

International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
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www.gynaecologyjournal.com
2020; 4(5): 274-278
Received: 10-07-2020
Accepted: 12-08-2020

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An assessment of the role of international ovarian tumor analysis system in the prediction of ovarian malignancy

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DOI: <https://doi.org/10.33545/gynae.2020.v4.i5e.716>

Abstract

Background: Ovarian cancer is the leading cause of mortality among gynecological malignancies. To date there is no single test with accurate sensitivity and specificity in the pre operative prediction of ovarian malignancy.

Objective: To evaluate the role of IOTA (International Ovarian Tumor Analysis) simple ultrasound rules in the pre operative prediction of ovarian malignancy and to correlate IOTA predictions with histopathology reports.

Methods: A prospective study was conducted on 50 patients with complex adnexal masses detected sonologically and planned for surgery in Father Muller Medical College Hospital, Mangalore. Based on ultrasonographic findings IOTA simple ultrasound rules were applied and preoperative prediction was compared with the final histopathology report.

Results: Sixty percentage of patients had benign masses, 8 % had borderline masses and 32 % had malignant masses. In our study IOTA had a sensitivity of 100%, specificity of 92.31 %, PPV of 87.5 %, NPV of 100% and diagnostic accuracy of 95%.

Conclusion: IOTA simple rules using ultrasonography has increased diagnostic accuracy and would serve as an excellent non invasive screening modality and as a diagnostic tool in predicting ovarian malignancy.

Keywords: Ovarian cancer, IOTA, ultrasonography, histopathology

Introduction

Ovaries are highly capable of producing both benign and malignant neoplasms throughout a women's lifetime. More than two-third of adnexal masses diagnosed by ultrasonography is of ovarian origin making it one of the most commonly encountered gynaecological problem. The prevalence of adnexal masses on routine ultrasonography is 0.17% to 5.9% in asymptomatic and 7.1% to 12% in symptomatic women^[1].

Adnexal masses of ovarian origin are of growing concern due to high case fatality rate associated with ovarian malignancy. Ovarian cancer is the most lethal among gynaecological malignancies. They are characterized by very few early symptoms, presentation at an advanced stage, and poor survival rates. It is three times more lethal than breast cancer². The differentiation of benign and malignant ovarian neoplasm is of great importance to determine the therapeutic approach. No single diagnostic tool (serum CA 125, ultrasonography, risk of malignancy index (RMI), magnetic resonance imaging, and computerized tomography) is accurate enough in preoperative diagnosis of malignancy in suspicious cases. Ultrasound, because of being relatively inexpensive, non-invasive, and widely available, is considered the initial method of choice in the evaluation of suspected ovarian masses.

Survival from ovarian cancer is related to the stage at diagnosis. The detection of early disease will largely improve outcome and survival rates.

To date, the IOTA study is the largest study in the literature on ultrasound diagnosis of ovarian pathology^[3]. The IOTA Simple Ultrasound Rules are a preoperative classification of ovarian tumors, consisting of five features typical for benign tumors (B-features) and five features typical for malignant tumors (M-features). The Simple Ultrasound Rules can be used to diagnose ovarian cancer in women who have at least one persistent adnexal (ovarian, para-ovarian, and tubal) tumor and are planned for surgery. Benign masses can be managed conservatively or with minimally invasive surgery, avoiding unnecessary morbidity. Based on which of the B- and M-features that apply, tumors are classified as Benign, Malignant or Inconclusive^[4].

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IOTA rules is 10 simple ultrasound rules that had have sensitivity and specificity and were applicable to a large number of tumours. Hence the need for this study to establish the diagnostic utility of these rules in complex ovarian masses 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.

Objectives

1. To evaluate the role of IOTA simple ultrasound rules in the pre-operative prediction of ovarian malignancy in complex ovarian masses.
2. To assess the diagnostic accuracy of IOTA rules prediction

with final histopathology reports.

Study Design: Prospective Study

Methodology

Women having complex adnexal masses detected sonologically using Affiniti 50 G Ultrasound and Doppler System, using a 3.75- 5 MHz sector transabdominal approach and planned for surgery in Father Muller Medical College Hospital, Mangalore were included in the study. Based on ultrasonographic findings IOTA simple ultrasound rules were applied. Patient were triaged according to IOTA findings. All predicted values obtained by IOTA score were compared with the final pathologic diagnosis.

