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Comparison of Two-Dimensional IOTA Simple Rules and Three-Dimensional Ultrasonography in Preoperative Assessment of Adnexal Masses

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Abstract

Objective Accurate preoperative characterization of adnexal masses is essential for optimal patient management. Two-dimensional ultrasonography (USG) based "International Ovarian Tumuor Analysis Simple Rules (IOTA-SR)" are used primarily in clinical practice. Three-dimensional (3D) USG is an emerging modality. The authors conducted this study to compare the performance of 3D USG with IOTA-SR for preoperative differentiation of benign and malignant adnexal masses.

Methods This prospective observational study recruited 84 patients with adnexal masses undergoing surgical management. IOTA-SR and 3D USG with power Doppler examination were applied to characterize the masses and correlated with histopathology. Logistic regression analysis defined individual 2D and 3D USG parameters' significance in predicting malignancy. The receiver operating characteristic (ROC) curve was plotted for significant variables, and area under the curves (AUCs) with cut-off values were calculated using the Youden index.

Results Out of the 84 adnexal masses, 41 were benign and 43 were malignant. IOTA-SR were conclusive in 88.1% (74/84) cases, with a sensitivity of 83.78% (95% confidence interval [CI]: 67.99–93.81%) and specificity of 89.19% (95% CI: 74.58–96.97%). The sensitivity and specificity of 3D USG with power Doppler were 84% and 88%, respectively, with an AUC of 0.96 (95% CI: 0.92–0.99). Ten cases were inconclusive by the IOTA-SR, and 3D USG could further correctly differentiate four of these cases.

Conclusion The diagnostic performance of both techniques is comparable. With good diagnostic performance and easy applicability, IOTA-SR remain the standard of care. 3D USG, although a more objective assessment, requires further validation and standardization.

Keywords
- benign adnexal mass
- International Ovarian Tumour Analysis
- IOTA simple rules
- malignant adnexal mass
- three-dimensional ultrasound
- power Doppler

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Introduction

Accurate preoperative differentiation of benign and malignant adnexal masses is essential to guide timely referral and personalized surgical planning. Clinicians use demographic parameters, tumor markers, and ultrasound predictors to classify adnexal masses in clinical practice.[1] Evidence-based, validated International Ovarian Tumour Analysis Simple Rules (IOTA-SR) are the most widely utilized ultrasonography (USG) predictors in clinical practice, owing to their simplicity and excellent performance. According to the original and subsequent validation studies by the IOTA group, these rules could be applied in 76 to 78% of adnexal masses with a sensitivity and specificity of 92 to 94% and 91 to 95%, respectively.[2,3] However, IOTA-SR is limited by being inconclusive in a fair proportion of cases, and these cases need further evaluation.[2,3]

The recently introduced three-dimensional (3D) power Doppler ultrasound offers the potential for volume measurements and quantification of echogenicity and blood flow in the whole target tissue, in contrast to the two-dimensional (2D) USG, which can assess the vascularization in only one subjectively chosen 2D plane.[4] Additionally, it is highly reproducible between sonographers.[5] The role of 3D USG in gynecologic oncology has yet to be proven and needs to be explored further. It is available only sometimes in daily clinical practice. Before introducing this technique in routine use, it is crucial to know whether 3D USG has added value for detecting malignancy over the widely practiced 2D ultrasound-based simple rules. We conducted the present study to evaluate and compare the diagnostic accuracy of 2D USG-based IOTA-SR and 3D USG for preoperative characterization of adnexal masses.

Methods

A prospective observational study was conducted in the Department of Obstetrics and Gynaecology and Department of Radiodiagnosis of All India Institute of Medical Sciences, New Delhi, India, from January 2019 to August 2020. Women older than 18 years with adnexal mass planned for surgical management were recruited in the study after signing an informed consent and institutional ethical clearance (IECPG-478/29.11.2017). We chose the mass with a more complex morphology or the larger size in patients with bilateral masses. Pregnant women with an adnexal mass, patients who failed to undergo surgery within 30 days of ultrasound examination, neoadjuvant chemotherapy recipients, and patients with histopathologically confirmed diagnosis before surgery were excluded from the study. Baseline characteristics and tumor marker values were recorded. Two investigators conducted 2D and 3D USG with power Doppler examinations for all the patients. For USG examination, both transvaginal sonography (TVS) and transabdominal approaches (TAS) were used. TAS was used to examine large masses that could not be visualized in their entirety using a transvaginal probe. Expert gynecologists performed all the examinations using the Voluson E8 USG machine (4–8 MHz).

