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Characterization of Adnexal Masses on Grey Scale Sonography and Color Doppler Imaging Using Simple IOTA (International Ovarian Tumour Analysis) Rules

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ABSTRACT

Aim: To assess the diagnostic performance of international ovarian tumour analysis (IOTA) simple rules to characterize adnexal masses as benign or malignant. **Methods:** A hospital based prospective cross sectional study was conducted. Patients with adnexal masses were evaluated using IOTA ultrasound rules and designated as benign or malignant. Findings were correlated with histopathological findings. Collected data was statistically analyzed using chi-square test and kappa statistical method. **Results:** Out of 83 patients, 80 patients were included in the final analysis who underwent surgery. IOTA simple rules were applicable in 70 out of 80 patients (87.5%). The sensitivity for the detection of malignancy in cases where IOTA simple rules were applicable was 95.83% and the specificity was 95.65%, the PPV was 92% and the NPV was 97.8%. Classifying inconclusive cases as malignant, the sensitivity, specificity, PPV and NPV were 96.3%, 83.02%,74.3% and 97.78% respectively. High level of agreement was found between ultrasound and histopathological diagnosis with Kappa value (K=0.784). **Conclusions:** IOTA simple ultra sound rules provide excellent discrimination between benign and malignant adnexal masses.

Keywords: IOTA SR, B rules, M rules, kappa statistics, ultrasound.

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INTRODUCTION

A woman presenting with adnexal mass is a common clinical problem. Correctly characterizing adnexal mass is critical as this ensures appropriate referral of patients with cancer to specialized surgeon, which is crucial to optimised patient care and survival.[1] By correctly recognising benign ovarian masses, conservative management may be adopted, leading to reduced morbidity. Different investigation tools, such as morphological scoring system and logistic regression analysis have been used to differentiate benign and malignant adnexal masses.[2-5] A systematic review in 2009 concluded that the risk of malignancy index is the best available test to triage patients with ovarian tumours for the referral to the Gynaec oncologist.[6,7] However, RMI which relies heavily on serum CA-125 for its prediction may not be useful in diagnosing germ cell malignancy in which other tumour markers such as AFP and LDH elevated. Therefore, if the study population contains a large number of germ cell tumours, then the sensitivity of RMI drops. Pattern recognition by an ultra sound examiner is an excellent method for discrimination between benign and malignant tumours.[8,9] In 2008, IOTA Group proposed simple ultra sound rules for the diagnosis of ovarian cancer.[10-12] Major highlight of the study were ten simple ultra sound rules that have 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 B rules or one or more B rules in the absence of 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 cannot be classified and is labelled as inconclusive.

Table 1: Simple Iota Rules for Predicting Benign or Malignant Ovarian Tumour

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 less 7 mm in largest diameter
M3- At least four papillary structures	B3- Presence of acoustic shadows
M4 - Irregular multilocular solid tumour with largest diameter greater 100 mm	B4 - Smooth multilocular tumour with largest diameter less than 100 mm
M5- Very strong blood flow (color score 4)	B5- No blood flow (color score 1)

Although large number of study are available providing the efficacy of the rule, 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

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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 & METHODS

This prospective cross sectional study was conducted in a tertiary care hospital. The protocol was approved by the institutional Ethics committee and all women gave informed consent. 83 patients with suspected ovarian pathology attending Gynaecology OPD were referred to Department of Radiodiagnosis SCB Medical College & Hospital, Cuttack during the period September 2018 to October 2020. Patients with suspicion of adnexal mass on pelvic examination or discovered during previous Sonographic examination were included and 2 pregnant patients and 1 patients not willing for surgery in our hospital were excluded. Transvaginal sonography was done on all the patients.[12-14] Examination was limited to transabdominal sonography in virgins and where it was not possible to completely visualize the mass by transvaginal probe. Sonography assessment of the given adnexal masses was done using wideband intra cavitary transducer having frequency 4-10 Mhz probe and 2-5Mhz trans abdominal curvilinear transducer connected to GE logiq F8 ultra sound machine. In cases of bilateral mass, the larger mass was considered. During the sonographic examination, the sonographers were blind folded for their results as well as histopathological findings. All patients included in the study underwent surgery (with 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

Out of 80 patients the mean age was 39.53 years. Youngest patient in the study was 14-year-old and the eldest was 70-year-old female. Malignancy was most common in 6th decade age group [Table 2]. Out of 80 patients, IOTA rules were applicable to 70 patients. In rest of the 10 patients where rules were not applicable or both B and M features applied, were termed as inconclusive. Among 70 applicable patients, 45 were indicative of benign and 25 indicatives of malignant.

