Research Article

The Accuracy of Modified Risk of Malignancy Index (RMI) in Predicting Malignancy of Epithelial Type Ovarian Tumor

Akurasi Modifikasi Risk of Malignancy Index dalam Memprediksi Keganasan Tumor Ovarium Tipe Epitel

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Abstract

Objective : To investigate the accuracy of modified Risk of Malignancy Index (RMI) in predicting malignancy of epithelial type ovarian tumour.

Methods : This research was comparative research using cross-sectional study design, which compared RMI modification and RMI method in predicting malignancy of epithelial type ovarian tumour. The sampling technique was consecutive sampling. This research was conducted on October 2017 until samples were fulfilled in Obstetrics and Gynecology Division of RSUP Dr. M. Djamil and Laboratory of RSUP Dr. M Djamil in Padang. Chi-square test was used to compare specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR, and accuracy of RMI modification and RMI with 95% CI (p≤0,05).

Results : A total of 61 subjects were recruited in this study. Sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy RMI modification scoring was 90.5%, 82.5%, 73.1%, 94.3%, 5.1, 0.1, dan 85.2%. Sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy RMI scoring was 66.7%, 70%, 53.8%, 80%, 2.2, 0.4, and 70%.

Conclusions : Modified RMI scoring method was more accurate in predicting the malignancy of ovarian type epithelial tumours than RMI.

Keywords : CA125, malignancy, ovarian tumor,pelvic mass, RMI.

Abstrak

Tujuan : *Mengetahui akurasi Risk of Malignancy Index (RMI) dalam prediksi keganasan tumor ovarium tipe epitel.*

Metode : *Penelitian ini merupakan penelitian komparatif dengan desain penelitian potong lintang yang membandingkan metode RMI modifikasi dan RMI dalam prediksi keganasan tumor ovarium tipe epitel. Jumlah sampel sebanyak 61 orang. Teknik pengambilan sampel berurutan. Penelitian di mulai pada bulan Oktober 2017 hingga jumlah sampel terpenuhi di Departemen Obstetri dan Ginekologi RSUP Dr. M Djamil dan Laboratorium RSUP Dr. M Djamil Padang. Untuk membandingkan spesifisitas, sensitivitas, nilai duga positif (NDP), nilai duga negatif (NDN), rasio kemungkinan positif (RKP), rasio kemungkinan negatif (RKN), dan akurasi RMI modifikasi dan RMI digunakan uji chi-square dengan 99% CI (p≤0,01).*

Hasil : *Sensitivitas, spesifisitas, NDP, NDN, RKP, RKN, dan akurasi skoring RMI modifikasi adalah 90,5%, 82,5%, 73,1%, 94,3%, 5,1, 0,1, dan 85,2%. Sensitivitas, spesifisitas, NDP, NDN, RKP, RKN, dan akurasi skoring RMI adalah 66,7%, 70%, 53,8%, 80%, 2,2, 0,4, dan 70%.*

Kesimpulan : *Metode skoring RMI modifikasi lebih akurat dalam memprediksi keganasan tumor ovarium tipe epitel dibandingkan RMI.*

Kata kunci : *CA125, keganasan, massa pelvik, RMI, tumor ovarium.*

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INTRODUCTION

Ovarian cancer is the third most cancer in women in Indonesia, which is 4.27 cases per 100000 women.[1]As the second most common gynaecological cancer in the world, most are epithelial types.[2]The absence of screening methods causes ovarian cancer is often diagnosed when the patient has a complaint or is already at an advanced stage. This brings difficulties and complexity in managing, which leads to a worse prognosis.[3]Management efficiency in patients with ovarian cancer can be improved by standardizing preoperative evaluations.