2D USG parameters noted were lesion diameter, septations, solid areas, acoustic shadow, presence of and the number of papillary projections, wall irregularities, free fluid, and echogenicity of the adnexal mass. After 2D grayscale ultrasound, tumor vascularity was assessed using resistance index (RI), pulsatility index (PI), and peak systolic velocity (PSV) by color Doppler examination. IOTA-SR using B and M features were applied, and a presumptive diagnosis of benign, malignant, or inconclusive was made. The mass was classified as malignant if one or more M features were present without B features. The mass was classified as benign if one or more B features were present without M features. If both B and M features could be applied or none of them were present, the mass was classified as inconclusive.[1]

3D USG and power Doppler examination were then performed by another investigator blinded to the 2D USG findings. The ultrasound examination was conducted using wall motion filter low 2, at 0.8-kHz pulse repetition frequency (PRF), gain 0.8, with high quality and line density of 8. 3D volume box was applied to cover the entire extent of the mass if possible. The contour of the mass was outlined by selecting the manual mode and after repeatedly rotating its image six times by 30 degrees, six tracings were obtained to complete a 360-degree rotation. Additional information on cyst volume, mean gray index (MGI), vascularization index (VI), flow index (FI), and vascularization flow index (VFI) was obtained to characterize benign and malignant masses.[5] The virtual organ computer-aided analysis (VOCAL) imaging software installed in the USG machine automatically calculated these indices (►**Figs 1** and **2**). The power Doppler images were acquired at the following setting: maximum radiant high-definition (HD) flow, with power doppler map 5, low wall motion filter, mid-frequency, and PRF of 0.8kHz, which were preset in the GE Voluson by the engineer to optimize image quality.

The mean value of the grayscale voxels was calculated as the MGI (scale: 0–100) using the "histogram" feature of the 3D View Function. MGI near zero refers to a sonolucent mass; higher values represent increased echogenicity.

Surgery was performed by laparoscopy or laparotomy, as per the hospital protocol. The excised mass underwent histopathological evaluation. According to the final histopathology report, tumors were classified into benign and malignant. For analysis, tumors with borderline histology were included in the malignant group.

2D USG-based IOTA-SR and 3D USG diagnostic accuracy were calculated using sensitivity, specificity, and positive predictive value (PPV)/negative predictive value (NPV). The study was powered to detect a 7% difference in sensitivity with 80% power and 95% confidence interval (95% CI; 5% level of two-sided significance). To assess the significance of individual USG features for identifying malignancy, logistic regression analysis was carried out by taking 2D and 3D ultrasound parameters separately. The receiver operating characteristic (ROC) curve was plotted for significant variables, and the areas under the curve (AUCs) with cut-off values using the Youden index were calculated. Sensitivity and specificity for 2D USG-based simple rules and 3D ultrasound were calculated. A two-sided probability of $p < 0.05$ was

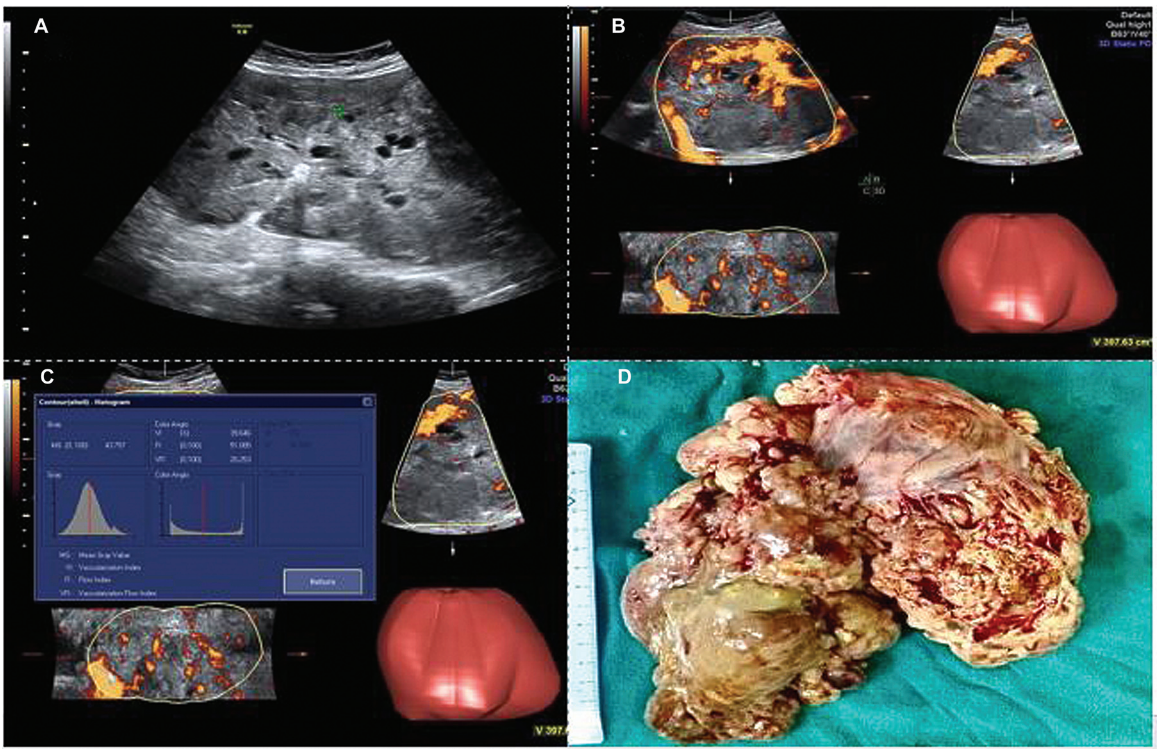

Fig. 1 (**A**) Two-dimensional grayscale image of an adnexal mass showing predominantly solid component with few cystic areas. (**B**) Three-dimensional power Doppler volume calculation of the adnexal mass using manual sampling. (**C**) Calculation of power Doppler indices using VOCAL software with histogram function. Three-dimensional and power Doppler indices were cyst volume of 397.60 cm^3, mean gray index (MGI) of 43.0, vascularization index (VI) of 33.0, flow index (FI) of 51.06, and vascularization flow index (VFI) of 20.25, which were also suggestive of a malignant nature. (**D**) Intraoperative picture of the adnexal mass. The final histopathology report was suggestive of high-grade serous carcinoma.