Table 2: Distribution of Adnexal Masses in Different Age Groups

Age group (in years)	Benign	Percentage	Malignant	Percentage
11 to 25	7	13.207	2	7.4
26 to 40	33	62.264	4	14.81
41 to 55	12	22.641	15	55.56
56 to 70	1	1.887	6	22.22
Total	53	100	27	100

Table 3: Distribution of Adnexal Masses According to Menopausal Status

	Premenopausal	Postmenopausal	Total
Benign	47	6	53
Malignant	11	16	27
Total	58	22	80

Table 4: Observed Combinations of Benign and Malignant Ultrasound Features of Iota Simple Rules

	Frequency	Benign	Malignant	Rate of malignancy
B1+B5	31	31	0	0%
B1+B3	3	3	0	0%
B2	1	0	1	100%
B3	1	1	0	0%
B3+B5	2	2	0	0%
B4	4	4	0	0%
B4+B5	3	3	0	0%
M1	2	1	1	50%
M1+M2	2	0	2	100%
M1+M2+M5	2	0	2	100%
M2+M4	16	0	16	100%
M2+M4+M5	2	0	2	100%
M4	1	1	0	0%
B2+M3+M4	1	0	1	100%
B2+M4	2	2	0	0%
B2+M5	1	1	0	0%
B4+M5	1	1	0	0%
M2+B5	1	0	1	100%
M2+M4+B5	1	0	1	100%
M4+B5	1	1	0	0%
Unclassifiable	2	2	0	0%
Total	80	53	27	33.75%

In the present study 20 different combinations of benign and malignant simple ultrasound features were encountered. Out of 20 combinations, most common was B1 and B5 combination (31 cases) showing no risk of malignancy on final histopathological analysis. 11 combinations showed 0% risk of malignancy. Out of 7 combinations having 100% rate of malignancy, the most frequent combination of was application of rule M2 with M4 having frequency of 16 cases [Table 4].

Table 5: Prevalence and Predictive Power of Benign Factors

Benign	Predicted	Result	%
B1	34	34	100%
B2	5	3	60%
B3	6	6	100%
B4	8	8	100%
B5	41	39	95.12%
At least one B	55	49	89.47%

Out of all benign factors, B5 is the most common occurring factor, however B1, B3 and B4 predicted the result most correctly (100%) followed by B5 and B2 [Table 5].

Table 6: Prevalence and Predictive Power of Malignant Factors

Malignant	Predicted	Result	%
M1	6	5	83.3%
M2	24	24	100%
M3	1	1	100%
M4	24	20	83.3%
M5	6	4	66.66%
At least one M	33	26	78.787%

M2 and M4 were found to be the most commonly occurring malignant factors followed by M1 and M5. M2 and M3 predicted the results most accurately followed by M4 and M1. [Table 6].

Table 7: Iota Simple Rules Vs Histopathology Cross Tab

Nature of mass as per IOTA rules	Benign(HPE + resolved on follow up scan after 2 months)	Malignant(H/P)	Total
Benign	44	1	45
Malignant	2	23	25
Inconclusive	7	3	10
Total	53	27	80

Table 8: Iota SR (Excluding Inconclusive Cases) Vs HPE Cross Tab

IOTA SR (excluding inconclusive cases)	Benign (HPE +resolved on follow up scan after 2 months)	Malignant (HPE)	Total
Benign	44	1	45
Malignant	2	23	25
Total	46	24	70

Pearson chi square value=57.49, p value<0.001<alpha

Kappa statistic (0.784) [Table 7] showed good level of agreement between sonology and histopthological findings (>0.75 –Excellent, 0.75-Good, <0.4-Poor). In our study, the sensitivity of IOTA simple rules for the detection of malignancy where applicable was 95.83% whereas specificity was 95.65%. It had the Positive predictive value of 92% with a comparatively high negative predictive value of 97.78% and accuracy of 95.71% [Table 8].

Results were found to be statistically significant as the chi square value=57.49, p value<0.001<alpha (Alpha =0.05, confidence interval is 95%).

There was one false negative case in our study where there was presence of papillary projections, later on turned out to be borderline papillary serous epithelial neoplasm.

Table 9: Final Pathological Diagnoses of 80 Adnexal Masses

Pathological Diagnosis	No(percentage)
Benign Adnexal Masses	51(63.75)
Serous cysts(simple cysts)	16(31.37)
Corpus luteal cyst	3(5.88)
Dermoid cyst	6(11.764)
Endometriotic cyst	4(7.84)
Follicular cyst	7(13.725)
Serous cystadenoma	10(19.61)
Mucinous cyst adenoma	3(5.88)
Fibroma	1(1.96)
Acute salpingoophoritis	1(1.96)
Malignant Adnexal Masses	27(33.75)
Serous cystadenocarcinoma	17(62.96)
Metastatic adenocarcinoma	3(11.11)
Mucinous cystadenocarcinoma	5(18.52)
Borderline papillary serous epithelial neoplasm	1(3.7)
Dysgerminoma	1(3.7)
Simple Cysts Which Resolved On Follow Up Scan After 2months	2(2.5)

Out of 80 patients, 10 had bilateral masses (larger and more complex one was considered for study). Of them 51(63.75%) were found to be benign and 2 simple cysts were found to have resolved in follow up scan after 2 months suggesting them to be benign follicular cysts. 27(33.75%) adnexal masses were found to be malignant on histopathology [Table 9].

