

## **Role of risk of malignancy index score in evaluation of adnexal masses**

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**How to citation this article:** Azhar un Nisa Quraishi, Ruksana Farooq, Afshana Salam, “Role of risk of malignancy index score in evaluation of adnexal masses”, IJMACR- November – December - 2021, Vol – 4, Issue - 6, P. No. 01 – 07.

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**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

### **Abstract**

**Background:** The aim of study was to evaluate effectiveness of risk of malignancy index score in the preoperative evaluation of benign and malignant ovarian masses.

**Methods:** This was a prospective study, carried out in all patients admitted with adnexal masses to the department of obstetrics and Gynecology, Sher-E-Kashmir Institute of Medical Sciences Soura, Srinagar from May 2019-june 2021. A total of 140 patients were taken in study and surgery was performed and histopathological diagnosis of specimens was taken as gold standard to calculate accuracy of RMI.

**Results:** Of the total masses, 67.1% had benign lesions and 32.9% had malignant lesions. Most of the patient was in the age group of 40-59 years. In our study the RMI score at the cutoff value of 225 had sensitivity 78.3%, specificity 97.9%, PPV 94.7%, NPV 90.2%, accuracy 91.4% and area under the ROC curve 0.831.

**Conclusions:** The study concluded that RMI was an effective diagnostic tool in differentiating benign and malignant ovarian masses.

**Keywords:** RMI, ROC, adnexal mass, CA125

### **Introduction**

Pelvic masses are commonly encountered gynecological problem.<sup>1,2</sup> They are one of the most common reasons for referral to gynecological oncology departments to assess the possibility of uterine or ovarian malignancies. The most common pelvic mass is ovarian mass that varies from benign cyst to malignant ovarian cancer. Most tumours produce few or only mild nonspecific symptoms. The most common symptoms include abdominal distension, abdominal discomfort, lower abdominal pressure sensation and urinary or gastrointestinal symptoms. Ovarian cancer ranks third after cervical and uterine cancer among gynecological malignancies.<sup>3</sup> The risk of a woman developing cancer of the ovary in her life time is 1:70 to 1:100. Patients of low parity, decreased fertility, delayed child bearing and those having strong

family history of ovarian, breast, endometrial and colon cancer, have strong predisposition to develop ovarian cancer. Most ovarian cancers are diagnosed at advanced stages with 5 year survival as low as 10%. Early diagnosis provides 5 year survival rate upto 90%.<sup>4</sup>

The increasing incidence of ovarian cancers mandates the need of investigations to identify the benign and malignant nature of ovarian masses before surgery and confirmation by histopathology examination of biopsy specimens. Proper preoperative evaluation of ovarian masses will help gynecologists to refer women with suspected malignancies to a gynecologist for appropriate treatment, which will improve survival rate.<sup>2</sup> At the same time, this will also reduce unnecessary referrals of low risk patients to oncology centers. Risk of malignancy index [RMI] score has been widely accepted as an efficient tool for preoperative assessment of ovarian masses. In 1995, Jacob et al<sup>5</sup> initially proposed RMI 1 as product of ultrasound findings\*serum CA125 levels\*menopausal status. Further RMI was extended to RMI2 and RMI3. The difference between three indices lies in the different scoring of ultrasound findings and menopausal status. For RMI 1, possible abnormal ultrasound findings [U] include parameters like multilocular cystic lesion, solid lesion, bilaterality, ascites and metastasis. If no USG parameter is found, U is taken as zero. If a single parameter is seen, it will be U=1, and if 2 or more parameters are found, it will be U=2. Menopausal status is taken either premenopausal [M=1], or if postmenopausal or age >50 with hysterectomy for any reason, then [M=3]. The serum concentration of CA125 is taken directly in the formula.<sup>5</sup> In present study a cutoff value of 225 for RMI revealed the best discrimination between benign and malignant ovarian masses, because of high sensitivity and specificity.

The objective of our study was to evaluate role of RMI1 in preoperative discrimination of benign and malignant masses.

