RESEARCH ARTICLE

Comparison of Effectiveness in Differentiating Benign from Malignant Ovarian Masses between IOTA Simple Rules and Subjective Sonographic Assessment

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Abstract

Background: To compare diagnostic performance in differentiating benign from malignant ovarian masses between IOTA (the International Ovarian Tumor Analysis) simple rules and subjective sonographic assessment. Materials and Methods: Women scheduled for elective surgery because of ovarian masses were recruited into the study and underwent ultrasound examination within 24 hours of surgery to apply the IOTA simple rules by general gynecologists and to record video clips for subjective assessment by an experienced sonographer. The diagnostic performance of the IOTA rules and subjective assessment for differentiation between benign and malignant masses was compared. The gold standard diagnosis was pathological or operative findings. Results: A total of 150 ovarian masses were covered, comprising 105 (70%) benign and 45 (30%) malignant. Of them, the IOTA simple rules could be applied in 119 (79.3%) and were inconclusive in 31 (20.7%) whereas subjective assessment could be applied in all cases (100%). The sensitivity and the specificity of the IOTA simple rules and subjective assessment were not significantly different, 82.9% *vs* 86.7% and 94.0% *vs* 94.3% respectively. The agreement of the two methods in prediction was high with a Kappa index of 0.835. Conclusions: Both techniques had a high diagnostic performance in differentiation between benign and malignant ovarian masses but the IOTA rules had a relatively high rate of inconclusive results. The IOTA rules can be used as an effective screening technique by general gynecologists but when the results are inconclusive they should consult experienced sonographers.

Keywords: Ovarian tumor - benign - malignant - masses - IOTA simple rules - subjective ultrasonography

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Introduction

Preoperative differentiation between benign and malignant ovarian masses is very helpful for decision-making since the two entities usually need different therapeutic interventions. For instance benign or functional ovarian cyst need less aggressive approach, only close follow-up or laparoscopic surgery or simple pelvic surgery which can be performed by general practitioners, whereas malignant masses usually need available oncologists or referral to a tertiary center. Several sonographic methods are proposed to differentiate the two conditions, e.g. morphology scoring systems(Sassone et al., 1991; Lerner et al., 1994; Hafeez et al., 2013), or Doppler velocity indices (Tongsong et al, 2009; Alcazar et al., 2011; Guerriero et al., 2011), subjective assessment (Tongsong et al,, 2007), or IOTA (the International Ovarian Tumor Analysis) simple rules(Timmerman et al., 2008) which have been more popular recently. The IOTA simple rules for differentiation between benign and malignant ovarian masses were first proposed in 2008 by Timmerman et al. (2008). The IOTA rules are developed for general practitioners to identify ultrasound findings indicating malignancy (M-features) or benignity (B-features). Because of simplicity and high diagnostic performance (Timmerman et al., 2010), the rules have been widely accepted currently. We have found that the IOTA simple rules are also effective in our population even by non-expert sonographers (Tantipalakorn et al., 2014; Tinnangwattana et al., 2015). However the accuracy of the IOTA simple rules has never been directly compared with other methods in the same study population. The objective of this study was to compare the diagnostic performance of the IOTA simple rules by general gynecologists and subjective sonographic assessment by the experienced sonographer in differentiating between benign and malignant ovarian masses.

Materials and Methods

This study was undertaken at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, between

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April 2014 and December 2015 with ethical approval by the institute review board. The study population was patients who were admitted for elective pelvic surgery due to an adnexal mass. The patients were counseled and invited to join the research with written informed consent. Inclusion criteria included 1) a woman who was diagnosed for an adnexal mass which was detected either by prior ultrasound or pelvic examination, and 2) no known diagnosis of the adnexal masses before surgery, either by prior laparoscopic examination or previous history of pelvic surgery. Exclusion criteria included 1) the patients who had an operation beyond 24 hours after ultrasound examination, and 2) post-operative diagnosis of a non-ovarian mass for example subserous leiomyoma, tubo-ovarian abscess etc.

