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Evaluation of Four Risk of Malignancy Indices (RMI) in the Preoperative Diagnosis of Ovarian Malignancy at Rajavithi Hospital

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ABSTRACT

Background: The discrimination between benign and malignant ovarian tumors is important considering to optimally plan for an appropriate surgical treatment. Women with malignant ovarian tumors should be referred to a gynecologic oncologist as the quality of cytoreductive surgery and lead to increased survival.

Objective: To evaluate the ability of four types of the risk of malignancy indices (RMI) based on serum levels of CA-125, ultrasound score, and menopausal status to discriminate between benign and malignant ovarian tumors.

Material and Method: This is a retrospective study of 255 women admitted at Rajavithi Hospital between January 2012 and December 2012 for elective laparotomy of ovarian tumor. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of four types of the risk of malignancy indices were calculated. And the Receiver Operating Characteristic (ROC) curves for RMI 1, RMI 2, RMI 3, and RMI 4 were calculated to compare the accuracy.

Results: Using a cut-off level of 200 to indicate malignancy for RMI 1, RMI 2 and RMI 3, and using a cut-off level of 450 to indicate malignancy for RMI 4. The RMI 2 gave the highest sensitivity (71%) while the RMI 1, RMI 3 and RMI 4 gave the sensitivity of 62–69%. The RMI 1 gave the highest specificity (80%) while the RMI 2, RMI 3 and RMI 4 gave the specificity of 71–78%. The positive predictive value of the four methods was 61-66% and the negative predictive value of the four methods was 66-80%. For the ROC curve, the greatest area under curve (AUC) was associated with the RMI 4 values (0.801) as compared to the ROC values for the RMI 1 (0.785), RMI 2 (0.782), and RMI 3 (0.778).

Conclusion: The RMI is able to discriminate between benign and malignant ovarian tumors. The RMI 4 was the most reliable in predicting malignancy in terms of area under the curves. It is a simple method that can be incorporated into clinical practice easily to enable the selection of patients for referral to a gynecologic oncologist.

Keywords: Ovarian tumor, Risk of malignancy index (RMI), serum levels of CA-125, Ultrasound score, Menopausal status

Introduction

Ovarian cancer is the second most common gynecologic cancer and accounts for 6% of all deaths in woman. The annual incidence is 5.1 per 100,000 women and increases with age[1]. The peak incidence of ovarian cancer is at about 56 to 60 years of age[2]. Women with ovarian cancer are often asymptomatic in early stage and resulting delays to diagnosis. Sixty percent of women are diagnosed at an advanced stage, which has a 5-year survival as low as 10%. When the disease is diagnosed at stage I (confined to the ovaries), the 5-year survival is in excess of 90%.This suggests that early detection of ovarian cancer may improve long term survival.

Standard treatment of ovarian cancer is complete surgical staging which comprises examination of peritoneal washings or ascitic fluid for cytology, exploration of all the intra-abdominal surfaces and viscera including the diaphragm, total abdominal hysterectomy with bilateral salpingo-oophorectomy, infra-colic omentectomy, bilateral pelvic lymphadenectomy and para-aortic lymphadenectomy. Additional therapy such as chemotherapy is indicated in high risk and advanced stage patients.

It is estimated that in pre and post-menopausal women, ovarian tumors are malignant in 24% and 60% of patients, respectively[3,4]. Many women with advanced ovarian cancer undergo suboptimal primary surgeries at local hospitals. The amount of tumor left after the primary cytoreductive surgery is one of the most important prognostic factors in ovarian cancers[5,6]. These specialized surgical procedures require the specific skills and experience provided by gynecologic oncology surgeons. Furthermore, appropriate and timely referral to a gynecologic oncologist has been proven to increase survival in patients with ovarian cancer[7].

The surgeon can be optimally prepared if the ovarian neoplasm is known to be benign or malignant in advance of surgery. Many investigators have employed a variety of sonographic variables and multiple tumor markers individually in an attempt to predict a malignancy, and many scoring systems and models for predicting the probability of ovarian cancer in women have been described[8-16].