### **Materials and Methods**

The study was a prospective study, carried out in all patients admitted with adnexal mass to the department of obstetrics and Gynecology Sher-I-Kashmir Institute of Medical Sciences Soura, Srinagar from May 2019 to June 2021. A total of 140 patients were taken in study. Only women who underwent surgery were taken in study as histopathological diagnosis was taken as gold standard to calculate accuracy of RMI. Women with non gynecological abdominal masses, known case of ovarian cancers and diagnosed cases of ectopic pregnancies were excluded from study. The written informed consent was taken from all participants and study was approved by Institutional Ethical Committee. A detailed preoperative history, clinical examination, serum tumour markers, Ultrasound imaging and other required diagnostic modalities were performed. The RMI 1 for each woman was calculated as the product of Ultrasound findings [U], Menopausal status [M] and serum CA 125 levels. Intraoperatively, tissue specimen was sent for histopathology. All Histopathologic examinations of the specimens were done by pathologists to whom ultrasonographic findings, tumour markers and intraoperative findings were not revealed. Histopathologic diagnosis was regarded as a gold standard for evaluation of results to classify benign and malignant masses.

### **Statistical Methods**

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and

Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were expressed as Mean±SD and categorical variables were summarized as percentages. Student’s independent t-test was employed for comparing continuous variables. Chi-square test was used for comparison of categorical variables. Sensitivity, specificity, PPV, NPV and diagnostic accuracy were calculated with reference to presence of benign and malignant disease. Receiver operating characteristics (ROC) curve of RMI was plotted to determine the appropriate cut-off value for discriminating between benign and malignant adnexal masses. A P-value of 0.05 was considered statistically significant.

**Results**

A total of 140 patients were taken in the study. Most of the patients were in the age group of 40-59 years[43.6%][table1].The age and parity distribution of patients is shown in table 1 and table 2. As per histopathological reports, 94 patients [67.1%] had benign tumours and 46 patients [32.9%] had malignant lesions. The benign lesions were serous cystadenoma (n=30) , dermoid cyst (n=19) , mucinous cystadenoma (n=15), chocolate cyst (n=8), papillary serous cystadenoma(n=7), papillary mucinous cystadenoma (n=6),simple serous cyst (n=5), fibroma (n=3) and fibro the coma (n=1).The malignant lesions were papillary serous cyst adenocarcinoma (n=17),mucinous cyst adenocarcinoma (n=6), serous cyst adenocarcinoma (n=5),papillary mucinous cyst adenocarcinoma (n=4), dysgerminoma (n=3), granulosa cell tumor(n=3), krukenberg tumour(n=3),yolk sac tumour(n=2), carcinosarcoma(n=2) and endometroid adenocarcinoma(n=1).

The age distribution of patients with respect to benign and malignant masses is shown in the table. Benign tumours are more common in mean age group of 36 years but

malignant lesions are more common in older age group with a mean age of 49 years, with a statistically significant p value of less than 0.001.

Age (Years)	Number	Percentage
< 20	8	5.7
20-39	53	37.9
40-59	61	43.6
≥ 60	18	12.9
Total	140	100
Mean ± SD=42.7±8.92		

Parity	Number	Percentage
Nulliparous	17	12.1
Para 1	26	18.6
Para 2	53	37.9
≥ Para 3	44	31.4
Total	140	100

Benign masses	Number	Percentage
Serous cystadenoma	30	21.4
Papillary serous cystadenoma	7	5.0
Mucinous cystadenoma	15	10.7
Papillary mucinous cystadenoma	6	4.3
Dermoid cyst	19	13.6
Chocolate cyst	8	5.7
Simple serous cyst	5	3.6
Fibroma	3	2.1
Fibrothecoma	1	0.7
Total	94	67.1

Table 4: Distribution of malignant adnexal masses according to histopathology

Malignant masses	Number	Percentage
Serous cyst adenocarcinoma	5	3.6
Papillary serous cyst adenocarcinoma	17	12.1
Mucinous cyst adenocarcinoma	6	4.3
Papillary mucinous cyst adenocarcinoma	4	2.9
Dysgerminoma	3	2.1
Granulosa cell tumor	3	2.1
Yolk sac tumor	2	1.4
Krukenberg tumor	3	2.1
Endometroid adenocarcinoma	1	0.7
Mmnt (carcinosarcoma)	2	1.4
Total	46	32.9

Table 5: Comparison based on age between benign and malignant masses

Age (Years)	N	Mean	SD	P-value
Benign	94	36.1	8.94	<0.001*
Malignant	46	49.4	11.73	

\*Statistically Significant (P-value<0.05)

The distribution of cases according to menopausal status, sonographic features, USG score. Serum CA125 levels and RMI is given in table [5].

