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ORIGINAL ARTICLE

IOTA Simple Ultrasound Rules for Triage of Adnexal Mass: Experience from South India

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Abstract

Objective To assess the diagnostic performance of International Ovarian Tumor Analysis (IOTA) simple ultrasound rules to discriminate adnexal masses as benign or malignant.

Methods A cross-sectional prospective study was conducted on women scheduled for elective surgery due to adnexal masses. Ultrasound examiner systematically assessed the tumors according to the IOTA simple rules to determine the risk of the tumor being malignant. If the simple rules yielded inconclusive result, pattern recognition was used to categorize the mass. Results were then compared with histologic findings after surgery. Diagnostic performance was assessed by calculating sensitivity and specificity.

Results Two hundred and five women undergoing surgery were included. The rules were applicable in 183 (89.3%) of the tumors; and for these tumors, sensitivity was 92.8% (95% CI 77–99%) and specificity was 92.9% (95% CI 88–96.4%). Of the tumors, 144 were benign and 39 were malignant. The simple rules yielded inconclusive results in 22 masses which were analyzed by pattern recognition.

Conclusion IOTA simple rules provide excellent discrimination between benign and malignant adnexal masses.

Keywords IOTA simple rules · Adnexal mass · Ultrasound · Benign ovarian tumor

Introduction

A woman presenting with an adnexal mass is a common clinical problem. Correctly characterizing ovarian tumors is critical, as this ensures appropriate referral of patients with cancer to specialized surgeons, which is crucial to optimize patient care and survival [1]. By correctly recognizing 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 tumors for the referral to the gynecologic 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 tumor markers such as AFP and LDH are elevated. Therefore, if the study population contains a large number of germ cell tumors, then the sensitivity of RMI drops. Pattern recognition by an experienced ultrasound examiner is an excellent method for discriminating between benign and malignant tumors [8, 9]. 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 [10–12].These rules are based on demonstration of certain sonographic findings, indicative of benignity(B features) and

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Table 1 IOTA simple rules to describe malignant or benign features

Rules for predicting a malignant tumor (M rules)		
M1	Irregular solid tumor	☐
M2	Presence of ascites	☐
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)	☐

some of which are suggestive of malignancy(M features). In 2013, Sayasneh showed that simple rules perform well in the hands of examiners with different background training or relatively little experience using ultrasonography [13]. In our center, doctors training and experience of performing transvaginal ultrasonography vary and they have level-I experience. In spite of previous studies [14–17] showing high diagnostic accuracy, IOTA rules have never been tested for reproducibility in our population. The aim of this study was to assess the ability of simple ultrasound rules to discriminate adnexal masses as benign or malignant.

