

The comparison of diagnostic accuracy of risk of malignancy index to IOTA simple rules in diagnosing adnexal masses



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ABSTRACT

Introduction: Ovarian cancer is one of the top three deadliest cancer in women and diagnosing this disease still leaves some challenges to overcome. Therefore, this study aimed to compare the diagnostic accuracy of the Risk of Malignancy Index (RMI) to International Ovarian Tumor Analysis (IOTA) simple rules in adnexal masses.

Methods: A retrospective study was conducted involving 29 patients diagnosed with ovarian tumors. RMI and IOTA Simple Rules were determined preoperatively and compared with histopathology examination as the gold standard. The accuracy of both methods was analyzed using SPSS.

Results: The mean age of the patients in this study was 45 years old. The sensitivity and specificity of RMI were 65% and 55,5%, respectively. The sensitivity and specificity of the IOTA SR were 90% and 55,5%, respectively. The values for the AUC for RMI and IOTA SR are 0.342 and 0.728, respectively. The AUC of the IOTA SR was significantly higher than the RMI ($P < 0.005$).

Conclusions: IOTA SR is a relatively useful diagnostic model in characterizing adnexal masses, while the RMI only performs fairly.

Keywords: adnexal, Risk Malignancy Index, International Ovarian Tumor Analysis simple rules.

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INTRODUCTION

Ovarian cancer ranks third-most common cancer among women. Based on 2018 GLOBOCAN data, the prevalence of ovarian cancer was 13,310 cases, about 7.1% of all cancer cases in women.¹ The high prevalence of ovarian cancer in Indonesia is a challenge for clinicians to increase the survival rate, one of which is a preoperative risk assessment so that patients can be appropriately managed if there is a potential for ovarian cancer.

The preoperative risk assessment is an initial and essential step for patients with an adnexal mass. Precise characterization of adnexal masses is imperative for optimal patient management. Patients with suspected ovarian malignancy receive appropriate management at a gynecologic oncology center, while patients with benign adnexal masses can be managed at a non-gynecologic oncology center.^{2,3}

Currently, there are various methods to predict whether an adnexal mass is malignant or benign, i.e., the IOTA simple

rules and the risk malignancy index (RMI).⁴

RMI is a predictive method based on mathematical calculation and is considered one of the effective preoperative methods to differentiate malignant from benign adnexal masses. This method has several advantages, such as being relatively simple and performed by a less experienced sonographer. In addition, this method can also reduce overtreatment and reducing healthcare costs. However, the drawback of the RMI examination is the limited sensitivity of the examination.⁵ The reason for low sensitivity is because RMI is mainly affected by serum CA-125, which only increases in approximately 40-50% of stage I ovarian cancer.⁶

Therefore, the IOTA group developed a prediction method known as Simple Rules (SR). The Simple Rules are a system that classifies adnexal masses preoperatively, consists of five features for benign tumors (B-features) and five features typical for malignant tumors (M-features). For

women with at least one adnexal (ovarian, para-ovarian, and tubal) tumor and who are known to need surgery, the Simple Rules may be used to diagnose ovarian cancer. Later on, the tumors are classified as Benign, Malignant or Inconclusive. The IOTA SR method has high sensitivity and specificity to differentiate malignant and benign ovarian tumors compared to the RMI score. However, the IOTA SR examination requires experience and expertise from the sonographer.^{7,8} Several studies had been made to evaluate both tools and the result shown that RMI has high diagnostic accuracy (Sensitivity: 100%; Specificity: 96.2%), while IOTA simple rules have a higher specificity value (up to 97%) and are applicable in 89.3% of adnexal masses.⁴ However, few studies have been conducted to compare both of them.

The purpose of this study was to compare the diagnostic output in the distinction between benign and malignant adnexal masses of the IOTA SR with the RMI score.

METHODS

A retrospective study of 29 patients diagnosed with ovarian tumor based on ultrasound and laboratory and histopathology examination as definitive diagnosis of the type of ovarian tumor. This study was conducted at the Division of Gynecological Oncology, Department of Obstetrics and Gynecology, Kandou General Central Hospital, Manado, Indonesia, for a period of 4 months of study from May to August 2020. All cases of ovarian tumors were taken from patients who were referred and treated in Kandou General central Hospital, Manado. All patients were examined using both transabdominal and transvaginal ultrasounds performed by residents under the supervision of Consultant Gynecologic Oncologists. All patients were also measured for CA-125 from laboratory examination. Both IOTA simple rules and RMI were determined preoperatively.