Jacobs et al. originated the concept of the Risk of Malignancy Index (RMI) in 1990 combining serum levels of CA-125, ultrasound score, and menopausal status into the assessment of a patient with an adnexal mass, and it is known as RMI 1. They found that the RMI 1 had a sensitivity of 85.4% and a specificity of 96.9% when using a cut-off level of 200 to indicate malignancy[12]. According to their results, the benign-malignant determination of ovarian tumors could be managed with higher sensitivity and specificity than with the use of ultrasound and serum levels of CA-125 individually, and also the main advantage of this method compared with other approaches such as color Doppler ultrasonography, or the use of different tumor markers, is that RMI can be used easily in less-specialized units[10,17-21].

Tingulstad et al. developed theirown model of the RMI in 1996 and it is termed RMI 2. Then they modified the RMI 3 in 1999[13,14]. The difference between the three indicies lies in the different scoring of ultrasound score (U) and menopausal status (M). In 2009, Yamamoto et al. createdthe RMI 4 by adding the parameter of the tumor size (S) to the RMI[15].

In Thailand, Leelahakorn et al. (2005) studied the ability of ultrasound score, serum levels of CA-125, menopausal status, and the RMI 1 in distinguishing benign from malignant ovarian tumors[22]. For the RMI 1, the sensitivity and specificity were 88.6% and 90.7%, respectively. Then Mooltiya et al. (2009) studied the performance of RMI 1 and RMI 2 in discriminating pelvic masses at Srinagarind Hospital[23]. Using a cut-off level of 200 to indicate malignancy, the RMI 1 gave sensitivity of 70.6%, specificity of 83.9%, positive predictive value of 75%, and negative predictive value of 80.6%. The RMI 2 gave sensitivity of 80%, specificity of 78.2%, positive predictive value of 71.6%, and negative predictive value of 85.1% and they found that the RMI 2 was significantly better in predicting malignancy than RMI 1.

The primary outcome of this study was to evaluate the ability of four types of the risk of malignancy indices to discriminate a benign from borderline or malignant ovarian tumor when the borderline ovarian

tumor was classified as a malignant tumor. The secondary outcome was to evaluate the performance of the four types of the risk of malignancy indices at Rajavithi Hospital, in order to identify cases of potential ovarian malignancy presenting at peripheral centers so that these patients would be referred to a gynecologic oncologist for appropriate treatment and survival might be increased in patients with ovarian cancer.

Methods

A retrospective review was made of the records of 255 consecutive women with ovarian tumors admitted for elective laparotomy at Rajavithi Hospital between January 2012 and December 2012. Prior to surgery, imaging by pelvic ultrasound was performed and a serum sample was taken for tumor marker analysis. Preoperative serum levels of CA-125, ultrasound findings, and menopausal status were noted. The patients who already had a histological diagnosis of malignant ovarian tumors, such as from tumor biopsy or ascites for cytology, or who have been operated on by emergency laparotomy or laparoscopic surgery were excluded.

The ultrasound was performed transvaginally by a 7.5 MHz transducer (GE, Voluson E8) or a 3.75 MHz abdominal transducer if a mass was found to be too large to observe completely transvaginally. Ultrasound score was calculated as follows : multilocularity, solid areas, bilateral lesions, ascites, and intra-abdominal metastases, scored as one point for each[12]. A total ultrasound score (U) was calculated for each patient. Tumor size (S) was measured by ultrasound for each patient. If the patients had bilateral ovarian tumor, the data of boths were obtained.

Patients were considered postmenopausal if they had at least 1 year of amenorrhea not related to other conditions or if they were at least 50 years old and had undergone a prior hysterectomy. All other women were considered premenopausal.

Preoperative measurement of serum levels of CA-125 was performed by using an eletrochemiluminescent immunoassay (ECLIA).

Based on the data obtained, RMI 1, RMI 2, RMI 3, and RMI 4 were calculated for all patients together with the sensitivity, specificity, positive and negative predictive values of the four methods as shown in Table 1.

Table 1. Definitions of RMI that were compared in this study.

Varieble	Scoring system			
	RMI 1*	**RMI 2***	**RMI 3***	**RMI 4****
Menopausal status (M)				
- Premenopause	1	1	1	1
- Postmenopause	3	4	3	4
Ultrasound score (U)				
- Multilocular				
- Bitaterally	No feature = 0			
- Solid	1 feature = 1	≤ 1 feature = 1	≤ 1 feature = 1	≤ 1 feature = 1
- Ascites	> 1 feature = 3	> 1 feature = 4	> 1 feature = 3	> 1 feature = 4
- Intraabdominal metastasis				
Serum level of CA-125	**Absolute level (U/mL)**			

* Calculation for RMI 1, RMI 2, RMI 3 = M x U x CA-125

** Calculation for RMI 4 = M x U x CA-125 x S (When S = single greatest diameter of tumor size (cm.). If size <7 cm. S = 1, size ≥7 cm. S = 2)

The histopathological diagnosis was considered the gold standard for definite outcome. When a borderline ovarian tumor was found, it was classified as malignant ovarian tumor.