Table 1: Iota Simple Rules

Benign	Malignant
B1- Unilocular	M1- Irregular Solid Tumor
B2- Presence of Solid Component With Solid Component <7MM	M2- Presence of Ascites
B3- Presence of Acoustic Shadows	M3- Atleast 4 Papillary Structures
B4- Smooth Multilocular Tumor With Largest Diameter <10CM	M4- Irregular Multilocular Solid Tumor With LARGEST Diameter >10CM
B5- NO Blood Flow	M5- Very Strong Blood Flow

Inclusion Criteria

- Women aged 15-65 years.
- Women having complex adnexal massess of size >5 cm detected sonologically.

Exclusion Criteria

- Women with simple cyst less than 5 cms in size.
- Women diagnosed with ovarian carcinoma or on concomitant chemotherapy.
- Women having adnexal masses of non-ovarian origin detected preoperatively or intraoperatively.

Statistical Analysis

Independent t test was used as test of significance. P value of <0.05 was considered as statistically significant.

Results

A total of 50 patients with complex adnexal masses were studied. The mean age in our study was 45 years. The youngest patient was 15 years and the oldest patient was 77 years. Twenty eight percentage (n=14) of patients were nulliparous. Fifty six percentage of patients had presented with pain abdomen as their presenting complaint and 26% had presented with mass per abdomen.

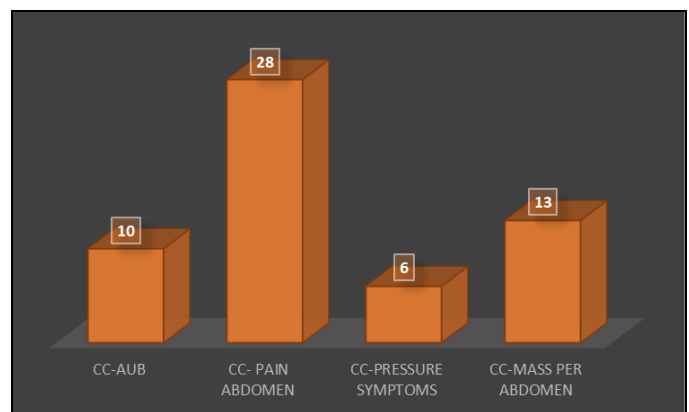


Fig 1: Presenting Complaints

Fifty four percentage (n=26) of patients had associated comorbidities like diabetes mellitus, hypertension, thyroid and cardiac disorders.

Thirty eight percentage (n=19) of patients belonged to the reproductive age, 38% (n=19) belonged to the postmenopausal age group and the remaining 24% (n=12) belonged to menopausal transition group.

IOTA simple rules applied pre operatively classified these patients as benign (n=24) when B rules were applicable, malignant (n=18) were M rules were applicable and inconsistent (n=8) when both rules applied or rules could not be applicable.

Table 2: Different Combinations of Iota Features in Our Study

S. No.	B1	B2	B3	B4	B5	M1	M2	M3	M4	M5	Frequency	Benign	Malignant	Percentage of Malignancy
1	1	0	0	0	0	0	0	0	0	0	1	1		0
2	1	0	1	0	0	0	0	0	0	0	3	3		0
3	0	0	0	1	0	0	0	0	0	0	7	7		0
4	0	1	0	1	0	0	0	0	0	0	1	1		0
5	0	0	1	1	0	0	0	0	0	0	1	1		0
6	0	0	0	0	1	0	0	0	0	0	1	1		0
7	1	0	0	0	1	0	0	0	0	0	4	4		0
8	0	0	1	0	1	0	0	0	0	0	2	2		0
9	0	0	0	1	1	0	0	0	0	0	4	4		0
10	0	0	0	0	1	1	0	0	0	0	1		1	100
11	0	0	0	0	0	0	0	0	1	0	1		1	100
12	1	0	0	0	0	0	0	0	1	0	1	1		0
13	0	0	1	0	0	0	0	0	1	0	1		1	100