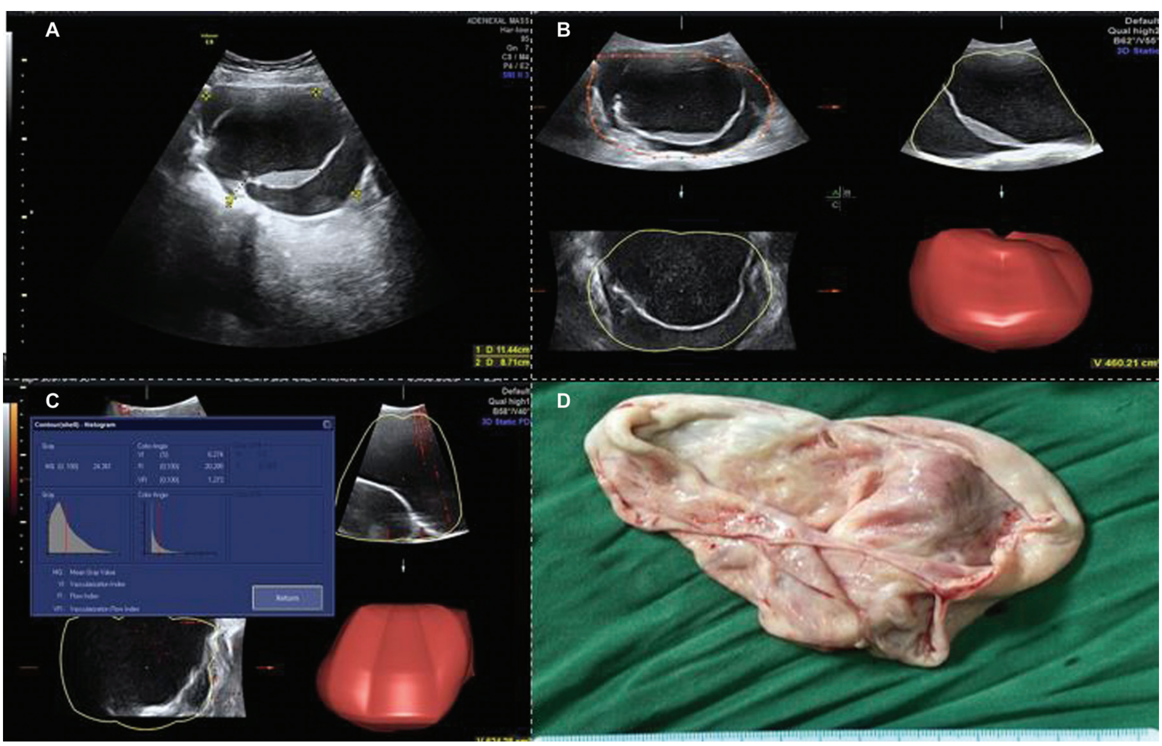

Fig. 2 (**A**) Two-dimensional grayscale image showing a multilocular cystic adnexal mass. (**B**) Three-dimensional power Doppler volume calculation of an adnexal mass using manual sampling method. (**C**) Calculation of power Doppler indices using VOCAL software with histogram function. Three-dimensional and power Doppler indices were cyst volume of 460.21 cm^3, mean gray index (MGI) of 24.3, vascularization index (VI) of 6.2, flow index (FI) of 20.2, and vascularization flow index (VFI) of 1.2, suggestive of the benign nature of the mass. (**D**) Intraoperative picture of the adnexal mass. The final histopathology report was suggestive of serous cystadenoma.

considered significant for all the statistical tests. The data analyses were carried out using STATA version 12.0 software.

Results

Eighty-four patients underwent surgical management during the study period, and histologically 41 (48.8%) of these were classified as benign and 43(51.1%) as malignant. The mean age (40.41 ± 16.83 vs. 46.05 ± 14.83 years; $p = 0.103$), body mass index (BMI; 23.97 ± 3.33 vs. 24.84 ± 2.53; $p = 0.17$), and mean parity (1.95 ± 1.92 vs. 1.79 ± 1.32; $p = 0.65$) of benign and malignant masses were comparable. The CA-125 concentration (U/mL) was significantly higher in malignant masses than in the benign group (131.44 ± 374.88 vs. 763.19 ± 933.55; $p < 0.001$).

