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A DESCRIPTIVE STUDY TO FIND ROLE OF RISK OF MALIGNANCY INDEX 3 IN PREOPERATIVE EVALUATION OF OVARIAN TUMOURS.

Gynaecology

Premlata Mital Department of Obstetrics and Gynaecology S.M.S. Medical College & attached Hospitals Jaipur, 302015, Rajasthan, Jaipur

Nupur Hooja* Department of Obstetrics and Gynaecology S.M.S. Medical College & attached Hospitals Jaipur, 302015, Rajasthan, Jaipur *Corresponding Author

Sunita Singhal Department of Obstetrics and Gynaecology S.M.S. Medical College & attached Hospitals Jaipur, 302015, Rajasthan, Jaipur

Richa Ainani Department of Obstetrics and Gynaecology S.M.S. Medical College & attached Hospitals Jaipur, 302015, Rajasthan, Jaipur

ABSTRACT

Background: Preoperative discrimination between benign and malignant ovarian tumours is a great challenge for Gynaecologists. In present study risk of malignancy index 3 has been used to discriminate benign ovarian tumours from malignant ovarian tumours preoperatively.

Material& methods: 180 patients diagnosed to have ovarian tumour were included in the study after written informed consent. RMI 3 was calculated by using S.CA 125, ultrasonography and menopausal status and correlated with histopathological diagnosis.

Results: Sensitivity, specificity, PPV, NPV and diagnostic accuracy of RMI 3 were 58.3% (95%CI 40.8 – 74.5), 98.6% (95%CI 95.1 – 99.8), 91.3 (95%CI 72.1 – 97.7), 90.5% (95%CI 86.5 – 93.3) and 90.6% (95%CI 85.3 – 94.4) respectively.

Conclusion: RMI with a high specificity of 98.6% can be used in daily clinical practice to rule out malignancy preoperatively even in a set up where sophisticated radiological and biochemical test may not be available.

KEYWORDS

Ovarian tumours, malignancy, menopausal status, risk of malignancy score

Introduction

Prognosis of survival from malignancy depends on staging of disease at the time of diagnosis. A pelvic mass is one of the most frequent indications for referral to specialist gynecologists. Often these pelvic masses are malignant and require surgical management. After cervical and breast carcinoma, ovarian malignancy is third most common cancer in females1 and unfortunately it remains clinically silent until advance stage of disease leading to higher mortality rate2. Various novel methods and marker have been introduced in clinical practice to discriminate benign ovarian tumours from malignant ovarian tumours preoperatively. Unfortunately these are costly methods and none of these methods has shown significantly better performance in detecting malignant tumors. Jacob et al3 originally developed the Risk of malignancy index (RMI) to increase the preoperative prediction of ovarian malignancy. Tingulstad et al4 in 1996 introduced RMI 2 which was further refined to RMI 3 again in 19995. RMI 4 was formed by Yamamoto et al6 in 2009.

The present study is designed to evaluate the ability of RMI 3 to discriminate benign ovarian tumor from malignant ovarian tumor preoperatively and to compare the performance of the RMI 3 with USG score, S.CA 125 level at a cutoff of 35U/ml and menopausal score.

Material and methods

The present prospective, cross-sectional study was conducted in Department of Gynecology and Obstetrics, SMS Medical College, Jaipur. 180 patients diagnosed to have ovarian tumour were included in the study after written informed consent. Pregnant women, advanced cases of ovarian malignancies, secondary ovarian malignancies, women with unilateral ovary were excluded from study. A detail history and clinical examination was done for all patients. USG whole abdomen was done by ultrasound machine Prosound ALOKA ALFA 6 using abdominal (3.75MHz) and vaginal probes (7.5 MHz). On ultrasonographic examination, findings of ovary particularly multilocularity, solidity, bilaterality, ascites, and presence of metastasis were noted. Ultrasound scans were scored 1 point for each characteristics and a total was done. A USG score 1 was given for total score of 0 or 1 and 3 was given for a total score between 2-5. Serum CA 125 was assayed by MEIA (micro particle enzyme immunoassay) technique for quantitative measurement. The optimal cut off value of serum CA 125 was 35 U/ml. Postmenopausal status is defined as more than one year of amenorrhea or age older than 50 years in women who had a hysterectomy. Women who did not meet these criteria were classified as premenopausal. Premenopausal status was assigned M=1, and postmenopausal as M=3. With all these score RMI 3 was calculated by mathematical formulas.

RMI 3 = S. CA 125 x M x U where M is menopausal score, U is ultrasonography score and absolute value of S. CA 125.

RMI 3 value ≥200 was considered as high risk score.