Statistical analysis was performed with STATA v11.1 (Stata Version 11.1, Stata Corp, College Station, Texas). Mean patient ages were compared by using the independent Student's t-test. The Chi-square (χ^2) test was used to test differences in differentiation of menopausal status, ultrasound score, serum levels of CA-125 and tumor size. Receiver operator characteristics (ROC) curves were constructed and the areas under the curve (AUC) with binomial exact 95% confidence intervals (95% CI) were calculated.

The diagnostic performance of the models was also expressed as sensitivity, specificity, positive and negative predictive values when using the recommended cut-off values for the each RMI.

For all statistical comparisons, a level of $p< 0.05$ was accepted as being statistically significant.

Results

A total of 255 women with ovarian tumors were enrolled in our study. According to the histopathological reports, 157 women (61.6%) had a benign tumor and 98 (38.4%) had a malignant tumor (Table 2).

The most common benign gynecological conditions were endometriotric cysts, mucinous cystadenomas, dermoid cysts and serous cystadenomas (Table 2).

The majority of the malignanttumors were epithelial originincludedborderline mucinous tumor, borderline endometrioid tumor, clear cell carcinoma, serous carcinoma and endometrioid carcinoma (Table 2). The non-epithelial primary ovarian tumors were granulosa cell tumor and neuroendocrine tumor. Along with the primary ovarian tumors, 5 extra-ovarian primary tumors with metastases toovary were diagnosed. The metastatic tumors were mainly of an endometrial or gastrointestinal origin. Another malignant tumors in our results was an endometrioid adenocarcinoma of fallopian tube (Table 2).

If a women with an ovarian cancer was diagnosed, it was staged according to the criteria of the International Federation of Obstetrics and Gynecology[24]. We found that 92 women had a primary ovarian cancer and were diagnosed at stage I of 58.7% (n=54), stage II of 13% (n=12), stage III of 27.2% (n=25), and stage IV of 1.1% (n=1).

Table 2. Histopathological classification of cases (N = 255)

Histological diagnosis	No.	Percentages
Total benign cases	**157**	**61.6**
1. Benign ovarian tumors		
- Endometriotic cyst	49	19.2
- Mucinous cystadenoma	33	12.9
- Dermoid cyst	29	11.4
- Serous cystadenoma	19	7.5
- Epithelial inclusion cyst	7	2.7
- Tubo-ovarian abscess	7	2.7
- Follicular cyst	2	0.8
- Fibroma	2	0.8
- Pseudo cyst	2	0.8
- Corpus luteal cyst	1	0.4

Table 2. Histopathological classification of cases (N = 255) (Cont.)

Histological diagnosis	No.	Percentages
Total benign cases	**157**	**61.6**
- Brenner tumor	1	0.4
2. Other benign tumors		
- Leiomyoma	4	1.6
- Degenerated myoma	1	0.4
Total malignant cases	**98**	**38.4**
1. Borderline ovarian tumors		
- Borderline mucinous tumor	22	8.6
- Borderline serous tumor	5	1.9
- Borderline endometrioid tumor	1	0.4
2. Primary ovarian cancers		
> Epithelial ovarian cancers		
- Clear cell carcinoma	19	7.5
- Serous carcinoma	13	5.1
- Endometrioid carcinoma	12	4.7
- Mucinous carcinoma	7	2.7
- Mixed epithelial carcinoma	7	2.7
- Adenocarcinoma NOS	2	0.8
>Non- epithelial ovarian cancers		
- Granulosa cell tumor	2	0.8
- Yolk sac tumor	1	0.4
- Neuroendocrine tumor	1	0.4
3. Metastases ovarian tumors		
- Metastatic adenocarcinoma	3	1.2
- Malignant lymphoma	1	0.4
- Metastatic sarcoma	1	0.4
4. Other malignant tumors		
- Endometrioid adenocarcinoma of fallopian tube	1	0.4
Total	**255**	**100**

The distribution of benign and malignant cases by age, menopausal status, ultrasound score, serum level of CA-125 and tumor size are described in Table 3. The mean age for benign and malignant ovarian tumors in our study was 45 and 51 years, respectively.