14	0	0	0	0	1	0	0	0	1	0	3	1	2	66.66667
15	0	0	0	0	0	1	0	0	1	0	1	1		0
16	0	0	0	0	0	0	1	0	1	0	1		1	100
17	0	0	0	0	0	1	1	0	1	0	1		1	100
18	0	0	0	1	0	0	0	0	0	1	1	1		0
19	0	1	0	1	0	0	0	0	0	1	1	1		0
20	0	0	0	0	0	1	0	0	0	1	5	1	4	80
21	0	0	0	0	0	1	1	0	0	1	1		1	100
22	0	0	0	0	0	0	0	1	0	1	1		1	100
23	0	0	0	0	0	0	0	0	1	1	2		2	100
24	0	0	0	0	0	1	0	0	1	1	3		3	100
25	0	0	0	0	0	1	1	0	1	1	1		1	100
26	0	0	0	0	0	1	1	1	1	1	1		1	100

As shown in the above table 26 different combinations of B and M features were found in our study. The most common was presence of B4 feature for benign neoplasm and combination of M1 and M5 feature for malignant neoplasm. After histopathological examination 60 percent of the tumors were

benign and 40 percent of tumors were malignant (including 8% borderline tumors). Among the malignant neoplasm 42% of malignant tumors were seen in menopausal group and 42% in perimenopausal group.

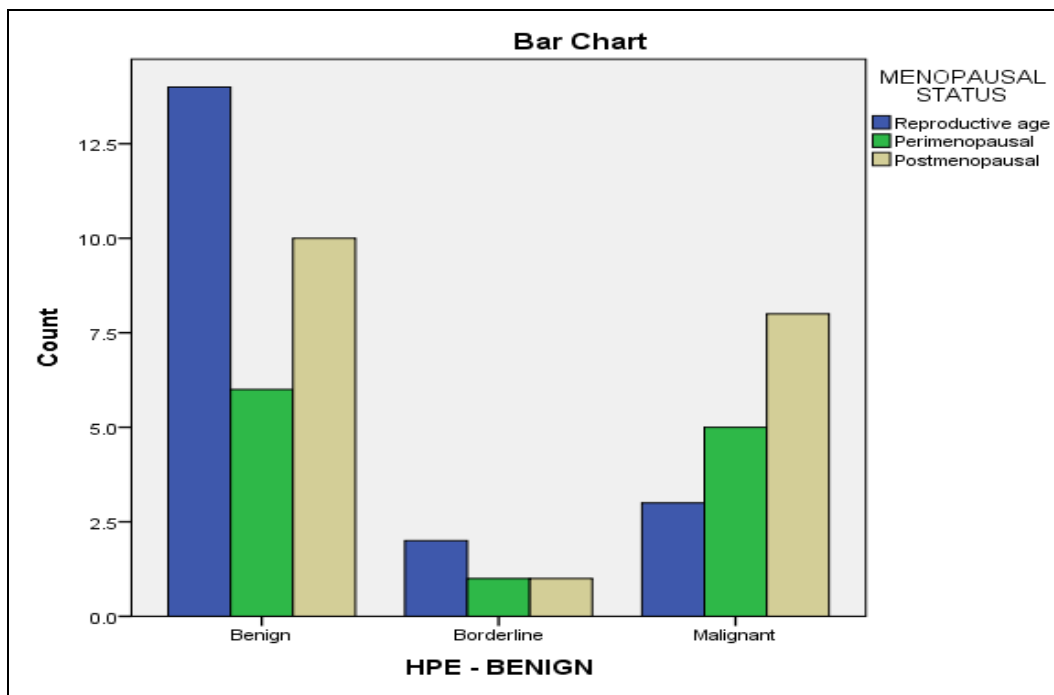


Fig 2: Comparison of Menopausal Status with Histopathology Features

Table 3: Correlation of Iota features with histopathology

Iota features	Predicted	HPE valid	Percentage
B1	9	8	89
B2	2	2	100
B3	7	6	86
B4	15	15	100
B5	15	9	60
M1	14	13	93
M2	5	5	100
M3	2	2	100
M4	16	9	56
M5	16	16	100

As shown in Table 3 B2, B4, M2, M3 and M5 features of IOTA had predictive index of 100%, while that of M4 feature had lowest predictive index of 56%.

