Research Article

International Ovarian Tumor Analysis (IOTA) Scoring System to Predict Ovarian Malignancy Pre-operatively

Sistem Skoring Internasional Ovarian Tumor Analisis untuk Memprediksi Keganasan Ovarium Prabedah

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Abstract

Objective: To compare diagnostic performance of International Ovarian Tumor Analysis (IOTA) scoring method with Risk of Malignancy Index-4 (RMI-4) and Sassone Morphology Index to predict ovarian malignancy preoperatively.

Method: Retrospective study with 119 subject who underwent surgical removal of ovarian tumor and performed histopathological examination at Dr. Cipto Mangunkusumo Hospital on January to December 2013. Demographic status, ultrasound scans, CA-125 level and histopathological result were collected to calculate the score of each method. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated by comparing each score with histopathology result. Comparison of diagnostic performance was analyzed by ROC curve.

Result: There were 51.26% subjects with benign tumor and 48.74% subjects with malignant tumor. Result was analyzed with sensitivity test (IOTA simple-rules, IOTA subgroup, RMI-4 and Sassone): 98%, 88%, 86% and 79%; specificity: 74%, 67%, 61% and 89%; positive predictive value: 78%, 72%, 68% and 87%; negative predictive value: 98%, 85%, 82% and 81%; and accuracy: 86%, 77%, 73% and 84%. AUC value for IOTA simple-rules, IOTA subgroup, RMI-4 and Sassone were: 0.86, 0.78, 0.73 and 0.84. Comparison of these results were significant with p = 0.000.

Conclusion: IOTA simple-rules had better sensitivity, negative predictive value and accuracy than IOTA subgroup, RMI-4 and Sassone morphology index to predict ovarian malignancy preoperatively.

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Keywords: iota, ovarian neoplasm, risk of malignancy, scoring

Abstrak

***Tujuan**: Membandingkan kemampuan diagnostik metode skoring International Ovarian Tumor Analysis (IOTA) dengan Risk of Malignancy Index-4 (RMI-4) dan Sassone Morphology Index dalam memprediksi keganasan ovarium prabedah.*

***Metode**: Uji diagnostik secara retrospektif pada 119 pasien yang menjalani pembedahan atas indikasi neoplasma ovarium dan dilakukan pemeriksaan histopatologi di RSUPN Dr. Cipto Mangunkusumo dari Januari hingga Desember 2013. Data demografi, ultrasonografi dan kadar CA-125 dikumpulkan untuk dikelola menurut metode skoring IOTA simple-rules, IOTA subgroup, RMI-4 serta Sassone dan dibandingkan dengan histopatologi. Nilai diagnostik dari keempat metode skoring dihitung dengan luaran: sensitivitas, spesifisitas, nilai prediksi positif, nilai prediksi negatif dan akurasi. Perbandingan ketiganya dihitung menggunakan kurva ROC.*

***Hasil**: Didapati 51,26% subjek dengan tumor jinak dan 48,74% subjek dengan tumor ganas. Dari perhitungan, didapat sensitivitas IOTA simple-rules, IOTA subgroup, RMI-4 dan Sassone adalah: 98%, 88%, 86% dan 79%. Spesifisitas: 74%, 67%, 61%, dan 89%. Nilai prediksi positif: 78%, 72%, 68%, dan 87%. Nilai prediksi negatif: 98%, 85%, 82%, dan 81%. Akurasi: 86%, 77%, 73% dan 84%. Nilai AUC IOTA simple-rules, IOTA subgroup, RMI-4 dan Sassone adalah: 0,86; 0,78; 0,73 dan 0,84. Perbandingan keempat nilai AUC ini memberikan hasil bermakna p = 0,000.*

***Kesimpulan**: IOTA simple-rules memiliki sensitivitas, nilai prediksi negatif dan akurasi lebih baik dibandingkan IOTA subgroup, RMI-4 dan Sassone Morphology Index dalam memprediksi keganasan ovarium prabedah.*

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***Kata kunci**: iota, kanker ovarium, keganasan ovarium, skoring, tumor ovarium*

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INTRODUCTION

Ovarian cancer is a primary malignancy of the ovary.[1] Approximately 192.000 new cases are discovered per year worldwide.[2] In United State, the prevalence of ovarian cancer is 23.100 cases per year, while in United Kingdom is 6.000 cases.[3,4] In Indonesia, according to the National Cancer Registry Indonesian Society of Gynecological Oncology (INASGO)[5], from 2000 - 2013, approximately 2930 cases were discovered. Ovarian cancer is the third most common malignancy in women after cervical and breast cancer.[6]

Survival rate of ovarian malignancy is very poor, a study was done in United Kingdom demonstrated that 5-years survival rate of early ovarian cancer was 73%, while in the advanced stage was 16%.[7] According to this study, it is important to detect in early stage, since delay in diagnosis correlates with

delay in treatment and more over poorer in prognosis. To minimize delay in diagnosis, it is important to evaluate the ovarian tumor whether it is a benign or malignant, because it will facilitate the referral to the tertiary level.