Most of patients in our study were premenopausal with 90 cases [64.3%],out of which 75 had benign and 15 had malignant diseases.50 cases[35.7%] were in the postmenopausal age group, out of which 19 had benign and 31 had malignant disease. Significantly malignant

disease was found more in postmenopausal group than premenopausal with a significant p value [p<0.001]

Analysis of 140 patients with ultrasound features showed that presence of solid areas, ascites and metastasis showed significant correlation with p<0.05.Bilaterality and multilocularity failed to prove malignancy in our study with p >0.05.Out of 86 patients with USG score of 1,77 cases were benign and 9 cases were malignant. Similarly out of 54 patients with USG score of 3,17 cases were benign and 37 cases were malignant. USG score proved to be statistically significant in our study with p<0.001.Similarly CA125 levels proved to be statistically significant in our study with p<0.001.Most of the cases with CA125 levels >35IU/MI were malignant, and those with CA125 levels<35IU/MI were benign.

Table 6: Distribution of cases according to menopausal status, sonographic morphology, USG score, serum CA125 levels and RMI

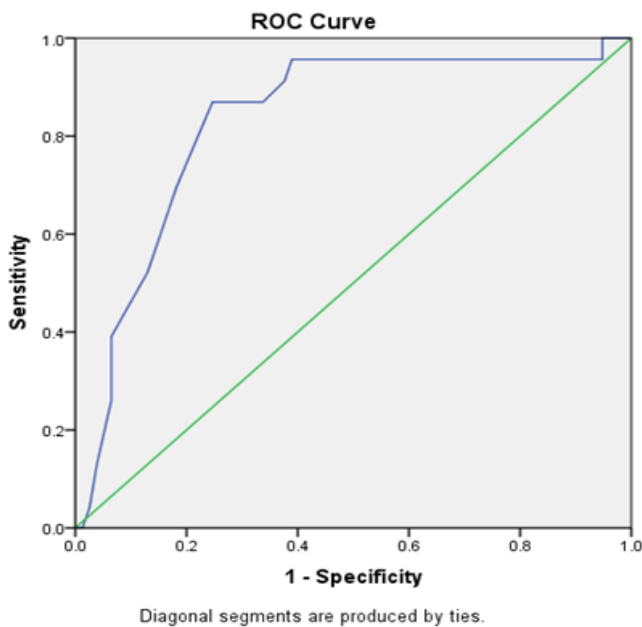
Variable	Benign [n=94]		Malignant [n=46]		Total		P-value	
	No.	%age	No.	%age	No.	%age		
Menopausal status	Premenopausal	75	79.8	15	32.6	90	64.3	<0.001*
	Postmenopausal	19	20.2	31	67.4	50	35.7	
Sonographic morphology	Bilateral	9	9.6	4	8.7	13	9.3	0.866
	Multilocularity	37	39.4	21	45.7	58	41.4	0.478
	Solid Areas	23	24.5	44	95.7	67	47.9	<0.001*
	Ascitis	7	7.4	27	58.7	34	24.3	<0.001*
	Metastasis	0	0.0	5	10.9	5	3.6	0.003*
USG Score	1	77	81.9	9	19.6	86	61.4	<0.001*
	3	17	18.1	37	80.4	54	38.6	
CA 125	< 35 U/mL	48	51.1	10	21.7	58	41.4	<0.001*
	≥ 35 U/mL	46	48.9	36	78.3	82	58.6	
RMI	< 225	2	2.1	36	78.3	38	27.1	<0.001*
	≥ 225	92	97.9	10	21.7	102	72.9	

\*statistically significant

Out of 38 cases with RMI<225, 36 cases had benign disease and 2 cases were malignant. Similarly, out of 102 cases with RMI>225, 92 cases were benign and 10 cases were malignant. RMI value at the cutoff of 225 proved to be statistically significant in our study in differentiating benign and malignant adnexal masses with p<0.001.

Table 7: Diagnostic performance of RMI in differentiating between benign and malignant adnexal masses

Parameter	Value	95% CI
Optimal cutoff	$\geq 225$	-
Sensitivity	78.3	63.6-89.1
Specificity	97.9	92.5-99.7
PPV	94.7	82.3-99.4
NPV	90.2	82.7-95.2
Accuracy	91.4	84.5-97.3
Area under the ROC curve (AUC)	0.831	0.743-0.898



Graph 1: ROC curve for RMI in differentiating between benign and malignant adnexal masses

Criteria	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
RMI $\geq 225$	78.3	97.9	94.7	90.2	91.4
CA 125 $\geq 35$	78.3	51.1	43.9	82.7	60.0
USG score 3	80.4	81.9	68.5	89.5	81.4

