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Comparison of Gi-Rads Ultrasonographic Stratification and IOTA Simple Rules in Distinguishing Benign Ovarian Masses from Malignant Ones

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ABSTRACT

Background: *Ovarian masses are common gynecological diseases which may appear and develop in any age group. Despite low prevalence rates, ovarian cancers still have a poor prognosis with high mortality rates, which can be effectively treated in the case of early detection and diagnosis.* ***Methods:*** *A total of 368 cases with ovarian masses treated from January 2016 to December 2017 were selected. These patients were diagnosed again by junior and senior blinded physicians using International Ovarian of Tumor Analysis simple rules (IOTA-SRs) and Gynecologic Imaging Reporting and Data System (Gi-Rads) respectively. Then the diagnostic efficiencies of 2 combined methods and individual ones were compared.* ***Results:*** *For the diagnosis of 368 patients, there were no significant differences between the sensitivity, PPV, NPV and DAR using IOTA-SRs and Gi-Rads by junior and senior physicians ($p>0.05$). Combining the 2 methods, it boosted the diagnostic performance, with the sensitivity, specificity, and DAR increasing to 96.3%, 92.31%, and 93.48% respectively. The sensitivity and NPV were significantly different ($p=0.021$, 0.032, $p<0.05$).* ***Conclusion:*** *Both IOTA-SRs and Gi-Rads had higher diagnostic performance and lower dependence on clinical experience. Combining the 2 methods may enhance the diagnostic performance, especially the sensitivity and NPV. Therefore, it is worthwhile to combine IOTA-SRs with Gi-Rads in the standardization and implementation of public reporting mechanism and the promotion of accurate pre-procedural stratification.*

Keywords: Ovarian masses, Ovarian cancer, IOTA, IOTA-SRs, Gi-Rads

INTRODUCTION

As common gynecological diseases, ovarian masses may appear and develop in any age group. Since malignant ovarian masses have unobvious early symptoms and are prone to spreading, approximately 60%-70% of the diagnosed cases are already in the advanced stage, and the 5-year survival rates of stage III and IV patients are <30%. Therefore, the mortality rate of ovarian cancer ranks first among those of all female malignant tumors [1,2]. In 2003-2007, the prevalence rate of ovarian cancer in China was 8.82 out of 100,000, accounting for 3.49% of the total one of Chinese female malignant cancers and ranking 8th. Besides, its mortality rate in China was 3.31 out of 100,000, which accounted for 2.51% of the total one of Chinese female malignant cancers and ranked 12th. The mortality rate of ovarian cancer grows with age and peaks at 75-79 years old (13.8/100.000) [3]. Ovarian masses are usually depicted by ultrasonography as benign or malignant to provide clinical treatment options, but the false positive rate of ultrasonographic diagnosis is as high as 24% [4,5]. Patients with malignant ovarian masses have a poor prognosis so their survival rates can be increased through early detection, diagnosis, and treatment. However, since surgeries are performed merely for suspected ovarian cancers with 1/3 being benign masses, it is key to elevate the diagnostic accuracy in order to decrease the treatment costs as well as to enhance the efficacy [1]. To increase the diagnostic rate and sensitivity, International Ovarian of Tumor Analysis simple rules (IOTA-SRs) and Gynecologic Imaging Reporting and Data System (Gi-Rads) have been proposed.

The aim of this study was to combine the IOTA-SRs with Gi-Rads to determine the stratification of benign and malignant ovarian masses, and to augment the diagnostic sensitivity and DAR.

MATERIALS AND METHODS

A total of 368 patients (14-82 years, mean: (37.63 ± 11.24) years) with ovarian masses diagnosed by gynecological sonography in Jinan Maternity and Child Care Hospital between September 2016 and September 2017 were studied retrospectively. About 7 patients (1.90%) developed bi-lateral or 2 and above masses, and 68 (18.48%) were in menopause. Surgeries were performed for cases with good pathological results.

