

# Evaluation of IOTA Simple Ultrasound Rules to Distinguish Benign and Malignant Ovarian Tumours

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## ABSTRACT

**Introduction:** IOTA stands for International Ovarian Tumour Analysis group. Ovarian cancer is one of the common cancers in women and is diagnosed at later stage in majority. The limiting factor for early diagnosis is lack of standardized terms and procedures in gynaecological sonography. Introduction of IOTA rules has provided some consistency in defining morphological features of ovarian masses through a standardized examination technique.

**Aim:** To evaluate the efficacy of IOTA simple ultrasound rules in distinguishing benign and malignant ovarian tumours and establishing their use as a tool in early diagnosis of ovarian malignancy.

**Materials and Methods:** A hospital based case control prospective study was conducted. Patients with suspected ovarian pathology were evaluated using IOTA ultrasound rules

and designated as benign or malignant. Findings were correlated with histopathological findings. Collected data was statistically analysed using chi-square test and kappa statistical method.

**Results:** Out of initial 55 patients, 50 patients were included in the final analysis who underwent surgery. IOTA simple rules were applicable in 45 out of these 50 patients (90%). The sensitivity for the detection of malignancy in cases where IOTA simple rules were applicable was 91.66% and the specificity was 84.84%. Accuracy was 86.66%. Classifying inconclusive cases as malignant, the sensitivity and specificity was 93% and 80% respectively. High level of agreement was found between USG and histopathological diagnosis with Kappa value as 0.323.

**Conclusion:** IOTA simple ultrasound rules were highly sensitive and specific in predicting ovarian malignancy preoperatively yet being reproducible, easy to train and use.

**Keywords:** Adnexal masses, Early diagnosis, Histopathology, Transvaginal sonography

## INTRODUCTION

To date, the IOTA study is the largest study in the literature on ultrasound diagnosis of ovarian pathology. It started years ago in 1999 and included nine European centers. The 5-year survival rate associated with ovarian cancer is less than 30%. The limiting factor for early diagnosis of ovarian tumour is lack of standardised terms and procedures in gynaecological sonography. A standardized technique for preoperative classification of adnexal masses was defined by IOTA group. Major highlight of the study were 10 simple ultrasound rules that had high sensitivity and specificity and were applicable to a large number of tumours. On application of one or more M-rules in the absence of a B-rule, or one or more B-rules in the absence of a M-rule, the mass is classified as malignant or benign respectively. If both M-rules and B-rules apply, or if no rule applies, the mass could not be classified [1], and was labeled as inconclusive. Although large no. of studies are available proving the efficacy of these rules, however a prospective study directly applying these diagnostic rules to the patient was lacking. This study was performed to truly establish the diagnostic utility of these rules in our country and to estimate and compare the sensitivity and specificity of given rules with histological diagnosis and establish their use as a tool in early diagnosis of ovarian malignancy.

## MATERIALS AND METHODS

The present study was a hospital based case control prospective study carried out in Department of Radiodiagnosis, Govt. Medical College and Rajindra Hospital, Patiala, Punjab, India. Case control study was done in 50 women with suspected ovarian pathology attending gynaecology clinic at Department of Obstetrics and Gynaecology during the period of December 2014 to October 2016. Mandatory written informed consent was taken from all the patient for participation in study. Patient with suspicion of adnexal mass

on pelvic examination or discovered during previous sonographic examination were included and pregnant patient and patient not willing for surgery in our hospital were excluded. Transvaginal sonography was done on all the patients. Examination was limited to Transabdominal sonography in virgins and where it was not possible to completely visualize the mass by a transvaginal probe. Permission from the hospital authority for conducting the study was obtained. Sonographic assessment of the given adnexal masses was done using wide band intracavitary transducer having frequency 5-7.5 MHz for transvaginal sonography and 2-5 MHz curved transducer for transabdominal sonography which was available in our department. Ultrasound was done by both experienced (experience of seven years or more in abdominopelvic sonography) and new sonographers and each patient were classified as benign or malignant on basis of IOTA simple rules [Table/Fig-1]. In cases of bilateral mass, the larger mass was considered. During the sonographic examination both the sonographers were blind folded for their results as well as the histopathological finding. All patients included in the study underwent surgery (within 120 days of sonographic examination). Histopathological diagnosis was obtained in all cases and used as the gold standard. Collected data was statistically analysed using chi square test and kappa statistical method.