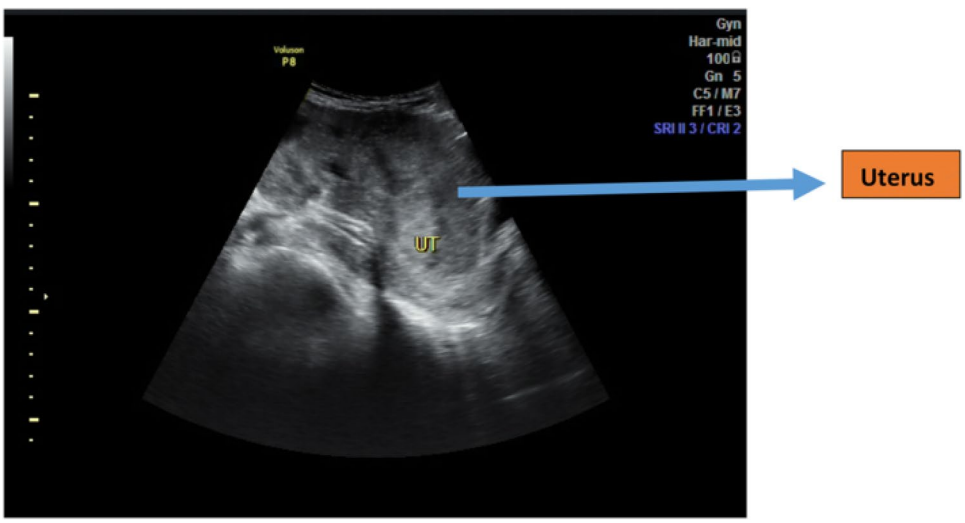
Methods

This prospective cross-sectional study was conducted in a tertiary care hospital. 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 (i) pregnancy, (ii) refusal of transvaginal ultrasonography, (iii) failure to undergo surgery within 120 days of the ultrasound examination

Transvaginal ultrasonography was performed using one of the available Voluson P8 or Phillips machines. Transvaginal ultrasonography was performed in the standardized manner previously published by the IOTA collaboration [12–14]. Transabdominal ultrasonography was performed if a large mass could not be fully assessed transvaginally. During the examination, assessment of sonographic morphology of the masses together with color Doppler study was performed to characterize the masses. Examiner evaluated the mass for the presence or absence of each benign or malignant ultrasound feature (Table 1). The resident (AS) filled the IOTA simple rules checklist by reading the original paper published by the IOTA group [12]. At the end of the examination, the mass was classified as benign if one or more B features were present in the absence of M features. 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 (Figs. 1, 2, 3, 4).

Surgery was performed in the case of a mass classified as persistent (i.e., still present 12 weeks after the initial scan). In cases of symptomatic masses, suspected malignancy, or at the

Fig. 1 Uterus



patient's request, surgery was performed more quickly, either by laparoscopy or laparotomy according to the surgeon's judgment. Histopathologic diagnosis of all patients was noted postoperatively. The masses with the pathological diagnosis of borderline tumors were categorized in the malignant group.

Statistical Analysis

Sample Size Calculation

$$n = \frac{(1 - \text{alpha}/2)^2 p(1-p)}{d^2}$$

$1 - \text{alpha}/2$ = confidence interval, p = population proportion (12%), d = margin of error (5%).

Sample size calculated by the above formula for the present study was 168. The sensitivity, specificity, positive predictive value and negative predictive value of IOTA simple ultrasound rules were calculated.

Results

A total of 207 patients were recruited. Data of excluded patients are depicted in the flow diagram (figure). The mean age was 37.5 (range 15–72 years), 27% (56) of the patients were nulliparous, and 23% (47) were postmenopausal (Table 2). In total, the simple rules yielded a conclusive result for 183(89%) of the tumors.

