Evaluation of Risk Malignancy Index (RMI) As Diagnostic Tool to Distinguish Between Malignant and Benign Adnexal Masses, while Taking Histopathlogy as Gold Standard

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Objective: To determine the diagnostic accuracy of risk of malignancy index (RMI) to distinguish between benign and malignant adnexal masses taking histopathology as gold standard.

Methods: This was an institutional based cross sectional study conducted at new radiology department of Services hospital Lahore, during the months of June to December 2016. Total of 165 females of age 25-70 years with adnexal masses on ultrasonography and admitted in gynecology ward for surgical exploration and histopathological diagnosis were included in the study, by using non probability consecutive technique.Ultrasound was performed by expert consultant radiologist. Preoperative serum CA 125 levels and menopausal status was also noted. RMI was calculated for every patient. All the collected data was entered and analyzed on SPSS version 14.0.1.

Results: The mean age of patients was 48.78±12.63 years. In total 165 females included, 80(48.48%) were premenopausal and 85(51.52%) were postmenopausal. The sensitivity of RMI was 89.06%, specificity of 96.04% and the diagnostic accuracy was 93.33% taking histopathology as gold standard.

Conclusions: ThAccording to our study results the RMI is reliable tool with high sensitivity, specificity and diagnostic accuracy values to distinguish between benign and malignant adnexal masses taking histopathology as gold standard.

Keywords: histopathology, RMI, malignant, benign, adnexal.

Introduction

Ovarian cancer is considered to be one of the most significant factors causing the death of women in the West and now it is equally affecting the Asian women too.[1]Every year, almost 200,000 women around the globe develop ovarian tumors, out of which 100,000 woman die from this disease. Ovarian cancer is one of the foremost causes of death and fourth most common ailment in Pakistani women.[2] According to a recent study,[3] 33.5% (4-63%) adnexal masses discovered are malignant. Especially in Pakistan where due to lack of sophisticated diagnostic tools, ovarian cancer has now been malicious and it is quite challenging to accurately diagnose a pelvic mass.[4]A palpable adnexal mass is a swollen lump in the adnexa of uterus and it can easily be identified during radiography imaging. Adnexal mass can be of following types:

i. Primary ovarian tumors (for example epithelial, germ cell and sex cord-stromal).
ii. Metastatic malignant tumors (gastrointestinal tract and breast).
iii. Lumps appearing in fallopian tubes (hydrosalpinx, pyosalpinx and primary Fallopian tube malignancies).
iv. Masses arising from the uterus (leiomyoma).
v. masses appearing in the gastrointestinal tracts (e.g. tumors of colons and appendix)
vi. Tumors of urinary tracts.
vii. Tumors caused by pelvic inflammatory diseases.
viii. It may be cysts arising from normal ovarian functions (follicular cysts and corpus luteum cysts).[5]
ix. psoas abscess.

In order to discriminate the malignant and benign tumor, there should be a less complicated and less expensive diagnostic tool to increase the survival rate. According to Bouzari[6], more than 50% of ovarian cancer is identified at the old age which characterizes the survival rate to be only 30% in which 20% are localized to ovaries. In order to recommend such patients to gynecologic oncology centers, the risk of malignancy index (RMI) was developed by Jacobs et al in 1990. As compared to other diagnostic procedures, this method is less complicated and does not involve complex techniques, such as whole-body positron emission tomography, magnetic resonance imaging, and computed tomography scan).[7]

There are four versions of risk of malignancy index (RMI) being known:

I. RMI 1: it is the basic diagnostic model used to evaluate the patients with pelvic masses.

ii. RMI 1 was modified in 1996 by Tingulstad et al. who named it RMI 2 which was further adjusted in 1999, known as RMI 3. A number of clinical studies have already validated these versions of RMI, with a cut off value of 200 stating the best differentiation between malignant and benign tumors. [8]

iii. In 2009, Yamamoto developed the RMI 4 in which tumor size was included as an additional parameter.

In the current study, RMI 1 will be used to differentiate between benign and malignant adnexal masses in Pakistani women.

A retrospective study done in Pakistan revealed the specificity and sensitivity of the risk malignancy index (RMI), to distinguish malignant from benign tumors as 92.2% and 53.8%, respectively having a cut off value of 200[9]. Nevertheless, another research shows the sensitivity and specificity of RMI to be 100% and 96.3% at the same cut off level. Through our study we want to assess the exact diagnostic accuracy,sensitivity and specificity of risk of malignancy index (RMI) so that we can implement the results of our study in local population in future.

