Original Research Article

Correlation of risk of malignancy index (RMI 3) of adnexal masses with the histopathology report and its significance

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Abstract

Background: Ovarian malignancy is the second most common gynecological malignancy. It is the most lethal gynecologic cancer as many women with ovarian cancer present with late stages of disease. The search for an ideal screening test for ovarian cancer has been going on for quite some time. RMI is a scoring system that is derived from a formula that combines menopausal status with serum cancer antigen 125 (CA-125) values and ultrasound variables of low complexity.

Aim: To calculate RMI of adnexal masses and correlate it with final histopathological diagnosis so as to determine the significance of RMI score in diagnosis of ovarian malignancy.

Materials and methods: A prospective cohort study was conducted of 48 women with an adnexal mass referred to a teaching hospital and managed surgically. RMI3 was calculated in all the cases and correlated with the intraoperative findings and histopathology.

Results: RMI 3 had a sensitivity of 100%, a specificity of 91.89%, a positive predictive value of 78.57%, and negative predictive value of 100% in diagnosing epithelial ovarian malignancy. RMI was more accurate than CA125 alone in distinguishing malignant from benign masses.

Conclusion: RMI is a standardized, easily reproducible, and relatively inexpensive, highly reliable procedure available even in low resource settings with good sensitivity, specificity, positive predictive value and negative predictive value in detecting epithelial ovarian malignancy.

Key words

Risk malignancy index, RMI, Adnexal mass, Histopathology, Correlation, Significance.

Introduction

Ovarian cancer is a leading cause of mortality among gynecological malignant tumors [1, 2, 3]. More than 75% of affected women are diagnosed at an advanced stage because early-stage disease is usually asymptomatic and symptoms of late-stage disease are nonspecific [7]. Women with suspected ovarian carcinoma should be referred for optimal cytoreductive surgery in a dedicated gynecological oncology unit because optimal cytoreductive surgery is one of the prognostic factors in the treatment [9]. The diagnostic gold standard includes vaginal ultrasound (US) along with serum biomarkers like traditionally CA125 which is commonly found to be raised in epithelial ovarian tumors.

In 1990, Jacobs, et al. [4] originally developed the RMI (termed as RMI1), which was the first diagnostic model which has combined demographic, sonographic and biochemical parameters for investigating patients with adnexal masses.

RMI 1 = U x M x CA 125; a total US score of 0 yielded U = 0, a score of 1 yielded U =1, and a score of >=2 yielded U = 3. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 3. The serum level of CA 125 was applied directly to the calculation.

Tingulstad, et al. [11] developed their version of the RMI in 1996, and it is known as RMI 2.

RMI 2 = U x M x CA 125; a total US score of 0 or 1 yielded U =1 and a score of >= 2 yielded U = 4. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 4. The serum level of CA 125 was applied directly to the calculation.

In1999, Tingulstad, et al. [8] modified the RMI, which is termed RMI 3

RMI 3 = U x M x CA 125; a total US score of 0 or 1 yielded U = 1 and a score of >= 2 yielded U = 3. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 3. The serum CA 125 level was applied directly to the calculation

In 2009, Yamamoto, et al. [12] added the parameter of the tumor size score (S) to the RMI and have termed it the RMI 4 but its validity is due to be confirmed in future studies [4, 8].

RMI 4 = U x Mx CA 125, where a total US score of 0 or 1 yielded U = 1 and a score of >= 2 yielded U = 2. Premenopausal status yielded M = 1 and postmenopausal status yielded M = 4. A tumor size (single greatest diameter) of < 7 cm yielded S = 1 and >= 7 cm yielded S = 2. The serum level of CA 125 was applied directly to the calculation.

The aim of this study was to evaluate the risk of malignancy index (RMI 3) efficiency in differentiation of benign from malignant adnexal tumors in clinical practice

Materials and methods

This study was a prospective study conducted in Obstetrics and Gynecology Department of King George Hospital Visakhapatnam, between June 2018 and April 2019.