## RESULTS

During the study 55 women were eligible but five were excluded as they deny for surgery. Out of 50 patients eight had bilateral masses (larger one was considered for study). The youngest patient in the present study was 18-year-old and the eldest was 77-year-old female, the mean age (SD) was 42.5 years. Malignancy was more common in 6<sup>th</sup> decade age group [Table/Fig-2]. Malignancy was more common in postmenopausal patients (71.43%) [Table/Fig-3]. Out of total 50 cases studied, IOTA Rules classified 45 patients, 29 as benign and 16 as malignant. Five cases where rules could not be

Rules for predicting a malignant tumour (M-rules)	Rules for predicting a benign tumour (B-rules)
M1 Irregular solid tumour	B1 Unilocular cyst
M2 Presence of ascites	B2 Presence of solid components where the largest solid component is <7 mm in largest diameter;
M3 At least four papillary structures	B3 Presence of acoustic shadows
M4 Irregular multilocular solid tumour with largest diameter ≥100 mm	B4 Smooth multilocular tumour with largest diameter <100 mm
M5 Very strong blood flow (color score 4)	B5 No blood flow (color score 1)

[Table/Fig-1]: Simple IOTA rules for predicting benign or malignant ovarian tumour.

Age Group (in years)	Benign		Malignant	
	Number	Percentage	Number	Percentage
11-25	6	16.67	0	0.00
26-40	23	63.89	1	7.14
41-55	4	11.11	3	21.43
56-70	2	5.56	9	64.29
71-85	1	2.77	1	7.14
Total	36	100.00	14	100.00

[Table/Fig-2]: Age distribution in benign and malignant ovarian masses (n=50).

Menopausal Status	Benign	%	Malignant	%
Postmenopausal	5	13.89	10	71.43
Premenopausal	31	86.12	4	28.57
Total	36	100	14	100

[Table/Fig-3]: Relation of menopausal status with ovarian tumours.

Nature of the Mass as per IOTA Rules	No.
Benign	29
Malignant	16
Indeterminate	5
Total	50

[Table/Fig-4]: Classification of cases as per IOTA simple ultrasound rules.

applied or where both B and M rules were applicable were labelled as indeterminate or inconclusive cases [Table/Fig-4].

In the present study, 23 different combinations of Benign and Malignant simple ultrasound features were observed as tabulated in [Table/Fig-5]. Out of all, most common was combination of Rules B1 and B5 (eight out of 23 combinations) showing no risk of malignancy on final histopathological analysis. Out of eight combinations having 100% rate of malignancy, most frequent combination was application of Rule M2 alone or in combination with M4 (two each out of eight combinations).

B5 was the most common occurring factor in all benign lesions, followed by B1. But B2 and B4 predicted the result most correctly (100%) followed by B5 and B1 [Table/Fig-6].

Rules M1, M2, M4 were all equally common factors each present in eight patients with suspected malignancy. Out of these best M factor was M2 (presence of ascites) which correctly predicted malignancy in all the eight patients in which it was found [Table/Fig-7].

Kappa statistics showed high level of agreement between USG and histopathological findings and it was statistically significant ( $K=0.323$ ) [Table/Fig-8]. The sensitivity for the detection of malignancy in cases where IOTA simple rules were applicable was 91.66% and the specificity was 84.84%. Accuracy was 88.88% [Table/Fig-9]. Classifying inconclusive cases as malignant the sensitivity and specificity was 93% and 80% respectively.

There was one false negative case in our study which on sonography had unilocular cyst and histopathological diagnosis of epithelial

Sr. No.	Applicable B-Factors					Applicable M-Factors					Frequency	Benign	Malignant	Rate of malignancy (%)
	B1	B2	B3	B4	B5	M1	M2	M3	M4	M5				
1	1	0	0	0	1	0	0	0	0	0	8	8	0	0.00
2	0	0	0	1	0	0	0	0	0	0	6	6	0	0.00
3	1	0	0	0	0	0	0	0	0	0	6	5	1	16.67
4	0	0	0	0	1	0	0	0	0	0	4	4	0	0.00
5	0	0	0	0	0	1	0	0	0	0	3	2	1	33.33
6	0	0	0	0	0	0	0	0	1	0	3	2	1	33.33
7	0	0	0	0	0	0	1	0	0	0	2	0	2	100.00
8	0	0	0	0	0	0	1	0	1	0	2	0	2	100.00
9	1	0	1	0	1	0	0	0	0	0	2	2	0	0.00
10	0	0	0	0	1	0	1	0	1	0	1	0	1	100.00
11	0	0	0	0	0	0	0	1	0	0	1	0	1	100.00
12	0	0	0	0	0	0	0	0	0	0	1	0	1	100.00
13	0	0	0	0	0	1	1	0	0	1	1	0	1	100.00
14	0	0	0	0	0	1	0	0	0	1	1	0	1	100.00
15	0	0	0	0	0	0	1	0	1	1	1	0	1	100.00
16	0	0	0	0	0	1	1	0	0	0	1	0	1	100.00
17	0	0	1	0	1	0	0	0	0	0	1	1	0	0.00
18	1	1	1	0	1	0	0	0	0	0	1	1	0	0.00
19	0	0	0	0	0	0	0	0	0	1	1	1	0	0.00
20	0	0	1	0	1	1	0	0	0	0	1	1	0	0.00
21	0	1	0	0	0	0	0	0	0	0	1	1	0	0.00
22	0	0	1	0	1	1	0	0	0	0	1	1	0	0.00
23	0	0	0	0	1	0	0	0	1	0	1	1	0	0.00