2D USG parameters are depicted in ►**Table 1**. Solid areas, random echogenicity, free fluid, and cyst wall irregularities were significantly more common in the malignant masses. When the IOTA-SR were applied, the masses were categorized as benign (39/74), malignant (35/74), and inconclusive (10/84). When the diagnostic accuracy of individual rules was assessed, it was observed that the B1 feature has the highest PPV of 93.3% for predicting the benign nature of adnexal masses. The M5 feature had the highest PPV of 100%, followed by M3 (91.67%) and M1 (91.30%), for predicting the malignant nature of the mass (►**Table 2**). These observations were compared with the final histopathology report, and the sensitivity, specificity, PPV, and NPV of IOTA-SR in conclusive cases were observed as 83.78% (95% CI: 67.99–93.81%),

Table 2 Diagnostic accuracy of individual B and M rules

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Diagnostic accuracy of B rules for predicting benign nature of adnexal mass				
B1	34.15	97.67	93.33	60.87
B2	4.88	97.67	66.67	51.85
B3	12.20	88.37	50.00	51.35
B4	19.51	95.35	80.00	55.41
B5	41.46	93.02	85.00	62.50
Diagnostic accuracy of M rules for predicting malignant nature of adnexal mass				
M1	48.84	95.12	91.30	63.93
M2	44.19	90.24	82.61	60.66
M3	25.58	97.56	91.67	55.56
M4	44.19	95.12	90.48	61.90
M5	32.56	100.00	100.00	58.57

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

Table 1 Two-dimensional (2D) and three-dimensional (3D) ultrasound parameters of benign and malignant adnexal masses

Feature		Benign ($N = 39$)	Malignant ($N = 35$)	p Value
2D gray scale parameters				
Mean cyst diameter (cm) Mean ± SD (range)		10.4 ± 5.2 (2.3–29.3)	12.4 ± 5.3 (3.7–27.7)	0.085
Solid areas		29.3% (12/41)	90.7% (39/43)	<0.001
Septations		56.1% (23/41)	60.4% (26/43)	0.68
Acoustic shadow		12.2% (5/41)	11.6% (5/43)	0.93
Free fluid		9.7% (4/41)	44.1% (19/43)	<0.001
Randomly echogenic		31.7% (13/41)	79.07% (20.9%)	<0.001
Cyst wall irregularities		14.6% (6/41)	34.8% (15/43)	<0.001
2D Doppler parameters				
PI (mean + SD)		1.02 ± 0.93	0.83 ± 0.63	0.315
RI (mean + SD)		0.75 ± 0.24	0.47 ± 0.24	0.001
PSV (cm/s)		27.25 ± 13.07	25.24 ± 11.36	0.51
Vessel characteristics	No flow	17 (41.46%)	3 (6.98%)	<0.001
	Suspect	3 (7.31%)	23 (53.48%)	
	Nonsuspect	21 (51.23%)	17 (39.54%)	
3D power Doppler parameters				
Cyst volume (cm^3)		462.71 ± 738.50	699.33 ± 799.16	0.163
MGI		22.29 ± 10.56	34.28 ± 8.67	<0.001
VI		5.08 ± 4.50	16.70 ± 10.40	<0.001
FI		22.96 ± 9.77	34.97 ± 7.15	<0.001
VFI		1.73 ± 1.59	6.32 ± 4.27	<0.001

Abbreviations: FI, flow index; MGI, mean gray index; PI, pulsatility index; PSV, peak systolic velocity; RI, resistance index; VFI, vascularization flow index; VI, vascularization index.

