Original Article

Efficacy of Risk Malignancy Index to differentiate the benign from malignant Ovarian Lesions

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Abstract

Objective: To evaluate the diagnostic accuracy of Risk Malignancy Index (RMI) to differentiate Benign from malignant ovarian masses taking histopathology as the gold standard.

Methodology: A total of 89 patients in department of gynecology and obstetrics, Civil Hospital Karachi from with ovarian masses identified on ultrasound findings according to International ovarian tumor analysis group (IOTA), who plan for surgical exploration were included in this study. After surgery, sample was sent for histopathology. RMI was calculated using formula RMI= U x M x CA-125. Based on RMI, lesions were interpreted, as benign and malignant, and Histopathological findings was considered as gold standard for defining the outcome. The data analysis was done by SPSS version 23.

Results: The average age of the patients was 37.21±11.69 years. The histopathological analysis revealed benign lesions in 83.15% and malignant lesions in 16.85% of cases. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of RMI in differentiating benign from malignant ovarian masses was 86.7%, 97.3%, 86.7%, 97.3% and 95.5% respectively. Additionally, the RMI maintained strong accuracy 96.7% in women under 40, 92.3% in those over 40, and 97.1% in premenopausal women, while the accuracy remained high across parity and BMI groups.

Conclusion: The Malignancy Index concluded to be a better estimate in diagnosing adnexal masses with high risk of malignancy, with an overall diagnostic accuracy of 95.5%, sensitivity of 86.7%, and specificity of 97.3%**.**

Keywords: Ovarian tumors, RMI, Benign, Malignant, differentiation.

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Introduction

Ovarian cancer has a notably high occurrence rate and ranks among the leading causes of mortality from reproductive system malignancies in women. According to the analysis across different ethnic groups, ovarian cancer shows the highest occurrence among Caucasian women, with an incidence rate of 12 per 100,000, followed by Hispanic women at 10.3 per 100,000, Asian women have a slightly lower rate of 9.2 per 100,000, while the lowest prevalence is seen among African-American women, with only 0.4 cases per 100,000.[1] Ovarian cancer represents a particularly aggressive form of ovarian malignancy. Since early-stage disease typically lacks distinct symptoms or noticeable clinical indicators, it often remains undetected until it progresses.[2] It has been indicating that merely 20–25% of cases are identified at an early stage, while around 60% of affected individuals receive their diagnosis only after the disease has advanced significantly.[2,3] Additionally the evaluating an adnexal mass before surgery is very important to determine whether it is benign or malignant, as this distinction directly influences both management strategy and counseling to patients.[4] Management of the malignant ovarian neoplasm is usually demanding in terms of surgical expertise or requiring a visit to a specialist center with gynecologic oncology practitioners, whereas benign lesions are usually easily managed by a general gynecologist, or safe with laparoscopic surgeries.[4] Early diagnosis of ovarian carcinoma and prompt referral to a gynecologic expert will allow such carcinoma to be properly staged and receive the best

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cytoreductive therapy and eventually improve the survival rates of the patients. Although histopathological examination remains the definitive diagnostic tool for ovarian cancer, an ideal biomarker for early detection has yet to be established. Furthermore, the diagnosis of ovarian cancer can often be achieved through a combination of clinical evaluation, blood tumor marker analysis, and imaging techniques such as ultrasound and CT.[2] Among these, MRI is especially favored because of its superior soft tissue contrast and detailed visualization capabilities.[5]

Though the proper distinguishing between the benign and malignant lesions still requires additional measurments.[2] Several studies have aimed to establish a reliable method for accurately distinguishing malignant lesions of the ovaries from the benign lesions.[6] Many serum biomarkers determined preoperative can be used to determine the possibility of ovarian carcinoma. The Carbohydrate antigen (CA) 125 is one of the most commonly used indicators among them with a cutoff point of 35 U/ml in cases of suspected malignancies.[7] But the sensitivity of it is limited in early-stage ovarian carcinoma, showing elevated levels in only about 23% to 50% of patients with Stage-I of the disease.[7] However the RMI is computed by multiplying the menopausal status, ultrasound score, and serum CA-125 level to estimate the probability of ovarian carcinoma.[7,8] As a result of its composite scoring approach that incorporates multiple clinical parameters, it can enhance the diagnostic accuracy in detection of ovarian malignancy.[9] Most important benefit of the RMI lies in its simplicity, as it can be easily implemented in routine clinical practice without the need for costly or complex techniques, making it a practical and efficient tool of diagnostic measurements. As the RMI is a widely applied scoring system in developed nations; however, its predictive reliability in developing regions remains undefine.