All recruited patients underwent ultrasound examination either transabdominal or transvaginal approach or both within 24 hours of surgery. All examinations were performed by the authors (general gynecologists; the residents who had taken a 2-week course of training for IOTA rules) who had no any clinical information of the patients, using a real-time machine Hitachi-Aloka model ProSound37 (Hitachi Aloka Medical Ltd, Inc., Tokyo, Japan). On ultrasound examination, sonographic morphology of the masses was evaluated by 2D real-time ultrasound and vascularization was assessed by color flow mapping. The sonographic characteristics of the masses were prospectively recorded in the research forms. The descriptions of the masses were interpreted based on the IOTA simple rules (Timmerman et al., 2008) to characterize whether the features were malignant (M) or benign (B), as presented in Table 1. If one or more M-rules applied in the absence of a B-rule, the mass was classified as malignant. If one or more B-rules applied in the absence of an M-rule, the mass was classified as benign. If both M-rules and B-rules applied or no rule applies, the mass was classified as inconclusive. During ultrasound examination, video clips of the masses, both real-time 2D cine and color flow mapping, were also recorded. The video clips were stored in the server for subjective assessment by the experienced author, who had experienced on ultrasound examination of adnexal masses for more than ten years. The experienced author had no any clinical information of the patients. The subjective assessment in differentiation between benign and malignant adnexal masses was based on sonographic pattern recognition (Tongsong et al., 2007), and color flow mapping of the masses on the video clips.

The definite diagnosis as a gold standard was based on pathological reports. In case of some benign masses without pathological specimens, the definite diagnosis was relied on the intraoperative diagnosis made by the surgeons. All of the masses were categorized into 2 groups as a benign and malignant group. The masses with pathological diagnosis of low malignant potential tumors were categorized in the malignant group.

Statistical analysis

The diagnostic performance of the IOTA simple rules and subjective assessment was calculated for sensitivity, specificity and predictive values. A comparison of the accuracy in differentiation between benign and malignant masses between the two methods was performed, using McNemar's chi-square test. The agreement of the two methods in predicting malignancy was evaluated using Cohen's kappa coefficient. The statistical analyses were performed using IBM SPSS version 21.0 (IBM SPSS Statistics for Windows, Released 2012. Armonk, NY: IBM Corp).

Results

A total of 164 adnexal masses, in 154 women, had been diagnosed as ovarian masses and were recruited into the study to undergo preoperative ultrasound examinations. Fourteen masses were excluded because of pathological diagnoses of non-ovarian lesions and surgery beyond 24 hours after sonographic examination. The remaining 150 ovarian masses in 144 women were included in analysis. The mean (+ SD) age of the women was 43.0+14.2 years (range 12-79 years). Two-thirds (101 women, 67.3%) were in reproductive age, 45 (30.0%) were post-menopausal and 4 (2.7%) were in early adolescent (less than 15 years). Forty-one (27.3%) were nulliparous.

Of 150 ovarian masses, 105 (70%) were benign and 45 (30%) were malignant. The final diagnoses of all ovarian masses are grouped and presented in Table 2. The IOTA simple rules could be applied in 119 (79.3%) and were inconclusive in 31 (20.7%) whereas subjective assessment could be applied in all masses (100%). The sensitivity and the specificity of the IOTA simple rules and subjective assessment were not significantly different, 82.9% vs 86.7% and 94.0% vs 94.3% respectively (Table 3, 4). The sensitivities and specificities of the two methods were not significantly different (McNemar's Chi square test; p-value: 0.83 and 0.95, respectively). The agreement of the two methods in prediction was high with the Kappa index of 0.835.

In the 31 masses of inconclusive results by the IOTA simple rules, 19 (61.3%) did not show the features of B-rule or those of M-rule; such as smooth multilocular tumors of more than 10 cm in diameter with very poor vascularization or some regular solid masses with scanty

Table 1. IOTA Simple Rules for Identifying a Benign or Malignant Tumor

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 largest diameter ≥100 mm	☐
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 largest diameter <100 mm	☐
B5	No blood flow (color score 1)	☐