Statistically significant differences were found regarding menopausal status, ultrasound score, serum level of CA-125 and tumor size between the groups with benign and malignant ovarian tumor.

Considering the odds ratio, we found that the postmenopausal women had an increased risk for malignant and borderline ovarian tumor which was 2.54

fold higher compared with the premenopausal women. The women who obtained an ultrasound score >1 were at increased risk for malignant and borderline ovarian tumor, 8.89 fold compared with those with an ultrasound score = 0. When the values of serum CA-125 levels were greater than, or equal to 35 U/ml a women's risk for malignant and borderline ovarian tumor increased 3.64 times. A tumor size greater than, or equal to 7 centimeters was associated with a 10.54 fold increased risk for malignant and borderline ovarian tumor.

Table 3. Distribution of Age, Menopausal status, Ultrasound score, Serum CA125 levels, and Tumor size between benign and malignant ovarian tumors.

Variables	Benign (n=157)	Malignant (n=98)	p	OR (95% CI)
Age (years)				
Mean ± SD	45 ± 15	51 ± 11		
Menopausal status			<0.001 * (¥)	
Premenopausal	103 (65.6)	42 (42.9)		1
Postmenopausal	54 (34.4)	56 (57.1)		2.54 (1.5 - 4.2)
Ultrasound score			<0.001* (¥)	
0	44 (28)	7 (7.1)		1
1	71 (45.2)	34 (34.7)		3.02 (1.2 - 7.6)
>1	42 (26.8)	57 (58.2)		8.89 (3.5 - 22.4)
CA 125 (U/ml)			<0.001 * (¥)	
<35	85 (54.1)	24 (24.5)		1
≥35	72 (45.9)	74 (75.5)		3.64 (2.1 - 6.4)
Tumor size (cm.) (*)			<0.001* (¥)	
<7	47 (29.9)	4 (4.1)		1
≥7	110 (70.1)	94 (95.9)		10.54 (3.6 - 31.3)

N (%) value, ¥= p-value from Chi-Square test, * significant at the 0.05 level

The results of evaluation by RMI 1, RMI 2, RMI 3 and RMI 4 are summarized in Table 4. By using a cut-off level of 200 to indicate malignancy for RMI 1, RMI 2, RMI 3, and using a cut-off level of 450 to indicate malignancy for RMI 4, the RMI 2 gave the highest sensitivity (71%) while the RMI 1, RMI 3 and RMI 4 gave the sensitivity of 62–69%. The RMI 1 gave the highest specificity (80%) while the RMI 2, RMI 3 and RMI 4 gave the specificity of 71–78%. The positive predictive value of the four methods was 61-66% and the negative predictive value of the four methods was 66-80% (Table 5).

The Receiver Operating Characteristic (ROC) curves for RMI 1, RMI 2, RMI 3, and RMI 4 were calculated to compare the accuracy of the four methods (Fig. 1). The greatest area under curve (AUC) was associated with the RMI 4 values (0.801), as compared to the ROC values for the RMI 1 (0.785), RMI 2 (0.782), and RMI 3 (0.778) (Table 6). As a result, we found that the RMI 4 was the most reliable in detecting the malignant ovarian tumor in terms of area under the curves and there was no statistically significant difference in performance of the four methods (p>0.05) as shown in Table 6.

Table 4. Results of RMI 1, RMI2, RMI 3, and RMI 4

RMI	Benign (n=157)	Malignant (n=98)	Total (n=255)
RMI 1			
< 200	125 (79.6%)	37 (37.8%)	162 (63.5%)
≥ 200	32 (20.4%)	61 (62.2%)	93 (36.5%)
RMI 2			
< 200	112 (71.3%)	28 (28.6%)	140 (54.9%)
≥ 200	45 (28.7%)	70 (71.4%)	115 (45.1%)
RMI 3			
< 200	119 (75.8%)	35 (35.7%)	154 (60.4%)
≥ 200	38 (24.2%)	63 (64.3%)	101 (39.6%)
RMI 4			
< 450	122 (77.7%)	30 (30.6%)	152 (59.6%)
≥ 450	35 (22.3%)	68 (69.4%)	103 (40.4%)

