International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Chandni et al. Int J Reprod Contracept Obstet Gynecol. 2024 Apr;13(4):1008-1012
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20240804

Original Research Article

Risk of malignancy index 4 for differentiating benign from malignant ovarian tumor

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Received: 25 February 2024
Accepted: 19 March 2024

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ABSTRACT

Background: Approximately 22% of gynaecologic cancers are of ovarian origin, but 47% of all gynaecologic cancer deaths occur in women who have ovarian cancer. Ovarian cancer is usually diagnosed at an advanced stage because most of the symptoms are nonspecific, hence, the difficulty in diagnosis at early stages. In general, there is no effective screening test for ovarian cancer. Aim was to evaluate the ability of risk of malignancy index 4 (ROMI 4) to differentiate benign from malignant ovarian tumors.
Methods: A prospective observational study was conducted in April 2019 to march 2020.
Results: In the present study the ROMI 4 score at cut-off ≥ 450 had sensitivity, specificity, PPV and NPV of 74.3%, 65.3%, 42.6% and 88% respectively for malignant ovarian tumor.
Conclusions: Preoperative ROMI 4 score ≥450 will lead to rational basis for further referral to higher centre or gynaecology oncologist timely for appropriate surgical intervention/ management.

Keywords: Ovarian cancer, ROMI 4, CA125, RMI, Adnexal mass, Benign, Malignant

INTRODUCTION

Worldwide ovarian malignancy is third most common cause of cancer of the female genital tract.[1] In the United States ovarian cancer is the seventh most common cancer, accounting for 3% of all malignancies, 6 % of deaths from cancer in women, almost one third of invasive malignancies of the female genital organs and fifth most common cause of death from cancer in women. A woman's risk at birth of having ovarian cancer at some point in her lifetime is 1% to 1.5% and that of dying from ovarian cancer is almost 0.5%.[2] In India annual percentage of increase in age standardized incidence rates ranged from 0.7-2.4%.[3] Ovarian cancers contribute 19.8% to total case of cancer in India.[4] Approximately 22% of gynecologic cancers are of ovarian origin, but 47% of all gynecologic cancer deaths occur in women who have ovarian cancer.[5-6] Parity is inversely related to the risk of ovarian cancer, having at least one child is protective for the disease, with a risk reduction of 0.3 to 0.4.[7] Whereas in the cases diagnosed at an early stage, the 5-year survival rate is about 90%.[8] Ovarian tumors commonly present with bizarre and atypical presentation like vague pain abdomen, menstrual complaints, abdominal distension and gastrointestinal symptoms etc. Adnexal mass may present as an impalpable asymptomatic incidental finding or even a large mass extended from pelvis to abdominal cavity. Accurate and timely diagnosis is a challenge.

Physical examination has sensitivity and specificity of 45% and 90%, respectively.[9] Ultrasonography has sensitivity and specificity of 62% and 73% respectively for diagnosis of ovarian malignancy.[11] Serum CA 125 testing in routine is problematic as CA 125 levels may be elevated by a number of other malignancies and benign conditions, including endometriosis, uterine leiomyoma, benign

adnexal masses, tubal inflammation or infection, liver disease or hepatitis, congestive heart failure, menses, and pregnancy. Elevation of serum CA 125 concentration at cut off level of 35 U/ml, the sensitivity and specificity were 60% and 66.6% respectively.[10]

In 1990, Jacobs introduced the risk of Malignancy Index (RMI) based on logistic regression analysis.[11] RMI was revised 3 times RMI 1-RMI 4. Tingulstad et al developed modified RMI in 1996 (RMI 2) and 1999 (RMI 3), with differences mainly in scorings of ultrasound findings and menopausal status.[12-13] RMI has been developed to improve diagnostic accuracy for ovarian malignancy. Yamamoto et al in 2009 developed RMI 4 by including tumor size as additional parameter.[14]

METHODS

A prospective observational study was conducted in department of obstetrics and gynaecology, Dr. Rajendra Prasad government medical college and hospital, Kangra at Tanda, Himachal Pradesh during the period of one year (April-2019 to March-2020).

Inclusion criteria

Patient admitted to Dr. RPGMC with adnexal masses suspected to be ovarian tumor for surgical management with age >18 years were included.