Inclusion Criteria

- Female patients who were aged 14 or above, and received surgery or intervention for adnexal masses in the Department of Gynecology of our hospital with known pathological results
- Patients who received preoperative gynecological sonography in our hospital within 2 weeks; sonography was performed by our physician with over 5 years of working experience in gynecological sonography, and complete and clear sonograms were saved, with detailed and standardized ultrasonographic reports
- Patients who received no medical and surgical treatment prior to admission
- Patients who received serum CA125 test within 1 week prior to surgery

Exclusion Criteria

- Incomplete baseline clinical data were saved
- Patients who did not receive gynecological sonography in our hospital
- Serum CA125 was tested by other methods
- Patients who were definitely diagnosed with reoperation
- Patients with illegible sonograms or incomplete ultrasonographic reports

Apparatus

Color Doppler ultrasonic diagnostic apparatus (GE Voluson 730 Expert, TOSHIBA Aplio 770/790) was used with a probe frequency of 3.0 ~ 9.0 MHz, a transabdominal probe frequency of 3.0 ~ 5.0 MHz and a transvaginal probe frequency of 5.0 ~ 9.0 MHz. Serum CA125 test was performed with a Siemens ADVIA Centaur CP system.

Methods

The 368 patients were examined by 2 gynecologists (A: junior physician with 5 years of working experience; B: a senior physician with over 20 years of working experience) blinded to previous diagnostic and surgical results. The subjects lay in the supine position for transabdominal or transvaginal ultrasonic diagnosis to scan pelvic organs such as the uterus and bi-lateral appendages, especially adnexal masses.

Ultrasonic scanning of ovarian masses: For patients with ovarian masses found (if 2 or above lesions existed, those with the highest risk of malignancy indicated in sonograms should be studied) by 2D ultrasonography, the position, morphology, size, boundary and internal echo of the masses, as well as the relationships with adjacent organs, were observed. We focused on the morphological indices recommended by IOTA-SRs, i.e. bilaterality of masses, smoothness of the sac wall, thickness of the sac wall (threshold: 3 mm), separation, appearance of papillary protuberance (length: >7 mm), appearance of solid region, internal echo, complication with ascites, etc. Color Doppler was employed to study the existence and amount of blood flow through masses and adjacent areas. Color sampling boxes were adjusted to optimize blood flow observation, and to test the peak systolic velocity and resistance index (RI).

Determination and analysis of benign and malignant ovarian masses by IOTA-SRs: The International Ovarian Tumor Analysis (IOTA) study aims to develop a simple diagnostic algorithm to help clinicians with different clinical experiences characterize adnexal pathology. In the 2000 year, the IOTA group published a consensus paper in order to standardize terms, definitions, and measurements to describe the sonographic features of adnexal tumors [6]. A major highlight of the study was 10 simple ultrasound rules (5 benign signs and 5 malignant ones) that had high sensitivity and specificity and were applicable to a large number of tumors [6]. In this study, benign and malignant ovarian tumors were diagnosed according to the classification criteria (Table 1).

Table 1 Simple IOTA rules for predicting benign or malignant ovarian tumor

Rules for predicting a malignant tumor (M-rules)	Rules for predicting a malignant tumor (B-rules)
M1: Irregular solid masses	B1: Unilocular cyst
M2: Presence of ascites	B2: Presence of solid portion (maximum diameter <7 mm)
M3: Minimum 4 papillary structures	B3: Presence of acoustic shadows
M4: Irregular multilocular solid tumor (maximum diameter ≥ 100 mm)	B4: Smooth multilocular tumor (maximum diameter <100 mm)
M5: Abundant blood flow signals (color score 4)	B5: without blood flow signal (color score 1)

The benign and malignant masses of all 368 patients were determined by physician A and physician B based on IOTA-SRs respectively, and postoperative pathological results were obtained. The benign and malignant tumors distinguished by IOTA-SRs were compared with the surgical results through statistical analysis (Figures 1-4).