However, the present study is designed to determine the diagnostic accuracy of the RMI in distinguishing benign from malignant ovarian masses, using histopathology as the reference standard. The findings may help clinicians make informed decisions regarding patient referral, surgical planning, and management, ultimately leading to improve the outcome of the patients.

Methodology

This descriptive cross-sectional study was conducted in the department of Gynecology and Obstetrics, Civil hospital, Karachi, during 12 months from November 2018 to November 2019. All women aged 18-75 years, married/unmarried, with any parity, admitted to department of obstetrics and gynecology, with ovarian masses identified on ultrasound findings according to International ovarian tumor analysis group (IOTA), who plan for surgical exploration were included in the study. All the women who did not provide consent, had a prior bilateral salpingo-oophorectomy, women with history of treated carcinoma, or those who declined surgical intervention were excluded from the study.

Demographic information of the patients including age, BMI parity, menopausal status, and physical examination were taken by the principal investigator and each woman will undergo detailed clinical examination. Before starting the data collection, informed consent was obtained from every participant after a clear and detailed explanation regarding objective and purpose of the study. The ovarian lesions were classified as benign if it exhibited at least one of the following characteristics as; a unilocular cyst, a smooth multilocular tumor measuring less than 10 cm, a solid component smaller than 7 mm in diameter, the presence of acoustic shadows, or the absence of a detectable signal of the Doppler scan. In the same way, a lesion was considered malignant if it showed at least one of these features: an irregular solid tumor, an irregular multilocular mass larger than 10 cm in diameter, the presence of four or more papillary projections, ascites, or a higher signal of the Doppler flow of blood. The WHO histological classification for ovarian tumor was used to categorized ovarian neoplasms. The RMI was determined using three parameters: the ultrasound score (U), menopausal status (M), and serum CA-125 level (IU/ml), following the formula RMI = U × M × CA-125. According to the calculated score, ovarian lesions were classified as benign when the RMI was less than 200 and malignant when it was equal to or greater than 200.

Transabdominal and/or transvaginal ultrasound examinations were performed, and each of the following features was assigned one point: multilocular cyst, solid areas, metastatic deposits, ascites, and lesions bilaterally. Score by ultrasonography was assigned as 0 when no feature was present, 1 when one feature was identified, and 3 when two or more features were detected. The menopausal status was also incorporated into the index, with a score of 1 given to premenopausal women and a score of 3 to postmenopausal women, defined as those who had no

menstrual period for at least one year or were over 50 years of age and had hysterectomy done. The serum CA-125 levels were measured preoperatively in IU/ml using a standardized immunoassay technique, with all samples processed in the same laboratory to ensure consistency. Final values of the RMI were calculated by multiplying the three parameters, and histopathological examination of the excised ovarian mass was used as the gold standard to confirm the benign or malignant nature of the lesions. All of the information was analyzed using SPSS 23. The categorical data like marital status, menopausal status, Histopathological type of ovarian tumor and RMI score were expressed as proportions and percentages. Continuous data like age, parity, BMI, will expressed as mean and SD. The diagnostic accuracy of the RMI in differentiating benign from malignant ovarian lesions was evaluated by calculating key statistical parameters, including sensitivity, specificity, PPV, and NPV. Stratification was done with respect to age, parity, menopausal status, marital status, BMI. Post stratification diagnostic accuracy was computed.

Results

The overall average age of 89 patients was 37.21±11.69 years and the mean BMI was 22.58 ± 3.12 kg/m². The average CA-125 level was 64.98 ± 115.28 IU/ml, and the mean RMI was 306.39 ± 913.91. Majority of the women were married (85.39%), premenopausal (77.53%), and nulliparous (46.07%). The histopathological analysis revealed benign lesions in 83.15% and malignant lesions in 16.85% of cases. Additionally, based on RMI, 83.15% had scores <200, while 16.85% had scores ≥200, consistent with a higher likelihood of malignancy. Table I.