The best diagnostic performance in our study was found for RMI at the cut-off value of 225, with highest area under the curve of 83.1%, sensitivity of 78.3%, specificity of 97.9%, PPV of 94.7%, NPV of 90.2% and accuracy of 91.4%. [Table 6]

The diagnostic performance of RMI  $> 225$ , against CA125  $> 35$  and ultrasound score  $> 3$  in differentiating benign and malignant adnexal masses is compared in Table [7]. Among the Criteria, RMI score  $> 225$  have highest specificity, PPV, NPV and accuracy compared to individual parameters. Among the individual parameters, USG score  $> 3$  has highest sensitivity, specificity, PPV, NPV and accuracy [80.4%, 81.9%, 68.5%, 89.5% and 81.4% respectively].

### Discussion

In our study, the disease was commonly seen in the age group of 40-59 years. This was consistent with the study of Ritanjali Behera et al<sup>6</sup> where most cases were found in the age group of 40-59 years. In our study, the mean age group in benign cases was 36.1 years and in malignant group was 49.4 years. This was consistent with the findings of Ashrafgangoe et al<sup>7</sup> and Simsek et al<sup>8</sup>, where mean age group in benign cases was found as  $37 \pm 8.79$ ,  $35.23 \pm 10.87$  years and  $50.8 \pm 12.9$ ,  $50.78 \pm 13.39$  in malignant groups respectively.

In our study, 67.4% malignant cases were seen in postmenopausal group and 32.6% were seen in premenopausal group. This was consistent with findings of Rao JH et al<sup>9</sup> and Kumari N et al<sup>10</sup>, showing similar incidence rates in postmenopausal patients. Similarly, in a study conducted by Meys EM et al<sup>11</sup>, malignant masses occurred more frequently in postmenopausal than in premenopausal women [42.4% and 24.2%, respectively]

In our study, most common benign mass seen was serous cystadenoma [32%] and most common malignant mass

was papillary serous cyst adenocarcinoma [28%], consistent with study of Manjunath et al<sup>12</sup>.

In our study, an ultrasound score of 3

Had the sensitivity 80.4%, specificity 81.9%,PPV 68.5%,NPV 89.5% and accuracy of 81.4%.This was consistent with observations of Ritanjali Behera et al<sup>6</sup> and Vasudevan et al<sup>13</sup>.

In our study, serum CA125 >35 in detecting malignant masses had sensitivity 78.3%,specificity 51.1%,PPV 43.9%,NPV 82.7% and accuracy 60%.This was consistent with observations made by Ratanjali et al<sup>6</sup>.Similarly in a study conducted by Shekhar NC et al<sup>14</sup>,serum CA125 >35IU/MI had sensitivity 80%,specificity 76%,PPV 42.42% and NPV 94.78%.In contrast a similar study by Singhal S et al<sup>15</sup> gave a sensitivity of 75% and a specificity of 90% for serum CA levels>35.

The best performance in our study was for RMI cut off of 225 with sensitivity 78.3%, specificity 97.9%, PPV 94.7%, NPV 90.2%, accuracy 91.4% and area under ROC curve 0.831.This was consistent with findings of Ritanjali Behera et al<sup>6</sup> where RMI cutoff of 225 was taken. Similarly in a study of Rojna Rai et al<sup>16</sup>,RMI 1 >200 was found to have sensitivity of 54.6%,specificity 85.7%,PPV 60%,NPV 82.8% and accuracy 76.9%.Hada A et al<sup>17</sup> found RMI1 at the cut off of 200 to have specificity of 93.8% and area under ROC curve to be 0.844,similar to observations in our study. Shekhar NC et al<sup>14</sup> in their study found that RMI 1 with cut off of 200 had specificity 92.12%,NPV 93.25% and area under ROC curve 0.899,consistent with our findings.

Thus our study confirmed that RMI 1 was effective in preoperative differentiation of benign and malignant masses, compared to individual parameters of USG score, serum CA125 levels and menopausal status.

## **Conclusion**

The present study concluded that RMI is an effective tool in preoperative evaluation of benign and malignant adnexal masses. It can be reliably used to triage patients as per RMI score of adnexal masses so that the suspected malignant masses are referred to higher gynecological oncology centres and evaluated on an urgent basis. At the same time, the low risk cases are managed at lower centres, thus avoiding unnecessary wastage of time, resources and other complex diagnostic modalities in such cases.

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