[Table/Fig-5]: Observed combinations of benign and malignant ultrasound features of IOTA simple rules ranked by frequency.

Benign	Predicted	Result	Percentage
B1	17	16	94%
B2	2	2	100%
B3	6	5	83%
B4	6	6	100%
B5	20	19	95%

[Table/Fig-6]: Prevalence and predictive power of benign factors.

Malignant	Predicted	Result	Percentage
M1	8	4	50%
M2	8	8	100%
M3	1	1	100%
M4	8	5	63%
M5	4	3	75%

[Table/Fig-7]: Prevalence and predictive power of malignant factors.

ovarian carcinoma, patient had history of contralateral ovarian carcinoma which was operated two years back.

On screening [Table/Fig-10], it shows Comparison between sonographic and histopathological findings of inconclusive cases.

Considering new residents in our institution as inexperienced sonographers in comparison to professors as experienced sonographers, no difference was found in interpretation of IOTA simple rules proving IOTA rules to be highly reproducible, easy to train and apply.

## DISCUSSION

In previous published studies the IOTA ultrasound rules were not directly applied during sonographic examination, the sonographic data was later collected from patients and was evaluated as per prediction models. Till date only few studies which applied this diagnostic test directly to patient have been performed. Our study overcomes this limitation by directly applying IOTA simple ultrasound rules on the patients. A total of 55 patients with suspected ovarian pathology were evaluated using transvaginal ultrasonography and transabdominal ultrasonography when transvaginal approach was not feasible. All the cases were examined first by an inexperienced sonographer (new residents with less than one year training in ultrasound) with prior knowledge of IOTA rules, the findings were noted. Same patient was later examined by an experienced sonographer and mass was again classified strictly as per IOTA rules. No expert opinion was taken into consideration. Both the rules were later compared with each other and 100% agreement was found between two results. Findings were correlated with histopathological findings. Out of 55 patients initially evaluated in the study, 50 patients were included in the final analysis who underwent surgery.

Nature of the Mass as per IOTA Rules	No.	Histopathological Result	
		Benign	Malignant
Benign	29	28	1
Malignant	16	5	11
Indeterminate	5	3	2

**[Table/Fig-8]:** Comparison of results of IOTA simple rules with histopathological findings.

Efficacy of IOTA Simple Rules	
Sensitivity	91.66%
Specificity	84.84%
PPV	68.75%
NPV	96.55%
Accuracy	88.88%

**[Table/Fig-9]:** Efficacy of IOTA simple rules.

Sonographic findings(IOTA RULES)	Histopathology
M4 + B5	Mucinous cystadenoma
M4+M2+B5	Epithelial ovarian carcinoma
M1+B3+B5	Tubo-ovarian abscess
Smooth,regular,solid tumour(>100 mm),no ascites and moderate blood flow(no rule applied)	Dysgerminoma
M1+B3+B5	Endometrioma

**[Table/Fig-10]:** Comparison between sonographic and histopathological findings of inconclusive cases.

Author and year of study	No. of Patients	Patients in whom rules are applicable	Malignant Tumours	Benign Tumours	Prevalence (%)	True Positive	False Positive	False Negative	True Negative	Sensitivity (%)	Specificity (%)
Timmerman D et al., [2] (2008)	507	386	-	-	29	106	25	6	249	95	91
Timmerman D et al., [3] (2010)	1938	1501	542	1396	25	340	49	29	1083	92	96
Fathallah K et al., [4] (2011)	122	109	14	108	10.10	8	3	3	95	73	97
Hartman CA et al., [5] (2012)	103	91	30	73	24.20	20	9	2	60	91	87
Sayasneh A et al., [6] (2013)	255	214	74	181	24.80	46	3	7	158	87	98
Alcazar JL et al., [7] (2013)	340	270	55	285	12.20	29	6	4	231	88	97
Nunes N et al., [8] (2012)	303	237	135	168	44.30	101	15	4	117	96	89
Present study (2016)	50	45	14	36	28.00	11	5	1	28	91.66	84.84

**[Table/Fig-11]:** Comparison of results of present study with the published data is shown.

Thus rate of inconclusive result was 10%. On histopathology, out of total 50 cases studied 14(28%) were malignant and 36 (72%) were benign. Out of 45 cases where IOTA simple rules were applicable, 16(35.5%) were malignant and 29(64.4%) were benign. Out of the five cases classified as inconclusive two were malignant and three were benign.