Table I: Baseline and clinical characteristics of the patients. (n=89)

Variables		Statistics
Age (Years)		37.21±11.69
BMI (kg/m^2)		22.58±3.12
CA-125 (IU/ml)		64.98±115.28
Risk of malignancy index		306.39±913.91
Marital Status	Married	76 (85.39%)
	Unmarried	13 (14.61%)
Parity Status	0	41 (46.07%)
	1-3	12 (13.48%)
	4-6	26 (29.21%)
	>6	10 (11.24%)
Menopausal Status	Pre-menopause	69 (77.53%)
	Post-menopause	20 (22.47)
Histopathology of the lesion	Benign	74 (83.15%)
	Malignant	15 (16.85%)
RMI Index	<200	74 (83.15%)
	>200	15 (16.85%)

Among all the benign lesions, serous cystadenoma in (31.1%) was most common whereas among malignant lesions mucinous adenocarcinoma (40%) was most diagnosed. Figure 1

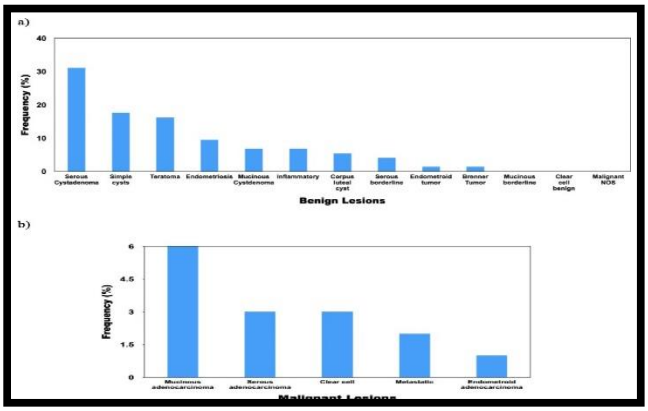

Figure 1. Frequency of Histopathological lesions. (n=89)

The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of RMI in differentiating benign from malignant ovarian masses was 86.7%, 97.3%, 86.7%, 97.3% and 95.5% respectively. Additionally, the RMI maintained strong accuracy 96.7% in women under 40, 92.3% in those over 40, and 97.1% in premenopausal women, while the accuracy remained high across parity and BMI groups. Table II

Table II: Diagnostic accuracy of RMI taking histopathology as gold standard additionally with stratification by age, marital status, parity and BMI. (n=89)

Variables	Sensitivity	Specificity	PPV	NPPV	Accuracy
RMI	86.7%	97.3%	86.7%	97.3%	95.5%
Age					
< 40	77.8%	100%	100%	96.3%	96.7%
>40	100%	90.9%	100%	75.0%	92.3%
Marital Status					
Unmarried	0	100%	100%	0	100%
Married	86.7%	96.7%	86.7%	96.7%	94.7%
Parity Status					
≤3	66.7%	100%	100%	95.9%	96.2%
>3	100%	92.6%	81.8%	100%	94.4%
Menopausal Status					
Pre-menopausese	75%	100%	100%	96.8%	97.1%
Post-menopauseuse	100%	84.6%	77.8%	100%	90%
BMI					
≤18.5	100%	80%	66.7%	100%	85.7%
18.5to25	80%	98.2%	88.9%	96.5%	95.4%

Discussion

The adnexal masses are common in clinical practice, and accurately distinguishing benign from malignant tumors is very important for proper diagnosis and treatment.[11] A standardized method for preoperative identification of probable malignant masses would allow optimization of first-line treatment for women with ovarian

cancer. The present study evaluated the diagnostic accuracy of the RMI in differentiating benign from malignant ovarian masses using histopathology as the gold standard, including 89 women aged 18–75 years with ultrasound-detected ovarian lesions (per IOTA criteria) scheduled for surgical exploration, where RMI scores <200 indicated benign and ≥200 indicated malignant masses. In this study the histopathological analysis revealed benign lesions in 83.15% and malignant lesions in 16.85% of cases, while based on RMI, 83.15% had scores <200, while 16.85% had scores ≥200, consistent with a higher likelihood of malignancy. In comparison, Liaqat B et al[12] reported that, based on RMI results, 25 (28.7%) patients tested positive and 62 (71.3%) tested negative, while histopathology confirmed 25 (28.7%) malignant and 62 (71.3%) benign ovarian masses.