Many women with advanced ovarian cancer undergo primary suboptimal surgery in regional hospitals. The amount of tumour tissue remaining

after primary cytoreductive surgery is one of the most important prognostic factors of ovarian cancer. The type of surgery also the experience of a doctor who performs surgery is another major factor affecting the prognosis. Therefore, proper preoperative diagnosis is very crucial and is still a challenge for gynaecologists. This temporary diagnosis is useful in referring patients who are appropriate to an oncology specialist and also useful in planning appropriate operative management. The increase in morbidity and mortality rates due to the unnecessary laparotomy performed to find early-stage ovarian cancer is a clinical dilemma.[4]

Ultrasound is a standard diagnostic test to evaluate pelvic masses. Ultrasound is not invasive, inexpensive, readily available and free of ionizing radiation. Whether ultrasound can be used to distinguish benign and malignant masses has been the subject of many studies. The principles of ultrasound include confirming the presence of a mass, differentiating ovarian mass from the mass originating from the tube or uterus, describing the internal appearance of the mass and finding other abnormal appearance. It may be possible to establish a malignancy based on ultrasound appearance, but a definite diagnosis cannot always be made. Ultrasound has a high specificity of 97.7% and a positive predictive value of only 1.5%.[5]

CA125 marker tumour has been tested for their ability to distinguish malignant and benign pelvic masses. Serum CA125 elevation often precedes clinical manifestations or ultrasound detection from residual diseases in 3-6 months. Although the single value of CA125 alone is not sufficiently specific and sensitive as initial detection, its specificity increases with periodic CA125 measurements and is combined with ultrasound.[5]

In 1990 introduced the risk of malignancy index (RMI), which is the first diagnostic model that combines demographic, sonographic and biochemical parameters to investigate patients with adnexa in mass. The RMI was first modified by Tingulstad et al in 1996 (RMI2) and the second time in 1999 (RMI3). These three versions of RMI are assessed in many prospective and retrospective clinical studies. Even made RMI 4, but the validity still needs to be confirmed in future studies. The difference between these three RMIs is in the difference in USG finding scores and menopausal status. These three RMIs were tested, with evidence of criteria for malignancy on ultrasound, such as liver metastases or distant metastases and they found that RMI2 had a better performance in detecting ovarian malignancies. The value of RMI 200 has proven to be the best limit for distinguishing benign and malignant adnexal masses, with a high degree of sensitivity and specificity (51% -90% and 51% -97%).[6]

The International Ovarian Tumor Analysis (IOTA) group in 2008 had a similar system, the USG Simple Rules (SR). SR classified the tumour into benign, malignant and indeterminate. SR sensitivity 92%, and specificity 96%.[7]

IOTA SR is not an ovarian cancer screening method but is the best predictor test in the preoperative classification of an adnexal tumour. IOTA SR is simple, easy to apply, and has been validated in many reports and should be widely used in everyday medical practice.[8]

One of the goals of IOTA is to establish a method for predicting ovarian malignancy that can make ultrasound examiners who are less experienced resemble USG results performed by an experienced expert. The IOTA method has shown a better performance than RMI if an ultrasound examination is performed by a person who is less experienced. Recent evidence was conducted on 124 women, where SR had a good performance test even though it was performed by a less experienced examiner. If these results persist, then an ultrasound-based prediction method such as SR can offer a better performance test compared to biomarkers such as CA 125 and HE4 to classify ovarian abnormalities, especially when performed on premenopausal women.[8]

SR has been well received by clinicians, and the Royal College of Obstetricians and Gynecologists (RCOG) have included SR in their top green guidelines for assessing and managing ovarian mass in premenopausal patients.[9]

Researchers predict that by including the IOTA scoring system into RMI, the specificity and sensitivity of RMI can be significantly improved. It is against this background that the author wants to investigate the accuracy of RMI that has been

modified by including IOTA SR in predicting the malignancy of epithelial type ovarian tumours.

METHODS

This study was comparative research with cross-sectionalstudy design, which compares RMI modification and RMI method to predict malignancy of epithelial type ovarium tumour.

The study was conducted from October 2017 until the number of samples was met at Obstetric and Gynecology Division of RSUP Dr. M. Djamil and Laboratory of RSUP Dr. M Djamil in Padang.

The population of this study were patients with a diagnosis of ovarian tumour which would be planned for surgery at RSUP Dr. M. Djamil with the inclusion criteria had never been diagnosed with ovarian cancer before and was willing to be a research sample. Sampling technique was consecutive sampling. Each sample will be explained about information for consent and sign an informed consent.

