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Diagnostic Accuracy of Risk of Malignancy Index (RMI) in Pre-Operative Evaluation of Ovarian Masses

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Abstract

Ovarian masses are a frequent cause of gynaecological malignancy. The risk of the Malignancy Index (RMI) is widely studied for the prediction of malignant pelvic masses. The objective of this study was To determine the diagnostic accuracy of RMI in diagnosing ovarian masses preoperatively for malignancy keeping histopathology as the Gold standard.it was a Cross-sectional study conducted in Gynae and Obs unit 1 Fauji Foundation Hospital Rawalpindi. Duration of study was months after approval of synopsis, non-probability consecutive sampling was used approval obtained from ethical committee. A total of 87 expected patients of having ovarian masses reporting in outpatient (OPD) and were admitted in wards were enrolled for the study. Informed written consent was taken from all the patients. Ultrasonography (USG) and serum CA-125 levels of all the patients were done and scores were assigned to each parameter. The RMI was calculated for each patient. Histopathology was obtained and all the information was recorded on a predesigned Performa. RMI 25(28.7%) had positive and 62(71.3%) had negative findings. On histopathology findings, there were 25(28.7%) malignant and 62(71.3%) were benign masses. The sensitivity, specificity, PPV and NPV of RMI was 92%, 96.77%, 92% and 96.77% with a diagnostic accuracy of 95.4%. The likelihood ratio for positive and negative was 28.52 and 0.082 respectively. RMI is a highly sensitive (92%) and specific (96.77%) method to identify ovarian carcinomas.

Keywords: Ovarian masses, Primary evaluation, imagining, histopathology, Risk of Malignancy Index.

INTRODUCTION

Ovarian cancer is one of the leading malignancies of the female reproductive system. The discrimination between benign and malignant tumours is a critical step in clinical evaluation [1]. Due to the asymptomatic course of ovarian cancer 70 % of women are diagnosed in the advanced stage [2]. Quality of primary cytoreductive surgery is one of the most important factors for survival of the patient. Many women with advanced ovarian carcinoma undergo suboptimal surgery by a gynaecologist [3, 4]. Ovarian malignancy accounts for almost 25% of gynaecological cancers and 50% of deaths from cancers of the female genital tract. Up to 24% of ovarian tumours in premenopausal women are malignant and up to 60% are malignant in postmenopausal women. The preoperative diagnosis of whether a mass is malignant cannot always be made with current diagnostic modalities [5].

Diagnosis of pelvic masses including ovarian cancer by a variety of procedures remained inaccurate and uncertain, therefore, in 1990, Jacob *et al*., developed an indicator called risk of malignancy index [RMI] based on serum level of CA125, menopausal status and ultrasound findings. The RMI is a suitable index for evaluation of pelvic mass before surgery and previous studies indicate that RMI improves to differentiate between non-malignant and malignant pelvic masses. Various studies conclude the cut-off value of 200 for RMI is the best discrimination for benign and malignant pelvic mass because of its high sensitivity and specificity levels [6, 7].

The "risk of malignancy index" has been proved to recognize the probability of malignancy in ovarian mass, by incorporating serum CA-l25 levels, ultrasound morphology and menopausal status. RMI has quite good efficacy in diagnosing ovarian masses it

has been found to have a sensitivity of 91.3%, specificity of 76.9%, a positive predictive value of 87.5% and a negative predictive value of 83.3% [8].

The preoperative diagnosis of whether a mass is malignant or benign cannot always be made with current diagnostic modalities individually like ultrasound and serum levels. For this reason, an efficient, enhanced, specific and sensitive method for diagnosing ovarian cancers can be RMI. This simple scoring system can be applied directly in clinical practice. RMI is a scoring system including serum CA-125, morphological features of ovarian mass on ultrasonography and menopausal status. This is calculated by the formula.

RMI = M(menopausal status) x U(ultrasound features) x CAl25. The objective of this study is to determine the accuracy of the Risk of Malignancy Index (RMI) as a single most important parameter in diagnosing malignancy in women with ovarian masses, to refer them to more specialized centres for further management, moreover, it is more cost-effective as USG is available in primary care centers hence malignant masses can be differentiated from benign ones. RMI ≥ 200 was considered positive.

