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# Predicting the risk of malignancy in suspected early ovarian neoplasms in our center (ASRAM)

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**Abstract: Background:** Ovarian neoplasms can be benign or malignant and accurate preoperative diagnosis is crucial for determining the appropriate surgical approach. Risk of malignancy index (RMI 4) is a useful tool that combines radiological findings, CA-125 levels, and tumor size to predict the likelihood of malignancy. The RMI 4 score is interpreted as either <450 or >450 and compared to the final histopathology report.
**Aim and Objectives:** The aim of this study is to evaluate the accuracy of RMI 4 in predicting the risk of malignancy in early ovarian neoplasms and to investigate its association with histopathological findings. The specific objectives are:
1) To determine the sensitivity of RMI 4 in predicting malignancy in suspected early ovarian neoplasms.
2) To compare the sensitivity of RMI 4 with CA-125 levels in predicting malignancy.
3) To examine the association between RMI 4 score and final histopathological examination findings.
**Methods:** This cross-sectional study was conducted in the Oncology OPD of ALLURI SITA RAMA RAJU ACADEMY OF MEDICAL SCIENCES (ASRAM) over a period of one year, from February 2021 to January 2022. We included 46 patients who met the inclusion criteria.
**Results:** The sensitivity of RMI 4 in predicting malignancy was found to be 52.4% for all cases, while it was 84.6% for serous and mucinous tumors. The sensitivity of CA-125 was 61.9% for all cases and 84.6% for serous and mucinous tumors. Our study found that RMI 4 and CA-125 are more predictive of malignancy in serous tumors compared to mucinous and other pathologies.
**Conclusion:** In conclusion, RMI 4 is a useful tool for differentiating malignant from benign ovarian lesions. Our study shows that RMI 4 and CA-125 are more sensitive in predicting malignancy in serous tumors compared to mucinous and other pathologies. Clinicians can use these tools to guide the appropriate surgical approach and improve patient outcomes.

**Keywords:** Ovarian neoplasms; RMI; Ca 125.

## 1. Introduction

Malignancy in ovarian neoplasms is typically suspected based on radiological findings [1] and CA 125 levels. However, identifying malignancy preoperatively in early ovarian neoplasms can be challenging. Solid mass, size greater than 6 cm, and multicystic nature are radiological features that may suggest malignancy. Furthermore, complex cyst and solid masses are associated with a significantly increased risk of ovarian cancer [2].

In advanced ovarian malignancy, histological diagnosis by trucut biopsy before commencing neoadjuvant therapy is safe [3]. However, performing fine-needle aspiration cytology (FNAC) or trucut biopsy in early ovarian malignancies is controversial to avoid upstaging of tumor or possible tumor seedlings along the track.

A preoperative diagnosis of malignancy is important in the approach to a tumor, as the surgical technique will be different in benign and malignant tumors. In benign tumors, only the neoplasm is removed, whereas in malignancy, a staging laparotomy is necessary, followed by hysterectomy, bilateral oophorectomy, infracolic omentectomy, and lymph node sampling. Surgical staging in epithelial ovarian cancer has prognostic importance and plays a significant role in the treatment of patients by gynecological oncologists [4]. Patients who undergo non-optimal surgical staging have worse overall survival and recurrence-free survival than optimally staged patients [5]. Non-optimal staged patients require adjuvant chemotherapy.

Frozen section is useful in clinical decision-making processes [6] per-operatively, but in centers where the facility is not available, the final histopathology can only diagnose malignancy. Risk of malignancy index (RMI) is helpful in predicting malignancy when compared to individual values [7]. RMI was originally developed by Jacobs *et al.* in 1990. RMI-1 was developed by Tingulstad *et al.* with slight modifications in score values for menopausal status and ultrasound score, while RMI-2 is known as RMI-3 and was modified in 1999 [8,9].

Any of the four risk of malignancy indices is useful in predicting malignancy preoperatively [7]. RMI 4= $U \times M \times S$ (size in centimeters) $\times CA - 125$,, where a total ultrasound score of 0 or 1 made U=1, and a score of =2 made U=4. Premenopausal status made M=1 and postmenopausal status made M=4. A tumor size (single greatest diameter) of <7 cm made S=1, and =7 cm made S=2. The serum level of CA-125 was applied directly to the calculation [10]. Ultrasound parameters taken are the presence of a multilocular cystic lesion, solid areas, a bilateral lesion, ascites, and intra-abdominal metastasis.