On ultrasound examination, we performed both transabdominal and transvaginally to assess the morphology of the tumors. We used 2D real-time ultrasound for the morphology and performed a color doppler to identify vascularization of the tumors. The morphology was described and interpreted based on IOTA simple rules. The Simple Rules are a method of preoperative classification of adnexal masses consisting of five characteristics typical for benign tumors (B-characteristics) and five features specific for malignant tumors (M-features). If one or more M-rules occur in the absence of a B-rule, the mass is labeled as malignant. In the absence of an M-rule, if one or more B-rules occur, the mass is labeled as benign. If both M-rules and B-rules appear, the mass is categorized as inconclusive or cannot be classified. If no rule applies, the mass cannot be classified as well. We documented each of the examinations for further evaluation and validation.

The RMI was assessed following the calculation $U \times M \times \text{serum CA-125 (U/mL)}$. The "U" represents the ultrasound with a maximum value of 3. It consists of locularity, papillary projections, bilateral, ascites, and intra-abdominal metastases. The "M" represents the menopausal state of the women, postmenopausal women

will be scored as 3, and premenopausal women will be scored as 1. We followed the menopause criteria according to the European Society of Human Reproduction and Embryology (ESHRE). The cut-off value for malignancy was defined as $RMI \geq 200$.

The definitive diagnosis was made from histopathology reports of each patient. All the tumors were categorized into two groups, benign and malignant groups. The masses with histopathology reports of borderline tumor or low malignant potential tumors were categorized as malignant.

Sensitivity, specificity, and predictive values were measured for the diagnostic accuracy of the IOTA rules and the RMI. A comparison of accuracy in differentiating tumors as benign or malignant were performed using ROC. $P < 0.05$ was considered statistically significant. The statistical analyses were performed using SPSS version 25.0.

RESULTS

In this study, 29 patients were thoroughly assessed for data. The mean age of the

patients in this study was 45 years old (16-75 y.o.). The mean serum level of CA-125 was 1425,91 U/mL. There were 19 (65%) patients categorized as pre-menopause and 20 (35%) patients categorized as post-menopause (Table 1).

The definitive diagnostic was made by histopathologic examination. On histopathological examination, there were 9 (31%) cases with benign examination results, 8 (28%) cases with borderline examination results, and 12 (41%) cases with malignant results. The benign group was evenly represented, while the malignant group was dominated by mucinous adenocarcinoma and borderline mucinous tumor (Table 2).

According to the analysis, the sensitivity and specificity of RMI were 65% and 55.5%, respectively, while IOTA SR showed higher diagnostic accuracy at 90% of sensitivity and 55.5% specificity. The Positive Predictive Value and Negative Predictive Value of RMI were 81.25% and 58.33%, respectively, while IOTA SR showed higher value at 81.81% and 71.42%, respectively.

Table 1. The Baseline Characteristics of Research Subjects

Patient Characteristics	Value
Mean age	45
Menopausal state	
Premenopausal	19 (65%)
Postmenopausal	20 (35%)
Definitive Histopathology	
Benign	9 (31%)
Borderline	8 (28%)
Malignant	12 (41%)
CA-125 Serum	
<35 U/mL	7
≥35 U/mL	22

Table 2. Histopathologic examination

Definitive Histopathology	Frequency
Benign	
Serous cystadenoma	1
Mucinous cystadenoma	2
Endometriotic Cyst	2
Simple epithelial cyst	2
Hemorrhagic cyst	2
Malignant	
Serous adenocarcinoma	4
Mucinous adenocarcinoma	6
Serous borderline tumour	1
Mucinous borderline tumour	8
Metastatic carcinoma	1
Total	29

Table 3. Diagnostic Performance of RMI and IOTA SR in characterizing ovarian tumours.

Method	Sensitivity	Specificity	PPV	NPV	AUC
RMI	65%	55.5%	81.25%	58.33%	0.689 (0.484-0.894)
IOTA SR	90%	55.5%	81.81%	71.42%	0.728 (0.508-0.948)

