



EVALUATION OF THE DIAGNOSTIC PERFORMANCE OF THE 'RISK OF MALIGNANCY INDEX' IN DIFFERENTIATING BENIGN FROM MALIGNANT OVARIAN TUMORS

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ABSTRACT Malignant ovarian tumors are the sixth most common female cancer and constitute 7.5% of all gynecological malignancies and 3.5% of all cancers in women (1). The overall mortality in ovarian malignancy is more than 80%, contributed largely by the delay in diagnosis. Early detection of ovarian cancer and timely referral, if required to a gynecological oncologist forms the corner stone to reduce mortality from ovarian malignancy.

Ovarian tumors are known to present late in the course of the disease and there is no definite test to define whether an ovarian mass is benign or malignant. The overall performance of the Ca 125 is rather poor, considering that it may be elevated in a number of benign conditions as well. Inter observer variability and the multitude of mimickers, precludes ultrasound as the sole tool to differentiate the two. A combination of the above along with the menopausal status promises to perform better in differentiating benign vs malignant masses. Hence rests the significance of the RMI in this study.

Also knowing whether an ovarian mass is benign or malignant will be helpful not only in prognosticating the disease and planning appropriate therapy, but it has the powerful advantage of deciding who should do the surgery – the general gynecologist or the oncosurgeon.

Aim : The objective of this study is to evaluate the diagnostic performance of the Risk of Malignancy Index (RMI) in differentiating between benign and malignant ovarian tumors.

Materials and methods : This study was conducted in the Department of Obstetrics and Gynecology – Government medical college Trivandrum for a period of one year. All patients above the age of 30 years, admitted to the wards with an ovarian mass were included in the study. RMI scores were calculated for all patients. The RMI scores were then compared to the histopathology reports, which is the gold standard for the diagnosis of malignancy. ROC curve was drawn to conclude on the cut off value.

Results : Out of the 102 patients in the study group, 24 (23.5%) had a malignant ovarian tumor. The sensitivity, specificity, PPV and NPV of RMI was 83.3%, 88.46%, 68.99% and 94.52% respectively. The sensitivity, specificity, and NPV of RMI is much higher than the individual performance of ultrasound, menopause or serum Ca 125 levels.

Conclusion : RMI has proved to be a good diagnostic method to differentiate benign and malignant ovarian tumors.

KEYWORDS : Risk malignancy index, Serum Ca 125, menopause, benign and malignant ovarian tumor.

INTRODUCTION :

Ovarian malignancy has the highest mortality amongst all the gynecological malignancies. The prognosis of ovarian malignancy is greatly influenced by appropriate first line surgery (2). In spite of the known benefit of meticulous comprehensive surgical staging and cytoreduction, many women do not receive appropriate first line surgery. This is because of the difficulty in making an accurate pre operative diagnosis of ovarian malignancy. Sensitive and specific methods for the diagnosis of ovarian malignancy are required, which may influence the selection of the institution where it will be done and also the seniority and expertise of the surgeon. This will provide a rational basis for referral before laparotomy (3).

The Risk of malignancy index (RMI) is a simple scoring system introduced in 1990, utilizing three diagnostic criteria – ultrasound finding, Serum Ca 125 levels and the menopausal status of the patient.

$RMI = \text{ultrasound score} \times \text{menopausal score} \times \text{absolute value of serum Ca 125.}$

To distinguish benign and malignant masses, the RMI is superior to the three individual variables in isolation. In addition, RMI utilizes currently available non invasive tests, which are applicable in clinical practice and provide a rational basis for specialist referral for better surgical clearance.

This study was conducted to validate the role of RMI in discriminating benign from malignant ovarian tumors in our population.

MATERIALS AND METHODS:

This study was conducted in the department of Obstetrics and Gynecology, Government medical college Trivandrum.

Inclusion Criteria:

All patients more than 30 years in age, with an ovarian mass as detected by clinical and ultrasound examination were included in the study.

Exclusion Criteria:

Ovarian tumors in pregnancy and inoperable masses were excluded

from the study, as were functional cysts or extra ovarian masses at sonography.

102 cases were included. For calculating the RMI, menopausal scores, ultrasound scores and Ca 125 levels were calculated.

Menopausal score :

premenopausal women were assigned a score of M=1, post menopausal (patients with more than 1 year of amenorrhoea or women > 50 years who underwent a hysterectomy), were given a score of M=3.

Ultrasound score :

ultrasonographic features studied were, unilateral/ bilateral, unilocular/ multilocular, solid areas, ascites and intra abdominal metastasis. A score of 1 was assigned for each criteria. Presence of 0/1criteria was given a score of 1(U=1) and 2-5criteria was given a score of 3(U=3).

