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Analysing Two Bulky Eggs In An Eagles Nest: Analysis Of Unenhanced & Contrast Enhanced Computed Tomography Study Of Adnexa To Reduce Radiation Exposure In Adnexal Pathologies.

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Abstract: *The primary goal of imaging study is to detect an abnormality, then characterize whether malignant or benign.Various modalities have been established,each having their own pros and cons.When it comes to gynecological imaging ,USG has dominated the imaging studies of female pelvis due to its easy accessibility, feasibility, most importantly it has limited radiation hazards, but has its own limitations.CT,a relatively new approach uses multidetector computed tomography (MDCT), which allows thinner sections, faster imaging, and good spatial resolution, has led to its more common use for further characterization of adnexal mass and staging work-up of ovarian malignancy [2-4]. CT protocol for the evaluation of abdomen and pelvis has even adopted multiphase CT scans, including scanning before and after contrast administration . Considering the dose-multiplication effect of extra phase, it is certain that inappropriate multiphase CT can be an important source of excess radiation exposure [5].*
The purpose of this study is to compare the diagnostic efficacy and radiation dose of contrast-enhanced CT (CECT) alone with that of combined unenhanced and enhanced CT (UE + CECT), for the assessment of adnexal mass.
Keywords: *computed TOMOGRAPHY(CT),UNENHANCED(UE),CONTRAST ENHANCED (CE)*

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I. Materials And Methods

This retrospective study was carried out at a tertiary care hospital -Medical College and Hospital, Kolkata , after the study protocol was approved by the Ethics Committee. Diagnosed cases of ovarian cancer by usg/histopathology referred for CT scan evaluation from gynecology/ Radiotherapy department were considered. The study was carried out from November 2017 to december 2018 and during this period 73 consecutive patients aged 20 to 80 years who gave written informed consent were included in this study. A total of 84 patients who did not give consent and did not turn up during the follow up were excluded.

Patients underwent contrast enhanced CT of abdomen and pelvis on 16 slice multi-detector CT scanner (Siemens) as per the standard protocol 11 ,120 kV and 160 mAs using Iohexol .Scans covered the thoracic cavity to the symphysis pubis. Delayed scans were performed in cases with suspicion of bladder involvement.

The indications for CT examination of all patients were as follows: evaluation of known ovarian tumor or adnexal mass (n = 43), evaluation of pelvic mass of unknown origin (n = 2), large amount of ascites (n = 2), lower abdominal or pelvic pain (n = 23), staging of non-ovarian malignancy (n = 3). Non-ovarian malignancy included cervix cancer (n = 2), endometrial cancer (n = 1).

Images obtained were analyzed by two experienced radiologists.

II. Imaging Analysis

The CT images were reviewed retrospectively on a picture archiving and communication system workstation by two radiologists with years of experience, respectively, in genitourinary and abdominal imaging independently. The readers were aware that the patients had undergone surgery/chemoradiation for adnexal mass, but they were blinded to the laterality of the surgery and any other clinical, pathologic, or radiologic findings of all patients. Both readers independently reviewed CECT images alone and UE + CECT images. The two data sets in each patient were randomly interpreted in different sessions at 4-week intervals. In each patient, both adnexa were evaluated for the presence of mass and the presence or absence of a mass in each adnexa was recorded. If an adnexal mass was regarded as being present, the size of the largest dimension at transverse scan was measured.

The readers also assessed the adnexal mass following imaging findings suggestive of malignant adnexal mass[1,3,4,6] : mass size larger than 4 cm, heterogeneity for a solid lesion, multilocularity (> 3 locules), irregular and thickened (> 3 mm) cystic septations or walls, and the presence of internal vegetations for a cystic lesion. In addition, the presence of ancillary imaging findings such as ascites, peritoneal implants, and pelvic lymphadenopathy, were recorded [1,3]. Each reader gave an overall impression of the likelihood of malignancy, using a rating scale of 1 to 5 (1, definitely benign; 2, probably benign; 3, indeterminate; 4, probably malignant; 5, definitely malignant).