## 2. Aim and objectives

1. To evaluate the diagnostic accuracy of the RMI4 score in predicting the risk of malignancy in suspected early ovarian neoplasms preoperatively.
2. To assess the association between RMI4 score and final histopathological examination findings in patients with suspected early ovarian neoplasms.

## 3. Methods

**Study design:** This is an analytical cross-sectional study conducted at Alluri Sitarama Raju Academy of Medical Sciences (ASRAM) in Eluru District, Andhra Pradesh.

**Study area and period:** The study was carried out over a one-year period from February 2021 to January 2022 in ASRAM, a tertiary care center with specialized facilities for the diagnosis and management of gynecological malignancies.

**Study population:** The study population consisted of all patients referred to ASRAM with suspected early ovarian malignancies based on radiological findings and serum CA 125 levels. Patients who met the inclusion and exclusion criteria during the study period were included in the analysis.

**Sample size:** A total of 46 patients were included in the study, based on the eligibility criteria.

**Study tools:** The risk of malignancy index (RMI) was used to calculate the risk of malignancy in suspected ovarian neoplasms. The RMI score was calculated using ultrasound score, serum CA 125 levels, menopausal status, and the size of the tumor, as shown in Table 1. The RMI score was used to predict the risk of malignancy in each patient, and the association between the RMI score and the final histopathological examination findings was analyzed.

The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all patients before the study. Data were collected using a pre-designed proforma and analyzed using appropriate statistical software.

**Table 1.** Showing the RMI4 score calculation

| **Parameter** | | **RMI 4 Score** |
|---|---|---|
| USG Score (U) | 1 feature | 1 |
| | = 2 | 4 |
| Menopausal score (M) | Pre menopausal | 1 |
| | Post menopausal | 2 |
| Size of the mass (S) | <7 cms | 1 |
| | = 7 cms | 2 |

Ultrasound score was based on the presence of solid content, multicystic nature, bilaterality, distant metastases, and ascites. A finding was scored as one, and two or more findings were scored as four. Premenopausal status was scored as one, and postmenopausal status was scored as two. Tumor size less than 7 cm was scored as one, and size greater than or equal to 7 cm was scored as two. The CA-125 level, measured in IU/mL, was multiplied by the scores obtained from the ultrasound findings and menopausal status, resulting in the calculation of RMI4 score using the following equation:

$$RMI4 = U \times M \times S \times CA - 125\,.$$

In our study group, all tumors were more than 7 cm in size. The RMI score was classified as <450 and >450.

### 3.1. Inclusion criteria

The following inclusion criteria were used in this study:

1. Patients who were referred to Alluri Sitarama Raju Academy of Medical Sciences (ASRAM) with suspected early ovarian malignancies based on radiological findings and CA 125 levels.

### 3.2. Exclusion criteria

The following exclusion criteria were used in this study:

1. Patients with advanced tumors, which had features such as ascites, peritoneal nodules, omental metastases, para-aortic nodes, pleural effusion, and other distant metastases.
2. Patients with simple cysts or tubo-ovarian masses were excluded.

### 3.3. Data analysis

The collected data were entered into Microsoft Excel 2007 and analyzed using SPSS version 26 software, trial version. Descriptive statistics were used to summarize the data, including means and standard deviations for continuous variables, and frequencies for categorical variables. The chi-square test and Fisher's exact test were used as appropriate. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined using ROC curve analysis. The results were presented in the form of charts and graphs, and a P value less than 0.05 was considered statistically significant.

### 3.4. Ethical issues

The institutional ethical committee provided clearance prior to the start of the study. Written consent was obtained from all patients prior to their participation. All patient information was kept confidential and the study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

## 4. Results

Table 2 shows the demographic and clinical characteristics of the study participants. The majority of patients, 45%, were between 40-59 years old, while 31.1% were above 60 years. Pre-menopausal status was observed in 63% of the patients. CA-125 level was found to be elevated (=35) in 54% of the patients. The RMI4 score was <450 in 69.6% of the patients, indicating a low risk of malignancy.

Regarding the histopathological findings, benign/borderline tumors were found in 54.3% of the patients, while malignant tumors were found in 45.7% of the patients. Among the malignant tumors, serous subtype was the most common, observed in 39.1% of the cases, followed by mucinous subtype, observed in 30.4% of the cases.