A total of 50 patients within a period of 11 months from June 2018 to April 2019, who attended the OP department with complaints of pain abdomen/ nausea, vomiting/ abdominal distension/ weight loss and on work up revealed an adnexal mass and for whom surgical treatment was planned, were taken up for the study.

Out of these 50 patients, 2 were excluded by the exclusion criteria mentioned below, leaving 48 patients included in the study.

Inclusion criteria:
- Women with adnexal mass for whom surgical treatment was planned.

Exclusion criteria:
- Pregnancy
- Coexistent Fibroid

- Patients who were known cases of endometriosis
- Patients whose HPE report turned out to be germ cell tumor origin

Obtained data included: age, menopausal status, clinical features at presentation, ultrasound findings and CA125 levels. RMI 3 was calculated for all patients.

The RMI-3 was calculated using the formula RMI=M x U x serum CA- 125
Where (M) refers to the patients' menopausal status, (U) refers to the ultrasound score and serum (CA -125) was the assayed level expressed in U/m.
Postmenopausal status is defined as more than 1 year of amenorrhoea
A score of M = 3 is given to postmenopausal women and M=1 for premenopausal status.
CA=125(U/ml) was entered directly into the equation.

Intraoperative findings of all the cases were recorded and correlated with histopathology in each case and the findings tabulated and analyzed. The diagnostic performances of CA-125, and RMI 3, were evaluated in sensitivity, specificity, NPV, and PPV with the pathologic report which was considered as gold standard and the results tabulated.

Results

A total of 48 patients with adnexal masses managed surgically were included in the study 31 out of 48 were premenopausal and 17 out of 48 were postmenopausal (**Table – 1**).

Table – 1: Number of patients.

Total no. of patients	Pre-menopausal	Post-menopausal
48	31	17
percentage	64.58%	35.41%

Out of the 48 women with adnexal masses who underwent surgical treatment, RMI was >200 in 14 out of 48 (**Table – 2**).

Table – 2: Surgical treatment and RMI.

Total no. of patients	RMI>200	RMI<200
48	14	34
Percentage	29.16%	70.83%

Table – 3: HPE.

Patients with RMI>200	HPE proven malignant lesions	HPE proven benign pathology
14	11	3
Percentage	78.57%	21.42%

Table – 4: RMI <200.

Patients with RMI<200	Malignant lesions	Benign lesions
34	0	34
Percentage	0%	100%

Out of these 14 women with RMI value >200, 11 had HPE proven ovarian malignancy. 4 out of these 11 were postmenopausal (36.2%). Remaining 3 out of the 14 women who had RMI >200 had benign lesions on HPE (**Table – 3**).
All the 34 women who had RMI <200 had benign lesions in HPE (**Table – 4**).

Sensitivity of RMI 3 to detect malignancy in adnexal pathology – 100%, specificity- 91.89%, Positive predictive value – 78.57%, and negative predictive value was 100% (**Table – 5**).

Out of the 11 women who had RMI>200 and had malignant lesions on HPE, the most common malignancy detected was Papillary serous cystadenocarcinoma – 3/11 - 27.27% (in two cases it was present alone and in another case it was detected to coexist with endometrioid carcinoma) as per **Table – 6**.

The mean value of RMI 3 in these cases was 3651.8. The mean CA125 value of these 11 cases was 1187. If measurement of CA125 value alone was considered in the study population: Sensitivity of CA125 to detect malignancy in adnexal pathology – 100%, Specificity- 64.86%, Positive predictive value – 45.83%, negative predictive value was 100% (**Table – 7**).

Table – 5: RMI and lesion.

	Malignant	Benign	Total
RMI>200	11	3	14
RMI<200	0	34	34
	11	37	48

Fishers exact test statistic value was <0.00001. The result was significant at p<0.01.

Table – 6: Distribution of various malignancies.