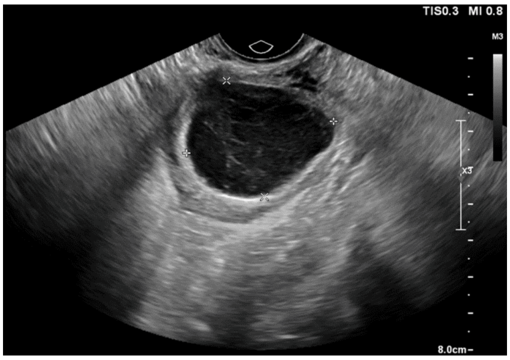

Figure 1 Transvaginal sonogram of an adnexal mass using IOTA-SRs diagnosis of benign tumors. Postoperative pathology proved that it was a luteal cyst

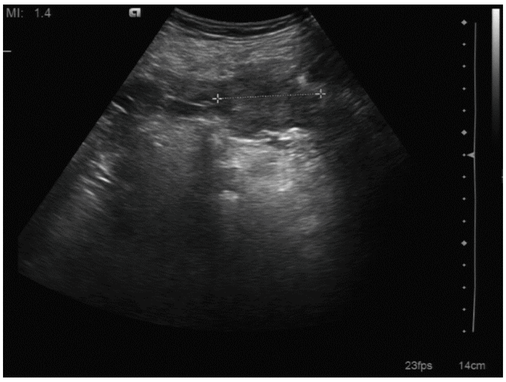

Figure 2 Transabdominal sonogram of an adnexal mass using IOTA-SRs diagnosis of malignant tumors. Postoperative pathology proved that it was metastatic adenocarcinoma

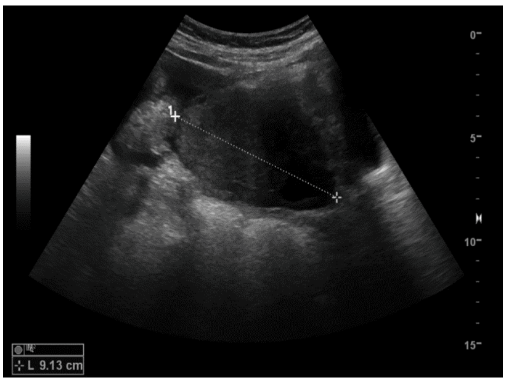

Figure 3 Transabdominal sonogram of an adnexal mass using IOTA-SRs diagnosis of borderline tumors. Postoperative pathology proved that it was a fibroma

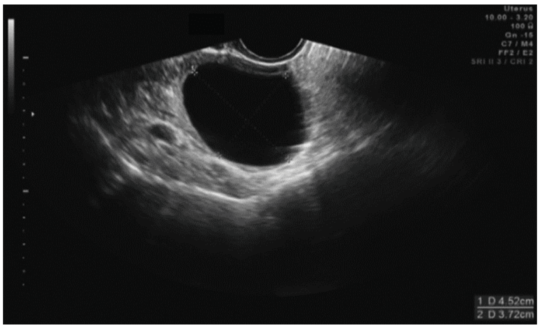

Figure 4 Transvaginal sonogram of an adnexal mass using IOTA-SRs diagnosis of borderline tumors. Postoperative pathology suggested malignant transformation

Determination of benign and malignant ovarian masses by ultrasonographic stratification using Gi-Rads: Ovarian tumors are classified by Gi-Rads ultrasonographic stratification into:

- Class 1: No obvious positive ovarian tumors are found by ultrasound, i.e. appendages are normal
- Class 2: High possibility of benign tumors, manifested as functional tissues (Figure 5)
- Class 3: Possibility of benign tumors, manifested as benign neoplastic ovarian tumors (Figure 6)
- Class 4: Suspected malignant tumors, with Class 2-3 lesions excluded and the following 1-2 malignant manifestation(s): large papillary prominence, thick wall separation, obvious solid region, abundant internal blood flow, a complication with ascites and minimum RI of <0.5 (Figure 7)
- Class 5: High possibility of malignant tumors which have 3 or more malignant manifestations listed in Class 4 (Figure 8).

All 368 patients with ovarian tumors were classified by physician A and physician B based on Gi-Rads ultrasonographic stratification respectively. The above results were compared with the “golden standard” through statistical analysis.

Class 1-4 lesions in Gi-Rads ultrasonographic stratification were considered as benign tumors, and Class 5 ones were considered as malignant tumors, which were then designated as Gi-Rads-1. Alternatively, Class 1-3 lesions were considered as benign tumors, and Class 4-5 ones were considered as malignant tumors, which were thereafter designated as Gi-Rads-2. The diagnostic efficiencies for Gi-Rads-1 and Gi-Rads-2 were analyzed.