Methods

The current study was conducted using the cross sectional research design in clinical setting of the New Radiology Department Services Hospital (SIMS) Lahore. It took almost 6 months to carry out the study. Sample size of 165 cases was calculated with 95% confidence level, 11% margin of error for 53.8% sensitivity, 4.5% margin of error for 92.2% specificity of RMI in differentiating between malignant and benign adnexal masses by taking expected percentage of adnexal masses i.e., 33.5% 10and taking histopathology as gold standard. Non-probability consecutive technique was used for sampling. Females of age 25-70 years with adnexal masses on ultrasonography and admitted in gynecology ward for surgical exploration and histopathological diagnosis was included in the study. However, on TVS pelvic masses less than 5 cm in size were excluded as they are considered to be most probably functional cysts. Also, the pregnant women, and patients with ovarian malignancy, intraperitoneal metastasis, hepatic or lung metastasis were also excluded from the study.

The Institutional Ethical committee approved the study and written informed consent was taken from all the patients prior to perform the study. The Department of Obstetrics and Gynecology Services Hospital Lahore chose all the patients with adnexal masses. In order to have the data of ultrasound of all cases, transvaginalultrasound was performed with Toshiba Xario 7.5 MHz TVS probe with an abdominal scan if needed by expert consultant radiologist. Menopausal status and preoperative serum CA 125 levels was also noted. RMI was calculated for every patient. Risk of malignancy index (RMI) is the product of ultrasound score (U), menopausal status (M) and CA 125. Thus, the RMI was calculated using the following formula: RMI = U x M x CA125

Where,

(U)Ultrasound data score;

U= 0 (for ultrasound score of 0);

U = 1 (for ultrasound score of 1);

U = 3 (for ultrasound score of 25)

Ultrasound scans are scored one point score for each of the following characteristics:

1. Multilocular cyst.
2. Evidence of solid areas.
3. Evidence of intraabdominal metastases.
4. Presence of ascites.

(M) Menopausal status score;

Score 1 for premenopausal women

Score 3 for postmenopausal women

CA 125 levels 0 - ∞

RMI < 200 (benign) RMI ≥ 200 (malignant)

Specificity, sensitivity, positive predictive value, and negative predictive value were also calculated for RMI using its cut off value of 200 and histopathological result as gold standard. Demographic information and study variables were documented in a pre-designed proforma. In order to evaluate the results, statistical analyses were performed using the Statistical Packages for the Social Sciences Version 14.0.1. From this analysis, Receiver Operating Characteristic Curve (ROC) was obtained which discovered the relationship between specificity and sensitivity of the CA 125, the ultrasound score, menopausal status, and the RMI 1 to differentiate between malignant and benign masses. Quantitative data like age, RMI were presented in the form of mean ± SD. Qualitative data like adnexal masses (Benign/ Malignant) on RMI and on histopathology were presented in the form of frequency and percentages. Data was presented in the form of 2×2 contingency table to estimate specificity, sensitivity, NPV, PPV, and accuracy of RMI with histopathology as gold standard. To address the effect modifier, the data was stratified by age and menopausal status. Moreover, in order to check the significance, post

stratification chi square test was applied with p-value ≤ 0.05 as significant.

Results

In the current study, a total of 165 patients were enrolled. The mean age of the subjects was 48.78±12.63 years with maximum and minimum ages of 70 and 25 respectively. Furthermore, the premenopausal women were 80(48.48%) and the postmenopausal women were 85(51.52%) (Figure 1). The mean value of CA125 of the patients was 61.96±21.65 with maximum and minimum values of 100 and 25 respectively. The results of this study showed that the patients with ultrasound score=0 were 47(28.5%), the patients with ultrasound score=1 were 57(34.5%) patients and the patients with ultrasound score 2-5 were 61(37%). Also, the mean value of RMI of the patients was 198.48 ± 236.061 with minimum and maximum values of 0 and 864 respectively. In this study the RMI diagnosed malignancy in 61(37%) patients and benign type was diagnosed in 104(63%) patients **(Table-1).**The histopathology diagnosed malignancy in 64(38.79%) patients and benign type patients was diagnosed in 101(61.21%) **(Fig-2)**.