Type of malignant lesion	Number (out of 11)	Percentage
Papillary serous cystadenocarcinoma	2	18.18%
High grade serous carcinoma	2	18.18%
Endometrioid carcinoma	1	9.09%
Papillary serous cystadenocarcinoma plus endometrioid carcinoma	1	9.09%
Papillary cystadenocarcinoma	1	9.09%
Papillary mucinous cystadenocarcinoma	1	9.09%
High grade papillary serous cystadenocarcinoma	1	9.09%
Serous cystadenocarcinoma	1	9.09%
Low grade papillary cystadenocarcinoma	1	9.09%

Table – 7: CA 125 and lesions.

	Malignant	Benign	Total
CA125>35	11	13	24
CA125<35	0	24	24
	11	37	48

Fishers exact test statistic value was <0.0002. The result was significant at p<0.01.

Table – 8: Distribution of benign lesions.

Type of lesion	Number (out of 34)	Percentage
Mucinous cystadenoma	18	52.94%
Simple serous cyst	5	14.7%
Corpus luteal cyst	3	8.82%
Papillary serous cystadenoma	2	5.88%
Seromucinous cystadenoma	2	5.88%
Serous cystadenoma	2	5.88%
Papillary cystadenoma	1	2.94%
Endometriotic cyst	1	2.94%

Of the 3 women who had RMI >200 but had benign lesions on HPE, one was ovarian fibroma, another was hemorrhagic corpus luteal cyst and the last was mucinous cystadenoma. All these 3 women had a CA 125 value above 35. Pain was the presenting symptom in 8 out of the 11 malignant cases (72.72%) Mass per abdomen was seen in 8/11 cases - 72.72%, Abdominal distension in 5/11- 45.45%, Weight loss in 7/11 cases - 63.63%. Out of the 34 women who had RMI <200, all had benign lesions on HPE. Most common benign lesion was mucinous cystadenoma seen in 17 out of 34 - 50% (**Table – 8**).

Discussion

Ovarian cancer carries the worst prognosis among all gynecological cancers, mainly due to the lack of effective screening methods for early stage detection of the disease. Transvaginal ultrasound can discriminate between benign and malignant ovarian tumors better than all other radiological methods. Serum CA125 level is a valuable parameter for both diagnosis and monitoring of epithelial carcinoma. However, CA125 as a single parameter does not distinguish sufficiently benign from malignant masses preoperatively, as it can be elevated in various benign diseases and even in physiological conditions.

Table – 9: Comparison of two tests.

	RMI 3 positive	RMI 3 negative	Total
CA 125 positive	14	10	24
CA 125 negative	0	24	24
Total	14	34	48

Mc Nemars chi- squared statistic was 10.00000, corresponding p value was 0.001565 (<0.01).

Mc Nemars chi- squared statistic with Yates correction of 0.5 was 9.025000, corresponding p value was 0.002663.

Mc Nemars chi- squared statistic with Yates correction of 1.0 was 8.100000, corresponding p value was 0.004427.

Result using binomial exact test was 0.001953.

The difference between the two tests if found to be significant.