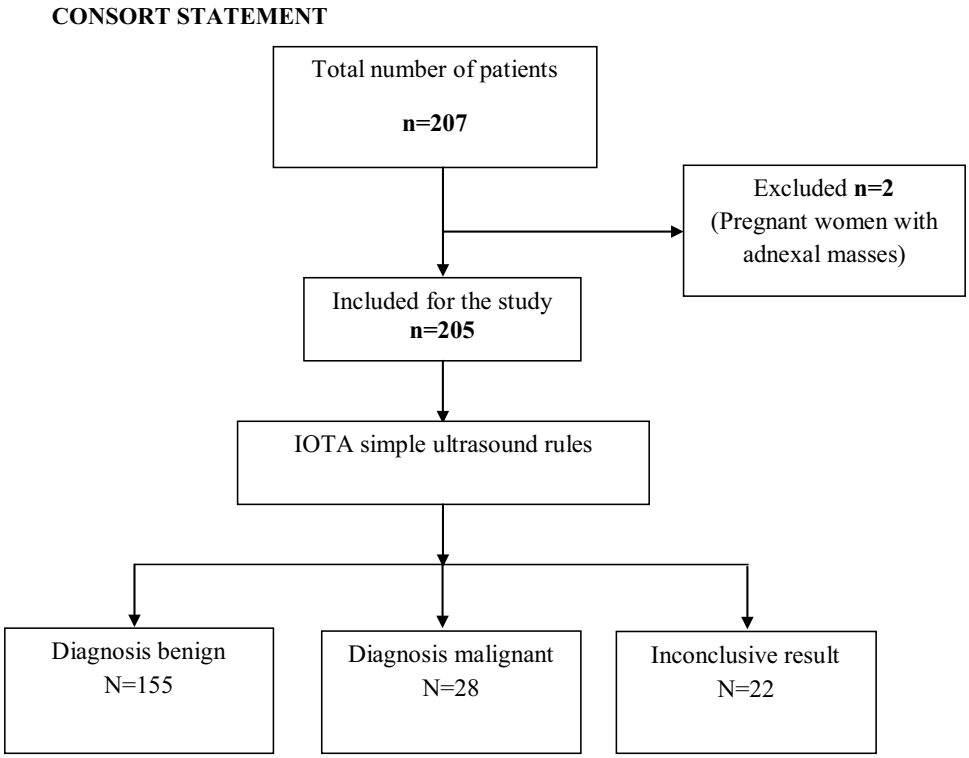
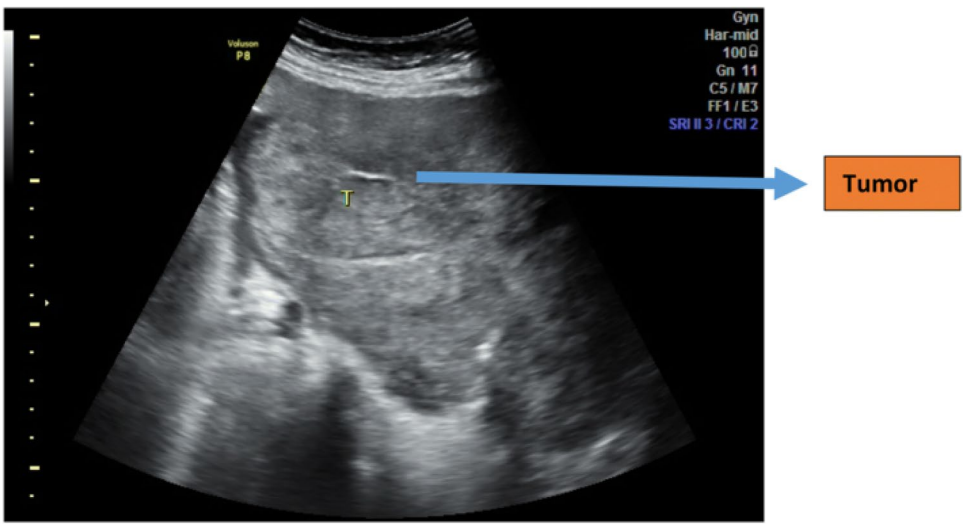