Chi-square test was used to determine specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR), and accuracy with 99% CI (p≤0,01). Data were analyzed by a computer program.

RESULTS

Table 1. Characteristics of Research Subject

Characteristic	Pathological Anatomy		*P-value*
	Malign (%)	Benign (%)	
Menopausal Status			0.1
Yes	10 (50)	10 (50)	
No	11 (26.8)	30 (73.2)	
Ultrasound score			0.9
3	12 (36.4)	21 (63.6)	
1	9 (32.1)	19 (67.9)	
IOTA			0.0001
3	21 (100)	0 (0)	
1	0 (0)	40 (100)	
CA125 level			0.0001
≥ 35	20 (54.1)	17 (45.9)	
< 35	1 (4.2)	23 (95.8)	

Based on Table 1 it is known that menopausal status and ultrasound score were not associated with ovarian cystic mass (p>0,01), whereas IOTA and CA125 level had a significant relationship with ovarian cystic mass (p<0,01).

Table 2. Table 2 x 2 RMI Modifikasi

RMI Modifikasi	Pathological Anatomy		Total
	Malign	Benign	
≥ 200	19	7	26
< 200	2	33	35
Total	21	40	61

Sensitivity = a/(a+c) x 100% = 19/21 x 100% = 90.5%
Specificity PPV = d/(b+d) x 100% = 33/40 x 100% = 82.5%
NPV = a/(a+b) x 100% = 19/26 x 100% = 73.1%
PLR = d/(c+d) x 100% = 33/35 x 100% = 94.3%
NLR = {a/(a+c) : b/(b+d)} = 0,9/0,175 = 5.1
Accuracy = {c/(a+c) : d/(b+d)} = 0,1/0,8 = 0.1
= a+d / (a+b+c+d) x 100% = 52/61 x 100% = 85.2%

Sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy of RMI modification are 90.5%, 82.5%, 73.1%, 94.3%, 5.1, 0.1, and 85.2%, respectively.

Table 3. Table 2 x 2 RMI

RMI Modifikasi	Pathological Anatomy		Total
	Malign	Benign	
≥ 200	14	12	26
< 200	7	28	35
Total	21	40	61

Sensitivity = a/(a+c) x 100% = 14/21 x 100% = 66.7%
Specificity PPV = d/(b+d) x 100% = 28/40 x 100% = 70%
NPV = a/(a+b) x 100% = 14/26 x 100% = 53.8%
PLR = d/(c+d) x 100% = 28/35 x 100% = 80%
NLR = {a/(a+c) : b/(b+d)} = 0,67/0,3 = 2.2
Accuracy = {c/(a+c) : d/(b+d)} = 0,3/0,7 = 0.4
= a+d / (a+b+c+d) x 100% = 42/61 x 100% = 70%

Sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy of RMI are 66.7%, 70%, 53.8%, 80%, 2.2, 0.4, and 70%, respectively.

To find out more accurate scoring method, an analysis was carried out comparing the accuracy of RMI modification and RMI to predict the malignancy of epithelial type ovarian tumour with the following result:

Table 4. Comparison of RMI Modification and RMI Diagnostic Values

Scoring method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR	NLR	Accuracy (%)	Chi-square (p) Kappa (R)
RMI	66.7	70	53.8	80	2.2	0.4	70	0.01
RMI modification	90.5	82.5	73.1	94.3	5.1	0.1	85.2	0.35 0.0001 0.69

There was a significant relationship between ovarian tumour with RMI modification and RMI ($p \leq 0,01$) (Table 4). The result of the suitability analysis showed that the kappa values was 0.69 in the modified RMI and 0.35 in the RMI.