Exclusion criteria

Patient not giving consent for study, age <18 years, previous treatment for ovarian cancer, cases that was inoperable, either who was poor surgical candidate or anaesthesia risk, patient who had advanced ovarian malignancy/secondary ovarian malignancy were excluded.

Methodology

All the women fulfilling inclusion criteria were undergone trans-abdominal ultrasound scan. Ultrasonography score was assigned using following features which is suggestive of malignancy: Multilocularity, solidity, bilaterality, associated ascites and presence of metastasis. One point was given to each criterion. So ultrasonographic score was assigned as follows: U=1, if 0 or 1 criteria fulfilled and U=4, if ≥2 criteria fulfilled. Size of ovarian tumor was measured and score=1, if size of tumor <7 cm and score=2, if size of tumor ≥ 7 cm. M=1, for pre-menopausal woman, M=4, for post-menopausal woman. ROMI 4 was calculated for all women undergone the study as follows: -ROMI 4=U×M×S×CA 125. Cut-off value of ROMI 4 was taken as 450. After that exploratory laparotomy proceed surgical staging and appropriate surgical procedure was done. The tissue specimen was sent for histopathological examination. HPE diagnosis was considered as gold standard. The data was collected, tabulated and analyzed for various parameters. Data was entered and statistically analyzed using the statistical package for social sciences (SPSS), version 21. Quantitative data was described as mean and standard deviation. Qualitative data was described as numbers and percentages. P≤0.05 was considered to be statistically significant. The sensitivity, specificity, diagnostic accuracy, positive and negative predictive values of the ROMI 4 and its individual parameters was calculated. To calculate sample size, data of previous similar studies was taken into consideration. The χ-test was used for determination of differences in distribution of age, menopausal status, tumor size, and ultrasound score. ROMI 4 was co-related with histopathological report.

RESULTS

In the present study more than half of women with benign ovarian tumor (55.4%) as well as malignant ovarian tumor (51.4%) were between 31 to 50 years. However, in younger age group below 30 years benign ovarian tumor were more than malignant ovarian tumor (20.7% vs 14.2%) and in older women >50 years malignant ovarian tumors were more common than benign ovarian tumor (34% vs 23.7%). It was observed that benign ovarian tumor was more prevalent in reproductive age group whereas malignant ovarian tumor was more prevalent among peri-menopausal and post-menopausal age group (p<0.0001). Serum CA 125 level had statistically significant correlation with malignant ovarian tumor and value <35 IU/ml was observed in women with benign ovarian tumor and >200 IU/ml in malignant ovarian tumor. In the present study among malignant cases 40% ovarian masses on USG were bilateral whereas only 15.8% benign cases had bilateral masses. This difference was statistically significant (p<0.003). Among malignant cases 77.1% were multilocular and in benign cases 61.3% were multilocular. In malignant cases 22.8% were solid where as in benign cases only 8.9% were solid. Ascites was present in 42.80% of malignant ovarian tumors whereas only 2.9% of benign ovarian tumor had ascites and the difference was statistically highly significant (p<0.0001). Metastasis was seen in 11.4% malignant ovarian tumor. Bilaterality, solidity, presence of ascites and metastasis on USG favors malignant ovarian tumor had statistically significant correlation. Whereas USG score 4 was observed more in malignancy (77.1%) as compared to benign (19.8%). This difference of USG score between benign and malignant ovarian tumor was found to be highly significant (p<0.0001). In present study there was no significant difference in the size of ovarian tumor of <7 cm and ≥7 cm on USG between benign and malignant ovarian tumor. In the present study higher ROMI score ≥450 correlated significantly with malignant pathology and <450 was associated with benign ovarian tumor.

In the present study the ROMI 4 score at cut-off ≥ 450 had sensitivity, specificity, PPV and NPV of 74.3%, 65.3%, 42.6% and 88% respectively for malignant ovarian tumor. Further positive likelihood ratio was observed 2.14 and negative likelihood ratio was 0.39. Diagnostic accuracy of ROMI 4 score was 67.64% in our study.

Table 1: USG features, (n=136).