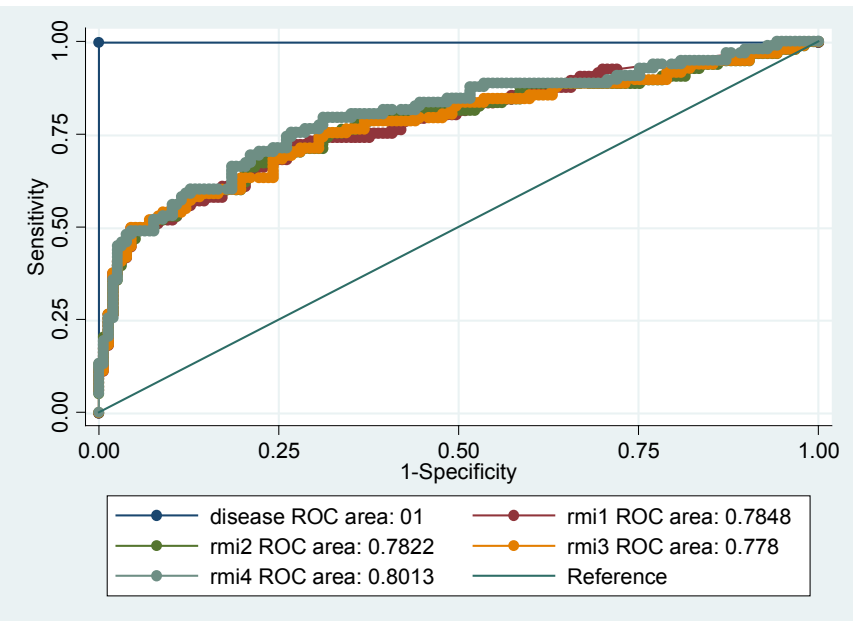

Fig. 1. Receiver Operating Charactersitics (ROC) curve showing the relationships between sensitivity and specificity oF RMI 1, RMI 2, RMI 3, and RMI 4 in discrimination between benign and borderline or malignant ovarian tumor.

Table 5. Diagnostic performance of RMI 1, RMI 2, RMI 3, and RMI 4

RMI	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
RMI 1	62 (52 - 72)	80 (72-86)	66 (55-75)	77 (70-83)
RMI 2	71 (61-80)	71 (64-78)	61 (51-70)	80 (72-86)
RMI 3	64 (54-74)	76 (68-82)	62 (52-72)	77 (70-84)
RMI 4	69 (59-78)	78 (70-84)	66 (56-75)	80 (73-86)

* Data represented as percentages ; 95%CI = 95% confidence interval

The cut off value used were 200 for the RMI 1, RMI 2, and RMI 3, and 450 for RMI 4.

Abbreviations : PPV = positive predictive value, NPV = negative predictive value

Table 6. Difference in the area under the curve (AUC) of the ROC curve for the diagnosis of malignant ovarian tumors with the corresponding 95% confidence intervals (95%CI) and p-value.

Scoring system	AUC (95%CI)	Difference	p
RMI 1	0.784 (0.724-0.845)	0.031	0.98
RMI 2	0.782 (0.720-0.844)	0.032	0.96
RMI 3	0.778 (0.715-0.841)	0.032	1.01
RMI 4	0.801 (0.742-0.862)	0.030	0.84

Discussion

The estimation of malignancy risk in patients with ovarian tumors is important to improve survival of patients with early ovarian cancer, as reported in several recent studies[5-7]. The most effective diagnostic tool should be accurate, easy to perform, and cheap. Furthermore, it should be helpful to prioritise treatment for high risk patients and in deciding the extent and time of surgery for low risk patients.

In 1990, Jacob et al.developed a risk of malignancy index (RMI) for predicting ovarian cancer[12]. Their prospective study evaluated 143 women. Using a cut-off level of 200, the sensitivity was 85.4% and the specificity was 96.9%. Other studies have since validated this scoring system, with similar results (Table 5)[13-15,22-23,25-29].

