Risk of Malignancy Index-3 and Histopathological Diagnosis of Ovarian Mass

Benju Pandit, Gehanath Baral

Paropakar Maternity and Women's Hospital, Kathmandu.

ABSTRACT

Aims: To find out the accuracy of Risk of Malignancy Index (RMI-3) to predict ovarian malignancy pre-operatively.

Methods: Intention to treat cross sectional study at Paropakar Maternity and Women's Hospital in Kathmandu in 2018-2019. Cases with ovarian mass were taken pre-operatively with serum tumor marker (CA-125) and ultrasound report, and histopathology report post-operatively. Pregnancy and diagnosed malignancy were excluded. Sensitivity, specificity, positive and negative predictive values of RMI-3 were calculated at different cut-off values using Receiver operator characteristics (ROC) curve.

Results: 36 cases of ovarian tumor from 15 to 60 years (mean=35) were studied. There were 31(86.1%) premenopausal and 5 (13.9%) in menopausal state; 26 (72.2%) were married and 10 (27.8%) unmarried; 19 (52.8%) were multiparous, 9 (25%) were nulliparous and 8 (22.2%) uniparous; 34 (94.4%) presented with pain in lower abdomen; 16 (44.4%) had lump in lower abdomen; 8 (22.2%) had bloody vaginal discharge. Eight out of 36 (22.2%) had malignant histopathology. Taking histopathology to diagnose ovarian malignant tumor RMI 3 score >200 has sensitivity, specificity, positive and negative predictive value of 75%, 92%, 75%, 92% respectively. Taking the cut off value of RMI 3 at >190.5, AUC is 0.906 for ovarian malignant tumor the sensitivity, specificity, positive and negative predictive values were 75%, 93%, 55% and 96% respectively.

Conclusions: Risk of Malignancy Index RMI-3 value of 190 or more is the best predictive cut-off to predict ovarian malignancy pre-operatively.

Keywords: Cut-off value; ovarian cancer; RMI-3

INTRODUCTION

Internationally, ovarian cancer is the 7th leading cancer diagnosis and 8th leading cause of cancer mortality among women.[1] It is often called the "silent killer" because the disease is not often detected until it reaches advanced stage due to anatomical location of ovaries and lack of screening tools.[2] Ovarian cancer is associated with an overall mortality of 75%, but can be cured in up to 90% of cases if diagnosed while still limited to the ovaries. So we need a reliable tool for timely diagnosis and suitable intervention.[3-4] Jacobs et all originally developed Risk Of Malignancy Index (R.M.I) which is simply calculated using the product of the ultrasound scan (U), the menopausal status (M) and serum CA-125 level (U/ml).[5] Gradually the subsequent versions of RMI were developed as RMI-2 in 1996,[6] RMI-3in 1999,[7] RMI-4 in 2009[8] and RMI-

5 in 2016.[9-10] This study was undertaken to determine the accuracy of risk of malignancy index (RMI) in pre-operative diagnosis of ovarian malignancy.

METHODS

It was intention to treat cross sectional study of subsequent 36 cases that underwent surgery for ovarian mass at Paropakar Maternity and Women's Hospital in Kathmandu from September 2018 to August 2019. Sample size was calculated by estimation of proportion at the study site taking 10.3% as its prevalence[11], maximum tolerable error of 10%. The sample size was 36. Research tools used are RMI calculation table and data collection forms [Table-1]. All patients attending at Gynecological clinic with adnexal mass and posted for scheduled surgery were taken; tumor marker CA 125, ultrasonography

CORRESPONDENCE

Dr Benju Pandit
Paropakar Maternity and Women's Hospital, Thapathali,
Kathmandu
Email: mebenzu@gmail.com; Mobile: +977-9840098660

reports recorded. Histopathology report collected from pathology lab after surgery. The cases with proven malignancy but were lacking either USG or CA-125 report or adnexal mass in pregnancy were excluded. Written informed consent was taken after IRC approval. There was no additional financial cost to the patient as the whole management process is a routine practice at the study site. MS Excel was used to generate descriptive value and charts, and SPSS 19 for inferential analysis. Sensitivity, specificity, accuracy, positive and negative predictive values of RMI-3 was calculated at different cut-off values. Optimal cut-off value for RMI-3 was determined by analyzing the greatest point of accuracy in the Receiver operator characteristics (ROC) curve.