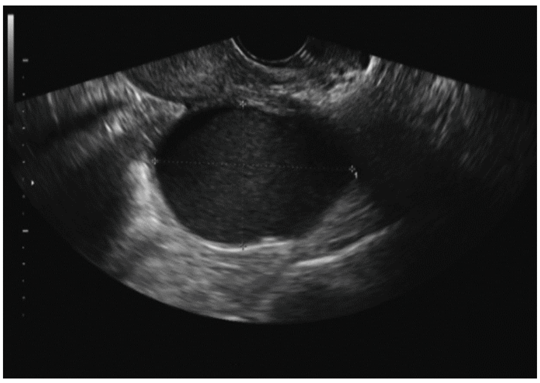

Figure 5 Transvaginal sonogram of an adnexal mass diagnosed as a corpus luteum cyst and classified as Gi-Rads-2. Surgery was performed, and the diagnosis was confirmed based on histopathological analysis

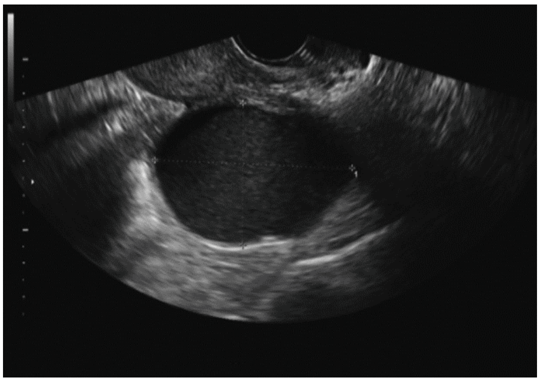

Figure 6 Transvaginal sonogram of an adnexal mass diagnosed as an endometrioid tumor and classified as Gi-Rads-3. Surgery was performed, and the diagnosis was confirmed based on histopathological analysis

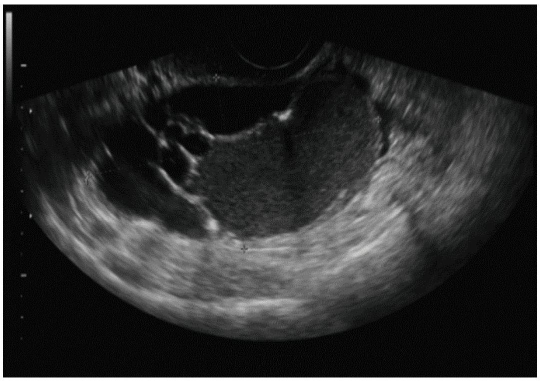

Figure 7 Transvaginal sonogram of an adnexal mass diagnosed as an ovarian mucinous cystadenoma with borderline malignancy and classified as Gi-Rads-4. Surgery was performed, and the diagnosis was confirmed based on histopathological analysis

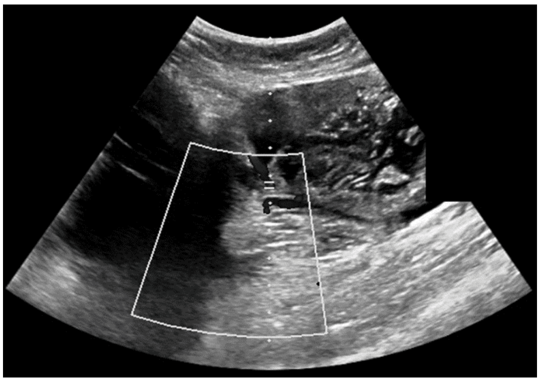

Figure 8 Transabdominal sonogram of an adnexal mass diagnosed as a mucinous ovarian carcinoma and classiied as Gi-Rads-5. Surgery was performed, and the diagnosis was confirmed based on histopathological analysis

Histopathological examination: Surgically dissected ovarian masses were examined histopathologically, using the pathological diagnosis results of paraffin sections given by 2 senior pathologists as standards.