The sensitivity and specificity of present study most closely related to study by Hartman CA et al., who reported a sensitivity and specificity of 91% and 87% respectively. The specificity of our study was lower as compared to these seven studies. This variation may be due to limited number of patients studied in the present study as compared to other studies [Table/Fig-11] [2-8].

Sub analyses was done for pre- and postmenopausal women in our study and compared with the literature [Table/Fig-12] [3,5-8].

It shows that sensitivity was higher in premenopausal women (100%) than in postmenopausal women (90.9%) while specificity was slightly lower (86.2% and 75% respectively). The increased sensitivity and specificity in premenopausal women compared to the postmenopausal women in present study may be explained by increased number of inconclusive cases in the premenopausal patients in present study where the simple rules could not be applied (10%).

The rate of inconclusive result in this study was 10%. Using a strategy classifying the inconclusive cases as malignant was adopted by many already published studies in this regard as shown in [Table/Fig-13] [3-5,7-9].

Applying this strategy in present study the sensitivity of the index test increased from 92% to 93% whereas specificity decreased from 85% to 80% respectively. This result correlated well with the published data and the sensitivity and specificity of present study was close to sensitivity and specificity as per study by Timmerman et al., [3].

## LIMITATION

The major limitation of this study was small sample size.

## CONCLUSION

The sensitivity for the detection of malignancy in cases where IOTA simple rules were applicable was 91.66% and the specificity was 84.84%. Accuracy was 88.88%. Classifying inconclusive cases as malignant the sensitivity and specificity were 93% and 80% respectively. The most important factor in ovarian malignancy is time of detection. With early detection, it is possible to improve the survival of patient significantly. USG offers inherent advantages of easy availability, low cost and lack of radiation exposure but being more subjective than other modalities. IOTA simple ultrasound rules can eliminate this problem as they are highly sensitive and specific in

Author and year of study	Patients with Rules Applicable	Prevalence of Malignancy (%)	Sensitivity	Specificity
<b>ALL WOMAN</b>				
Timmerman D et al., [3] (2010)	796	22.2	96	96
Hartman CA et al., [5] (2012)	91	24.2	87	87
Sayasneh A et al., [6] (2013)	214	24.8	98	98
Alcazar JL et al., [7] (2013)	270	12.2	97	97
Nunes N et al., [8] (2012)	237	44.3	89	89
Present Study (2016)	45	28	91.66	84.84
<b>PREMENOPAUSAL</b>				
Timmerman D et al., [3] (2010)	526	9.5	90	97
Hartman CA et al., [5] (2012)	39	23.1	89	90
Sayasneh A et al., [6] (2013)	143	15.4	82	100
Alcazar JL et al., [7] (2013)	217	7.4	88	97
Nunes N et al., [8] (2012)	130	22.3	90	89
Present Study (2016)	30	3.33	100	86.2
<b>POSTMENOPAUSAL</b>				
Timmerman D et al., [3] (2010)	270	47	91	94
Hartman CA et al., [5] (2012)	36	30.6	91	80
Sayasneh A et al., [6] (2013)	71	43.7	90	93
Alcazar JL et al., [7] (2013)	53	32.1	88	100
Nunes N et al., [8] (2012)	107	71	99	87
Present Study (2016)	15	73.33	90.9	75

**[Table/Fig-12]:** Comparative sensitivity and specificity of published data with the current study in pre and postmenopausal women [3,5-8].

predicting ovarian malignancy yet being reproducible, easy to train and use.

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Study	Sensitivity If SR Applicable	Specificity If SR Applicable	Sensitivity With SR+MA	Specificity With SR+MA
Timmerman D et al., [3]	91	96	94	80
Fathallah K et al., [4]	73	97	79	88
Hartman CA et al., [5]	91	87	94	76
Alcazar JL et al., [7]	88	97	93	81
Nunes N et al., [8]	96	89	97	70
Tantipalakorn C et al., [9]	83	95	87	81
Present study	92	85	93	80

**[Table/Fig-13]:** Test performance of different simple rules (sr) strategies in the IOTA studies.

SR-simple rules; SR+MA- simple rules+ inconclusive result considered as malignant.

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