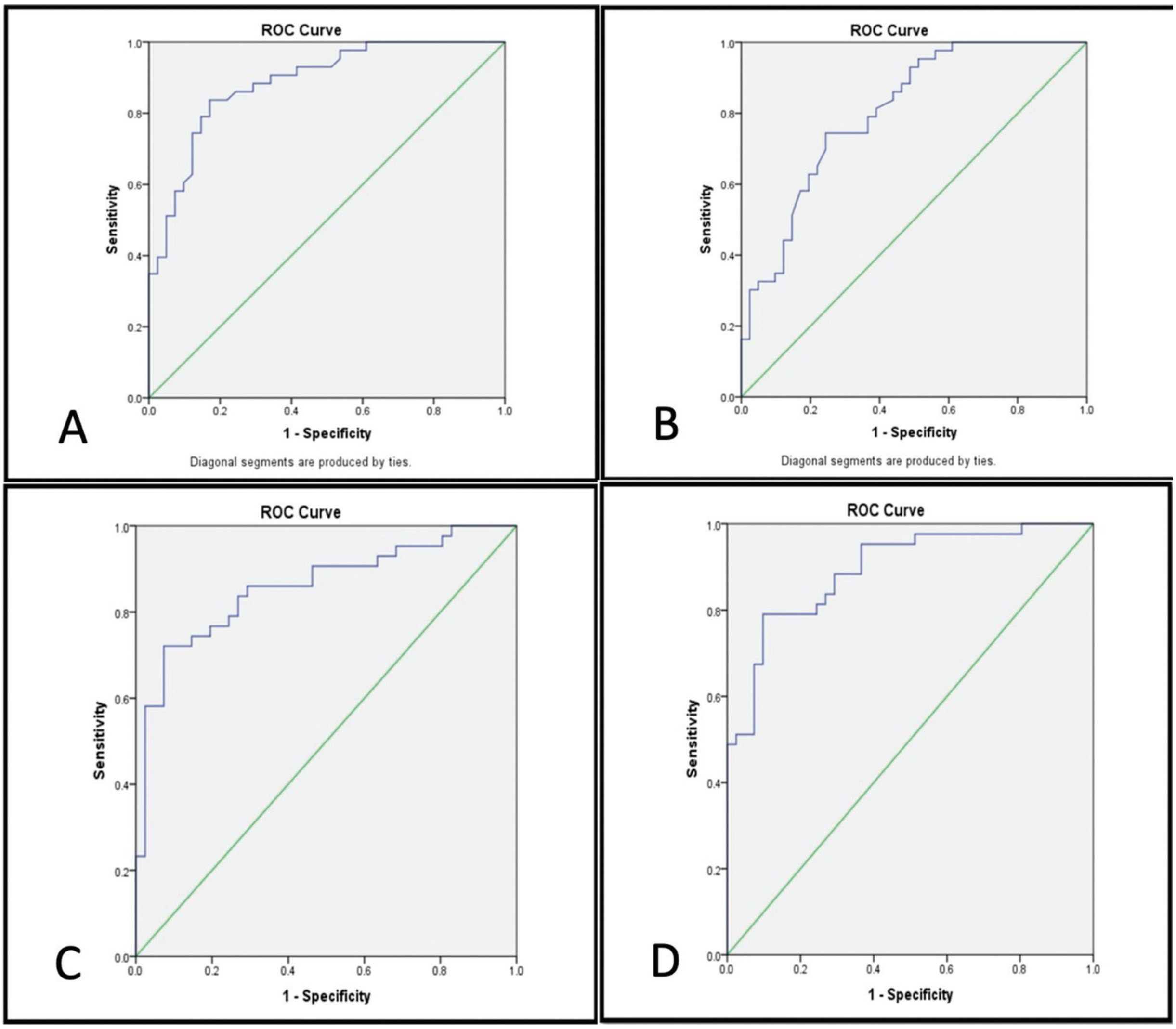

Fig. 3 Receiver operating characteristic (ROC) curve for three-dimensional (3D) ultrasonography (USG) parameters. (**A**) Vascularization index (cut-off: 8.4; area under the curve [AUC]: 0.89). (**B**) Mean gray index (cut-off: 28.2; AUC: 0.81). (**C**) Flow index (cut-off: 29.6; AUC: 0.86). (**D**) Vascularization flow index (cut-off: 3.1; AUC: 0.89).

89.19% (95% CI: 74.58–96.97%), 88.6% (95% CI: 75.2–95.2), and 84.62% (95% CI: 72.51–92.02), respectively.

Among the 3D power Doppler ultrasound parameters, MGI, VI, FI, and VFI were found to be significantly associated with increased risk of malignancy using multivariate logistic regression analysis ($p = 0.036$, 0.028, 0.032, and 0.019, respectively; ►**Table 1**). There are no established cut-off values for 3D ultrasound and power Doppler indices; hence, the cut-off values for each were calculated using the ROC curve (►**Fig. 3**). Among all the power Doppler indices, the VI showed the highest sensitivity of 83% for a cut-off value of 8.4 (►**Table 3**). Overall, the sensitivity and specificity of 3D USG and power Doppler were 84 and 88%, respectively, with an AUC of 0.96 (95% CI: 0.92–0.99) and was comparable with IOTA-SR.

Inconclusive findings were observed when IOTA-SR were applied in 11.9% (10/84) cases. Out of these 10 masses, both B and M features were present in 8 masses, and 2 had none of

Table 3 Sensitivity, specificity of estimated cut-off values for three-dimensional ultrasound and power Doppler parameters

Variable	Cut-off value	Sensitivity	Specificity	AUC	95% CI
MGI	28.2	74%	73%	0.81	0.71–0.89
VI	8.4	83%	83%	0.89	0.82–0.96
FI	29.6	77%	76%	0.86	0.78–0.94
VFI	3.1	79%	78%	0.89	0.83–0.96

Abbreviations: AUC, area under the curve; CI, confidence interval; FI, flow index; MGI, mean gray index; VFI, vascularization flow index; VI, vascularization index.

Table 4 Three-dimensional characteristics of inconclusive cases

Sl. no.	IOTA-SR characteristics	Histopathology	3D USG characteristics				
			Cyst volume (cm^3)	MGI (estimated cut-off: 28.2)	VI (estimated cut-off: 8.4)	FI (estimated cut-off: 29.6)	VFI (estimated cut-off: 3.1)
1	B4M2	High grade serous cancer (HGSC)	118.53	41.41	10.66	36.55	3.9
2	B3M1	Endometrioid adenocarcinoma	767.0	23.17	6.80	36.96	2.54
3	B1M2	Tuberculosis	239.00	30.38	10.40	29.22	3.05
4	No feature	Tuberculosis	100.45	28.34	7.60	46.33	3.50
5	B3M1M2	Endometrioma	97.81	13.00	16.24	25.00	4.10
6	B3M4	Dysgerminoma	831.00	47.20	10.31	34.34	3.54
7	B2M5	Endometrioid adenocarcinoma	337.02	30.29	15.83	39.54	6.26
8	No feature	Borderline mucinous tumor	691.26	32.15	16.91	29.11	4.92
9	B1B5M3	Borderline serous tumor	441.77	26.00	2.50	20.00	0.90
10	B5M3	Serous cystadenoma	666.32	0.00	0.00	0.00	0.00