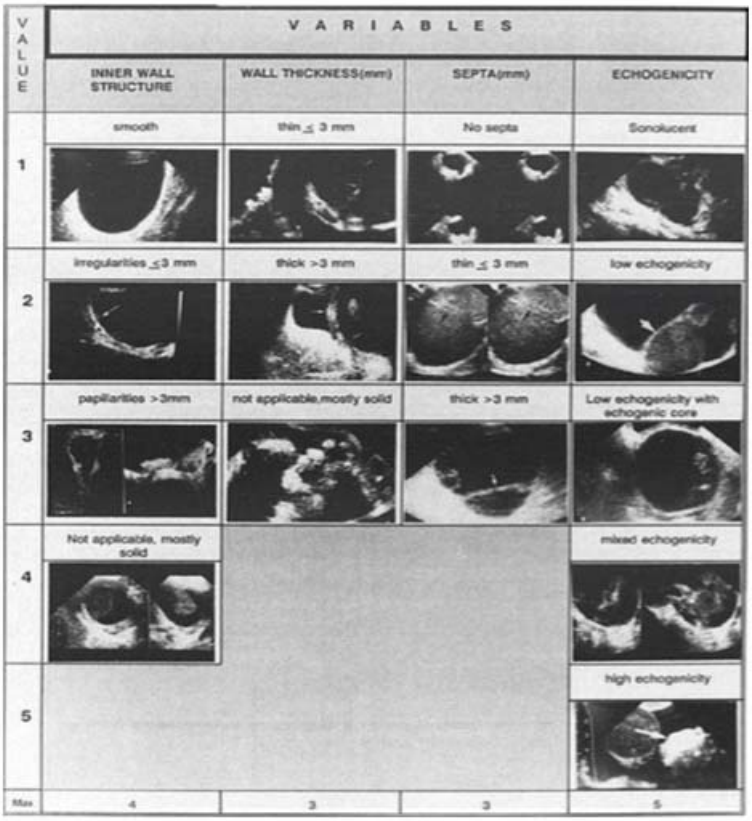
Ultrasonography has developed many scoring systems to predict ovarian malignancy, which is: Sassone Morphology Index (1991), Risk of Malignancy Index (Jacob, 1991), and International Ovarian Tumor Analysis (IOTA, 2000-2013).[8] Each of the scoring system has good sensitivity and specificity in predicting malignancy in ovarian tumor.

Unfortunately, there is no data that compare the diagnostic performance of each scoring systems and its applicability in Indonesian population. Therefore, this study aims to demonstrate the diagnostic performance of IOTA, Sassone Morphology Index and RMI-4.

METHODS

This was a retrospective study with subject population was patients who underwent surgical removal of ovarian tumor and histopathological examination in National General Hospital Dr. Cipto Mangunkusumo on January to December 2013. Medical records, along with the ultrasound scans, were reviewed by gynecological oncology consultant. Incomplete medical records or ultrasound scans and borderline histopathology tumor were excluded from this study.

Each scoring method was calculated on every subjects, based on IOTA simple-rules, IOTA subgroup, Sassone Morphology Index and RMI-4 to evaluate the tumor for malignancy possibility. The reference standard of this study was histopathology examination using World Health Organization classification. The operational definition of IOTA simple-rules, subgroup, RMI-4 and Sassone Morphology Index can be found on Table 1, 2, 3 and Figure 1. The outcome of the study was sensitivity, specificity, positive predictive value, negative predictive value and accuracy that were performed by ROC curve. Statistical significancy was determined by p value < 0.05. SPSS v.21 was used to do the statistical calculation.