Fig. 2 Solid tumor



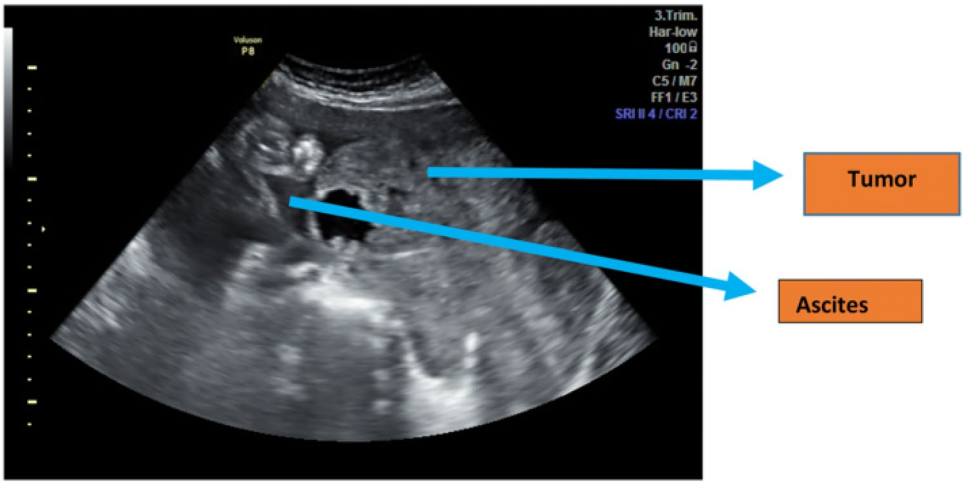


Fig. 3 "M" features

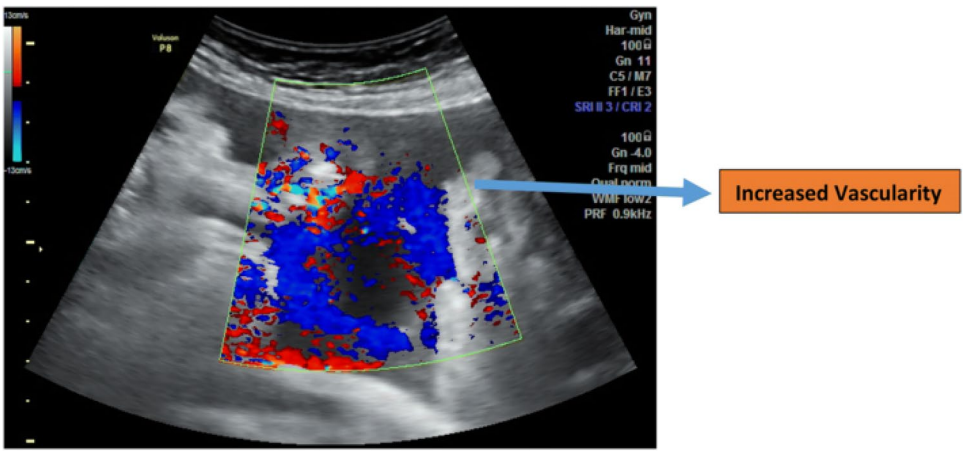


Fig. 4 Colour Doppler feature with strong blood flow

In 174 cases, at least one B feature was present, and in 155 (88%) of these no M features were present. Of the 155 masses predicted to be benign by the simple rules, 93% (144) were benign according to histopathology. In 51 cases, at least one feature for a malignant tumor was present, and in 28 (55%) of these no B feature was present. Of the 28 masses predicted to be malignant by the simple rules, 93% (26) were malignant according to histology. Table 3 shows the diagnostic performance of simple rules for which it yielded a conclusive result (183 cases). Pathological diagnoses of 183 adnexal masses predicted using simple rules are presented in Table 4.

Among the tumors for which the simple rules yielded an inconclusive result, pattern recognition was used as the second-stage test. In the 22 cases which were inconclusive by

Table 2 Demographic characters of patients based on histopathological classification of adnexal tumors as benign and malignant

Characteristics		Total No. of patients		Benign group by histopathology		Malignant group by histopathology		*P* value
		n = 205	%	*n* = 153	%	*n* = 52	%	
Mean age in years		37.5 ± 12.7		34.1 ± 10.5		47.6 ± 13.4		
Parity	Nullipara	56	27.3	32	20.9	12	23.1	0.03
	Multipara	149	72.7	121	79.1	40	76.9	
Menopausal status	Premenopausal	158	76.1	132	86.3	24	46.1	0.02
	Post menopausal	47	23.9	21	13.7	28	53.9	
Family history of ovarian/breast cancer	Present	10	4.9	4	2.6	6	11.5	0.01
	Absent	195	95.1	149	97.4	46	88.5	

Table 3 Diagnostic indices of IOTA simple ultrasound rules in predicting malignant adnexal masses

IOTA simple ultrasound rules	Pathological diagnosis Malignant $n=37$	Pathological diagnosis Benign $n=146$	Total
Malignant	True malignant $n=26$	False malignant $n=2$	28
Benign	False benign $n=11$	True Benign $n=144$	155
Diagnostic indices			
Sensitivity		92.8% 95% CI—77% to 99%	
Specificity		92.9% 95% CI—88% to 96.4%	
Positive predictive value		70.2% 95% CI—53% to 84%	
Negative predictive value		98.6% 95% CI—95% to 99%	

simple rules, 19 (86.4%) masses exhibited one B feature and one M feature and three masses did not exhibit any feature.