Abbreviations: 3D, three-dimensional; FI, flow index; OITA-SR, International Ovarian Tumuor Analysis Simple Rules; MGI, mean gray index; USG, ultrasonography; VFI, vascularization flow index; VI, vascularization index.

the B and M features. Six were malignant, and four were benign, per the final histopathology report. The histological diagnosis of 10 inconclusive cases is shown in ►**Table 4**. These masses were irregular solid masses with the presence of acoustic shadow (B3M1), multilocular irregular masses more than 10 cm with acoustic shadow (B3M4), multilocular masses less than 10 cm with the presence of ascites (B4M2), and other combinations. Of these 10 inconclusive cases, 4 were malignant, 2 were borderline tumors, 2 were tuberculosis, and 1 each was endometrioma and serous cystadenoma. These masses were triaged using 3D ultrasound with power Doppler. 3D parameters could correctly differentiate 40% (4/10) of SR inconclusive masses (a malignant disease in three and a benign disease in one patient; ►**Table 4**).

Discussion

Adnexal masses are frequently encountered in clinical practice. The accurate preoperative assessment facilitates timely referral, route, and extent of surgery. Clinical and laboratory parameters like age, menopausal state, personal or family history of breast or ovarian cancer, CA-125 level, and imaging are used to differentiate benign and malignant masses. Various ultrasound models are available for preoperative assessment of adnexal masses.

Among the USG-based reporting systems, IOTA-SR are commonly utilized because of their simplicity and good diagnostic accuracy. Several investigators have evaluated the diagnostic performance of IOTA-SR. In a systemic review, pooled sensitivity and specificity of IOTA-SR were 0.93 (95% CI: 0.89–0.95) and 0.81, respectively.[6] Similar findings were observed by Meys et al, with a pooled sensitivity and specificity of 0.93 (95% CI: 0.91–0.95) and 0.80 (95% CI: 0.77–0.82), respectively.[7] In the present study, sensitivity and specificity of simple rules were 83.78% (95% CI: 67.99–93.81) and 89.19% (95% CI: 74.58–96.97), respectively, which were similar to the results of a study reported by Auekitrungrueng et al, who reported sensitivity and specificity of 83.8% (95% CI: 77.1–90.40) and 92.0 (95% CI: 88.8–95.2), respectively.[8] However, other authors have reported higher sensitivity to simple rules than our observations.[9,10] The marginal variations reported in the diagnostic performance could be because of the heterogeneous nature, variations in the prevalence of malignant masses, and different levels of examiners conducting the test across these investigations.

The proportion of conclusive results using simple rules varied from 76 to 92% in different studies.[1,3,8,9,11–13] The interpretation of simple rules is affected by the experience of the examiners. In a study by Knafel et al, the proportion of conclusive results was 82.4% (lower than our results) when level 1 examiners (with less experience) performed the examination; this increased to 91.2% with level 2 examiners.[9] Most differences resulted from evaluating acoustic shadow, motion artefacts, and subjective interpretation of color flow in adnexal masses. In our study, all the examinations were done by experienced investigators, which explains the relatively higher proportion of conclusive cases.

3D ultrasound allows visualization of adnexal masses in multiple planes, thus better characterizing an adnexal mass. With surface rendering mode, the surface of an adnexal mass can be visualized more precisely, and it also allows the 3D reconstruction of vessels. Other features like inversion mode allow better visualization of areas of cystic contents. With the addition of 3D power Doppler, the vascular architecture can be visualized more clearly. In 3D Doppler, vascular indices (VI, FI, and VFI) are calculated, which provides a more objective assessment of vascularity and would probably decrease the subjective variation in the assessment of vascularity. However, 3D ultrasound is still under evaluation, and its use is limited by cost and availability. In the current study, sensitivity and specificity for 3D USG for discriminating adnexal masses were calculated as 84 and 88%, respectively, with AUC of 0.96 (95% CI: 0.92–0.99). A study by Perez-Medina et al found a sensitivity and specificity of 84.6% and 81.9%, respectively.[14] Huchon et al found a sensitivity and specificity of 82 and 90%, respectively, and Alcazar et al reported a sensitivity and specificity of 97.8 and 79.2%, respectively.[15,16] A summary of available studies conducted to evaluate the efficacy of 3D USG is depicted in ►**Table 5**.[4,14,15,17,18,20]

Our study has demonstrated numerically increased cyst volume, significantly increased MGI, and raised vascular indices in malignant masses (►**Table 1**). Malignant masses are highly vascular due to neovascularization and the vascularization index reflects the density of blood vessels in an adnexal mass. The results of our study corroborated with the existing data, which also demonstrated a higher value of VI in malignant masses (16.70 ± 10.40 vs. 5.08 ± 4.50). A wide variation is observed in absolute VI values in different studies. However, all studies have consistently demonstrated higher values of VI in malignant masses, except the studies by Perez-Medina et al and Ohel et al, where no significant difference was demonstrated between the two benign and malignant masses, which could be attributed to the small study sample size.[4,14] The observed variation in the value of vascular indices may be due to a difference in technique and lack of standardization. FI is the sum of weighted color voxels divided by the total number of color voxels. It reflects the number of blood corpuscles in the vessels of the volume examined. Additionally, the chaotic architecture of vessels and complex branching patterns in adnexal masses were noted. The results of our study are consistent with the study by Huchon et al, which also showed higher values of FI in malignant masses.[15] However, other studies did not find any significant differences (►**Table 5**). Hence, FI's role in discriminating the adnexal masses must be explored further. VFI is the total number of weighted color voxels divided by the total number in the region of interest. It reflects the density of blood within the region and the number of corpuscles in the vessels in the volume. Like our observations, a higher value of VFI in malignant masses was observed in the published literature.