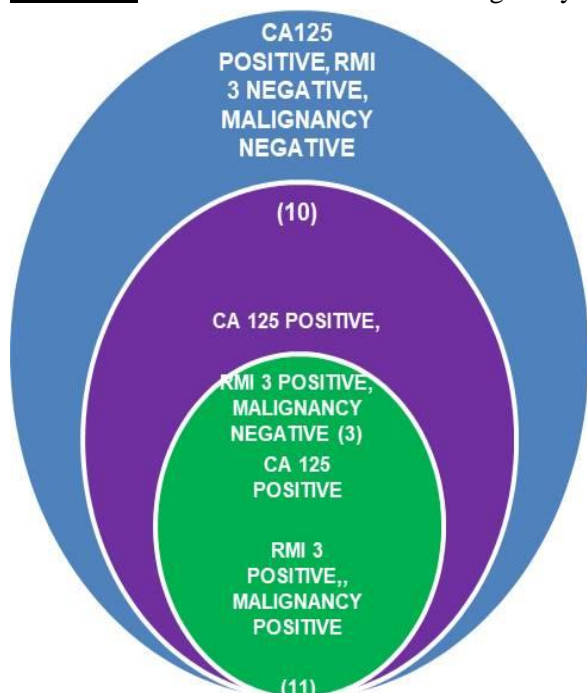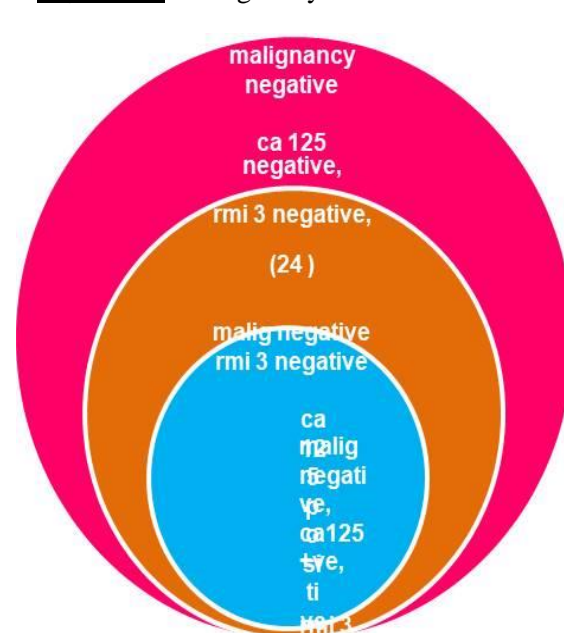**Figure – 1:** CA 125 +ve – RMI 3 – Malignancy.

Figure – 2: Malignancy -ve – CA 125 – RMI 3

These three versions of RMI (RMI 1, 2, 3) were assessed in many prospective and retrospective clinical studies. The RMI value of 200 has been proven to be the best for distinction of benign from malignant adnexal masses, with the high level of sensitivity (51% - 90%) and specificity (51% - 97%) [5, 6, 10].

In the present study, the sensitivity of RMI 3 to detect malignancy in adnexal pathology – 100%,

specificity was 91.89%, positive predictive value was78.57%, negative predictive value was 100%. In our study, benign pathology was commonly found in the study population and RMI3 was found to be low in 100 percent of the cases with benign pathology highlighting that benign tumors will always have low RMI values. That is also confirmed by high negative predictive values. Tests with better specificity and negative predictive value are more useful in early diagnostic phases and in population screening. This can avoid unnecessary or overly radical surgery in order to reduce the risk of surgical procedures.

RMI was more accurate than any individual criterion in distinguishing malignant from benign masses.

In this study, whereas both CA125 as an individual parameter as well as RMI 3 both had a sensitivity and negative predictive value of 100% in detecting ovarian malignancy, they differed in the specificity and the positive predictive value.

RMI 3 had a specificity of 91.89%, compared to Ca 125 which had a specificity of 64.86%. RMI 3 had a PPV of 78.57 % in detecting ovarian malignancy, as compared to Ca 125 measurement, which, used alone had a PPV of 45.83% in detecting ovarian malignancy.

Comparing the two tests i.e. RMI 3 and CA125 in the test population using Mc Nemars test was as per **Table – 9**.

CA125 positive cohort and its relationship with RMI 3 values and malignancy in the study population can be represented by **Figure – 1**.

Malignancy negative cohort and its correlation with the CA 125 and RMI 3 values in them can be represented as per **Figure – 2**.

Conclusion

Ovarian malignancy is common in women of all age groups both pre and postmenopausal and it can present with vague symptoms like pain abdomen, nausea and vomiting of which pain is the most common symptom and weight loss and mass per abdomen were the most common signs in this study.

High index of suspicion and early evaluation using simple but highly sensitive and specific tools like RMI3 is very efficacious and reliable in distinguishing benign from malignant lesions early such that cases with high RMI can undergo appropriate staging laparotomy in dedicated gynec oncology units and the remaining cases can be confidently and reasonably dealt with in a routine gynecological surgical practice.

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