses. While the pathological diagnosis of SI max, WIR, and WOR showed statistically significant differences. To assess the AUC for each distinct perfusion parameter, a ROC curve was built. When employing WOR, SI max, and then WIR, the least overlap and greatest AUC were seen. This offers the most accurate enhancing information for identifying benign from borderline/cancerous tumors. 100% sensitivity, specificity, NPV, PPV, and accuracy were generated by using the WOR>6 cutoff value. (Table 2)

### Relation of conventional, diffusion, perfusion and combined diagnosis with pathological results

In ROC curve analysis, malignancy was predicted based on conventionally based diagnosis., diffusion-based diagnosis and perfusion-based diagnosis. Between the three diagnostic techniques and the pathological diagnosis, there were statistically significant differences. However, compared to conventional based diagnosis, diffusion and perfusion-based diagnostic had greater AUC, sensitivity, specificity, and accuracy. Both perfusion- and diffusion-based diagnoses use the same values on the ROC curve.

**Table 1:** ROC curve analysis for prediction of malignancy according to diffusion restriction and ADC value

| Variable | Diffusion restriction | ADC value |
|---|---|---|
| Optimal cutoff point | Restricted | ≤ 1 |
| AUC (Area Under Curve) | 0.78 | 0.96 |
| 95% CI (Confidence Interval) | 0.61-0.88 | 0.87-0.99 |
| Sensitivity | 100 | 100 |
| Specificity | 55.60 | 77.10 |
| PPV (Positive Predictive Value) | 76.1 | 89 |
| NPV (Negative Predicative Value) | 100 | 93.8 |
| Accuracy | 81.8 | 90.9 |

**Table 2:** ROC curve analysis for prediction of malignancy according to curve type and semi-quantitative assessment of perfusion

| Variable | Curve type | | SI max | WIR | WOR |
|---|---|---|---|---|---|
| Optimal cutoff point | 2 or 3 | 3 | >1284 | >17.8 | >6 |
| AUC (Area Under Curve) | 0.95 | | 0.98 | 0.94 | 1 |
| 95% CI (Confidence Interval) | 0.84-0.99 | | 0.88-1 | 0.82-0.99 | 0.92-1 |
| Sensitivity | 100 | | 57 | 100 | 91 |
| Specificity | 89 | | 95 | 94 | 100 |
| PPV (Positive Predictive Value) | 92.5 | | 93.5 | 96.4 | 96 |
| NPV (Negative Predicative Value) | 100 | | 61 | 100 | 89.7 |
| Accuracy | 95.6 | | 72 | 97.8 | 93.10 |

## Discussion

Recently, functional techniques like MR dynamic contrast enhanced imaging and MR diffusion have been put to the test to boost MRI's sensitivity, specificity, and accuracy in order to increase diagnostic confidence [12]. This study's objective is to assess the additional value of DCE-based perfusion and DWI MRI over traditional MRI imaging for characterizing ovarian cancers.

In this study, there was a difference of no statistical significance among borderline epithelial ovarian tumors and malignant tumors of epithelial ovarian regarding their appearance on DWI as well as the mean ADC values. In a different study by Zhao *et al*. 2018, the effectiveness of the ADC value in separating benign from malignant sex cord stromal ovarian tumors was examined in 85 individuals with ovarian tumors [13]. They presume that the benign ovarian tumors had an ADC mean value of about 1.28 0.23 10-3 mm2/s while the malignant ovarian tumors had an ADC mean value of about 0.86 0.17 10-3 mm2/s. Compared to our study, the measurements for malignant lesions were very close to our measurements while the measurements for benign lesions were lower than our measurements. This can be explained by the difference in sample size [13]. Mclemore *et al* reported ovarian cancer symptom index (OCSI) consisting of bloating, pelvic or abdominal pain, feeling full quickly and urinary symptoms of urgency and frequency [14]. If any of these symptoms were reported >12 times in one month, OCSI was positive with sensitivity of 56.7% to detect early-stage disease and 79.5% for detection of advanced stage disease. Post-menopausal bleeding is another symptom which warrants screening as it indicates presence of available circulating estrogen and points to granulosa cell tumor. Our findings are comparable to those of Hai-Ming Li *et al*. who found that the TIC type was effective at differentiating between malignant and benign ovarian tumors, nonetheless, there was a substantial overlap among the borderline and malignant tumors [15].

According to the proposed pathophysiology of tumor growth idea, tumors must stimulate angiogenesis in order to proliferate. The vessels are highly permeable to a variety of macromolecules due to the wide gaps among the endothelial cells, the endothelium, and also the basement membranes, as well as among the basement membranes and the angiogenetic arteries involved pericytes produced by tumors. DCE-MRI can use these characteristics to its advantage. Differential enhancement is created when MR contrast chemicals, which leak slowly through healthy blood arteries, flow through tumor vessels more quickly. The tumor microcirculation can be functionally examined because of how quickly the contrast is washed in and out [16]. In 2003, Sohaib *et al.*[17] investigated the percentage rise in the intensity of the signals of the solid parts of adnexal masses at 60 sec (early) and 120 sec (late) of enhancement. They discovered that, when compared to benign lesions, malignant lesions exhibit higher enhancement during the early enhancement phase than the late enhancement phase [17].

Our investigation's threshold value for SI max was >1285. (Malignant tumors are those whose SI max is greater than that value.). 100% sensitivity and 94% specificity were measured. Although those measurements conflict with those results, Dilks *et al*. suggested a threshold value of >250 for malignancy prediction with a 100% sensitivity and specificity [18]. WIR was cut off at >9.5 by Bernardin *et al*. (Malignant lesions are those that have a WIR of 9.5 or higher). The cut off value of ourstudy (>17.9) was greater than that value, which is also comprehensible given the study's unequal distribution of cases and larger-than-average proportion of individuals with hyper vascular characteristics.

The limitation of the study is that present study is a single institution-based study with a small group. Results of present study may not reflect the actual pattern and age distribution; a large multicentric approach is needed to compare present study results. The studies also involves a small case number having epithelial borderline ovarian tumors. Young patients of reproductive age make up the bulk of epithelial borderline tumor cases; therefore, to preserve fertility, a cautious surgical approach rather than a radical one may be indicated. Additional research including more samples and better pathological distribution is advised. We should mention that our study excluded other nonovarian adnexal lesions as tubo-ovarian abscess which is not rare in clinical practice. Addition of those cases to the study will be valuable.

## Conclusion

Ovarian neoplasia is one of the most common and lethal malignancy in female reproductive tract in older age group. The diagnostic accuracy of conventional MRI has significantly increased with the addition of DWI and DCE MR sequences. DCE MRI offers extra details on tumour vascularity.

## Conflict of interest

No! Conflict of interest is found elsewhere considering this work.

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