Benign if score < 9; Malignant if ≥ 9

Figure 1. Sassone morphology index[12]

Table 1. IOTA Simple-rules[9]

B-rules	M-rules
Unilocular	Irregular solid
Solid part with diameter < 7 mm	Ascites
Multilocular with regular border size < 100 mm	Multilocular with irregular border > 100 mm
Acoustic shadow	At least 4 papillary projections
No blood flow	Strong blood flow

Table 2. IOTA subgroup[10]

Unilocular	Multilocular	Weight	Solid component, no papillation	Weight	Papillation	Weight
	Ascites	2	Ascites	7	Ascites	3
	Number of locules	1	Irregular wall and:		Age ≥ 50 years	1
	Max lesion D ≥ 100 mm	1	Completely solid tumor	5	Number of papillations ≥ 4	2
	Age ≥ 50 years	1	Multilocular solid with max lesion D ≥ 100 mm	3	Papillary flow	2
			Other	1		
			Blood flow color score:		Blood flow color score:	
			No flow	-4	Very strong flow	2
			Minimal flow	-1		
			Moderately strong flow	0		
			Very strong flow	2		
			Max solid D:		Max solid D:	
			< 10 mm	-3	< 10 mm	-3
			10-19.9 mm	-1	10-19.9 mm	-1
			20-29.9 mm	0	20-29.9 mm	0
			30-39.9 mm	1	30-39.9 mm	1
			40-49.9 mm	2	40-49.9 mm	2
			≥ 50 mm	3	≥ 50 mm	3
			Bilateral	2		
			Acoustic shadow	-3	Acoustic shadow	-3
					Personal history of ovarian cancer	3
	Total < 3 → benign		Total < 4 → benign		Total < 2 → benign	
Benign	Total ≥ 3 → malignant		Total ≥ 3 → malignant		Total ≥ 3 → malignant	

Table 3. RMI-4[11]

	RMI-4
	U x M x S x CA125
U	Parameters: solid, multilocular, bilateral, ascites, metastasis Ultrasound score: 1 or 4. Put 1 if ≤ 1 parameters, 4 if > 1 parameters
M	Menopausal status: 1 or 4. Put 1 if premenopause, 4 if post menopause
S	Size of tumor mass: 1 or 2. Put 1 if size < 7 cm, 2 if size ≥ 7 cm
CA125	CA125 value

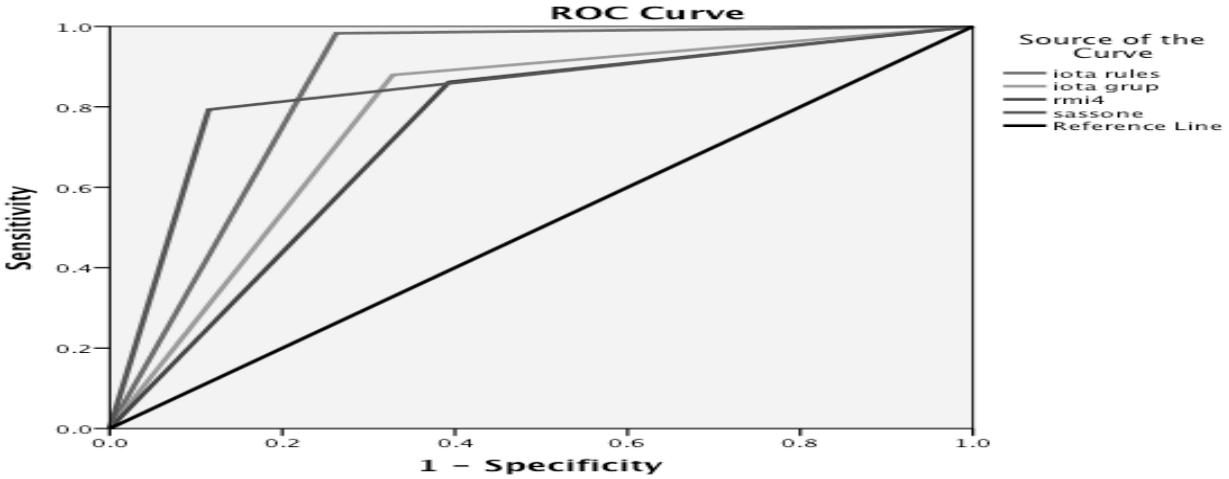


Figure 2. ROC curve of each scoring method

RESULTS

From this study, we confirmed that 61 (51.26%) subjects with benign tumor and 58 (48.74%) subjects with malignant tumor, with approximately 69% of the population were aged above 40 years and 4.2% were aged below 19 years. Mean size of tumor was 152 mm (50 - 480 mm) for benign and 139 mm (53 - 450 mm) for malignant tumor and the mean value of CA-125 was 129 U/ml (5 - 816 U/ml) for benign and 658 U/ml (7 - 7490 U/ml) for malignant tumor. The majority of the population with benign and malignant tumor was found in premenopausal status (68.9% and 58.6%, p = 0.246).