III. Statistical Analysis

Descriptive variables were reported as the mean and standard deviation, and categorical variables were reported as frequencies and percentages. The two-tailed paired t test with exact p values was used for comparison of the radiation dose between ECT images alone and UE + ECT images. The area under the receiver operating characteristic curves (AUC) with confidence intervals (CIs) was estimated for reader performance. The sensitivity and specificity were estimated with a score of 3 or greater as positive for malignancy. The AUC for ECT images alone and UE + ECT images was compared using a nonparametric method proposed by Obuchowski[7]. Differences with p values of 0.05 or less were considered statistically significant. Inter-reader agreement was assessed by using weighted or unweighted κ statistics with quadratic weights for the detection of adnexal mass or for the evaluation of adnexal malignancy. Weighted and unweighted κ statistics were interpreted using the following scale: slight agreement, < 0.20; fair agreement, 0.21-0.40; moderate agreement, 0.41-0.60; substantial agreement, 0.61-0.80; and almost perfect agreement, 0.81-1.0 [8]. Ninety-five percent CIs were reported for the estimated κ statistics.

IV. Results

Histopathologic Results

We found 89 adnexal masses in 73 patients; 67 masses were benign and 22 masses were malignant. 16 underwent bilateral salpingo-oophorectomy and 57 patients underwent unilateral salpingo-oophorectomy. The histopathologic diagnoses of the 89 masses are detailed in the table below. The most common malignant tumor was endometrioid adenocarcinoma and the most common benign tumor was teratoma

BENIGN LESIONS	NO. OF CASES
TERATOMA	22
ENDOMETRIOMA	12
MUCINOUS CYSTADENOMA	9
CORPOUS LUTEAL CYST	5
SEROUS CYSTADENOMA	5
PARATUBAL CYST	4
FOLLICULAR CYST	3
HYDROSALPINX	2
STRUMA OVARII	2
FIBROMA	1
PSEUDO CYST	1
TUBO OVARIAN ABSCESS	1

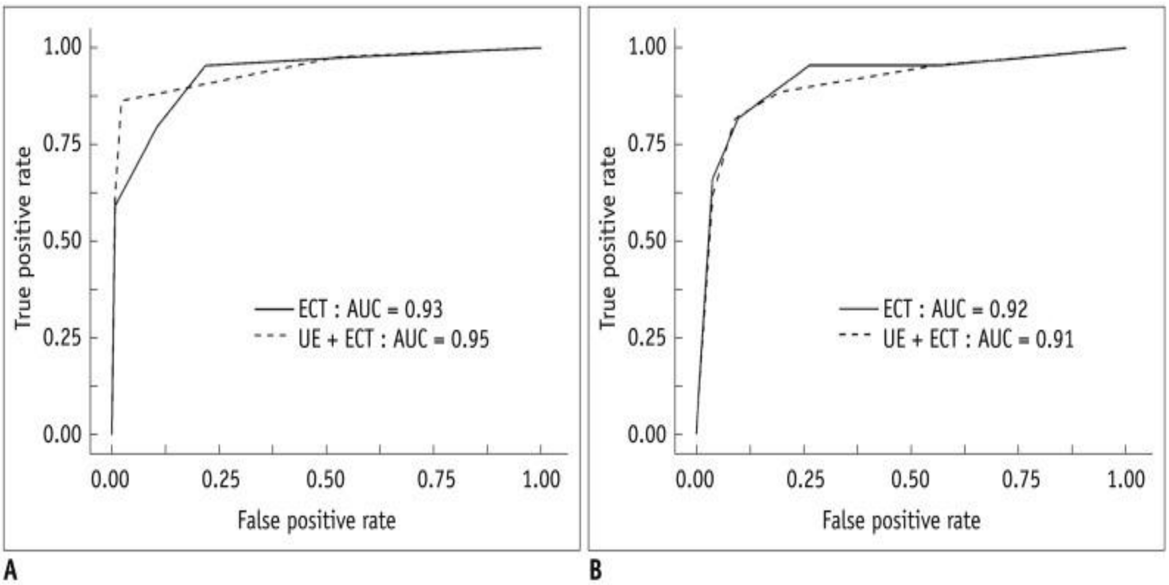
MALIGNANT LESIONS	NO. OF CASES
ENDOMETRIOID ADENOCARCINOMA	5
CLEAR CELL CARCINOMA	3
SEROUS CARCINOMA	2
SEROUS PAPILLARY CARCINOMA	2
BORDERLINE SEROUS TUMOR	1
BORDERLINE SEROMUCINOUS TUMOR	1
BORDERLINE SEROUS CYSTADENOMA	2
BORDERLINE MUCINOUS TUMOR	1
LYMPHOMA	0
KRUKENBERG TUMOR	1
SMALL CELL CARCINOMA	1
DYSGERMINOMA	1
GRANULOSA CELL TUMOR	1
FIBROSARCOMA	1
FALLOPIAN TUBE ADENOCARCINOMA	0