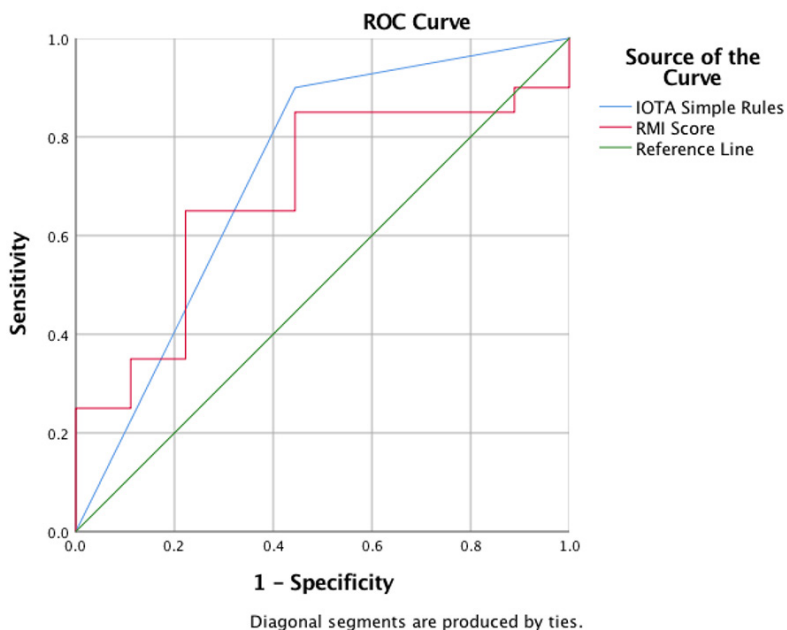


Figure 1. ROC of IOTA Simple Rules and RMI Score

Figure 1 shows the ROC curve to assess the accuracy of both methods in preoperatively classified adnexal masses, calculated for the RMI and IOTA SR to compare the AUC of these models. The values for the AUC for RMI and IOTA SR are 0.342 and 0.728, respectively. The AUC of the IOTA SR was significantly higher than the RMI ($P < 0.005$).

DISCUSSION

Before the operation, the classification of adnexal masses and the distinction between benign and malignant characteristics are imperative to reduce unnecessary anxiety and allow efficient decision-making on optimal care. In this study, the results of the IOTA SR analysis showed that the results of sensitivity, specificity, PPV, and NPV were higher than the RMI Score examination.^{7,9}

Another study showed that RMI performed better than the result of our evaluation. A systematic review conducted by Geomini et al showed the sensitivities and specificities of an RMI I score of 200 in the detection of ovarian malignancies to be: RMI I sensitivity 78% (95% CI 71-85%), specificity 87% (95% CI 83-91%).¹⁰ Whereas in our study, the sensitivity of

the RMI was only 65% with a specificity of 55.5%.

The IOTA Group has published a study investigating the use of ultrasound to differentiate the malignant and benign adnexal masses. The simple ultrasound rules, known as IOTA SR, were developed to help classify masses preoperatively as benign (B-rules) or malignant (M-rules).^{5,7,8} The reported sensitivity for IOTA SR was convincing. It had 95% sensitivity, 91% specificity, a positive likelihood ratio at 10.37, and a negative likelihood ratio of 0.06.11. In our study, the sensitivity on the IOTA SR examination was 90%, with a specificity of 55.5%. This study shows several advantages of ultrasound examination using IOTA SR in determining the characteristics of the adnexal mass. These results are consistent with a study conducted by Sayasneh et al., where the RMI sensitivity was only 72% compared to IOTA SR with a sensitivity of 91%.¹² The same results were obtained from the study of Mulder et al., where they got an RMI sensitivity of 72% versus an IOTA SR sensitivity of 90%.¹³ A systematic review and meta-analysis of RMI conducted by Kaijser et al. also showed similar results to ours, where the sensitivity was 72% and specificity was 92%; compared with the

IOTA SR sensitivity and specificity at 93% and 81%, respectively.¹⁴

Compared with several previous studies, this study showed an advantage of the IOTA SR examination compared to the RMI examination. The ultrasonographic variables are easier to obtain, and the rules are applicable in clinical practice than are many mathematical models. Moreover, consistent with when the RMI is used, no blood sample for a serum CA 125 is needed. The IOTA SR from ultrasound findings gives a general gynecologist or beginner sonographer an optimal and sufficient ability to differentiate between benign and malignant adnexal masses. Because the IOTA SR offers a direct result of accurately characterizing about 75% of adnexal masses, their use could reliably and sufficiently differentiate malignant and benign masses in almost all cases.^{2,3}

On the RMI examination, one of the variables is the serum CA-125 level. CA-125 is considered to have low sensitivity and specificity in differentiating adnexal masses regarding their malignancy features in premenopausal women because of the increased rate of false positives.^{7,15} This problem is caused by CA-125 is also raised in some benign gynecologic cases, such as fibroids, adenomyosis, endometriosis, and pelvic infection. CA-125, a primary marker of epithelial carcinoma, is also raised in only 50% of early-stage diseases. On the other hand, the RMI score is reproducible and straightforward, but its utility is negatively affected in premenopausal women. It is primarily because premenopausal women are still highly affected with endometriomas, non-epithelial ovarian tumours, borderline ovarian tumours, and other benign gynaecologic conditions.²⁻⁴

CONCLUSION

Correctly classifying the nature of ovarian pathology is a common diagnostic problem in gynecology, and accurate identification of cancer in these cases is the key to ensure patients access appropriate treatment. This study showed that the IOTA SR is a relatively useful diagnostic model in characterizing adnexal masses, while the RMI only performs fairly. However, a more extensive study is needed to confirm our findings.

CONFLICT OF INTEREST

All authors declared that there is no conflict of interest regarding this article

ETHICS APPROVAL

This study has been approved by the ethics commission of Universitas Sam Ratulangi with ethical clearance number: KE/FK/0218/EC/2020

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AUTHOR CONTRIBUTION

All authors contributed equally in the study and the writing of this article

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