Statistical Analysis

Data were analyzed with SPSS version 20.0 software. Normally distributed categorical data were expressed as mean ± standard deviation $\overline{\chi} \pm S$, whereas abnormally distributed ones were expressed in medians (M). Inter-group comparisons were conducted quantitatively with the t-test or rank test, and multiple samples were compared by one-way analysis of variance or the rank test. Numerical data were compared by using the χ^2 test. The α=0.05 was set as the test level, $p<0.05$ indicated that the difference was statistically significant, and $p<0.01$ suggested a markedly significant difference.

RESULTS

Results of IOTA-SRs

Of the 368 patients, 117 received transvaginal ultrasonic scans and the other 251 received transabdominal ones. Based on IOTA-SRs, physicians A and B determined 253 (68.75%) and 253 benign tumors (68.75%) respectively, 51 (13.86%) and 57 malignant tumors (15.49%) ($p>0.05$) respectively, as well as 64 (17.39%) and 58 inconclusive tumors (15.76%) respectively (Tables 2-4). Statistical analysis was conducted for both physicians in classifying all inconclusive cases as malignant by using IOTA-SRs.

Table 2 Results and pathology obtained by physician A using IOTA-SRs (case)

IOTA-SRs Classification	Histopathology		Total	DAR (%)
	Malignant	Benign		
Malignant	90	25	115	88.32%
Benign	18	235	253	
Total	108	260	368	

Table 3 Results and pathology obtained by physician B using IOTA-SRs (case)

IOTA-SRs Classification	Histopathology		Total	DAR (%)
	Malignant	Benign		
Malignant	92	23	115	89.40%
Benign	16	237	253	
Total	108	260	368	

Table 4 Diagnostic performances of physicians A and B by using IOTA-SRs alone

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	DAR (%)
Physician A	83.330%	90.380%	78.260%	92.890%	88.320%
Physician B	85.190%	91.150%	80.000%	93.680%	89.400%
χ^2	0.140	0.092	0.105	0.126	0.230
p-value	0.709	0.762	0.746	0.722	0.631

The sensitivity, specificity, and DAR in classifying all inconclusive cases as malignant by physicians A and B using IOTA-SRs alone were 83.33% vs. 90.38%, 88.32% vs. 85.19%, and 91.15% vs. 89.40% respectively (Table 4). The χ^2 test indicated that the diagnostic results of the 2 physicians were similar.

For the distinguishing of benign and malignant tumors, IOTA-SRs are sensitive, specific, targeted and easily usable, without needing computer software. Moreover, there were no significant differences between physicians with various lengths of clinical practice ($p>0.05$). Accordingly, IOTA-SRs may be an ideal tool for inexperienced ultrasonographers and community hospitals to preliminarily distinguish benign ovarian masses from malignant ones [7].

Diagnostic Performance of Gi-Rads in Distinguishing Benign Ovarian Masses from Malignant Ones

The 368 patients were classified by physician A and physician B based on Gi-Rads ultrasonographic stratification respectively. Class 1-4 lesions were considered as benign tumors, and Class 5 ones were considered as malignant tumors, which were then referred to as Gi-Rads-1. They were determined as follows: 263 (71.47%) and 263 benign tumors (71.47%) respectively; 105 (28.53%) and 105 malignant tumors (28.53%) respectively ($p>0.05$) (Table 5).

Table 5 Diagnostic performances of physicians A and B by using Gi-Rads-1 alone

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	DAR (%)
Physician A	84.260%	94.620%	86.670%	93.540%	91.570%
Physician B	86.110%	95.380%	88.570%	94.300%	92.660%
χ^2	0.147	0.162	0.176	0.133	0.309
p-value	0.702	0.687	0.675	0.715	0.578

In addition, Class 1-3 lesions were considered as benign tumors, and Class 4-5 ones were considered as malignant tumors, which were thereafter referred to as Gi-Rads-2. They were determined as follows: 252 (68.48%) and 247 benign tumors (67.12%) respectively; 116 (31.52%) and 121 malignant tumors (32.88%) respectively ($p>0.05$) (Table 6).