Furthermore, in this study RMI demonstrated a sensitivity of 86.7%, specificity of 97.3%, PPV of 86.7%, NPV of 97.3%, and an overall diagnostic accuracy of 95.5% in distinguishing malignant from benign ovarian masses. In aligns to this study Disasa FA et al[13] reported that the overall, when applying an RMI cutoff point of 220, the index showed strong diagnostic performance, showing a 84.2% sensitivity, 77% specificity, 69.5% PPV, 88.7% NPV, and an overall accuracy of 79.8% in distinguishing malignant ovarian tumors from benign ones.[12] In the study Liaqat B et al[12] reported consistent findi8ngs where RMI demonstrated a 92% sensitivity**,** 96.77% specificity of**,** PPV of 92%**,** and 96.77% NPV, resulting in an overall diagnostic accuracy of 95.4%.

Another study by Naurin R et al[14] reported that, by using histopathology as the gold standard, the RMI achieved a sensitivity of 100%**,** specificity of 90.6%**,** 72.7% PPV**,** 100% NPV**,** and an overall diagnostic accuracy of 92.5%. in the study by Binte Afzal H et al[15] reported that the among patients with ovarian masses, the RMI demonstrated an overall diagnostic accuracy of 88.04%**,** with a sensitivity of 87.5%**,** specificity of 88.9%**,** 92.45% PPV**,** and 82.05% NPV. Furthermore**,** the study analysis by Mongan SP et al[16] showed that the RMI had 65% sensitivity**,** 55.5% specificity**,** 81.25% PPV**,** and 58.33% NPV, while the IOTA (SR) demonstrated 90% sensitivity**,** 55.5% specificity**,** 81.81% PPV**,** and 71.42% NPV, indicating better overall diagnostic performance. Almost all of the studies reported positive findings; however, some variations in results were observed, which may be attributed to differences in population characteristics, geographical variations, sample sizes, sample selection criteria, and the diagnostic methods employed in each study. Another study conducted in Pakistan reported 82.3% and 88.3% sensitivity and specificity of RMI in predicting ovarian cancer in comparison to ultrasound and CEA-15which less than reported in our study.[20]

Although, study reported inferior results for RMI in detecting ovarian cancer.[21] Additionally present study also evaluated the diagnostic accuracy of RMI across different demographic groups. It has been reported that the risk of developing ovarian cancer increases with age, as physiological changes such as heightened inflammation occur over time. Similarly, premenopausal women have been shown to have a 1.1 to 1.5 times higher risk of developing ovarian cancer. The findings of this study are particularly notable regarding the prediction of ovarian malignancy in overweight women, a significant consideration in Pakistan, where the majority of women fall into this category. Being overweight has been strongly associated with an increased risk of ovarian cancer (approximately 16%).[17]

Few other studies also showed good sensitivity, specificity, PPV and NPV.[18-20] Furthermore, in this study RMI demonstrated 100% diagnostic accuracy in detecting malignancy among overweight women, indicating the importance of considering age, menopausal status and BMI in evaluating ovarian cancer risk. Liaqat B et al[12] also reported that the RMI demonstrated the greatest specificity across the entire study group as well as within the postmenopausal subgroup, showing values of 92.4%**,** 87.1%**,** and 95.7%**,** respectively. However, the study has certain limitations, most notably a relatively small sample size, followed by potential selection bias**,** demographic homogeneity, and the single-center design, which may limit the generalizability. Hence, further large-scale, multicenter studies are recommended to validate these findings, explore the influence of demographic and physiological factors in greater detail, and support the development of tailored, population-specific diagnostic strategies for cancer of ovaries.

Conclusion

RMI observed is a reliable, simple, and cost-effective diagnostic tool for differentiating benign and malignant lesions from masses of the ovaries, with an overall diagnostic accuracy of 95.5%, sensitivity of 86.7%, and 97.3% specificity. The strong agreement observed of RMI with histopathological findings, validating its usefulness as an effective preliminary screening

technique. Overall method can serve as a valuable tool for early detection, risk stratification, and timely referral with the suspected malignancy of the ovaries, specifically in limited resources health settings where access to advanced diagnostic modalities is not easily obtainable.

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