The scoring methods were applied to the subjects and resulted with sensitivity (IOTA simple-rules, IOTA subgroup, RMI-4 and Sassone): 98%, 88%, 86% and 79%; specificity: 74%, 67%, 61% and 89%; positive predictive value: 78%, 72%, 68% and 87%; negative predictive value: 98%, 85%, 82% and 81%; and accuracy: 86%, 77%, 73% and 84%. The AUC value for IOTA simple-rules, IOTA subgroup, RMI-4 and Sassone were: 0.86, 0.78, 0.73 and 0.84 respectively. Comparison of these results were significant with p = 0.000.

DISCUSSION

Compared with its predecessor study, the sensitivity of IOTA simple rules in this study was quite consistent. Timmerman et al[9] demonstrated that simple rules method had sensitivity of 95% and specificity of 91%. Validation of this system by Timmerman et al[9] and Kaijser et al[13] showed a sensitivity of 90%. The specificity result of this study was different from the initial study. There was a 20% difference. It can be explained from the morphological characteristics of benign tumors that truly benign and malignant tumors that suspected benign. Approximately 43.8% of benign tumors suspected malignancy had ascites, 31.3% had multilocular appearance with irregular border, 18.8% had strong blood flow and 18.8% had papil more than 4. These factors could contribute to increasing the false-positive interpretation. Based on further analysis, the presence of ascites correlated significantly in improving the false-positive rate (r = 0412; p = 0.005).

The sensitivity of IOTA subgroup in this study also had consistent result with previous research. Ameye et al[10] demonstrated that this subgroup method had sensitivity of 88% and specificity of 90%. There was a 23% difference in the specificity resulted from this study with the original research.

Morphological characteristic of the tumor was also considered as a factor that increased the number of false-positives result in this group. In multilocular dominant appearance group of tumor, 37% histopathological benign multilocular tumor was suspected malignant by this scoring method. This was due to several factors such as: ascites, number of locules, tumor size, and the age of the patient. Approximately, 62.5% histopathological-benign tumor which were suspected malignant had locules more than 5.25% had ascites, 100% had tumor size more than 100 mm, and 75% found in subjects over 50 years. In tumors with solid appearance, 44% of histopathological benign tumors

were suspected and classified as a malignancy. Approximately, 57% of this benign solid tumors had ascites, irregular border (42.9%), and appearance of blood flow (28.6%). In tumors with papillary projection, 60% of histopathological benign tumor were suspected malignant. All of histopathological benign tumors with papillary projection which suspected malignant had papil more than 4. The other parameters which contribute to increasing number of false-positives were: ascites (33.3%) and the appearance of blood flow (33.3%). Based on further analysis, the presence of ascites had a significant strong positive correlation in improving the false-positive rate (r = 0667; p = 0.027).

The sensitivity results for RMI-4 in this population was also consistent with previous research. Yamamoto et al[11] gained 86.8% sensitivity and 91% specificity. Wide differences between this study and Yamamoto's was also due to the characteristic of the tumor, size of the tumor and menopausal status. Approximately, 91.7% of histopathological benign tumors were diagnosed as malignant by RMI-4 had a tumor size above 100 mm, 41.7% of the population were in the post-menopausal state. Ultrasound scoring equal to 4 was also contribute to 68.8% of this group. Based on further analysis, ultrasound scoring equal to 4 had a weak positive correlation in increasing the number of false-positive but it was not significant (r = 0:25; p = 0.126).

Sassone's previous studies obtained a sensitivity of 100% and specificity of 83%.[12] Geomini et al[14] validated this scoring method and gained 84% sensitivity and 83% specificity. This study found a 21% false-negative. This was also due to some morphological characteristics of benign ovarian tumors in histopathological malignant tumors. This study found: 41.7% of tumors had regular wall, 50% with wall thickness less than 3 mm, and 41.7% had sonolucent or low echogenicity. Based on further analysis, it was found that the wall thickness of less than 3 mm had a weak positive correlation in increasing the numbers of false-negative (r = 0:25; p = 0.313).

The ROC curve showed that the AUC value of IOTA simple-rules and Sassone morphology index had over 80% (86% and 83%), demonstrating the diagnostic test had a strong interpretation. While IOTA subgroups and RMI-4 showed the AUC above 70% (78% and 73%) which showed moderate interpretation.

CONCLUSION

IOTA simple rules scoring system had better sensitivity, negative predictive value and accuracy than RMI-4 and Sassone Morphology Index in predicting ovarian malignancy. Careful interpretation needs to be done in a presence of ascites as this was correlated with false-positive.

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