Lesion Detection

For detecting the presence of an adnexal mass, reader 1 detected 87 of 89 adnexal masses on ECT images alone and 88 of 89 adnexal masses on UE + CECT images. Reader 2 detected 83 of 89 adnexal masses on ECT images alone and 88 of 89 adnexal masses on UE + CECT images. There was no statistical difference in the detection rate between UE +CECT images and CECT images alone for both readers ($p > 0.05$). Readers 1 or 2 failed to detect 12 adnexal masses on CECT images alone. The benign adnexal masses that were not detected on CECT images alone (n = 8) were mucinous cystadenoma (n = 3), endometrioma (n = 2), teratoma (n = 1), paratubal cyst (n = 1), and fibroma (n = 1). The malignant adnexal masses that were not detected on ECT images alone (n = 4) were serous carcinoma (n = 1), clear cell carcinoma (n = 1), lymphoma (n = 1), and borderline seromucinous tumor (n = 1). Both readers failed to detect 1 adnexal mass on UE + CECT images, which was clear cell carcinoma. The patient with adnexal mass not detected by both readers had bilateral ovarian malignancies, where an obvious mass was preoperatively identified in one adnexa, whereas due to the very small size of the tumor in the other adnexa, it was only confirmed based on pathology. Inter-readeragreement for the detection of adnexal mass was moderate, with unweighted κ statistics of 0.54 for both ECT images alone and UE + ECT images.

Lesion Characterization

For the detection of malignant adnexal mass, the AUC of reader 1 was 0.94 (95% CI: 0.89-0.97) on CECT images alone and 0.95 (95% CI: 0.90-0.97) on UE + CECT images . The AUC of reader 2 was 0.92 (95% CI: 0.87-0.95) on ECT images alone and 0.91 (95% CI: 0.85-0.94) on UE +CECT images . Both readers had no significantly greater AUC for UE + CECT images than for CECT images alone . Sensitivity, specificity, positive and negative predictive values of ECT images alone and UE + CECT images for the detection of malignant adnexal mass are shown in the table below. Inter-reader agreement for the detection of malignant adnexal mass was moderate, with weighted κ statistics of 0.60 for ECT images alone, and 0.59 for UE + CECT images.