Serum Ca 125 levels :

The absolute value as measured by a Elecsys Ca 125 2 assay was considered.

RMI calculation :

was done using the formula
 $RMI = M \times U \times \text{absolute value of Ca 125}$
 Values above 200 indicate malignancy.

All these patients underwent a staging laparotomy and the subsequent histopathology report was the gold standard for the diagnosis of malignancy.

The sensitivity, specificity, positive and negative predictive value were calculated for the various parameters.

Multivariate logistic regression analysis was performed to assess the Odds ratio of different factors for each group.

Receiver operated characteristic (ROC)analysis was done and the

ROC curve was drawn to obtain the cut off value of RMI and Ca 125 levels.

RESULTS :

Out of the 102 patients recruited in the study group, 24 (23.5%) had a malignant ovarian tumor. 87.5% had an epithelial ovarian tumor with serous tumors predominating. The proportion of malignant tumors increased as age advanced, and the mean age for malignant lesions was 50.3 years.

52% of the cases were pre menopausal . The proportion of benign to malignant ovarian tumors in the post menopausal group was higher than that in the pre menopausal group.

Table 1 : Menopausal score :

Menopausal score M	HPR		Total
	malignant	Benign	
M1 (score 1)	8 (33.3%)	45 (57.7%)	53 (52%)
M3 (score 3)	16 (66.7%)	33 (42.3%)	49 (48%)

P<0.05
Sensitivity 66.6%, specificity 57.6%, PPV 32.6%, NPV 84.9%

Table 2: Distribution as per ultrasound findings :

Sl No		HPR		Total	P value
		Malignant	Benign		
1	unilateral	14 (58.3%)	71(91.00%)	85 (83.3%)	P<0.001
	bilateral	10 (41.70%)	7 (9.00%)	17 (16.7%)	
2	Solid area negative	4 (16.70%)	62 (79.5%)	66 (64.7%)	P<0.001
	Solid area positive	20 (83.30%)	16 (20.5%)	36 (30%)	
3	multilocular	24 (100%)	56 (71.8%)	80 (78.4%)	P<0.01
	unilocular	0	22 (28.2%)	22 (21.6%)	
4	Ascites negative	10 (41.7%)	72 (92.3%)	82 (80.39%)	P<0.001
	Ascites positive	14 (58.3 %)	6 (7.70%)	20 (19.6%)	

Table 3: Analysis of ultrasound score

Ultra sound score	HPR		Total
	Malignant	Benign	
Score -1	4 (16.67%)	61(78.2%)	65 (63.7%)
Score -3	20 (83.33%)	17 (21.8%)	37 (36.3%)

p<0.001

This shows a significant co relation between ultrasound score 3 and ovarian malignancy.

(Sensitivity 83.33%, specificity 78.21%, PPV 54.05%, NPV 93.85%)

Table 4: Analysis of the serum Ca125 levels

Serum Ca 125 levels	HPR		Total
	Malignant	Benign	
High > 35	19 (79.20%)	19 (24.40%)	38 (37.30%)
Normal < 35	5 (20.80%)	59 (75.60%)	64 (62.70%)

Taking a cut off 35u/ml for malignancy, the sensitivity, specificity, PPV and NPV were 79.1%,75.6%, 50%, and 92.1% respectively .

Table 5: Analysis of RMI

RMI	HPR		Total
	Malignant	Benign	
High > 200	20 (83.30%)	9(11.5%)	29(28.4%)
Normal < 200	4 (16.7%)	69 (88.5%)	73 (71.6%)
P <0.001			

Sensitivity 83.33%, specificity 88.46%, PPV 68.97%and NPV 94.52%.

The sensitivity, specificity and NPV of RMI is much higher than the individual scores of ultrasound, menopause and serum Ca 125 levels.