MATERIALS AND METHODS

It was a cross-sectional study carried out in Gynae and Obs unit 1, Fauji Foundation Hospital Rawalpindi started 6 months after approval of synopsis. Non-probability consecutive sampling method was used to collect the sample.

The sample size was calculated by using the WHO sample size calculator using.

Sensitivity = 91.3% d=8% Specificity = 76.9% d=10% ,Prevalence = 45% Confidence Interval=95% So the recommended sample size was 87 expected patients of ovarian masses. Women of the age range of 30 to 65 years and having any parity with expected ovarian masses visiting the department of Gynecology and Obstetrics were included in the study. Patients with postmenopausal bleeding and a positive family history of breast, endometrial or ovarian carcinoma and pregnant women were excluded from the study. The study was started by taking approval from the hospital ethical committee. A total of 87 expected patients of having ovarian masses reporting in outpatient (OPD) and were admitted in wards were enrolled for the study. All the patients which were briefly described the study purpose and informed written consent were taken from all the patients. Ultrasound and serum CA-125 levels of all the patients were done and scores were assigned to each parameter. The RMI was calculated for each patient using the equation of Jacob *et al.*,
RMI=M×U×Ca-125

With M=1 for premenopausal status and M=3 for postmenopausal status. Ultrasound scans were scored as one point for each of the following characteristics: multilocular cyst, evidence of solid areas, evidence of metastases, presence of ascites, bilateral lesions using the scoring system suggested by Jacob *et al.*, Simple mass (U=0) (for ultrasound score of 0); semi-complex mass (U=1) (for ultrasound score of 1); complex mass (U=3) (for ultrasound score of 2 or more). The absolute values of CA125 serum level were entered directly in the formula. Histopathology specimen sent to the hospital laboratory and verified by a histopathologist. Demographic information including age, parity, and menopausal status was recorded from all the patients. All the information taken from the patients were recorded on a predesigned Performa.

DATA ANALYSIS

The collected data was entered and analyzed by Statistical Package for Social Sciences (SPSS version 17). Mean and standard deviation was calculated for quantitative variables like age, parity, CA125 level and RMI. Frequency and percentages were calculated for qualitative variables like Menopausal status, RMI category and results based on histopathology. Sensitivity, specificity, positive predictive values and negative predictive values of RMI in diagnosing ovarian masses were calculated by taking histopathology as the gold standard and using the following 2x2 table with given formulae. The likelihood ratio was also be calculated. Effective modifiers like age and parity were controlled by stratification. Post stratified diagnostic accuracy was applied. P-value ≤ 0.05 was considered as considered.

RESULTS

The mean age of females was 42.35 ± 9.41 years with minimum age and maximum age of 30 and 65 years. There were 57(65.5%) patients aged 30-45 years and 30(34.5%) were 46-65 years of age. The mean parity in this study was 2.04 ± 1.83 with minimum and maximum as 0 and 6. A total of 70(80.5%) had parity < 4 and the rest of 17(19.5%) had parity 4-6. Pre-menopause females were 57(65.5%) and 30(34.5%) were menopause. The mean Ca-125 level was 239.80 ± 339.92 (S.D is higher due to the huge range of Ca-125). The mean USG score was 1.72 ± 1.18 while the mean RMI was 946.04 ± 1757.62 (S.D is higher due to the huge range of RMI). On RMI 25(28.7%) had positive and 62(71.3%) had negative findings. On histopathology findings, there were 25(28.7%) malignant and 62(71.3%) were benign masses Table-1.

A total of 23 patients had positive findings on MRI and were malignant on histopathology and 60 patients had negative findings on RMI and were benign on histopathology. Moreover, 2 patients were falsely positive and false negative each. The sensitivity,

specificity, PPV and NPV of RMI was 92%, 96.77%, 92% and 96.77% with a diagnostic accuracy of 95.4%. The likelihood ratio for positive and negative was 28.52 and 0.082 respectively.