In terms of the ultrasound score, the majority of patients (69.6%) had a score of one, indicating a low likelihood of malignancy. This finding is consistent with the high percentage of patients with low RMI4 score. Overall, these results suggest that the majority of suspected early ovarian neoplasms in our study had a low risk of malignancy.

**Table 2.** Showing percentages of various parameters

| Variable | | Frequency | Percentage (%) |
|---|---|---|---|
| **Aage** | <20 years | 3 | 6.5% |
| | 20-39 years | 11 | 23.9% |
| | 40-59 years | 21 | 45.7% |
| | = 60 years | 11 | 23.9% |
| **Menopause** | Premenopause | 29 | 63.0% |
| | Postmenopause | 17 | 37.0% |
| **CA125** | <35 | 21 | 45.7% |
| | =35 | 25 | 54.3% |
| **RMI4** | <450 | 32 | 69.6% |
| | =450 | 14 | 30.4% |
| **Types of Tumour** | Benign/borderline | 25 | 54.3% |
| | Malignant | 21 | 45.7% |
| **USG** | 1 | 38 | 82.6% |
| | 4 | 8 | 17.4% |
| **Subtypes of malignany** | Serous | 18 | 39.1% |
| | Mucinous | 14 | 30.4% |
| | Germcell | 6 | 13.0% |
| | Fibroma | 4 | 8.7% |
| | Endometrial cyst | 1 | 2.2% |
| | Yolk sac | 1 | 2.2% |
| | Dysgerminoma | 1 | 2.2% |
| | Seromucinous | 1 | 2.2% |

In the present study, the age range of participants varied from 17 years to 76 years, with a mean age of 46 years. Table 3 provides more detailed information on the age distribution of the study population.

**Table 3.** Showing the descriptive statistics of Age

| Variable | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age | 46 | 17 | 76 | 46.09 | 16.319 |

Table 4 provides important insights into the findings of our study, from which the following conclusions can be drawn:

**1. Age categorization:** Our study group revealed that malignant tumors are typically seen in the less than 20 years age group and in the 38-45% range in the middle age group. In the greater than 60 years age group, 54% of tumors are malignant, with 45% being benign tumors. These results suggest that malignancy can occur at any age, and benign tumors can occur even in older age groups.

**2. Menopausal status:** Postmenopausal women had a higher percentage of malignant tumors (53%) compared to premenopausal women (43%). This finding suggests that postmenopausal women may be more susceptible to ovarian malignancies.

**3. CA125:** 38% of malignant tumors showed CA125 levels less than 35 IU/ml, while 48% of benign/borderline tumors had CA125 values greater than 35 IU/ml. When we further categorized CA125 levels in different ovarian neoplasms, the sensitivity of CA125 in detecting malignancy increased from 61% in all cases to 84% in serous tumors alone.

**4. RMI4 score:** RMI4 scores less than 450 are considered benign, while scores greater than 450 are considered malignant. In our study group, RMI scores less than 450 were observed in 34% of malignant tumors and scores greater than 450 were seen in 28% of benign tumors. When we further categorized neoplasms as serous, mucinous, and others, the sensitivity of detecting malignancy increased from 52% to 84%, with a statistically significant p-value of 0.016 (Table 5).

Overall, these findings highlight the importance of considering age, menopausal status, CA125 levels, and RMI4 scores in the evaluation of ovarian neoplasms.