Table 2. Frequencies of the Final Diagnoses of the Ovarian Masses

Diagnostic Categories	Final Diagnoses	Number	Percent
Benign tumors		105	70.0
	Endometriotic cyst	35	23.3
	Mature teratoma (Dermoid cyst)	21	14.0
	Mucinous cystadenoma	15	10.0
	Serous cystadenoma / simple cyst	13	8.7
	Hemorrhagic cyst	5	3.3
	Fibroma	4	2.7
	Struma ovarii	3	2.0
	Other Benign tumors	9	6.0
Borderline tumors		9	6.0
	Mucinous low malignant potentials	6	4.0
	Serous low malignant potentials	3	2.0
Malignant tumors		36	24.0
	Clear cell carcinoma	8	5.3
	Mucinous cystadenocarcinoma	6	4.0
	Endometrioid carcinoma	5	3.3
	Serous cystadenocarcinoma	5	3.3
	Metastatic adenocarcinoma	3	2.0
	Sex cord stromal tumor	2	1.3
	Endodermal sinus tumor	2	1.3
	Other malignant tumors	5	3.3
Total		150	100.0

color Doppler flow and 12 (38.7%) masses showed at least one B-feature and one M-feature, such as irregular solid tumors with scanty blood flow, acoustic shadowing or unilocular cysts with more than four papillary projections.

Discussion

We have found that the IOTA simple rules by general gynecologists were as effective as subjective sonographic assessment by the experienced sonographer in differentiating between benign and malignant ovarian masses. Additionally, the IOTA simple rules and subjective assessment had a high agreement in prediction as indicated by the high Kappa's index value (0.835). Nevertheless, the IOTA rules had a relatively high rate of the inconclusive results.

Though several studies on the IOTA simple rules have been reported, most are confined to the few groups of the western researchers (Timmerman et al., 2010; Di Legge et al., 2012; Alcazar et al., 2013; Kaijser et al., 2013a; Sayasneh et al., 2013). Our studies, as an external validation, showed that the result of high effectiveness of the IOTA simple rules could be reproducible in other groups and even among non-expert examiners. Together with its simplicity, this study suggests that the rules are clinically practical, and we believe that the rules are likely to be reproducible when applied by general practitioners or even non-expert examiners, though they certainly need a proper training course or practice under supervision for a short time period. Additionally, the rules may be used as an alternative to the risk of malignancy index (RMI), which is used in many guidelines concerning management of ovarian masses currently. This is supported by the recent study reported by Kaijser et al. (2013b) who demonstrated that an ultrasound based prediction model (developed by IOTA) showed a better diagnostic performance than ROMA for the characterization of a pelvic mass in both pre- and postmenopausal women.

Based on this study and previous reports (Timmerman et al., 2010; Alcazar et al., 2013; Sayasneh et al., 2013), though the IOTA simple rules yielded high diagnostic performance, approximately 20-30% of examinations were inconclusive while there were no inconclusive results when evaluated by the experienced sonographer. Inconclusive results are the main disadvantage of the IOTA simple rules. This indicates that a significant number of cases need to consult the expert sonographers. Such a disadvantage may raise a concern for widely use.

The strengths of this study included: 1) The comparison of the two methods was performed on the same ultrasound examinations, making them perfect for comparison in terms of patients, the ultrasound machine, and time of examinations. To the best of our knowledge this is the first study aimed to directly compare the effectiveness of the two methods using the same settings of ultrasound examinations. 2) The examiners performing IOTA simple rules could properly represent general gynecologists or general practitioners because they were in the residency training program and had not much experience on gynecologic ultrasound. This suggests that the high effectiveness results of the IOTA simple rules could be expected when widely used by general gynecologists or general practitioners.

The weaknesses of this study were as follows: 1) The subjective assessment by the expert was performed on the video clips instead of real practice. This was due to the inconvenience of practice for both the patients and the examiners to exam twice on each patient at the same time. 2) The IOTA simple rules were assessed by the residents, representing general gynecologists, who were in early learning curves of their practice. Therefore, the results might probably be less reliable. However, the results of relatively high effectiveness and high agreement with the expert assessment in predicting malignancy or benignity indicate that the method is simple and may be successfully trained in no time. 3) Selection bias might have existed because only the cases undergoing surgery were included. This was essential since the final diagnosis which was based on surgical or pathological findings was required for determining diagnostic indices. Nevertheless, such a bias seemed not to affect the conclusion since masses requiring no surgery is usually simple and benign or functional and easier to be categorized by ultrasound.

In conclusion, both techniques had a high diagnostic performance in differentiation between benign and malignant ovarian masses but the IOTA rules had a relatively high rate of the inconclusive results (approximately 20% of cases). Because of simplicity to practice with no need of highly-skilled expertise and high effectiveness, the IOTA rules are probably suitable for

widely use by any general gynecologists. Nevertheless when the IOTA simple rules are inconclusive they should consult the experienced sonographers.

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