Table 6 Diagnostic performances of physicians A and B by using Gi-Rads-2 alone

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	DAR (%)
Physician A	87.040%	91.540%	81.030%	94.440%	90.220%
Physician B	88.890%	90.380%	79.340%	95.140%	89.950%
χ^2	0.175	0.211	0.107	0.123	0.016
p-value	0.676	0.646	0.743	0.726	0.900

The determination results given by senior and junior physicians using Gi-Rads stratification were not significantly different (Table 6), i.e. similar results were obtained either by considering Class 1-4 lesions as benign tumors and Class 5 ones as malignant tumors, or Class 1-3 lesions as benign tumors and Class 4-5 ones as malignant tumors.

Diagnostic Performance of Combining IOTA-SRs with Gi-Rads Stratification

Table 7 shows the results of combining IOTA-SRs with Gi-Rads stratification to distinguish benign and malignant ovarian tumors. A total of 124 positive cases were diagnosed by the combined methods, of whom 104 cases were in accordance with the golden standard and 20 were not. There were 244 negative cases, with 240 cases being in accordance with the golden standard and 4 being not. Combining IOTA-SRs with Gi-Rads in color Doppler examination may improve the diagnosis of benign and malignant ovarian masses. Particularly, the sensitivity, specificity, and DAR were increased to 96.30%, 92.31%, and 93.48% respectively. Both sensitivity and NPV had statistically significant differences (p=0.021, 0.032, p<0.05).

Table 7 Diagnostic performances of combining IOTA-SRs with Gi-Rads stratification to distinguish benign ovarian masses from malignant ones

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	DAR (%)
IOTA-SRs*	85.190%	91.150%	80.000%	93.680%	89.400%
Gi-Rads**	88.890%	90.380%	79.340%	95.140%	89.950%
IOTA-SRs*+Gi-Rads**	96.300%	92.310%	83.870%	98.360%	93.480%
χ^2	7.767	0.612	0.957	6.902	4.376
p-value	0.021	0.736	0.620	0.032	0.112

IOTA-SRs* indicates the examination results given by senior physician B; Gi-Rads** indicates the examination results given by senior physician B when considering Class 1-3 lesions in Gi-Rads ultrasonographic stratification as benign tumors and Class 4-5 ones as malignant tumors. In the case of combined examination, either positive item indicates a positive result

DISCUSSION

Currently, benign and malignant tumors are optimally distinguished by experienced ultrasonographers who, however, may sometimes be lacking [8]. Therefore, IOTA developed IOTA-SRs to assist clinicians to depict the pathological characteristics of ovarian masses regardless of their skill levels. In 2000, IOTA issued a consensus document that defined the terminology, definition and measurement standardization to evaluate ovarian pathology [8]. In 2008, different IOTA methods, such as SRs which indicated benign lesions based on 5 B features and malignant lesions based on 5 M features, were put forward by a prospective study on ovarian masses in non-screening patients [9]. As IOTA-SRs can be facilely used without any calculation, they have been widely validated and adopted as international codes with extensive applications [10]. This method has thus become one of the best tools to distinguish benign ovarian masses from malignant ones [8,11]. In this study, the tumor diagnostic performances of different physicians using IOTA-SRs were similar (p>0.05), suggesting that this method hardly depended on clinical experience.

Gi-Rads stratification, which is adapted from the Breast Imaging Reporting and Data System to classify adnexal masses in a similar way, is used to diagnose benign and malignant ovarian tumors and to avoid high false positive rates caused by inexperienced ultrasonographers or clinicians who have inadequate information [12]. Herein, Gi-Rads stratification gave a false positive rate of lower than 24% which was reported by Timmerman [5]. When Gi-Rads stratification was combined with IOTA-SRs, PPV further decreased to 83.87%.

CONCLUSION

Both IOTA-SRs and Gi-Rads stratification had satisfactory diagnostic performances which were further boosted upon their combination. Notably, the sensitivity, specificity, and DAR were raised to 96.30%, 92.31%, and 93.48%

respectively. The differences between both sensitivity and NPV were statistically significant. Therefore, it is of great significance to combine IOTA-SRs with Gi-Rads ultrasonographic stratification in standardizing and implementing public reporting mechanism as well as promoting accurate pre-procedural stratification and appropriate management.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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