DISCUSSION

Based on the results of the study, it was found that Ca125 levels and ultrasound examination with the SR IOTA approach were associated with ovarian malignancy, while menopausal status and ultrasound examination with a pattern recognition approach did not have a significant relationship with ovarian malignancy. The results of Akturk et al (2011) found that Ca125 levels, menopausal status, and ultrasound examination with a pattern recognition approach had a significant association with ovarian tumour malignancy ($p < 0.001$).[10] Likewise with research conducted where there was a relationship between menopausal status, ultrasound examination with pattern recognition approach, and serum Ca125 with ovarian tumour malignancy ($p = 0.0001$.[11, 12]

In this study, a new scoring modified the RMI by replacing the ultrasound examination approach from the pattern recognition approach with the SR IOTA. The results of the analysis showed that the sensitivity of the modified RMI diagnostic test was higher at 90.5% while the RMI was 66.7%. This means that 90.5% of patients with malignant ovarian tumours will be detected with modified RMI scoring while in RMI scoring 66.7% of patients. Modification of RMI specificity was also obtained higher at 82.5% and RMI 70%. This shows that 82.5% of patients with benign ovarian tumours will give negative diagnostic tests on modified RMI scoring while RMI 70% of patients.

Modified RMI scoring method shows PPV and NPV are 73.1% and 94.3% which means that the probability of a person suffering from malignant ovarian tumours is 73.1% and the probability of someone not suffering from malignant ovarian tumours is 94.3%. PPV and NPV values using the modified RMI scoring method are higher than RMI.

The accuracy of the modified RMI scoring method is higher than the RMI of 85.2%. This means that the modified RMI diagnostic test provides more accurate results compared to the RMI method. The results showed that sensitivity, specificity, PPV, NPV, PLR, and modified RMI accuracy were higher than RMI. Statistical tests showed both scorings could be used in predicting ovarian tumour malignancy ($p \leq 0.01$), and kappa values on RMI and RMI modification were 0.35 and 0.69 which means modified RMI was better than RMI in predicting ovarian tumour malignancy.

In addition, several studies regarding RMI scoring have been carried out. All research that has been done shows that RMI can be used to predict ovarian malignancy before surgery with a value of $p < 0.01$ with various sensitivity values, specificity, PPV, NPV, PLR, NLR, and accuracy.

According to some previous studies, the IOTA SR has high sensitivity and specificity. Timmerman's research was delivered in 2010 with a sensitivity and specificity of 92% and 96%.[13]Likewise in a study with a sensitivity and specificity of 87% and 98% and which conducted an external study of one flashlight validation on 122 ovarian tumors within 4 years with the results of sensitivity and specificity of 73% and 97%. However, they did not evaluate the strategy if the IOTA SR found inconclusive results.[14]Ideally, patients with inconclusive IOTA SR results should be referred to a gynaecological ultrasound expert for further assessment[15].However, for ultrasound examiners who find it inconclusive at IOTA SR should classify it into malignancy if there is no gynaecological ultrasound expert. According to Bernardin if there is no experienced ultrasound examiner available, another alternative is to do MRI in patients.[16]However, further research is

needed for this protocol.

Another study, published in the year, was conducted on 2403 samples by comparing ADNEX models with CA125 and without CA 125, IOTA SR and RMI. Produces similar specificity of 80%, but with different levels of sensitivity, namely for ADNEX and SR IOTA between 92.3 - 93.0% compared to only 81.7% of RMI. This shows that the ADNEX and IOTA SR models have a better ability to predict malignancy than RMI.[17]In this study, it was found that the modified RMI scoring by replacing the pattern recognition ultrasound variable with IOTA SR ultrasound can be used in predicting ovarian malignancy with a p-value <0.01. If the modified RMI is compared to RMI, it is seen that the RMI modification is better than RMI. So that modified RMI can be used as a new score for predicting ovarian malignancy before surgery.

CONCLUSION

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR), and accuracy of RMI modification scoring are 90.5%, 82.5%, 73.1%, 94.3%, 5.1, 0.1, and 85.2%, respectively. Sensitivity, specificity, PPV, NPV, PLR, NLR, and accuracy of RMI scoring are 66.7%, 70%, 53.8%, 80%, 2.2, 0.4, 0.7, and 70%, respectively. RMI modification scoring method are more accurate to predict malignancy of epithelial type ovarian tumour than RMI.

We recommend that the pattern recognition ultrasound examination for comparison be done by the same and qualified people. For further research, it is expected that the inclusive value in IOTA will be included in malignancy to increase the sensitivity value.

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