Table 4: Comparison of IOTA prediction with HPE report

Diagnosis based on IOTA rules		HPE valid	Valid percent
Benign	24	24	100
Inconclusive	8	2	25
Malignant	18	14	78
Total	50	40	80

Thus by Table 4 IOTA simple rules had an agreement of 40 out of 50 cases in our study i.e., 80%.

In our study there were 2 false positive patients, whose final histopathology reported as mature cystic teratoma.

The overall sensitivity of IOTA simple rules in our study was 100%, specificity was 92.31%, positive predictive value was 87.5% and negative predictive value was 100% with overall diagnostic accuracy was 95%. Kappa value in our study was

0.658 which indicates good agreement with a P value of <0.001 .

Discussion

This study was conducted to evaluate the use of IOTA simple ultrasound rules as a tool in the preoperative prediction of malignancy in southern India. The presence of B features was considered as Benign, M features as Malignant and both B and M features was considered as inconclusive.

Table 5: Comparison of Results of Present Study with Published Studies

Study	No of patients	Prevalence of malignant tumors	Sensitivity	Specificity
Our study	50	40%	100%	92.31%
Garg S <i>et al.</i> [3]	50	28%	91.66%	84.84%
Nunes N <i>et al.</i> [5]	303	44.30%	97%	89%
Timmerman D <i>et al.</i> [6]	507	29%	95%	91%
Saysaneh <i>et al.</i> [7]	255	24.8%	95%	95%
Timmerman D <i>et al.</i> [8]	1936	25%	92%	96%
Hartman <i>et al.</i> [9]	103	24.20%	91%	87%
Alcazar J <i>et al.</i> [10]	340	12.2%	88%	97%
Fathallah K <i>et al.</i> [11]	122	10.1%	73%	97%

As seen in Table 5 the prevalence of malignant tumors in our study was 40% which was similar to the study conducted by Nunes N *et al.* [5] 44.3% and in contrast with the other studies.

Timmerman D *et al.* [6] in his multicentric study of 507 patients noted that when prospectively tested IOTA rules had a sensitivity of 95%, specificity of 91%, PPV of 80% and NPV of 97%. This study correlates with the results of our study which had a sensitivity of 100%, specificity of 92.31%, PPV of 87.5% and NPV of 100%.

In a single center prospective study of 303 patients Nunes N *et al.* [5] reported a sensitivity of 97%, specificity of 89%, PPV was 78% and NPV 95.2%. The results of this study was also similar with the results of our study.

Saysaneh *et al.* [7] in her multicentric study of 1165 women reported sensitivity and specificity of 95% and 95% which was similar to our study which had a sensitivity of 100% and specificity of 92.31%.

Dirk Timmerman *et al.* [8] in his large cohort study of 1936 patients reported IOTA to have a sensitivity of 92% and specificity of 96%. There is a positive correlation with the specificity of this study and our study 92.31%, though our study had a higher sensitivity of 100%.

Garg S *et al.* [3] in his study reported a sensitivity of 92%, specificity of 85%, PPV of 69% and NPV of 97% when simple rules were applied which contrasted the results of our study which had a sensitivity of 100% and specificity of 92.31%, PPV of 87.5% and NPV of 100%.

The reports of studies done by Hartman *et al.* [9], Alcazar J *et al.* [10] and Fathallah K *et al.* [11] were in contrast with the results of our study.

Overall our study showed high sensitivity, specificity and negative predictive value when IOTA simple rules were applied. The diagnostic accuracy of our study was 95%. Thus our study proves the efficiency of simple ultrasonography as an effective diagnostic and screening tool for differentiating benign and malignant ovarian neoplasm by application of IOTA simple

rules.

Conclusion

Survival from ovarian cancer is related to the stage at diagnosis. A number of screening modalities continue being researched and developed to develop an efficient test to preoperatively predict ovarian malignancy which would greatly improve outcome of the disease. IOTA simple rules using ultrasonography has increased diagnostic accuracy and would serve as an excellent non invasive screening modality and as a diagnostic tool in predicting ovarian malignancy. This would go a long way to help triage patients for appropriate treatment largely improving survival rates.

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