Several authors have investigated the cut-off values of Doppler indices, and different cut-off values with variable accuracy have been shown in the literature. A cut-off value of 3.1 for VFI has demonstrated sensitivity and specificity of 79 and 78%, respectively, for the detection of malignancy. Geomini et al calculated the VFI cut-off value of 2.0 to predict the risk of malignancy with an odds ratio of 0.74 (0.45–1.23) for VFI <2 and 0.92 (0.74–1.25) for VFI >2.[19] These authors also calculated the cut-off value of FI as 30 to predict the risk of malignancy with an odds ratio of 0.83 (0.74–0.94) (95% CI) for FI <30 and 1.07 (0.99–1.15) for FI >30. Our study's cut-off value of 29.6 for FI demonstrated a sensitivity and specificity of 77 and 76%, respectively. Wilson et al suggested a cut-off value 2.3 for VI with a sensitivity and specificity of 75% and 90%, respectively.[20] In the present study, the cut-off value of 8.4 for VI demonstrated both sensitivity and specificity of 83%. Despite similar observations, the absolute value of VI was different in their study than ours, and this could be explained by the fact that our study used power processing and frequency-based color Doppler.

Hence, it is evident that there has yet to be a clear cut-off value established so far for the power Doppler indices to differentiate between benign and malignant masses due to variations in tissue attenuation and machine settings, such as gain and pulse repetition by different examiners. There is insufficient evidence to support the application of this technology in clinical practice.

Both modalities (IOTA-SR and 3D ultrasound) have demonstrated good diagnostic performance in the studies. The significant benefits of IOTA-SR over 3D ultrasound are that

Table 5 Review of studies evaluating diagnostic performance of 3D USG

Study	Mean VI	Mean FI	Mean VFI
Abbas et al[17]	10.98 ± 9.17 vs. 16.36 ± 15.18; $p < 0.05$	20.15 vs. 20.16; $p > 0.05$	2.13 ± 2.01 vs. 3.91 ± 3.83; $p < 0.01$
Perez et al[14]	5.38 ± 6.61 vs. 6.29 ± 5.77; $p = 0.53$	29.63 ± 10.29 vs. 33.81 ± 10.39; $p = 0.15$	1.68 ± 2.10 vs. 2.37 ± 2.72; $p = 0.24$
Huchon et al[15]	7.2 ± 8.0 vs. 35.5 ± 20.8; $p < 0.0001$	37.0 ± 11.5 vs 48.2 ± 11.0; $p = 0.003$	2.9 ± 3.6 vs. 17.6 ± 12.5; $p < 0.0001$
Ohel et al[4]	6.5 ± 4.2 vs. 6.2 ± 4.6	41.6 ± 9.8 vs. 36.0 ± 8.6	
Jokubkiene et al[18]	5.1 (0.03–60.53) vs. 35.6 (4.73–78.61); $p < 0.001$		
Wilson et al[20]	1.3 ± 1.6 vs. 4.7 ± 3.9; $p < 0.01$		
Present study	5.08 ± 4.50 vs. 16.70 ± 10.40; $p < 0.001$	22.96 ± 9.77 vs. 34.97 ± 7.15; $p < 0.001$	1.73 ± 1.59 vs. 6.32 ± 4.27; $p < 0.001$

Abbreviations: 3D, three-dimensional; FI, flow index; VFI, vascularization flow index; USG, ultrasonography; VI, vascularization index.

they are easy to learn, simple to use with a short learning curve, and can be used by nonexpert examiners.[8,20] The main concern with IOTA-SR remains the proportion of inconclusive cases. Several strategies like three-step assessment, logistic regression models, Assessment of Different NEoplasias in the adneXa (ADNEX model), and expert USG assessment have been investigated.[21,22] We also evaluated the role of 3D ultrasound with power Doppler for evaluating the IOTA inconclusive cases. 3D USG could correctly classify three malignant masses and one benign mass out of 10 inconclusive cases. So, 3D ultrasound with power Doppler could be used as a second-stage test to evaluate the inconclusive masses. Nevertheless, this needs further confirmation in large-scale prospective studies.

The study's strength was that the comparison of both techniques was performed using the same ultrasound machine and settings, which allowed an ideal comparison of both techniques. The limitations were the small sample size and the ultrasound was performed only for patients planned for surgery.

Conclusion

IOTA-SR and 3D USG have similar diagnostic performances in discriminating benign and malignant adnexal masses. 3D USG does not provide any added advantage over IOTA-SR. However, the potential use of 3D ultrasound as a second-stage test in inconclusive masses should be further evaluated. More large-scale studies are required to develop a standardized technique and cut-off values for power Doppler parameters before its implementation in routine clinical practice.

