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The Use of Risk of Malignancy Index for Adnexal Masses

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Abstract

Objective: To evaluate the effectiveness of the Risk of Malignancy Index (RMI) to identify cases with high potential of ovarian malignancy

Methods: A total of 106 patients with adnexal masses were included in this prospective, observational study. The ultrasound findings, menopausal status and serum CA125 level were documented.

Ultrasound characteristics, documented preoperatively, and assessed with RMI scoring to detect the relationship between benign and malign groups. The statistical analysis was done using statistical software (NCSS 2008). The sensitivity, specificity, positive and negative predictive value of serum CA125, ultrasound findings and menopausal status were calculated separately and combined into RMI.

Results: The best cut-off value for the RMI was 189 with a sensitivity of 84.8%, a specificity of 81.6%, a PPV of 78% and a NPV of 87.5%.

Conclusion: The present study demonstrated that RMI was a reliable method detecting pelvic masses with high risk of malignancy. Herewith, RMI leads selecting patients who need to be referred to gynecologic oncologists.

Keywords: Ovarian; Mass; Malignancy; Index

Introduction

Ovarian cancer causes for 4% of all female genital tract cancers and it is the leading cause of the death due to female genital tract cancer in industrialized countries [1]. Ovarian cancer prognosis remains poor with overall 5 year survival about 44%, according to SEER data [2]. The increase in overall survival is associated with the management of patients with optimal debulking surgery for epithelial ovarian cancer [3]. Also, recent studies have shown that surgery by gynecologic oncologists improves survival [4,5]. Pre-operative discrimination between benign and malignant ovarian tumors enables referring patient to oncology centers.

Preoperative evaluation of an adnexal mass is rather complicated process. So, differentiation of benign and malignant adnexal mass is critical. However, when evaluated individually, the efficacy of ultrasound, demographics and biochemical values are incapable of distinguishing benign from malignant. CA-125, one of the biochemical marker, is often used for distinguishing malignant tumors. However, CA-125 has limited value. The level of CA-125 is elevated in less than half of epithelial ovarian cancers [6]. Also, premenopausal benign pathologies and postmenopausal medical problems are associated with increased CA-125 serum levels [6]. The specificity and sensitivity of CA-125 can be improved when the test is combined with pelvic ultrasonography [7]

The original form of 'Risk of Malignancy Index' (RMI) was first presented by Jacobs et al. in 1990 [7]. Second version of RMI was developed in 1996 by Tingulstad et al., which we termed RMI-2 [8]. The RMI 2 was modified by same authors in 1999, and it's known as RMI 3 [9]. The RMI is a simple method that can be applied directly into clinical practice rather than high-priced or complex methods such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT).

The RMI is based on CA 125 level, the Ultrasound score (U) and the Menopausal status score (M). RMI: CA-125xUxM. All versions of RMI were validated by many retrospective and prospective studies and the best cut-off value for RMI was found to be 200, with a sensitivity of 81-92%, a specificity of 82-85% [7-21].

The present study was designed to confirm the effectiveness of the RMI to identify cases with high potential of ovarian malignancy in order to refer these patients to gynecologic oncologists. Additionally, we revealed the most accurate cut-off value for differentiation of benign masses from malignants.

Materials and Methods

This was a prospective, observational study, including 106 patients who underwent surgery because of an adnexal mass between January 2008 and October 2010 and comparing the RMI with pathological final results. Approval for the trial protocol and written informed consent of all patients were obtained.

Age, parity, medical history, pelvic and physical examination, laboratory findings, including CA-125 of all cases were recorded. Ultrasound examination was performed with a GE Medical U/S (Logic

alpha 200 GE Medical A/S Milwaukee, USA) with 6.5 MHz transvaginal transducer, by the same doctor. The transabdominal ultrasonography was also performed when necessary.

Patients with amenorrhea more than a year or who had hysterectomy and older than 50 years were described as postmenopausal women and they scored M=3. Other patients scored M=1.

The ultrasound findings were evaluated according to RMI scoring system. One point was given for each: multilocularity, presence of solid areas, presence of ascites, bilaterality or presence of intraabdominal metastases. A total of 2 or more points gives U=3, zero or one point give U=1. The numeric value of CA-125 level was entered directly into the formula. Histopathologic diagnosis regarded as a gold standard for evaluation of results. The histological classification of tumors was done according to WHO (World Health Organization) classification [21].

The statistical analysis was done using statistical software (NCSS 2008) and Student's t and Mann-Whitney U tests were used, as appropriate. The proportion of malignant and benign cases with different sonographic parameters was compared with chi-square and Fisher's exact tests. A Receiver Operating Characteristics (ROC) curve was used to determine the best cut-off value for discriminating benign and malignant adnexal masses. Significance level was defined as 0.05.

Results

Of 60 patients with benign final pathologic results, 23 had nonneoplastic tumors and 34 had neoplastic tumors.

Histological type	n	%
Non-neoplastic tumors	23	38.4
Follicular cyst	13	21.7
Endometrioma	6	10
Tubo-ovarian abscess	4	6.7
Neoplastic Tumors	34	56.6
Mature cystic teratoma	8	1.3
Epithelial tumors	14	23.3
Mucinous cystadenoma	3	5
Serous cystadenoma	11	18.3
Sex-cord stromal tumors	12	20
Fibrothecoma	6	10
Thecoma	2	3.3
Adenofibroma	4	6.7
Others	3	5
Intraligmantary leiomyoma	1	1.7
Genital tuberculosis	2	3.3
Total	60	100

Table 1: The pathological final results of the benign masses.