All patients underwent laparotomy/staging laparotomy after PAC clearance. Surgically removed specimens were sent for histopathological examination. Prediction of risk of malignancy indices were correlated with histopathological diagnosis. Statistical analysis was done by standard statistical methods and a p value <0.05 was considered significant. Performance of RMI 3 was analyzed in the form of sensitivity, specificity, PPV, NPV and diagnostic accuracy. Performance of RMI 3 was compared with that of USG score, menopausal status and S.CA 125.

Results

The present study was performed on a total of 180 patients having ovarian tumours. Distribution of patients according to age, menopausal status, USG score and S.CA 125 levels were shown in table 1. 80.6% patients with malignant ovarian tumours were above 30 years in contrast to 55.6% patients with benign ovarian tumours. On univariate analysis the difference in the two groups was statistically significant (p-.006). Mean age of the patient was significantly higher for malignant tumours (43.59 ± 14.48) than for benign tumours (34.08 ± 13.48) p value .003. 41.7% women with malignant ovarian tumours were postmenopausal in contrast to 15.3% women with benign ovarian tumours. On univariate analysis the difference was statistically significant (p - .004. 80.6% patients with malignant ovarian tumours had a USG score between 2 to 5 in contrast to 6.3% with benign tumours and the difference was statistically significant (p .00). Serum levels of CA 125 was >35U/ml in 77.8% patients with malignant ovarian tumours as compared to 8.3% patients with benign ovarian tumours. The difference in the S. CA 125 levels was significantly difference (p .00). Mean serum CA 125 level was significantly more in patients with malignant ovarian tumours (p 0.0000).

Performance of RMI 3 is shown in table 2. In our study 36 patients had malignant ovarian tumours on histopathology, out of which 21were malignant by RMI 3 (true positive) and 15 had benign tumours by RMI

3 (false negative). Out of 144 patients with benign ovarian tumours on histopathology, 142 had benign ovarian tumour (true negative) and 2 had malignant tumour by RMI 3 (false positive).

Sensitivity, specificity, PPV, NPV and diagnostic accuracy of RMI 3 were 58.3% (95%CI 40.8 – 74.5), 98.6% (95%CI 95.1 – 99.8), 91.3 (95%CI 72.1 – 97.7), 90.5% (95%CI 86.5 – 93.3) and 90.6% (95%CI 85.3 – 94.4) respectively (Table 2).

In table 3 performance of RMI 3 is compared with individual parameters S.CA 125, USG score and menopausal status. Sensitivity of USG score and S CA 125 was better than RMI 3. Specificity and PPV of RMI 3 were highest.

Discussion

This study has addressed the performances of RMI 3 at a cut off value of 200 in preoperative evaluation of ovarian tumours. Disease prevalence was 20% in our study. Our results were consistent with the study of Yorito Yamamoto et al[7] 2015 where 25% patients had malignant disease and 75% had benign disease. The disease prevalence in our study was significantly lower than that of earlier reports of 30-54.8%.[3,8,9,10]

Mean age of the patients with malignant tumours (43.59 ± 14.48) was significantly higher than age of the patients with benign tumours (34.08 ± 13.48) p value .006. Our results were consistent with that observed by Tahereh Ashrafgangooei 201111, Dora et al 2017[8].

41.7% women with malignant ovarian tumours were postmenopausal in contrast to 15.3% women with benign ovarian tumours. On univariate analysis the difference was statistically significant (p - .004). Our results were similar to that observed by Radhamani and Akhila 2017.[12] 80.6% patients with malignant ovarian tumours had a USG score between 2 to 5 in contrast to 6.3% with benign tumours and the difference was statistically significant (p .00). Our results were in accordance with Watcharada Moolthiya et al 2009[13], Tahereh Ashrafgangooei et al 2011[11], Javdekar et al14 2015 and Dora et al 20178 who in their studies observed significant difference in the USG score between benign and malignant tumours.(p-value <0.000, 0.000, 0.0004 & 0.001 respectively) Mean serum CA 125 level was significantly more in patients with malignant ovarian tumours (p 0.0000). Our results were consistent with previous studies done by Watcharada Moolthiya et al 2009[13] , Tahereh Ashrafgangooei et al 201111, Javdekar et al14 2015 and Dora et al8 2017.

Sensitivity, specificity, PPV, NPV and diagnostic accuracy of RMI 3 were 58.3% (95%CI 40.8 – 74.5), 98.6% (95%CI 95.1 – 99.8), 91.3 (95%CI 72.1 – 97.7), 90.5% (95%CI 86.5 – 93.3) and 90.6% (95%CI 85.3 – 94.4) respectively. Sensitivity of RMI 3 in our study was lower and specificity was higher than that observed by Tingulstad et al 1996.4, Yamamoto et al 20096, Manjunath et al 2001[15], Andersen ES et al 2003[16], Obeidat et al 200417 , Ulusoy S et al 2007[18], Van Den Akker et al2011[19]. A.B.F. Mohammed et al.201420 observed that RMI 3 has a sensitivity, specificity, PPV, NPV and diagnostic accuracy as 80.7%, 93.1%, 70%, 96% & 91% respectively.