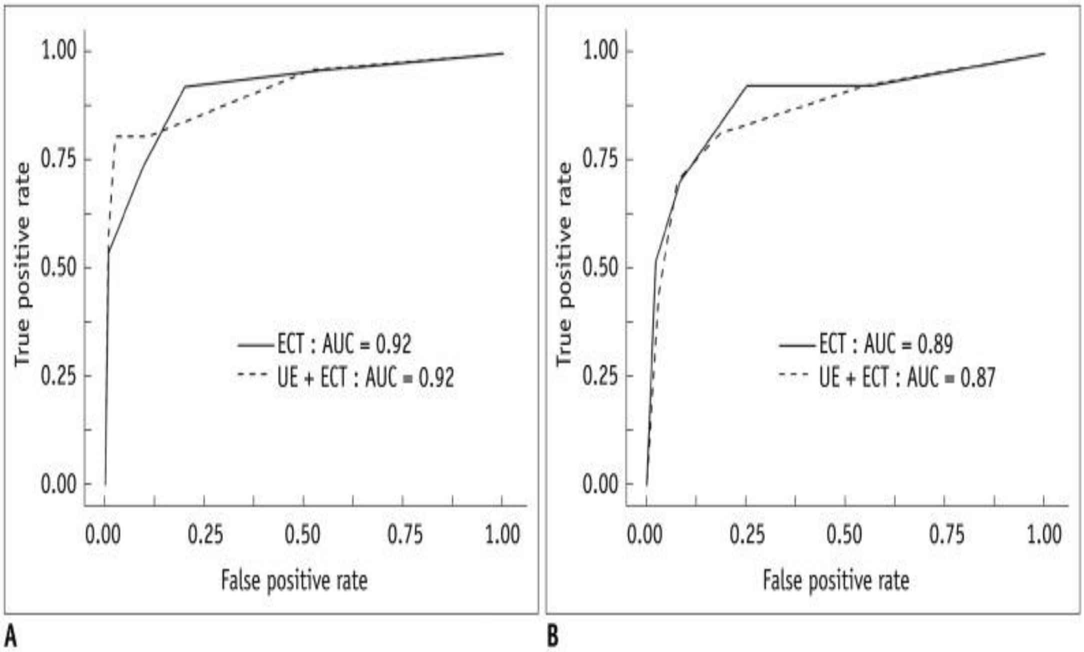


Diagnostic Performance of 2 Readers for Detection of Malignant Adnexal Mass

	Reader 1			Reader 2		
	ECT	UE + ECT	P	ECT	UE + ECT	P
AUC	0.93 (0.89-0.97)	0.95 (0.90-0.97)	0.50	0.92 (0.87-0.95)	0.91 (0.85-0.94)	0.30
Sensitivity	0.95 (0.84-0.99)	0.89 (0.76-0.96)	0.25	0.95 (0.84-0.99)	0.89 (0.76-0.96)	0.25
Specificity	0.78 (0.70-0.84)	0.87 (0.80-0.92)	0.006	0.74 (0.66-0.80)	0.80 (0.73-0.86)	0.007
Positive predictive value	0.59 (0.48-0.70)	0.70 (0.57-0.80)	0.27	0.55 (0.43-0.65)	0.60 (0.48-0.71)	0.67
Negative predictive value	0.98 (0.93-0.99)	0.96 (0.90-0.98)	0.62	0.98 (0.93-0.99)	0.96 (0.90-0.98)	0.66

Note.- Data in parentheses are 95% CIs. AUC = area under curve, ECT = enhanced CT, UE + ECT = combined unenhanced and enhanced CT, CIs = confidence intervals

In 120 patients, reader 1 did not identify any ancillary findings as ascites, peritoneal implants, and pelvic lymphadenopathy on UE + ECT images. In 127 patients, reader 2 did not identify any ancillary findings on UE + ECT images. The κ statistic was 0.58, indicating a moderate agreement between readers in identifying patients without ancillary findings. For assessing adnexal malignancy in patients without ancillary findings, the AUC of reader 1 on ECT images alone was 0.92 (95% CI: 0.86-0.96), the same value as that on UE + ECT images . The AUC of reader 2 was 0.89 (95% CI: 0.83-0.93) on ECT images alone and 0.87 (95% CI: 0.80-0.92) on UE + ECT images . Sensitivity, specificity, positive and negative predictive values of ECT images alone, and UE + ECT images, for the detection of malignant adnexal mass without ancillary findings are shown in the table below..



Diagnostic Performance of 2 Readers for Detection of Malignant Adnexal Mass without Ancillary Findings

	Reader 1			Reader 2		
	ECT	UE + ECT	P	ECT	UE + ECT	P
AUC	0.92 (0.86-0.96)	0.92 (0.86-0.96)	0.98	0.89 (0.83-0.93)	0.87 (0.80-0.92)	0.19
Sensitivity	0.92 (0.75-0.99)	0.81 (0.62-0.92)	0.25	0.93 (0.76-0.99)	0.81 (0.63-0.92)	0.25
Specificity	0.80 (0.72-0.86)	0.89 (0.82-0.94)	0.006	0.75 (0.67-0.82)	0.82 (0.74-0.87)	0.008
Positive predictive value	0.50 (0.36-0.63)	0.62 (0.45-0.76)	0.39	0.43 (0.31-0.56)	0.48 (0.34-0.62)	0.76
Negative predictive value	0.98 (0.92-0.99)	0.96 (0.90-0.98)	0.66	0.98 (0.93-0.99)	0.96 (0.90-0.99)	0.66