USG	Benign, (n=101)		Malignant, (n=35)		P value
	N	%	N	%	
Unilateral/bilateral					
Unilateral	85	84.1	21	60	0.003
Bilateral	16	15.8	14	40	
Unilocular/ multilocular					
Unilocular	39	38.6	08	22.8	0.091
Multilocular	62	61.3	27	77.1	
Solid/ cystic					
Solid	09	08.9	08	22.8	0.032
Cystic	92	91.1	27	77.1	
Ascites					
Present	03	02.9	15	42.8	<0.0001
Absent	98	97.1	20	57.1	
Metastasis					
Present	00	00	04	11.4	0.001
Absent	101	100	31	88.6	

Table 2: Distribution of case according to ROMI 4 score (U×M×S ×CA 125), (n=136).

ROMI 4	Benign, (n=101)		Malignant, (n=35)		P value
	N	%	N	%	
USG score					
1	81	80.1	08	22.8	<0.0001
4	20	19.8	27	77.1	
Menopausal status*					
Pre-menopausal	69	68.3	12	34.3	<0.0001
Post-menopausal	32	31.6	23	65.7	
CA 125 value					
<35 IU/mL	53	52.4	08	22.8	0.002
35-200 IU/mL	38	37.6	15	42.8	0.584
>200 IU/mL	10	9.9	12	34.2	0.001
Tumor size**					
<7 cm	20	19.8	10	28.6	0.281
≥7 cm	81	80.1	25	71.4	
ROMI 4					
<450	78	77.2	07	20	<0.0001
≥450	23	22.7	28	80	

*Pre-menopausal: multiply by 1, post-menopausal: multiply by 4, ** tumor size <7 cm: multiply by 1, tumor size ≥7 cm: multiply by.

DISCUSSION

In the present study mean age of women with benign ovarian tumor was 42.89 years. Similarly in the studies by Campos et al and Yamamoto et al mean age of women with benign ovarian tumor was 45.9 years and 43.6±15.4 years respectively, which is comparable to our study. The mean age of women with malignant ovarian tumor in our study was 45.71 years, which was comparable to study done by Singhal et al (44.1%) and Ali et al (43.4%).[21] In the present study 68.3 % patients with benign ovarian tumor were pre-menopausal which is comparable to similar studies conducted by Campos et al and Yamamoto et al where 61% and 74.8% respectively women with benign ovarian tumor was premenopausal. In the present study 34.3% of patients with malignant ovarian tumor were pre-menopausal which is comparable to the studies conducted by Campos et al and Yamamoto et al in which 40% and 36.5% respectively of the women with malignant ovarian tumor were premenopausal. In our study 65.7% women with malignant ovarian tumor were post-menopausal. Similarly in the studies conducted by Campos et al and Yamamoto et al 60% and 63.5% of patients with malignant ovarian tumor were postmenopausal. In our study 65.7% women with malignant ovarian tumor were post-menopausal. Similarly in the studies conducted by Campos et al and Yamamoto et al 60% and 63.5% of patients with malignant ovarian tumor were postmenopausal.[19,20]

Table 3: Performance of ROMI 4.

Variables	Park et al, (n=547)[15]	Yamamoto et al, (n=296)[16]	Campos et al, (n=158)[17]	Ali et al, (n=91)[18]	Singhal et al, (n=200)[1]	Present study, (n=136)
Sensitivity (95% CI)	75.2	77	75	75	67.5	74.3
Specificity (95% CI)	87.5	92.3	82	97.3	98.7	65.3
PPV (95% CI)	61.2	77	-	85.7	93.1	42.6
NPV (95% CI)	93.1	92.3	-	94.8	92.4	88
PLR (95% CI)	6.02	10.0	4.29	28.12	54	2.14
NLR (95% CI)	0.28	0.25	0.3	0.26	0.33	0.39
Diagnostic accuracy (95% CI)	85	-	81	93.4	92.5	67.64

Table 4: ROMI 4 score.

Variables	Benign (%)		Malignant (%)	
	<450	**≥450**	**<450**	**≥450**
Campos et al, (2016) (n=136)[17]	82	18	23	77
Ali et al, (2018) (n=91)[18]	94.8	5.2	14.3	85.7
Singhal et al, (2018) (n=200)[1]	98.8	1.2	32.5	67.5
Present study, (n=136)	77.2	22.7	20	80

Limitation

Fallacy of our study is less number of malignant ovarian tumors and presence of more number of cases of benign ovarian tumor. The study has more number of women in reproductive age group. Duration of study was only 1 year. ROMI need improvement for better detection of mucinous carcinoma and germ cell tumors.

Strength of the study

Good number of women with benign ovarian tumor. We have concluded which features have statistically significant importance to discriminate between malignant ovarian tumor and benign ovarian tumor.