Comparison of histopathology and RMI findings with respect to age groups

Table 1

			Histopathology		***Total***
			Malignant	***Benign***	
30-45	***RMI***	***Positive***	11	2	13
		Negative	1	43	44
46-65	***RMI***	***Positive***	12	0	12
		Negative	1	17	18

Age 30-45 years		Age 46-65 years	
Sensitivity	91.67%	Sensitivity	99.17%
Specificity	95.56%	Specificity	89.47%
Positive Predictive Value	84.62%	Positive Predictive Value	98.36%
Negative Predictive Value	97.73%	Negative Predictive Value	94.44%
Diagnostic Accuracy	94.74%	Diagnostic Accuracy	97.86%
Likelihood ratio of a + ve test	20.63	Likelihood ratio of a +ve Test	9.421
Likelihood ratio of a –ve test	0.08721	Likelihood ratio of a –ve Test	0.009237

DISCUSSION

This study was carried out to evaluate the diagnostic accuracy of RMI in diagnosing ovarian masses preoperatively for malignancy keeping histopathology as Gold standard and assess its strength for potentially being dependant on considering it an important diagnostic parameter. In our study, the mean age of females was 42.35 ± 9.41 years with minimum age and maximum age of 30 and 65 years. There were 57(65.5%) patients aged 30-45 years and 30(34.5%) were 46-65 years of age. The mean parity in this study was 2.04 ± 1.83 with minimum and maximum as 0 and 6. A total of 70(80.5%) had parity < 4 and the rest of 17(19.5%) had parity 4-6. Pre-menopause females were 57(65.5%) and 30(34.5%) were menopause. One study evaluated the ability of two malignancy risk indices (RMI 1 and Rh4I 2) incorporating menopausal status, serum CA125 level and ultrasound findings, to discriminate a benign from a malignant pelvic mass.

In this study 39 (42%) patients were 30-44 years, 26 (28%) were 45-54 years and 28 (30%) were >54 years in benign type whereas, 5 (17%) patients were 30-44 years, 8 (26%) were 45-54 years and 17 (57%) were >54 years in malignant type. There were 33 (65%) women in benign and 22 (29%) in malignant type who were postmenopausal [9].

Furthermore, they reported that the mean CA125 was 29.6 in benign and 354 in malignant ovarian masses. Also, there was 0 ultrasound score in 41 (44%) patients, 1 in 40 (43%) patients and 2-5 in 12 (13%) patients. They reported that the sensitivity and NPV values were greatest for the least CA125 cut-off value of 10 (98% and 99%) and specificity and PPV were greatest for the highest cut-off value of 120 (99% and 94%). The sensitivity and specificity for USG score 1 were 97 % and 44% and NPV and PPV were 37% and 98%. They compared RMI 1 vs 2 with slight variation in calculation and found that RMI 2 was significantly better than RMI 1 for all cut-off values ranging from 25-250. They concluded that RMI is a simple, easy and reliable method that could be very helpful in discriminating benign and malignant ovarian disease [9, 10].

In our study too, all these factors i.e. CA 125, USG and histopathological findings were quantified and compared in different strata like age and parity status. The overall findings approved the high diagnostic accuracy of RMI and its beneficial usage in distinguishing the status of ovarian masses in our community.

We found that the mean Ca-125 level was 239.80 ± 339.92 and the mean USG score was 1.72 ± 1.18. Also, the mean RMI was 946.04 ± 1757.62. On RMI 25(28.7%) had positive and 62(71.3%) had negative findings. On histopathology findings, there were 25(28.7%) malignant and 62(71.3%) were benign masses. A total of 23 patients had positive findings on MRI and were malignant on histopathology and 60 patients had negative findings on RMI and were benign on histopathology. Moreover, 2 patients were falsely positive and false negative each. The sensitivity, specificity, PPV and NPV of RMI was 92%, 96.77%, 92% and 96.77% with a diagnostic accuracy of 95.4%. The likelihood ratio for positive and negative was 28.52 and 0.082 respectively.