One of the patients had intraligamentary leiomyoma and 2 of the patients had genital tuberculosis. Table 1 shows the pathological results of benign masses.

Two patients had borderline mucinous tumors. In addition, 44 patients had malignant ovarian tumors according to their final pathological results, as shown in table 2.

Histological type	n	%
Borderline Ovarian Tumors	2	4.3
Borderline mucinous Tumor	2	4.3
Malignant Ovarian Tumors	44	95.7
Epithelial Tumors	35	76.1
Mucinous cystadenocarcinoma	5	10.9
Serous cystadenocarcinoma	24	52.1
Endometrioid cystadenocarcinoma	4	8.7
Clear-cell adenocarcinoma	2	4.4
Granulosa cell tumor	5	10.9
Metastatic ovarian cancer	4	8.7
Total	46	100

Table 2: The pathological final results of the malignant masses

The mean age of the patients was 53.3 ± 13.05 years.

Variable	Benign	Malignant	P-value
Age (mean ± SD)	48.6 ± 13.1	59.3 ± 10.2	0.001
Serum CA-125 (u/ml)* (range)	22.1 (12-35.5)	515.5 (168.25-801.75)	0.001
RMI* (range)	57 (30-150.5)	3771 (518.25-7215.75)	0.001
Menopausal status			0.001
Premenopausal	40	10	
Postmenopausal	20	36	
Sonographic morphology			
Multilocularity	39	46	0.001
Presence of solid areas	40	44	0.001
Presence of ascites	2	34	0.001
Bilaterality	4	13	0.003
Evidence of metastases	4	13	0.003
Ultrasound score			0.001
	1	33	0
	≥ 2	27	46

Table 3: Results of univariate analysis. *median

Patients with malignant final pathologic results were significantly older than others. Menopausal status, CA-125 levels and median values of the RMI of the cases were presented in table 3.

All 5 parameters (age, Ca-125 levels, menopausal status, RMI and Ultrasound score) were found to be associated predictors of malignancy using ROC analysis (Figure 1). RMI was the most accurate factor for predicting malignancy.

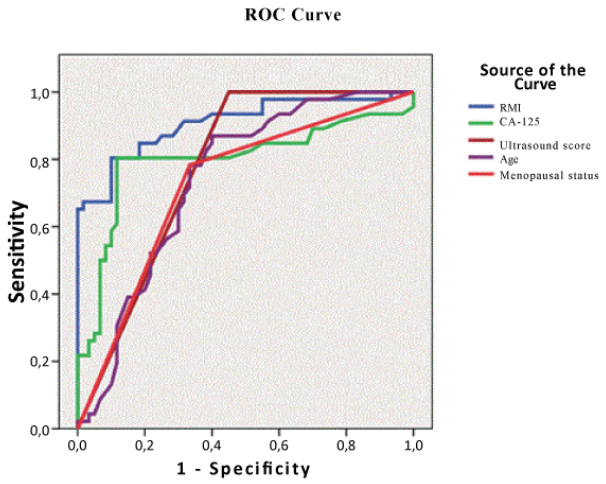

Figure 1: ROC curves of individual predictors for differentiating ovarian malignancy from benign masses

The best cut-off value for the RMI was 189 with a sensitivity of 84.8%, a specificity of 81.6%, a PPV of 78% and a NPV of 87.5%.

Discussion

Our findings are in line with previous studies which the RMI was found to be effective to classify ovarian masses according to their potential for malignancy. We detected that CA-125 is the most useful individual criteria of RMI to discriminate benign and malign of ovarian masses with sensitivity and a specificity of 75% and 77%, respectively. In their study, Jung-Woo Park et al. reported similar findings [23]. However, the values of serum CA 125 levels are limited for postmenopausal women. Endometriosis, pelvic inflammatory disease and menstruation can increase CA 125 values [24]. Second useful individual criteria of RMI are ultrasound score with sensitivity and a specificity of 100% and 65%, respectively. Jacobs et al. was achieved a sensitivity of 71% and specificity of 75% for CA-125, and a sensitivity of 71% and a specificity of 83% for ultrasound score [7].

RMI has proven its success in discriminating benign and malignant adnexal masses compared with individual parameters such as Ultrasound score CA-125 levels and menopausal status. Nonetheless, the most accurate cut-off value for the RMI has been investigated and a value of >200 was found to be best with a sensitivity, a specify, a Positive Predictive Value (PPV) and a Negative Predictive Value (NPV) of 89-92%, 82-96%, 62-98% and 77-98%, respectively [21,25]. Supporting this data, we achieved a 77.5% of sensitivity and 85.9 % of specificity when a cut-off value of >200 was used. However, in our study, the best cut-off value for the RMI was 189 with a sensitivity of 84.8%, a specificity of 81.6%, a PPV of 78% and a NPV of 87.5%. If the cut-off value of RMI was set 189 instead of 200, it would cause a reduction of 2 false-negative cases. Still, 7 patients with invasive malignancies had scores of RMI under 189. 4 of these were diagnosed as mucinous carcinoma and 3 were diagnosed as germ cell tumor. Of the 6 women with mucinous carcinomas, 4 were false negative. False positive results occurred in the 11 cases; 6 had endometriomas, 2 fibrotecoma, 2 adenofibroma, and 2 genital tuberculosis.

In conclusion, the present study demonstrated that RMI was a reliable method detecting pelvic masses with high risk of malignancy. Herewith, RMI leads selecting patients who need to be referred to gynecologic oncologists. However, RMI may need improvement for better detecting of mucinous carcinomas and germ cell tumors.

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