CONCLUSION

ROMI 4 is reliable, cost effective, non-invasive, easily accessible and applicable, good multivariate scoring system for differentiating between benign and malignant ovarian tumor from suspected adnexal masses. But presence of endometrioma could be the confounding factor. Preoperative ROMI 4 score ≥450 will lead to rational basis for further referral to higher centre or gynaecology oncologist timely for appropriate surgical intervention/ management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Singhal S, Rajoria L, Mital P, Batar A, Ainani R, Agarwal M, et al. Risk of malignancy index 4 in preoperative evaluation of patients with ovarian tumours. Int J Rep Contracept Obstet and Gynecol. 2018;7(6):2467-71.
2. Berek JS, Berek and Novak's Gynecology in chapter 39, ovarian, fallopian tube, and peritoneal cancer, 16th edition, New Delhi, Wolter Kluwer. 2020;1078.
3. Murthy NS Shalini S, Suman G, Srekantaiah P, Aleyamma M. A changing trends in incidence of ovarian cancer-the Indian scenario. Asian Pac J Cancer Prev. 2009;10(6):1025-30.
4. Takiar R, Nadayil D, Nandkumar A. Projections of cancer cases in India (2010-2030) by cancer groups, Asian Pacific J Cancer Prev. 2011;21(4);1045-104.
5. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65(1):5.
6. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011. CA Cancer J Clin. 2011;61(4):212-36.
7. Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Williams Gyneacology, United States, in chapter 35, epithelial ovarian cancer. 3rd edition. Mac Graw hill. 2016;762-3.
8. Ertas S, Vural F, Tufekci EC, Ertas AC, Kose G. Predictive value of malignancy risk indices for ovarian masses in premenopausal and postmenopausal women. Asian Pac J Cancer Prev. 2016;17(4):2177-83.
9. Karimi-Zarchi M, Mojaver SP, Rouhi M, Hekmatimoghaddam SH, Moghaddam RN, Yazdian-Anari P, et al. Diagnostic value of the risk of malignancy index (RMI) for detection of pelvic malignancies compared with pathology. Electronic Physician. 2015;7(7):1505.
10. Shintre SA, Survase RM, Patil NA, Sayyed RL. Effectiveness of risk of malignancy index to

differentiate benign from malignant ovarian masses-a cross sectional study. Int J of Health Sci Res. 2017;7(5):52-9.
11. Oram JI, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol. 1990;97:922.
12. Jacobs IJ, Skates S, Davies AP, Woolas RP, Jeyerajah A, Weidemann P, et al. Risk of diagnosis of ovarian cancer after raised serum CA 125 concentration: a prospective cohort study. BMJ. 1996;313(7069):1355-8.
13. Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomised controlled trial. The Lancet. 1999;353(9160):1207-10.
14. Yamamoto Y, Yamada R, Oguri H, Maeda N, Fukaya T. Comparison of four malignancy risk indices in the preoperative evaluation of patients with pelvic masses. Eur J Obstet Gynecol Reprod Biol. 2009;144(2):163-7.
15. Park JW, Park JH, Song ES, Lee BI, Lee JH, Kim KW, et al. Four risk of malignancy indices in evaluation of pelvic masses. Korean J Obst Gynecol. 2012;55(9):636-43.
16. Yamamoto Y, Tsuchida A, Ushiwaka T, Nagai R, Matsumoto M, Komatsu J, et al. Comparison of 4 risk-of-malignancy indexes in the preoperative evaluation of patients with pelvic masses: a prospective study. Clin Ovarian Cancer Other Gynecol Malig. 2014;7(1-2):8-12.
17. Campos C, Sarian LO, Jales RM, Hartman C, Araújo KG, Pitta D, et al. Performance of the risk of malignancy index for discriminating malignant tumors in women with adnexal masses. J Med Ultrasound. 2016;35(1):143-52.
18. Ali MN, Habib D, Hassanien AI, Abbas AM, Makarem MH. Preoperative evaluation of patients with ovarian masses using the risk of malignancy index 4 model. Proc Obstet Gynecol. 2018;8(1):29.

Cite this article as: Chandni, Bind NK. Risk of malignancy index 4 for differentiating benign from malignant ovarian tumor. Int J Reprod Contracept Obstet Gynecol 2024;13:1008-12.