**Table 4.** Showing the association of various parameters with type of tumours

| Variable | | Benign/ Borderline | | Malignant | | Chi- square/ Fisher's exact test value | df | P value |
|---|---|---|---|---|---|---|---|---|
| | | Count | Row N % | Count | Row N % | | | |
| **Age** | <20 years | 1 | 33.3% | 2 | 66.7% | 1.368 | 3 | .713 |
| | 20-39 years | 6 | 54.5% | 5 | 45.5% | | | |
| | 40-59 years | 13 | 61.9% | 8 | 38.1% | | | |
| | = 60 years | 5 | 45.5% | 6 | 54.5% | | | |
| **Menopause** | Premenopause | 17 | 58.6% | 12 | 41.4% | .577 | 1 | .447 |
| | Postmenopause | 8 | 47.1% | 9 | 52.9% | | | |
| **CA125** | <35 | 13 | 61.9% | 8 | 38.1% | .889 | 1 | .346 |
| | =35 | 12 | 48.0% | 13 | 52.0% | | | |
| **RMI4** | <450 | 21 | 65.6% | 11 | 34.4% | 5.389 | 1 | .020* |
| | =450 | 4 | 28.6% | 10 | 71.4% | | | |
| **USG** | 1 | 23 | 60.5% | 15 | 39.5% | 3.362 | 1 | .067 |
| | 4 | 2 | 25.0% | 6 | 75.0% | | | |
| **Subtypes of malignancy** | Serous | 9 | 50.0% | 9 | 50.0% | 2.528 | 2 | .282 |
| | Mucinous | 10 | 71.4% | 4 | 28.6% | | | |
| | Others | 6 | 42.9% | 8 | 57.1% | | | |

**Table 5.** Showing the association of type of tumour with RMI4 among different subtypes of malignancy

| Variable | | Serous | | Mucinous | | Others | |
|---|---|---|---|---|---|---|---|
| | | Benign / borderline | Malignant | Benign / borderline | Malignant | Benign / borderline | Malignant |
| | | N (%) | N (%) | N (%) | N (%) | N (%) | N (%) |
| **RMI4** | **<450** | 6(85.7%) | 1(14.3%) | 10(76.9%) | 3(23.1%) | 5(38.5%) | 8(61.5%) |
| | = 450 | 3(27.3%) | 8(72.7%) | 0(0.0%) | 1(100%) | 1(100%) | 0(0.0%) |
| **Fisher's exact test** | | 5.844 | | 2.692 | | 1.436 | |
| **df** | | 1 | | 1 | | 1 | |
| **P value** | | 0.016 | | 0.101 | | 0.231 | |

Table 6 presents a statistically significant association between different subtypes of malignancy and RMI4 score, with a p-value of 0.000. This indicates that the RMI4 score is a useful tool in distinguishing between different subtypes of malignancy.

Furthermore, Table 5 shows a statistically significant association between the type of tumor and RMI4 score in serous type of malignancy, with a p-value of 0.016. This suggests that the RMI4 score can be particularly useful in identifying serous tumors.

Moreover, in Table 7, we can observe that the sensitivity of RMI4 score is 52.4% in all cases, while in serous and mucinous subtypes it is 84.6%. This highlights that the RMI4 score has a higher sensitivity in detecting malignancy in serous and mucinous tumors compared to all cases combined. Similarly, the sensitivity of Ca125 is 61.9% in all cases and 84.6% in serous and mucinous subtypes, indicating that Ca125 is also a useful marker in detecting malignancy in these subtypes.

**Table 6.** Showing the overall association of subtype of malignancy with RMI4

| Variable | | RMI4 | | | | 2 value | df | P value |
|---|---|---|---|---|---|---|---|---|
| | | <450 | | =450 | | | | |
| | | Count | Row N % | Count | Row N % | | | |
| **Subtypes of malignancy** | **Serous** | 6 | 33.3% | 12 | 66.7% | 18.335 | 2 | .000 |
| | **Mucinous** | 13 | 92.9% | 1 | 7.1% | | | |
| | **Others** | 13 | 92.9% | 1 | 7.1% | | | |

**Table 7.** Showing the sensitivity, specificity, PPV and NPV of RMI4 and Ca125

| Variable | All cases | | | | Only Serous and Mucinous | | | |
|---|---|---|---|---|---|---|---|---|
| | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
| **RMI4** | 52.4 | 89.9 | 83.84 | 65.38 | 84.6 | 89.50 | 88.95 | 85.31 |
| **CA125** | 61.9 | 60.0 | 60.74 | 61.16 | 84.6 | 57.90 | 66.77 | 78.99 |

In Figure 1, we can observe that RMI4 has a sensitivity of 52.4%, specificity of 89.9%, and an area under the curve (AUC) of 70.4%, indicating that RMI4 is a useful diagnostic tool for distinguishing between benign and malignant ovarian tumors. The statistical significance of this finding is noteworthy.

Similarly, in Figure 2, RMI4 has a sensitivity of 84.6%, specificity of 89.5%, and an AUC of 86.2%, indicating that RMI4 is a more reliable tool for the diagnosis of serous and mucinous tumors. The statistical significance of this finding is also noteworthy.