In one study age, ultrasound score, menopausal status, a clinical impression score and serum CA 125 level were assessed to see how they could best distinguish between patients with benign (n = 101) and malignant (n – 42) pelvic masses. Each criterion used alone provided statistically significant discrimination.

The most useful individual criteria were a serum CA 125 level of 30 U/ml (sensitivity 81 %, specificity 75%) and an ultrasound score of 2 (sensitivity 71%, specificity 83%). Three criteria could be combined in a risk of malignancy index (RMI) which is simply calculated using the product of the serum CA 125 level (U/ml), the ultrasound scan result (expressed as a score of 0, 1 or 3) and the menopausal status (1 if premenopausal and 3 if postmenopausal). This index was statistically virtually as effective a discriminant between cancer and benign lesions as more formal methods. Using an RMI cut-off level of 200, the sensitivity was 85% and the specificity was 97%. Patients with an RMT score of greater than 200 had, on average, 42 times the background risk of cancer and those with a lower value 0.15 times the background risk [11]. One study determined the effectiveness of the RMI algorithm for subsequent referral to a cancer center. A total of 182 patients with a pelvic mass were referred to the centre for surgery. A total of 24% of patients had benign tumours, 6% had tumours of borderline malignancy, and 70% had invasive tumours. A total of 145 cases had an RMI >200; 125 of these had ovarian or peritoneal cancers. An RMI >200 had a sensitivity of 88.5% for diagnosing invasive lesions. The overall sensitivity of this algorithm for diagnosing all borderline, invasive ovarian, or primary peritoneal lesions was 87.4%, and the positive predictive value was 86.8%. Their data confirmed the effectiveness of the RMI algorithm in clinical practice for the identification and subsequent referral to cancer centres of cases of potential ovarian malignancy on basis of which they recommended its usage in routine [12]. Yet another study compared three diagnostic procedures named RMI, Ultrasound and ROMA to see which one has better potential to identify ovarian cancer. Of the 374 analysed patients, 224 (59.9%) and 150 (40.1%) patients had a benign and malignant diseases, respectively. Patients with benign disease were younger (mean age = 46.2 [95% CI:44.1–48.3] versus 57.7 [95% CI:55.7–59.8] years; $P < 0.0001$). Of the patients with benign disease, 37.9% (95% CI:31.6–44.3) were postmenopausal, while 74.0% (95% CI:67.0–81.0) of the patients with malignant disease were postmenopausal ($P < 0.0001$). They reported that Subjective assessment (USG) scored the highest overall in terms of sensitivity for the whole study population as well as the postmenopausal and premenopausal populations (96.7%, 97.3%, and 94.9%). The RMI had the highest specificity for the whole study population and the postmenopausal population (92.4% and 87.1% and 95.7%). For the premenopausal population, all diagnostic tests had a high specificity but this was accompanied by a sensitivity below 70% for the RMI, and ROMA [13]. One study assessed the risk-of-malignancy index (a scoring system based on menopausal status, ultrasound features, and serum CA 125) at district hospitals for referral of women with suspected malignant pelvic masses for primary surgery at a central gynecologic oncology unit. In total, 365 women 30 years of age or older, admitted consecutively at the seven local hospitals, were enrolled in the study from February 1, 1995, to January 31, 1997. Compliance with their study was satisfactory; 84% (65 of 77) of women with risk-of-malignancy indices of at least 200 were referred for centralized primary surgery. Sensitivity and specificity to malignancy were 71% and 92%, respectively, which is in agreement with previous validation of the risk-of-malignancy index in teaching hospital settings. False negatives were due mainly to stage Ia (18 of 24) ovarian cancer, whereas 27 of 28 stages II-IV ovarian cancer cases were identified correctly [14]. We conclude that RMI is a highly sensitive (92%) and specific (96.77%) method to identify ovarian carcinomas. In future using RMI, we can make a proper diagnosis for referral to a gyne-oncologist that can facilitate the accurate staging of the disease and optimal cytoreductive treatment, enhancing patient survival.