Discussion

In this study, we showed the ability of simple rules to discriminate between benign and malignant adnexal masses. To our knowledge, this study represents the first external validation of the IOTA simple ultrasound rules by examiners with a range of experience and training in South Indian population. As most ovarian pathology is probably examined by doctors who do not have a special interest in gynecologic ultrasonography (level II), it seems reasonable to suggest that our findings offer clinicians a clearer idea on the usefulness of simple rules. Most proposed sonographic assessments [18], which need high expertise, limit them from wide use in clinical practice. Pattern recognition has been shown to be the best method for classifying adnexal masses as benign or malignant [8, 19]. However, this requires expertise that not all ultrasound examiners have. In our hospital, sonographies were done by an OBGYN consultant with 3–10 years experience. The resident (AS) observed the images to fill the simple tick box system and could predict the mass as benign or malignant without the need for a mathematical model. 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. This skill is not easily transferable to less experienced ultrasound operators. A simple form using tick boxes that might be easily used in clinical practice to help less experienced examiners is shown in Table 1.

Compared to the previous studies [5, 14, 21] the sensitivity and specificity ranged from 88 to 93% and 90 to 97%, respectively, and our results were compatible with that of the literature. More recently, Hartman et al. reported a prospective study in a series of 110 adnexal tumors and they found that the simple rules could be applied in 82% of the tumors [20]. Usefulness of simple rules is related to its prevalence of malignancy in the study population. In our study,

Table 4 Distribution of pathological diagnosis of the adnexal masses

Benign tumors	No. of cases $n=146$	Percentage (%)
Endometriotic cyst	59	28.7
Serous cystadenoma	23	10.7
Mucinous cystadenoma	12	10.7
Dermoid cyst	18	8.7
Functional cyst	8	5.9
Paraovarian cyst	9	4.4
Hemorrhagic cyst	5	2.4
Hydrosalpinx/tuboovarian abscess	4	1.5
Peritoneal inclusion cyst	8	1.5
Borderline tumors	4	
Malignant tumors		
Serous cystadenocarcinoma	19	9.3
Immature teratoma	5	2.4
Mucinous cystadenocarcinoma	2	1
Dysgerminoma	1	0.5
Endometrioid carcinoma	1	0.5
Clear cell carcinoma	1	0.5
Sex cord stromal tumor	3	
Cellular fibroma of low malignant potential	1	0.5

malignancy prevalence was found to be 25%. Fathallah et al. [22] performed a prospective study using simple rules. This is the only study which reported low sensitivity (73%). Sensitivity was much lower than that in the IOTA studies and was probably because of the low malignancy rate (11%).

The limitation of this technique is that approximately 10% were inconclusive results, which needed further evaluation by pattern recognition. Recently, Tinnangwattana et al. [23] reported that inconclusive results were found in only 6% of the cases, better than that observed in the previous studies. The reason for better diagnostic performance in this study may be due to the extensive training imparted to the residents 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.

Conclusion

In conclusion, the IOTA simple rules have high diagnostic performance in differentiating between benign and malignant adnexal masses. IOTA rules were able to correctly characterize about 89% of adnexal masses. Where the rules yield an inconclusive result, this group must be referred for pattern recognition by an experienced ultrasound examiner. If we use simple rules as a triage test and pattern recognition by an experienced ultrasound examiner as a second-stage test in those masses for which the simple rules result was inconclusive, we obtain the same diagnostic performance as when pattern recognition is used in all masses. Therefore, the use of simple rules has the potential to reduce the burden of work on experienced ultrasound examiner.

Compliance with Ethical Standards

Conflict of interest None.

Informed Consent Informed consent in studies with human subjects: informed consent taken and ethical committee clearance obtained

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