Pooja Sharma
Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu, Jammu and Kashmir, India

Tarini Singh
Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu, Jammu and Kashmir, India

Ankita Sharma
Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu, Jammu and Kashmir, India

IOTA simple ultrasound rules for triage of ovarian masses: A prospective cross-sectional study in a tertiary care hospital

Pooja Sharma, Tarini Singh and Ankita Sharma

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Abstract
Background: A woman presenting with an adnexal mass is a common clinical problem. Correctly characterizing ovarian tumors is critical as it helps in recognizing benign ovarian masses, conservative management may be adopted, leading to reduced morbidity. In 2008, IOTA group proposed simple ultrasound rules for the diagnosis of ovarian cancer by demonstration of certain sonographic findings, indicative of benignity (B features) and some of which are suggestive of malignancy (M features).
Aim: The aim of this study was to establish the diagnostic utility of IOTA ultrasound rules, 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 in our tertiary care centre.
Methods: This was a prospective cross-sectional study conducted in SMGS hospital, Jammu, J&K from Jan 2019 to 2020. Women with at least one adnexal mass were recruited into the study. In the case of bilateral adnexal masses, the mass with the most complex ultrasound morphology was included in the analysis. Assessment of sonographic morphology of the masses together with color Doppler study was performed to characterize the masses. Sonological and histopathological correlation was established appropriate statistics methods.
Result: In a total of 79 patients with USG using iota rules: 49 were benign, 24 were malignant whereas 5 were inconclusive. On final HPE report of the 49 masses predicted to be benign by the simple rules, 47 were benign according to histopathology. Of the 24 masses predicted to be malignant by the simple rules, 21 were malignant according to histology.
Conclusion: IOTA simple rules provide excellent discrimination between benign and malignant adnexal masses.

Keywords: Ovarian masses, ovarian tumors, adnexal masses, IOTA rules, IOTA triage, ultrasound

Introduction
Adnexal masses are a common clinical problem among women. Correctly characterizing these ovarian tumors is critical, as it helps in recognizing benign ovarian masses. In these benign masses conservative management may be adopted, leading to reduced morbidity. The most prevalent type of pelvic masses is ovarian masses, which include cysts and tumors. The size of the mass, its mobility, consistency, shape, possible internal aqueous component, and associated pain are helpful features for diagnosis of the nature of the mass [1]. Different investigation tools, such as morphological scoring system and logistic regression analysis, have been used to differentiate benign and malignant adnexal masses [2]. RMI (risk of malignancy index is the best available test to triage patients with ovarian tumors. However, RMI which relies heavily on serum CA 125 for its prediction may not be useful in diagnosing germ cell malignancy in which other tumor markers such as AFP and LDH are elevated, hence the sensitivity of RMI drops. Pattern recognition by an experienced ultrasound examiner is an excellent method for discriminating between benign and malignant tumors. However, this type of expertise is available only in specialized ultrasound centers. In 2008, IOTA group proposed simple ultrasound rules for the diagnosis of ovarian cancer. These rules are based on demonstration of certain sonographic findings, indicative of benignity (B features) and some of which are suggestive of malignancy (M features).
Rules for predicting a malignant tumor (M rules)
M1 Irregular solid tumor
M2 Presence of ascites

Corresponding Author:
Ankita Sharma
Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu, Jammu and Kashmir, India

M3 At least four papillary structures

M4 Irregular multilocular solid tumor with the largest diameter ≥ 10 cm

M5 Very strong blood flow (color score 4)

Rules for predicting a benign tumor (B rules)

B1 Unilocular

B2 Presence of solid components with the largest diameter < 7 mm

B3 Presence of acoustic shadows

B4 Smooth multilocular tumor with the largest diameter < 10 cm

B5 No blood flow (color score 1)

Materials and method

This was a prospective, cross-sectional study conducted in a SMGS hospital, Jammu, J&K which is a tertiary care centre. It was carried out from Jan 2019 to 2020. The protocol was approved by the ethics committee, and all women gave informed consent.

Women with at least one adnexal mass were recruited into the study. In the case of bilateral adnexal masses, the mass with the most complex ultrasound morphology was included in our analysis.

The exclusion criteria were pregnancy, refusal of transvaginal ultrasonography, failure to undergo surgery within 120 days of the ultrasound examination.

Transvaginal ultrasonography was performed in all patients. Transabdominal ultrasonography was performed if a large mass could not be fully assessed vaginally. During the examination, assessment of sonographic morphology of the masses together with color Doppler study was performed to characterize the masses. The mass was classified as malignant if one or more M features were present in the absence of B features. If both B rules and M rules were applied or none were present, the mass was classified as inconclusive. Sonological and histopathological correlation was then performed.

Statistical analysis

Data was analyzed using using kappa statistics to establish the usefulness of IOTA simple rules for correlating sonological and histopathological reports of the ovarian masses.

Results

A total of 78 patients were included in our study. The mean age was 40.5 (range 15-72 years), 27% of the patients were nulliparous, and 33% were postmenopausal.

On USG using iota rules: 49 masses were benign, 24 were malignant whereas 5 were inconclusive

On final HPE report of the 49 masses predicted to be benign by the simple rules, 47 were benign according to histopathology. Of the 24 masses predicted to be malignant by the simple rules, 21 were malignant according to histology. There seemed to be strong agreement between ultrasonography findings and histopathological reporting (Table 1).