The most common benign adnexal mass was found to be serous cysts(31.37% of benign masses) followed by serous cyst adenoma (19.61%)and follicular cysts(13.725%). Other benign lesions in final HPE study were dermoid cyst(11.76%), endometriotic cyst(7.84%),mucinous cystadenoma(5.88%), corpus luteal cysts(5.88%), fibroma(1.96%) and acute salpingoophoritis(1.96%). Serouscystadenocarcinoma was found to be the most common malignant adnexal tumor accounting for 62.96%% of total malignant masses followed by mucinous cystadenocarcinoma(18.52%) and metastatic adenocarcinoma (11.11%). There was one borderline papillary serous neoplasm and one dysgerminoma in the present study [Table 9].

DISCUSSION

Till date only few studies which applied this diagnostic test directly to patient have been

performed. In this study, we have attempted to prospectively validate the ability of the IOTA simple ultrasound rules to discriminate between benign and malignant adnexal masses. The results of this study confirmed that when the rules yielded a conclusive result, they reliably discriminated between benign and malignant adnexal masses.

The IOTA SR is unable to classify all adnexal masses into benign or malignant in about 12% of the cases limiting its usefulness and requires subjective pattern recognition by an expert examiner to classify the inconclusive cases.

In addition to it, we divided the study group into premenopausal and post-menopausal group and the results were depicted in [Table 3]. The sensitivity and specificity is higher in premenopausal (100%, 97.56%) as compared to post-menopausal (93.75%, 80%) because of more number of inconclusive cases in premenopausal group.

Overall prevalence of malignancy of 80 adnexal masses was found to be 33.75% while the prevalence of malignancy excluding inconclusive cases was found to be 34.28%. the prevalence of malignancy was also much more in postmenopausal age group (73%) in comparison to premenopausal group.

Bilateral masses, presence of solid components/papillary projections, multilocularity, solid masses, presence of ascites, irregular cyst wall, large masses(size >10cm) and increased vascularity on color doppler were all associated with an increased risk of malignancy in the present study(with malignancy rates of 90%, 75%, 61.76%,83.3%, 100%, 79.4%, 60% and 69.23% respectively). There were 6 AM with presence of acoustic shadows all of which turned out to be benign mature cystic teratoma /dermoid cyst on final HPE.

Table 10: Comparison of Results of Present Study with the Published Data is shown.

Author and year of study	No of patients	Patients in whom rules are applicable	Malignant tumors	Benign tumors	Prevale-nce of maligna-ncy	Sensiti-vity	Specifi-city
Timmerman et al, 2008.[12]	507	386	-	-	27%	95%	91%
Timmerman et al, 2010.[13]	1938	1501	542	1396	25%	92%	96%
Fathallah K et all,2011.[15]	122	109	14	108	10.1%	73%	97%
Nunes N et al, 2012.[14]	303	237	135	168	44.3%	96%	89%
Hartman CA et al,2012.[16]	103	91	30	73	24.20%	91%	87%
Present study	80	70	45	25	34.28%	95.83%	95.65%

D. timmerman et al in 2008,[12] prospectively tested the simple rules on 507 patients. When prospectively tested the rules were applicable in 76% (386/507) of the tumors, where they had a sensitivity of 95% (106/112), a specificity of 91% (249/274), LR+ of 10.37, and LR− of 0.06.[12] The sensitivity of the present study was found to be almost similar to that of D.timmerman et all(2008) while the specificity was found to be slightly more.

The IOTA simple rules were prospectively validated by the IOTA group D. Timmermann et al in 2010.[13]Of the 1938 patients with an adnexal mass, 1396 (72%) had benign tumours, 373 (19.2%) had primary invasive tumours, 111 (5.7%) had borderline malignant tumours, and 58 (3%) had metastatic tumours in the ovary. The simple rules yielded a conclusive result in 1501 (77%) masses, for which they resulted in a sensitivity of 92% (95% confidence interval 89% to 94% and a specificity of 96% (94% to 97%).[13] The specificity of the present study where rules yielded conclusive result was found to be 95.65% which is almost similar to the study by the IOTA group.

In a metaanalysis study by N.Nunes et al in 2012,[14] The rules were applicable in 237 (78.2%) of the 303 tumours .For these women in whom the rules were applicable, the simple rules had a sensitivity of 96.2% and a specificity of 88.6%.[14] The accuracy was 92.0%. The diagnostic accuracy of the present study where rules yielded conclusive result were found to be 90%, similar to that of N.Nunes et al.

Limitation of study

1. Small sample size
2. All cases are from a single hospital

CONCLUSION

In conclusion, the IOTA simple rules have high diagnostic accuracy in differentiating between benign and malignant adnexal masses. Application of the IOTA simple rules yielded acceptable results in terms of sensitivity,specificity and malignancy rates which were comparable to recommended rates by previous literature. These rules are fairly simple and easily reproducible even in the hands of an inexperienced sonographer. However, their disadvantage is that these rules do not yield conclusive results in about 12.5% cases and require subjective pattern recognition approach by an expert sonographer. But wherever applicable, they have a high diagnostic efficacy.

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