Radiation Dose

In the patients that underwent CT examination in the 16-channel MDCT scanner (LightSpeed Pro 16 CT) (n = 49), the mean $CTDI_{vol}$ was 12.5 ± 2.7 mGy (95% CI: 11.3-13.7) and the mean DLP was 627.3 ± 149.1 mGy·cm (95% CI: 562.8-691.7) of ECT scan alone, whereas, the mean $CTDI_{vol}$ was 22.5 ± 2.7 mGy (95% CI: 21.3-23.6) and the mean DLP was 943.9 ± 158.4 mGy·cm (95% CI: 562.8-691.7) of UE + ECT scan. Mean $CTDI_{vol}$ and DLP of ECT scan alone was significantly lower than those of UE + ECT scan ($p < 0.0001$). In the patients that underwent CT examination in the 64-channel MDCT scanner (LightSpeed VCT XT) (n = 97). The mean $CTDI_{vol}$ was 12.6 ± 2.0 mGy (95% CI: 12.2-13.2) and the mean DLP was 645.8 ± 133.9 mGy·cm (95% CI: 613.7-678.0) of ECT scan alone, whereas, the mean $CTDI_{vol}$ was 21.2 ± 2.6 mGy (95% CI: 20.6-21.9) and the mean DLP was 916.8 ± 159.6 mGy·cm (95% CI: 878.5-955.2) of UE + ECT scan. Mean $CTDI_{vol}$ and DLP of ECT scan alone was also significantly lower than those of UE + ECT scan ($p < 0.0001$). In the overall comparison of mean $CTDI_{vol}$ and DLP between ECT scan alone and UE + ECT scan, irrespective of CT scanner, mean

$CTDI_{vol}$ (12.6 ± 2.2 mGy; 95% CI: 12.2-13.1) and DLP (641.2 ± 137.2 mGy; 95% CI: 612.8-669.6) of ECT scan alone was significantly lower than mean $CTDI_{vol}$(21.5 ± 2.7 mGy; 95% CI: 21.0-22.1) and DLP (923.6 ± 158.8 mGy; 95% CI: 890.7-956.5) of UE + ECT scan ($p < 0.0001$).

V. Discussion

Several studies have suggested that contrast-enhanced MDCT can be highly accurate in the detection and characterization of adnexal mass, and can have an important role in the diagnosis of malignant ovarian tumor[2-4,9,10]. Zhang et al. reported that MDCT shows a sensitivity of 86-90% and specificity of 77-84% for differentiating benign and malignant adnexal masses. Tsili et al. also described that MDCT can accurately categorize adnexal mass into benign and malignant for 89-93% of cases. Our result demonstrated that ECT alone has a sensitivity of 92-95%, and a specificity of 74-80% for the diagnosis of malignant adnexal mass, which is comparable to the results of previous literature.

Since widespread acceptance of MDCT for the scanning of abdomen and pelvis, various multiphase CT imaging protocol have been used[11-13]. Although general guidelines recommend that pelvis CT with or without contrast is usually inappropriate for clinically suspected adnexal mass, due to the associated radiation hazard [14], some institutions have used a UE + ECT protocol for the evaluation of adnexal mass or lower abdominal pain in routine clinical practice[15-17]. In these circumstances, as Guite et al. suggested, un-indicated multiphase CT scans can add excess radiation dose, the clinical usefulness of added unenhanced CT images for the evaluation of adnexal mass need to be verified. This study is the first comparative study about diagnostic performance for the evaluation of adnexal mass between ECT images alone and UE + ECT images. It was obvious that UE + ECT scan increases 58.6% of $CTDI_{vol}$ and 69.4% of DLP, when compared with ECT scan alone. Otherwise, in terms of detection and characterization of adnexal mass, our results demonstrated ECT images alone can provide comparable diagnostic information to UE + ECT images. Even in the case of adnexal mass without ascites, peritoneal implants, and pelvic lymphadenopathy, which can indicate the early stage of ovarian cancer, unenhanced CT images also could not add significant diagnostic value to enhanced CT images.

There were a few limitations to our study. First, our study, as a retrospective study, may have selection and verification biases, especially in the proportion and stage of adnexal malignancy, which mainly depend on the status of the institution, community, and/or referral hospital. Notably, in the advanced stage of adnexal malignancy, the characterization of adnexal masses could be affected by extra-adnexal findings as ascites, peritoneal implants, and pelvic lymphadenopathy. Second, non-uniform CT scanners were used in the study, although this reflects actual clinical practice.