This present study showed the ability of the RMI to discriminate correctly between benign and malignant ovarian tumors, and confirmed the moderately high sensitivity and specificity of the RMI by using the cut-off level of 200 for RMI 1, RMI 2, RMI 3, and using a cut-off level of 450 for RMI 4. RMI 1, RMI 2, RMI 3, and RMI 4 gave the sensitivity of 62%, 71%, 64% and 69%, respectively, and the specificity of 80%, 71%, 76%, and 78%, respectively. As a result, we found that RMI 2 was slightly more sensitive but less specific than the other three risk of malignancy indices. If RMI 2 is to be chosen for use in our population, there will be a benefit to patients of detecting more cancers but a gynecologic oncologist will end up operating on more benign cases. Similarly, RMI 1 was the most specific but less sensitive than other indices.Malignancy will be wrongly diagnosed as benign in some cases and these patients will not be referred to a gynecologic oncologist. The best results in our study were obtained when RMI 4 was used. There was an increase in the sensitivity of the test without any major loss of specificity and it had a highest accuracy in terms of area under the curve.

In 2009 Yamamoto et al. developed their own RMI by using tumor size and called it RMI 4[15]. Their study confirmed that, at a cut-off level of 450, the accuracy of the RMI 4 was better than RMI 1, RMI 2, and RMI 3 with a cut-off level of 200. They observed that, at a cut-off level of 450, the sensitivity, specificity,

positive predictive value, negative predictive value and accuracy were respectively, 86.8%, 91%, 63.5%, 97.5%, and 90.4%[15]. In our study, we found a sensitivity, specificity, positive predictive value, and negative predictive value of 69%, 78%, 66%, and 80%, respectively, and RMI 4 was more reliable than RMI 1, RMI 2, and RMI 3, similar to the results of Yamamoto et al[15].

The prevalence of malignancy in this study was 38.4%, which was similar to the other previous studies in which it ranged from 29-35%[12-13,27-28]. The sensitivity and specificity of these four risk of malignancy indices in discriminating malignancy were lower than those reported by the previous studies as shown in Table 7. One possible reason may be that we had a higher percentage of early stage ovarian cancer (stage I)and borderline ovarian tumor than in the previous studies, the prevalence of stage I of primary ovarian cancer was 22% while the prevalence was 32.7% in our study[12-13]. Because the elevated serum level of CA-125 (>35 U/mL) could be detected in approximately 50% of patients with stage I and in more than 90% of those with advanced disease, so that made the RMI slightly elevated in these groups and resulted in low sensitivity and specificity of the RMI in our study[30].

Table 7. Comparison the diagnostic performance of our results with previous studies.

Study	No.	sensitivity	specificity	PPV	NPV
Jacobs et al.1990[12]	143	85.4	96.9		
Davies et al.1993[28]	100	87	89		
Tingusled et al.1996[13]	173	71	96	89	88
Tingusled et al.1999[14]	365	71	92	69	92
Morgante et al.1999[26]	124	58	95	78	87
Obeidat et al.2004[25]	100	90	89	96	78
Leelahakorn et al.2005[22]	175	88.6	90.7	70.5	97
Ulusoy et al.2006[27]	296	71.7	80.5	67	84
Sharon et al.2009[29]					
RMI1	163	72	87		
RMI2	163	76	81		
RMI3	163	74	84		
Yamamoto et al.2009[15]					
RMI1	253	75	89	62	93
RMI2	253	75	85	55	93
RMI3	253	75	87	57	93
RMI4	253	86.8	91	63.5	97.5
Mooltiya et al.2009[23]					
RMI1	209	70.6	83.9	75	85.1
RMI2	209	80	78.2	71.6	85.1
Our study					
RMI 1	255	62	80	66	77
RMI 2	255	71	71	61	80
RMI 3	255	64	76	62	77

Value were represented percentages

Abbreviations : PPV = positive predictive value, NPV = negative predictive value

We found that the four risk of malignancy indices demonstrated better performance when borderline ovarian tumors were classified as benign ovarian tumors. RMI 1 sensitivity increased from 62% to 77%, RMI 2 sensitivity increased from 71% to 84%, RMI 3 sensitivity increased from 64% to 79 and RMI 4 sensitivity increased from 69% to 84% when these tumors were classified as benign. Although the classification of borderline ovarian tumors remains controversial, clinical and biological evidence suggests that these tumors can be classified as benign. Borderline ovarian tumors are associated with a good prognosis and 5-year survival rates are approximately 98% for stage I tumors and 90% for stage III tumors with non invasive implants[31]. But in our study, the borderline ovarian tumors were classified as malignant ovarian tumors because metastatic implants may occur with borderline ovarian tumors, especially invasive implants. This group has a higher likelihood of developing into progressive, proliferative disease in the peritoneal cavity, which can lead to intestinal obstruction and death[32,33]).