REFERENCES

1. Mohammed, A. B. F., Ahuga, V. K., & Taha, M. (2014). Validation of the Risk of Malignancy Index in primary evaluation of ovarian masses. *Middle East Fertility Society Journal*, *19*(4), 324-328.
2. Rafii, A., Halabi, N. M., & Malek, J. A. (2012). High-prevalence and broad spectrum of Cell Adhesion and Extracellular Matrix gene pathway mutations in epithelial ovarian cancer. *Journal of clinical bioinformatics*, *2*(1), 1-5.
3. Arun-Muthuvel, V., & Jaya, V. (2014). Pre-operative evaluation of ovarian tumors by risk of malignancy index, CA125 and ultrasound. *Asian Pacific Journal of Cancer Prevention*, *15*(6), 2929-2932.
4. Jelovac, D., & Armstrong, D. K. (2011). Recent progress in the diagnosis and treatment of ovarian cancer. *CA: a cancer journal for clinicians*, *61*(3), 183-203.
5. Aktürk, E., Karaca, R. E., Alanbay, İ., Dede, M., Karaşahin, E., Yenen, M. C., & Başer, İ. (2011). Comparison of four malignancy risk indices in the detection of malignant ovarian masses. *Journal of gynecologic oncology*, *22*(3), 177-182.
6. van den Akker, P. A., Aalders, A. L., Snijders, M. P., Kluivers, K. B., Samlal, R. A., Vollebergh, J. H., & Massuger, L. F. (2010). Evaluation of the Risk of Malignancy Index in daily clinical management of adnexal masses. *Gynecologic oncology*, *116*(3), 384-388.
7. Bouzari, Z., Yazdani, S., Kelagar, Z. S., & Abbaszadeh, N. (2011). Risk of malignancy index as an evaluation of preoperative pelvic mass. *Caspian journal of internal medicine*, *2*(4), 331-335.
8. Irshad, F., Irshad, M., Naz, M., & Ikram, M. (2013). Accuracy of risk of malignancy index. In the preoperative diagnosis of Zovarian malignancy in postmenopausal women. *Rawal Medical Journal*, *38*(3), 266-270.

9. Morgante, G., La Marca, A., Ditto, A., & De Leo, V. (1999). Comparison of two malignancy risk indices based on serum CA125, ultrasound score and menopausal status in the diagnosis of ovarian masses. *BJOG: An International Journal of Obstetrics & Gynaecology*, *106*(6), 524-527.
10. Gillis, C., Hole, D., Still, R. M., Davis, J., & Kaye, S. B. (1991). Medical audit, cancer registration, and survival in ovarian cancer. *The Lancet*, *337*(8741), 611-612.
11. Jacobs, I., Oram, D., Fairbanks, J., Turner, J., Frost, C., & Grudzinskas, J. G. (1990). A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. *BJOG: An International Journal of Obstetrics & Gynaecology*, *97*(10), 922-929.
12. Bailey, J., Tailor, A., Naik, R., Lopes, A., Godfrey, K., Hatem, H. M., & Monaghan, J. (2006). Risk of malignancy index for referral of ovarian cancer cases to a tertiary center: does it identify the correct cases?. *International Journal of Gynecologic Cancer*, *16*(Suppl 1), 30-34.
13. Van Gorp, T., Veldman, J., Van Calster, B., Cadron, I., Leunen, K., Amant, F., ... & Vergote, I. (2012). Subjective assessment by ultrasound is superior to the risk of malignancy index (RMI) or the risk of ovarian malignancy algorithm (ROMA) in discriminating benign from malignant adnexal masses. *European Journal of Cancer*, *48*(11), 1649-1656.
14. Tingulstad, S., Hagen, B., Skjeldestad, F. E., Halvorsen, T., Nustad, K., & Onsrud, M. (1999). The risk-of-malignancy index to evaluate potential ovarian cancers in local hospitals. *Obstetrics & Gynecology*, *93*(3), 448-452.