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Conflict of Interest
None declared.

References

1 Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. Ultrasound Obstet Gynecol 2008;31(06):681–690
2 Timmerman D, Ameye L, Fischerova D, et al. Simple ultrasound rules to distinguish between benign and malignant adnexal masses before surgery: prospective validation by IOTA group. BMJ 2010;341:c6839
3 Fathallah K, Huchon C, Bats AS, et al. External validation of simple ultrasound rules of Timmerman on 122 ovarian tumors. Gynécol Obstét Fertil 2011;39(09):477–481
4 Ohel I, Sheiner E, Aricha-Tamir B, et al. Three-dimensional power Doppler ultrasound in ovarian cancer and its correlation with histology. Arch Gynecol Obstet 2010;281(05):919–925
5 Geomini PMAJ, Coppus SFPJ, Kluivers KB, Bremer GL, Kruitwagen RFPM, Mol BWJ. Is three-dimensional ultrasonography of additional value in the assessment of adnexal masses? Gynecol Oncol 2007;106(01):153–159
6 Kaijser J, Sayasneh A, Van Hoorde K, et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis. Hum Reprod Update 2014;20(03):449–462
7 Meys EMJ, Kaijser J, Kruitwagen RFPM, et al. Subjective assessment versus ultrasound models to diagnose ovarian cancer: a systematic review and meta-analysis. Eur J Cancer 2016;58:17–29
8 Auekitrungrueng R, Tinnangwattana D, Tantipalakorn C, et al. Comparison of the diagnostic accuracy of International Ovarian Tumor Analysis simple rules and the risk of malignancy index to discriminate between benign and malignant adnexal masses. Int J Gynaecol Obstet 2019;146(03):364–369
9 Knafel A, Banas T, Nocun A, et al. The prospective external validation of International Ovarian Tumor Analysis (IOTA) Simple Rules in the hands of level I and II examiners. Ultraschall Med 2016;37(05):516–523
10 Ning CP, Ji X, Wang HQ, Du XY, Niu HT, Fang SB. Association between the sonographer's experience and diagnostic performance of IOTA simple rules. World J Surg Oncol 2018;16(01):179
11 Alcázar JL, Pascual MÁ, Olartecoechea B, et al. IOTA simple rules for discriminating between benign and malignant adnexal masses: prospective external validation. Ultrasound Obstet Gynecol 2013;42(04):467–471
12 Ruiz de Gauna B, Rodriguez D, Olartecoechea B, et al. Diagnostic performance of IOTA simple rules for adnexal masses classification: a comparison between two centers with different ovarian cancer prevalence. Eur J Obstet Gynecol Reprod Biol 2015;191:10–14
13 Kaijser J, Bourne T, Valentin L, et al. Improving strategies for diagnosing ovarian cancer: a summary of the International Ovarian Tumor Analysis (IOTA) studies. Ultrasound Obstet Gynecol 2013;41(01):9–20
14 Perez-Medina T, Orensanz I, Pereira A, et al. Three-dimensional angioultrasonography for the prediction of malignancy in ovarian masses. Gynecol Obstet Invest 2013;75(02):120–125
15 Huchon C, Metzger U, Bats AS, et al. Value of three-dimensional contrast-enhanced power Doppler ultrasound for characterizing adnexal masses. J Obstet Gynaecol Res 2012;38(05):832–840
16 Alcázar JL, Castillo G. Comparison of 2-dimensional and 3-dimensional power-Doppler imaging in complex adnexal masses for the prediction of ovarian cancer. Am J Obstet Gynecol 2005 Mar;192(03):807–812
17 Abbas AM, Sheha AM, Salem MN, Altraigey A. Three-dimensional power Doppler ultrasonography in evaluation of adnexal masses. Middle East Fertil Soc J 2017;22(04):241–245
18 Jokubkiene L, Sladkevicius P, Valentin L. Does three-dimensional power Doppler ultrasound help in discrimination between benign and malignant ovarian masses? Ultrasound Obstet Gynecol 2007;29(02):215–225
19 Geomini PMAJ, Kluivers KB, Moret E, Bremer GL, Kruitwagen RFPM, Mol BWJ. Evaluation of adnexal masses with three-dimensional ultrasonography. Obstet Gynecol 2006;108(05):1167–1175
20 Wilson WD, Valet AS, Andreotti RF, Green-Jarvis B, Lyshchik A, Fleischer AC. Sonographic quantification of ovarian tumor vascularity. J Ultrasound Med 2006;25(12):1577–1581
21 Ngu SF, Chai YK, Choi KM, et al. Diagnostic performance of risk of malignancy algorithm (ROMA), risk of malignancy index (RMI) and expert ultrasound assessment in a pelvic mass classified as inconclusive by International Ovarian Tumour Analysis (IOTA) Simple Rules. Cancers (Basel) 2022;14(03):810
22 Hiett AK, Sonek JD, Guy M, Reid TJ. Performance of IOTA Simple Rules, Simple Rules risk assessment, ADNEX model and O-RADS in differentiating between benign and malignant adnexal lesions in North American women. Ultrasound Obstet Gynecol 2022;59(05):668–676