In our study, we had false positive and false negative rates of about 20.4-28.7% and 28.6-37.8%, respectively. The majority of histological diagnoses in the false positive cases were endometriotic cysts (38.1-45.9%), mucinous cystadenomas (8.9-22.7%), and dermoid cysts (6.5-12.7%). A recent published study has shown that elevated serum CA-125 level could be found in many benign conditions such as menstruation, pregnancy, functional cysts, pelvic infection and endometriosis[19,26,30,34-37]. So the false positive about elevation of serum CA-125 in endometriotic cyst can be explained. For mucinous cystadenomas and dermoid cysts, the false high ultrasound scores can be explained by the fact that multi-locular cystic lesions may be found in mucinous cystadenomas and solid parts are found in dermoid cysts. The false negative cases were borderline mucinous ovarian tumors (45.7-57.8%), clear cell carcinomas (15.8-20%), and borderline serous ovarian tumors (10.7-15.8%). Jacobs et al.[30] demonstrated that elevated serum CA-125 could be detected in approximately 50% of patients with stage I and in more than 90% of those with advanced disease and Gadducci et al.[34] reported that mucinous tumors expressed CA-125 less frequently than non-mucinous tumors. The observation that mostly women with false negative results in the present study had stage I ovarian cancer, borderline mucinous tumor is 33.3%, clear cell carcinoma is 24.1%, and borderline serous tumor is 9.3%, is similar to those previously reported. The low level of CA-125 in mucinous type and clear cell carcinomas,including stage I ovarian cancer may explain the false negative results.

Recently, laparoscopic surgery is being performed widely for the treatment of ovarian tumors[38]. The safety of laparoscopic surgery for ovarian tumors is still unclear because of possible complications such as intraoperative cyst rupture, spillage of cyst contents, chemical peritonitis, and unexpected malignant tumors[38]. Hence, preoperative diagnoses to estimate the risk of malignancy in patients with ovarian tumors who are admitted for laparoscopic surgery can enable the surgeon to be optimally prepared before surgery. The present study showed the RMI was able to discriminatebetween benign and malignant ovarian tumorsbut our study had afalse negative rate of about 28.6-37.8%. This means that in one of three cases, the tumor will be wrongly diagnosed as benign. These patients will not be referred to a gynecologic oncologist and may be operated on by laparoscopy, which is associated with an increased risk of spillage of cyst fluid and decrease inoverall survival[39].

A significant problem associated with CA-125 is that it can be expressed in numerous benign and malignant conditions, which leads to false positive results and it is only expressed by about 50% of early stage ovarian cancers,which leads to false negative results[30]. Another tumor marker which has gained attention is the human epididymis secretory protein 4 (HE4). HE4 is expressed in 100% of endometrioid adenocarcinomas, 93% of serous adenocarcinomas and 50% of clear cell ovarian cancers but not expressed in normal surface epithelium[40]. Moore et al. developed an algorithm, the risk of malignancy algorithm (ROMA), which is based on both CA-125 and HE4. They studies the RMI and ROMA in 457 patients; the results were the ROMA had a sensitivity of 94.3% while the RMI had

a sensitivity of 84.6% (p=0.0029)[41]. Thus in our setting, if we use the combined HE 4 with CA 125 we may improve the sensitivity and specificity for distinguishing malignant from benign ovarian tumors but the disadvantages of HE 4 are that it is expensive and difficult to perform in peripheral centers.

Conclusion

The RMI is a simple and useful method to apply in clinical practice, and it uses commonly available techniques and tests. The comparison of the four risk of malignancy indices in our study did not reveal any obvious statistical difference between the sensitivity and specificity of these tests. However, in our study, RMI 4 had a better sensitivity and specificity in predicting malignancy and we have chosen to adopt the RMI 4 as a tool to selection the patients for referral to a gynecologic oncologist in our unit.