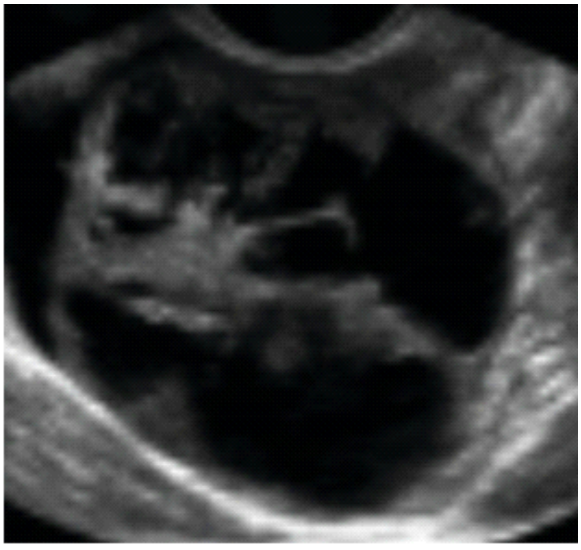

Fig-1: Mucinous ovariancystadenocarcinoma.

In our study the sensitivity of RMI was 89.06% with specificity of 96.04%, the PPV value was 93.44%, NPV value was 93.27% and the diagnostic accuracy was 93.33% taking histopathology as gold standard **(Table-2).**This study revealed t=another important result that that in up to 50 years patients, the sensitivity, specificity and diagnostic accuracy was 73.68%, 100% and 94.32% respectively. Similarly in above 50 years patients the sensitivity, specificity and diagnostic accuracy was 95.56%, 87.5% and 92.21% respectively **(Table-3).** The study results showed that in premenopausal patients, the sensitivity, specificity and diagnostic accuracy was 68.75%, 100% and 93.75% respectively. Similarly in postmenopausal patients the sensitivity, specificity and diagnostic accuracy was 95.83%, 89.89% and 92.94% respectively **(Table 4).**

Table-1: Frequency Distribution of RMI.

		Frequency	Percentage
RMI	Malignant	61	37.0
	Benign	104	63.0
	Total	165	100.0

Table-2: Frequency distribution of RMI with Histopathology.

		Histopathology		
		Maligant	Benign	Total
RMI	Malignant	57	04	61
	Benign	07	97	104
	Total	64	101	165

Sensitivity	*89.06%*
Specificity	*96.04%*
PPV	*93.27%*
NPV	*93.27%*
Diagnostic accuracy	*93.33%*

Table-3: Frequency distribution of RMI with histopathlogy stratified by age.

Age (in years	RMI	Histopathology		
		Maligant	Benign	Total
≤50	Malignant	14	0	14
	Benign	05	69	74
	Total	19	69	88
>50	Malignant	43	04	47
	Benign	02	28	30
	Total	45	32	77

Table-4: Frequency distribution of RMI with histopathlogy stratified by menopause.

Age (in years	RMI	Histopathology		
		Maligant	Benign	Total
≤50	Malignant	14	0	14
	Benign	05	69	74
	Total	19	69	88
>50	Malignant	43	04	47
	Benign	02	28	30
	Total	45	32	77

Discussion

The current cross sectional research was conducted at New Radiology department Services hospital (SIMS) Lahore in order to determine the diagnostic accuracy of risk of malignancy index (RMI) to distinguish between malignant and benign adnexal masses taking histopathology as gold standard. Mostly women are

referred to a gynecologist due to the presence of an adnexal mass. In such patients, the decisions regarding clinical management and surgical procedures solely depend upon the discrimination between the malignant and benign adnexal masses.[11] As the quality of lymph node dissection/surgical staging and cytoreductive surgery are crucial diagnostic factors in case of ovarian cancer, so the patients having malignant tumors are supposed to be referred to gynecological oncologist.[12]

In our study the sensitivity of RMI was 89.06% with specificity of 96.04%, the PPV value was 93.44%, NPV value was 93.27% and the diagnostic accuracy was 93.33% taking histopathology as gold standard. There are a number of studies already done whose results are in favor of our study. The result values of these studies correspond well with our values of sensitivity (72%) and specificity (87%). Few of them are discussed below:

A previous study conducted by Aslam[13] using MRI 2 showed the sensitivity to be 74% and specificity to be 89%. Similarly, Andersen[14] found out the sensitivity value 71% and specificity as 89%. Another similar study was conducted by Manjunath[15] whose sensitivity and specificity values were 76% and 82%, respectively. A study done in Pakistan found out the specificity and sensitivity of RMI to be 96.3% and 100% respectively.

RujutaJavdekar and Nandita Maitra[16] stated the fact that RMI is a cost effective, simple and reliable diagnostic tool with a sensitivity of 70.5% and specificity of 87.8%.

Conclusion

According to our study results, the RMI is a reliable tool with high sensitivity, specificity and diagnostic accuracy values to distinguish between malignant and benign adnexal masses taking histopathology as gold standard.

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