Dora et al 20178 in their study reported diagnostic accuracy, sensitivity, specificity, PPV,NPV of RMI at cut off point of 200 as 84.13%, 73.9%, 96.5%, 96.2% & 75.3% respectively.

Sensitivity, specificity, PPV, NPV and diagnostic accuracy of S CA 125 at cutoff of 35U/ml were 77.8%, 91.7%, 70%, 94.3% and 88.9% respectively. Our results were consistent with that of G.O.Abdulrahman Jr et al 201421, who in their study observed that at a cutoff of 35U/ml S.CA 125 had a sensitivity, specificity, PPV and NPV of 76%, 67%, 56% and 84% respectively.

Sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG score were 80.6%, 93.8%, 76.3%, 95.1% and 91.1% respectively. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of menopausal status were 41.7%, 84.7% 40.5%, 85.3% and 76.1% respectively. Jung-Woo Park et al 201222 observed sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG score as 94.7%, 62.2%, 39.5%, 97.8% and 68.9% respectively. They also observed sensitivity, specificity, PPV, NPV and diagnostic accuracy of menopausal status as 43.4%, 75.3%, 31.4%, 83.6% and 68.7% respectively. Javdekar et al 201514 observed sensitivity, specificity, PPV and NPV of CA 125 as 76.4%, 85.3%, 68.4% and 89.7% respectively. They also observed sensitivity, specificity, PPV, NPV and diagnostic accuracy of menopausal status as 41.1%, 58.5%, 29.1% and 70.5% respectively and sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG score of 76.4%, 75.6%, 56.5% and 88.5% respectively. Similar results were also observed by Veluswamy Arun-Muthuvel and Vijayaraghavan Jaya 201423. Specificity and PPV of RMI 3 was better than that of individual parameters. The risk-of-malignancy index 3 was better in discriminating benign ovarian tumours from malignant ovarian tumours than CA 125, USG and menopausal status individually. Use of RMI 3 in daily clinical practice by gynaecologists will help to choose appropriate surgical approach.

Conclusion

The Risk of malignancy index incorporates serum CA 125 levels, ultrasonographic score and menopausal status to discriminate between benign and malignant ovarian tumour preoperatively. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of RMI 3 were 58.3% (95%CI 40.8 – 74.5), 98.6% (95%CI 95.1 – 99.8), 91.3 (95%CI 72.1 – 97.7), 90.5% (95%CI 86.5 – 93.3) and 90.6% (95%CI 85.3 – 94.4) respectively. RMI with a high specificity of 98.6% can be used in daily clinical practice to rule out malignancy preoperatively even in a set up where sophisticated radiological and biochemical test may not be available.

Conflict of interest: "The author(s) declare(s) that there is no conflict of interest regarding the publication of this article."

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Ethical guidelines: All ethical guidelines were followed and all work was conducted in accordance with the Declaration of Helsinki (1964).

Table 1: Distribution of patients according to age, menopausal status, USG score and S.CA125 levels.

Variables	Benign (n = 144)		Malignant (n = 36)		p value
	No.	%	No.	%	
Age (years)					
<30	64	44.4	7	19.4	0.006
>30	80	55.6	29	80.6	Significant
Menopausal status					
Premenopausal	122	84.7	21	58.3	0.0004
Postmenopausal	22	15.3	15	41.7	Significant
USG Score					
1	135	93.7	7	19.4	0.00
4	9	6.3	29	80.6	Significant
S.CA 125(U/ml)					
<35	132	91.7	8	22.2	0.00
>35	12	8.3	28	77.8	Significant

Table 2: Performance of RMI 3

RMI 3	Benign (n = 144)		Malignant (n = 36)		Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
	No.	%	No.	%					
<200	142	97.9	15	44.4	58.3	98.6	91.3	90.5	90.6
>200	2	2.1	21	55.6	40.8-74.5	95.1-99.8	72.1-97.7	85.3-94.4	85.3-94.4

Table 3: Comparison of performance of CA 125, USG score, menopausal status with RMI 3

Variables	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
S.CA 125 (U/ml)	77.8	91.7	70	94.3	88.9
USG Score	80.6	93.8	76.3	95.1	91.1
Menopausal status	41.7	84.7	40.5	85.3	76.1
RMI 3	58.3	98.6	91.3	90.5	90.6

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