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การประเมินดัชนีความเสี่ยงของการเป็นมะเร็งในเนื้องอกรังไข่ก่อนการผ่าตัดในโรงพยาบาลราชวิถี

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ความเป็นมา : เนื่องจากผู้ป่วยมะเร็งรังไข่ หากได้รับการผ่าตัดรักษาจากแพทย์ผู้เชี่ยวชาญด้านมะเร็งนรีเวช จะมีอัตราการรอดชีพที่เพิ่มขึ้น การวินิจฉัยแยกระหว่างก้อนเนื้องอกรังไข่ชนิดธรรมดา และก้อนเนื้องอกรังไข่ที่เป็นมะเร็ง จึงมีความสำคัญในการวางแผนก่อนการผ่าตัด และส่งต่อผู้ป่วยไปยังโรงพยาบาลที่มีแพทย์ผู้เชี่ยวชาญด้านมะเร็งนรีเวช เพื่อให้ได้รับการรักษาที่มีความเหมาะสม

วัตถุประสงค์ : เพื่อศึกษาความสามารถของการใช้ดัชนีความเสี่ยงของการเป็นมะเร็ง (Risk of Malignancy Index: RMI) ทั้ง 4 วิธี โดยใช้ลักษณะทางเครื่องตรวจคลื่นเสียงความถี่สูง ค่าของระดับ CA-125 ในเลือด และภาวะการหมดระดู ในการวินิจฉัยแยกระหว่างก้อนเนื้องอกรังไข่ชนิดธรรมดา และก้อนเนื้องอกรังไข่ที่เป็นมะเร็ง

วัสดุและวิธีการ : เป็นการศึกษาย้อนหลังเก็บรวบรวมข้อมูลผู้ป่วยก้อนเนื้องอกรังไข่จำนวน 255 คนที่เข้ารับการผ่าตัดในโรงพยาบาลราชวิถีตั้งแต่เดือนมกราคม พ.ศ.2555 ถึงเดือนธันวาคม พ.ศ.2555 และคำนวณหาค่าความไว ความจำเพาะ ค่าพยากรณ์เป็นบวก (positive predictive value) และค่าพยากรณ์เป็นลบ (negative predictive value) ในการวินิจฉัยก้อนเนื้องอกรังไข่ที่เป็นมะเร็ง และเปรียบเทียบความแม่นยำของดัชนีความเสี่ยงของการเป็นมะเร็งทั้ง 4 วิธีโดยใช้ขนาดพื้นที่ใต้กราฟของ ROC curve

ผลการวิจัย : เมื่อใช้คะแนนมากกว่าหรือเท่ากับ 200 ในการบ่งชี้ความเป็นมะเร็งสำหรับ RMI 1, RMI 2, RMI 3 และคะแนนมากกว่าหรือเท่ากับ 450 ในการบ่งชี้ความเป็นมะเร็งสำหรับ RMI 4 พบว่า RMI 2 มีค่าความไวสูงสุดเท่ากับ 71% ส่วน RMI 1, RMI 3 และ RMI 4 มีค่าความไว 62-69% RMI 1 มีค่าความจำเพาะสูงสุดเท่ากับ 80% ส่วน RMI 2, RMI 3 และ RMI 4 มีค่าความไว 71-78% ค่าพยากรณ์เป็นบวกของดัชนีความเสี่ยงของการเป็นมะเร็งทั้ง 4 วิธีเท่ากับ 61–66% และค่าพยากรณ์เป็นลบของดัชนีความเสี่ยงของการเป็นมะเร็งทั้ง 4 วิธีเท่ากับ 66–80%

สำหรับ ROC curve ของดัชนีความเสี่ยงของการเป็นมะเร็งทั้ง 4 วิธี พบว่า RMI 4 มีขนาดของพื้นที่ใต้กราฟมากที่สุดโดยมีค่าเท่ากับ 0.801 เมื่อเปรียบเทียบกับ RMI 2, RMI 3 และ RMI 4 ซึ่งมีค่าเท่ากับ 0.785, 0.782 และ 0.778 ตามลำดับ

สรุป : ดัชนีความเสี่ยงของการเป็นมะเร็ง (Risk of Malignancy Index: RMI) สามารถใช้ในการวินิจฉัยแยกระหว่างก้อนเนื้องอกรังไข่ชนิดธรรมดาและก้อนเนื้องอกรังไข่ที่เป็นมะเร็งได้ โดย RMI 4 มีความแม่นยำมากที่สุดในการบ่งชี้ความเป็นมะเร็งเมื่อเปรียบเทียบกับ RMI 1, RMI 2, และ RMI 3 ซึ่งเป็นวิธีการที่ทำได้ง่าย และสามารถใช้ในการคัดเลือกผู้ป่วยเพื่อส่งต่อไปยังผู้เชี่ยวชาญด้านมะเร็งนรีเวชเพื่อให้ได้รับการรักษาที่เหมาะสม