Overall, these figures provide strong evidence to support the use of RMI4 as a diagnostic tool for ovarian tumors, especially for the detection of serous and mucinous tumors.

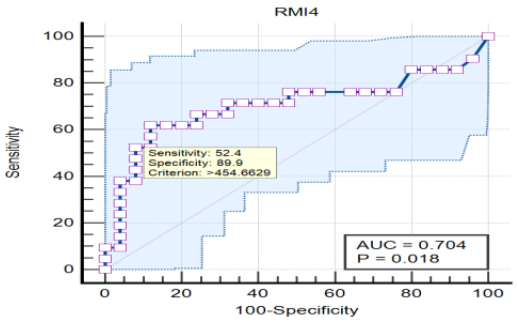


**Figure 1.** Showing the ROC curve of RMI 4 of all cases

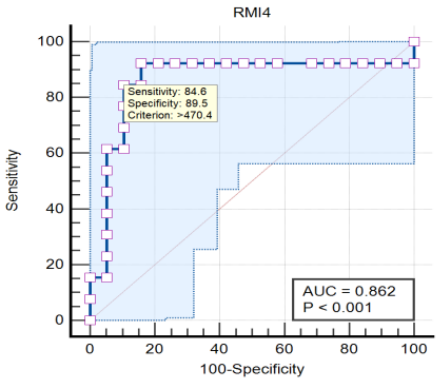


**Figure 2.** Showing the ROC curve of RMI 4 for serous and mucinous cases

## 5. Discussion

The preoperative diagnosis of ovarian malignancy is essential for the treating oncologist to determine the appropriate surgical staging and adjuvant chemotherapy decisions, which have a significant impact on prognosis. Numerous studies have demonstrated the prognostic importance of surgical staging in epithelial malignancies [4,5].

The risk of malignancy index is a valuable diagnostic tool for predicting ovarian malignancy, and RMI 4 is useful for assessing the risk of ovarian malignancy by considering ultrasound score, menopausal status, Ca125, and tumor size [10]. In our study, germ cell tumors were found to be the most common malignancy in patients under the age of 20, which is consistent with previous studies [11,12]. However, the sample size was too small to draw a definitive conclusion.

Our study found that 38-45% of the middle age group had a risk of malignancy, indicating a significant risk of ovarian malignancy in this age group. The mean age of presentation was 46 years, and postmenopausal status was a risk factor in western countries. However, an increasing trend of ovarian malignancy has been observed in middle and older age groups in the Indian population, with ovarian malignancy being one of the most common malignancies affecting Indian women [13,14].

In our study, 45% of suspected ovarian neoplasms were found to be benign, indicating that the size of the tumor and postmenopausal age do not always suggest malignancy. A study conducted by R. Goswami et al. found that transvaginal ultrasound revealed that 39% of ovarian neoplasms were benign [15]. CA 125 is a valuable marker in the pre-operative diagnosis and monitoring of ovarian malignancy and is also a prognostic indicator for this disease [16,17]. However, the role of CA 125 in screening for early-stage ovarian cancer and the diagnosis of early ovarian cancer is not significant.

Our study found that the Ca 125 level was significantly higher in serous tumors than in mucinous and germ cell tumors. This finding is consistent with other studies [18,19].

## 6. Conclusion

The present study highlights the importance of using RMI in the preoperative evaluation of ovarian masses, as it is a simple, reliable, and clinically applicable scoring system. Our results suggest that RMI is more accurate in differentiating malignant from benign lesions compared to individual parameters. Additionally, our study findings indicate that Ca 125 and RMI 4 are more predictive of malignancy in serous tumors compared to mucinous and other pathologies. These results suggest that other markers may be more helpful in nonepithelial malignancies.

It is important to note that preoperative diagnosis of ovarian malignancies in early stages can be challenging, particularly in mucinous and other pathologies. Furthermore, our study revealed that malignant tumors can occur in the middle age group and that benign tumors can occur in postmenopausal or older age groups. Therefore, clinicians should consider using RMI and Ca 125 in their diagnostic evaluations, especially in cases where malignancy is suspected, but further diagnostic workup is required. Further studies are needed to validate the use of RMI and Ca 125 in the diagnosis of ovarian malignancies across diverse patient populations.

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