Table 1: Kappa value (95% CI) = 0.843 (0.613-0.981)

Nature or mass as per IOTA rules	NUMBER	HISTOPATHOGICAL	
		BENIGN	MALIGNANT
BENIGN	49	47	2
MALIGNANT	24	3	21
INCONCLUSIVE	5	3	2

IOTA simple rules seemed to be 91.3% sensitive and 94% specific in differentiating between benign and malignant masses,

excluding the inconclusive cases. Table 2 and Table 3 depicts its diagnostic accuracy.

Table 2: Diagnostic accuracy of IOTA simple rules taking histopathology as gold standard (excluding inconclusive cases)

Parameter	Value	95% CI
Sensitivity	91.3	73.2-97.6
Specificity	94.0	83.8-97.9
PPV	87.5	69.0-95.7
NPV	95.9	86.3-98.9
Accuracy	93.2	84.9-97.1

Table 3: Diagnostic accuracy of IOTA simple rules taking histopathology as gold standard (Taking inconclusive cases as Malignant)

Parameter	Value	95% CI
Sensitivity	92.0	75.0-97.8
Specificity	88.7	77.4-94.7
PPV	79.3	61.6-90.2
NPV	95.9	86.3-98.9
Accuracy	89.7	81.1-94.7

Discussion

There are several diagnostic methods to predict the nature of ovarian tumours as benign or malignant. These include clinical assessment, CA125 [3], sonographic morphology [4] or Doppler sonography. Initially the use of usg for assessment of ovarian tumors was a complex one requiring great expertise, this was overcome by IOTA simple rules in 2008 and subsequently their usefulness was demonstrated by several clinical studies. We applied these usg simple rules in patients presenting to our tertiary care centre to elucidate and establish their use as a tool in early diagnosis of ovarian malignancy.

In our study we included 78 patients, in whom 49 (62.8%) masses were suggested to be benign, 24 (30.7%) malignant and 5 (6.4%) inconclusive according to IOTA simple rules. This was almost similar to Sharma B *et al.,* [5] where according to usg IOTA rules 67.2% masses seemed benign and 26.2% as malignant.

Timmerman D *et al.,* [6] in their study found out the sensitivity and specificity of IOTA simple rules as 91% and 96% excluding inconclusive masses respectively and 94% and 80% taking inconclusive masses as malignant. In study by Fathallah k *et al.,* [7] the findings were sensitivity of 73% and 79%, specificity of 97% and 88%, without consideration and with consideration of inconclusive as malignant respectively. The figures comprehended by Nunes N *et al.,* [8] were 96% sensitivity and 89% specificity, excluding the inconclusive masses and 97% sensitivity and 70% specificity taking inconclusive as malignant masses. All these observations make IOTA rules extremely useful to differentiate between benign and malignant lesions. Our findings were in line with these studies. It showed a sensitivity of 91.3% and specificity of 94% disregarding the inconclusive masses and sensitivity of 92% and specificity of

88.7% regarding the inconclusive masses as malignant.

In a similar study by Sharma B *et al.,* [5] the sensitivity of IOTA simple rules for the detection of malignancy was 92.8%, whereas the specificity was 93%, it had the positive predictive value of 81.2%, with a comparatively high negative predictive value of 97.5% and the accuracy of 92.9%. Our study showed positive predictive value of 87.5%, negative predictive value of 95.9% and accuracy of 93.2% excluding the inconclusive masses. With inconclusive masses taken as malignant the PPV was 79.3%, NPV was 95.9% and accuracy of 89.7% was found out.

Tantipalakorn C *et al.*, [9] evaluated the diagnostic performance of IOTA simple rules in differentiating between benign and malignant ovarian tumors and found out sensitivity of 82.9% and specificity of 95.3%.

In a prospective study by Alcáza J *et al.,* [10] again IOTA simple rules were applied to find out the nature of ovarian masses. In these cases, sensitivity was 87.9% and specificity 97.5%. They concluded that application of the IOTA simple rules yielded acceptable results in terms of specificity even in the hands of examiners that were not so expert.

These IOTA simple rules have been included by the Royal College of Obstetricians in their guidelines for evaluating adnexal masses in premenopausal women. Most women diagnosed as having an adnexal mass are first evaluated by non-expert examiners. These rules are simple and easy to learn. Non-expert examiners using these rules provide reasonable good results.

Our study showed the ability of simple rules to discriminate between benign and malignant adnexal masses. Pattern recognition has been shown to be the best method for classifying adnexal masses as benign or malignant. Our results show that these rules are reasonably reproducible among observers with different levels of experience. This study indicates that the main advantage of simple rules is that they are user-friendly and does not require complicated computer software. Experienced ultrasound examiners take clinical and ultrasound information into account when they estimate the risk of malignancy in an adnexal mass, and they subconsciously apply a set of rules based on their previous observations when evaluating a tumor.

Conclusion
Usefulness of simple rules is related to its prevalence of malignancy in the study population. The limitation of this technique is that approximately 6.4% were inconclusive results, which needed further evaluation by pattern recognition. The reason for better diagnostic performance in this study may be due to the extensive training provided to the resident doctors before embarking on the study. In our opinion, the IOTA simple rules constitute a simple user-friendly way to classify an adnexal mass as benign or malignant.

Declarations
Conflict of interests: The authors declare that they have no conflict of interest.

Ethical standards: The study was performed after approval from the institutional ethical committee.

Informed consent: A written informed consent was taken from each patient for inclusion in the study. The patients who refused were excluded from the study.

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