VI. Conclusion

In summary, using unenhanced CT scan in addition to contrast-enhanced CT scan did not improve the detection of adnexal malignancy, but increased radiation exposure.

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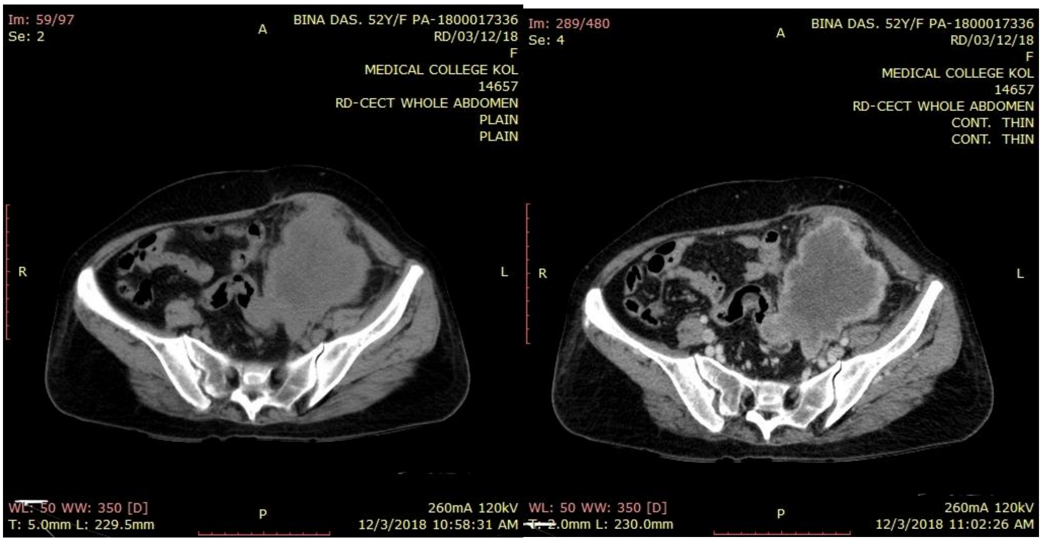
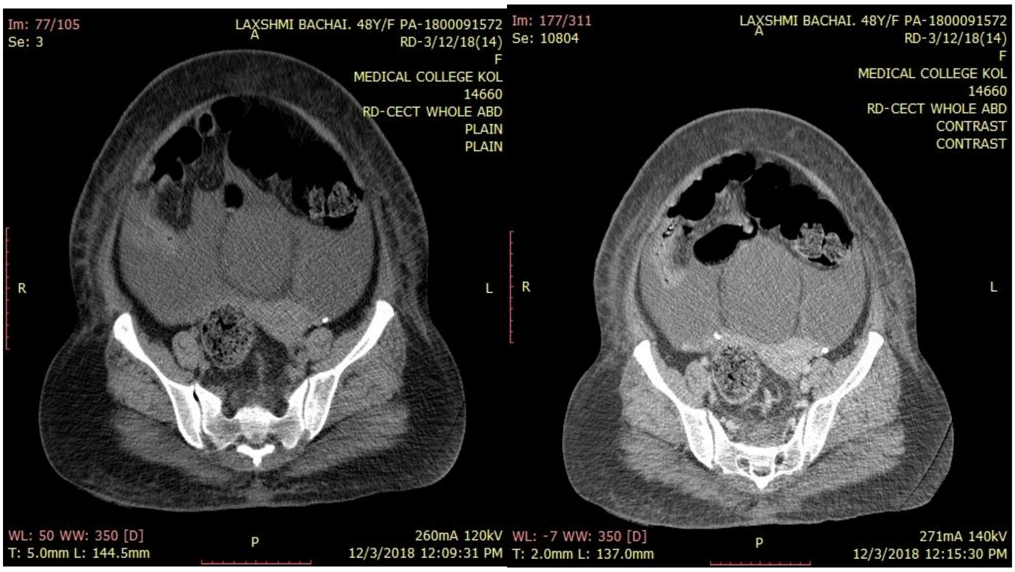


Unenhanced contrast enhanced

A large cystic SOL with enhancing walls and solid parts with lobulated margin in left pelvic region.



Unenhanced contrast enhanced

Thin walled cyst in bilateral ovary

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