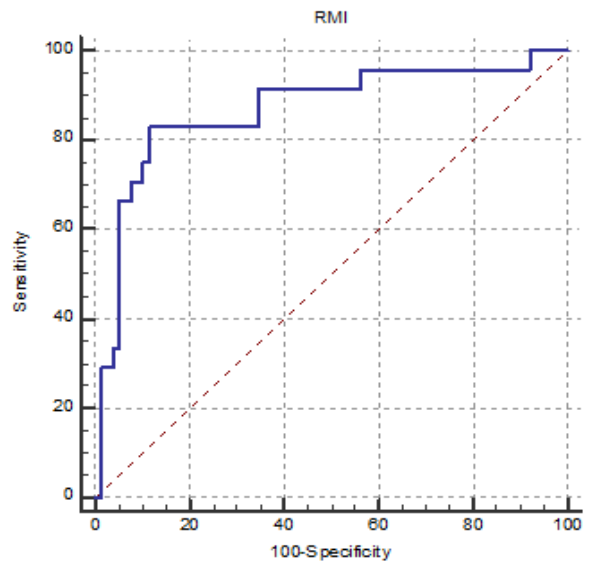


Figure 1: Receiver operator characteristic curve for RMI

Table 6: Co ordinates for ROC

Criterion	Sensitivity	Specificity	+LR	-LR	+PV	-PV
≥0.4	100	0	1		23.5	
>6.3	100	7.69	1.08	0	25	100
>6.54	95.83	7.69	1.04	0.54	24.2	85.7
>19.2	95.83	43.59	1.7	0.096	34.3	97.1
>20	91.67	43.59	1.62	0.19	33.3	94.4
>40.2	91.67	65.38	2.65	0.13	44.9	96.2
>50.4	83.33	65.38	2.41	0.25	42.6	92.7
>186.3	83.33	88.46	7.22	0.19	69	94.5
>205.2	75	88.46	6.5	0.28	66.7	92
>210.6	75	89.74	7.31	0.28	69.2	92.1
>213	70.83	89.74	6.91	0.33	68	90.9
>254	70.83	92.31	9.21	0.32	73.9	91.1
>268.2	66.67	92.31	8.67	0.36	72.7	90
>336	66.67	94.87	13	0.35	80	90.2
>1026	33.33	94.87	6.5	0.7	66.7	82.2
>1059	33.33	96.15	8.67	0.69	72.7	82.4
>1272.6	29.17	96.15	7.58	0.74	70	81.5
>1935	29.17	98.72	22.75	0.72	87.5	81.9
>5292	0	98.72	0	1.01	0	76.2
>6084	0	100		1		76.5

DISCUSSION :

RMI is a reliable diagnostic scoring system to differentiate benign from malignant ovarian tumors. We performed this study to test the validity of RMI. Hence the sensitivity, specificity and predictive values of serum Ca 125, ultrasound score and menopausal score and RMI to differentiate benign from malignant ovarian masses was determined and compared.

Statistical analysis of the menopausal score shows a low negative predictive value, sensitivity and specificity. Thus a menopausal score alone cannot be used to differentiate benign from malignant ovarian tumors.

Ultrasound score gives a sensitivity, specificity and NPV of 83.3%, 78.2% and 93.85% respectively. This is comparable with the diagnostic performance of other complicated scoring systems like Ferrazi et al and Sassone et al (4,5) where the sensitivity and specificity ranges from 74-88% and 40-65% respectively. Because of the low specificity of the ultrasound score, ultrasound alone cannot be used to differentiate benign from malignant masses. The advantage of the ultrasound scoring system is that, due to its simplicity, it can be used easily by the general gynecologist or the sonologist.

Taking a Ca 125 cut off of 35u/ml for malignancy, the sensitivity, specificity and NPV for the study group was 79.1%, 75.6% and 92.18% respectively. This low value can be due to the inclusion of many benign conditions like endometriosis, which also show elevated Ca 125 values. Among the individual parameters, the ultrasound score

appears to be the most useful diagnostic modality in distinguishing benign from malignant ovarian tumors.

Analyzing the diagnostic performance of the RMI, we found that it performed much better than any individual test in differentiating benign from malignant tumors at the optimal cut off score of > 200 to indicate malignancy.

Of the 102 cases, 29 had an elevated RMI of which 20 were malignant. Of the 9 cases that were falsely positive, we encountered endometriosis (3), tuberculosis (1), fibro thecoma with ascites (2) and serous cystadenoma (3).

Out of the 73 cases with normal RMI, 4 turned out malignant. They were mainly non epithelial tumors - (malignant lymphoma ovary, immature teratoma grade 3, Krukenberg tumor) and one case of stage I mucinous cystadenocarcinoma.

The sensitivity, specificity and NPV of the diagnostic performance of RMI was 83.3%, 88.46% and 94.52% respectively which is comparable to the results of Jacobs et al (6), Tingulstad et al (7), Morgante(8) et al, and Bailey et al (9) which ranged from 71-87%, 84-97% and 89-93% respectively.

Thus RMI has proved to be a good diagnostic tool to differentiate benign and malignant ovarian tumors. This 2. by the general gynecologist working in the periphery and refer the suspect cases to a higher oncology centre, thereby improving the survival and prognosis of women undergoing surgery for ovarian masses.

CONCLUSION :

The increased negative predictive value, sensitivity and specificity of the RMI, has proven that it is a good diagnostic method to differentiate benign from malignant ovarian tumors. Amongst all the individual diagnostic modalities, ultrasound has been found to have a better diagnostic performance in differentiating benign from malignant ovarian tumors.

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