Table-1: Details of Risk of Malignant Index-3[7]

RMI 3 [1999] = U x M x CA125	Ultrasound score (U)		Menopausal Status (M)	
	Characteristics	Score	Characteristics	Score
	≤1 features presen	1	Premenopausal	1
	≥ 2 features present	3	Postmenopausal	3
Cancer Antigen-125 (CA-125) in U/ml. Ultrasound findings (U) were scored with one point for each of the following: Multi-locular cyst, evidence of solid areas, evidence of metastases, presence of ascites, bilateral lesions			Post-menopausal status: if the woman had more than one year of amenorrhea or was over 50 years of age if she had undergone hysterectomy.	
Interpretation: Minimum score of ≥ 200: cut-off for malignancy				

RESULTS

Out of 36 cases of ovarian mass, 29 cases (80.5%) fell between the age of 20 and 50; 11.1%, 33.3%, 27.8%, 19.4% and 8.3% respectively in each age group. The mean age was 35 years with minimum 15 years and maximum 60 years. Age group of 40-60 years had higher proportion of malignant condition than the younger age group and there is increasing proportion of malignancy by increased in age [Figure-1].
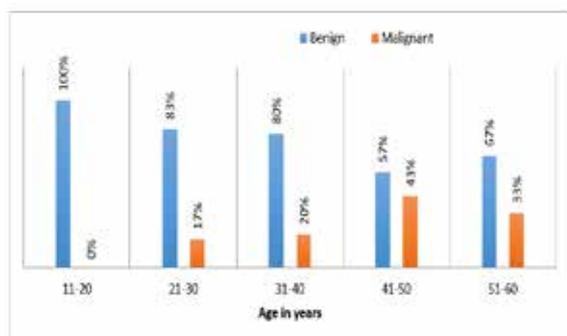

Figure-1: Distribution of ovarian mass according to age group [N=36]

Outof total 36 cases of ovarian mass 31 (86.1%) were premenopausal and 5 (13.9%) were in menopausal state; 26 (72.2%) cases were married and 10 (27.8%) cases were in unmarried. None of the cases were smoker and one each has used OCP and used to consume alcohol; 19 (52.8%) were multiparous, 9 (25%) nulliparous and 8 (22.2%) uniparous.

Lower abdominal pain, abdominopelvic lump and irregular menstrual cycles were the common presentations [Table-2].

Table-2: Clinical presentation of ovarian mass [n=36]

Presentation	Frequency	%
Pain in lower abdomen	34	94.4%
Normal uterine size	30	83.3%
Irregular menstrual cycle	26	72%
Vaginally palpable adnexal mass	25	69.4%
Lump in lower abdomen	16	44.4%
Palpable abdominal mass	16	44.4%
Bloody vaginal discharge	8	22.2%
Primary infertility	2	5.5%

Outof total 36 cases of ovarian mass 8 (22.2%) were malignant and other common histopathological findings were endometriotic cysts, teratoma and mucinous cystadenomas [Table-3].

Table-3: Histopathology of ovarian mass (n=36)

Histopathology	Number	Percentage
Endometriotic cyst	9	25%
Mature cystic teratoma	8	22.2%
Mucinous cyst adenoma	6	16.7%
Cystadenocarcinoma	5	13.9%
Cystic follicle	2	5.5%
Adenocarcinoma	1	2.8%
Benign mucinous cystadenoma + Brenners	1	2.8%
Dysgerminoma	1	2.8%
Granulosa cell tumor	1	2.8%
Mucinous Borderline	1	2.8%
Ovarian Fibroma	1	2.8%

By ultrasound findings there were 15 cases (41.7%) of unilocular cysts, 12 (33.3%) multilocular cysts, 5 (13.9%) unilocular solid cysts, 2 (3.3%) multilocular solid cysts and 2 (3.3%) solid tumor.

Taking histopathology to diagnose ovarian malignant tumor RMI 3 score >200 hassensitivity,specificity,positivepredictivevalueand negative predictive value of 75%, 92%, 75%, 92%respectively [Table-6].

Area under curve (AUC) is 0.906, so RMI 3 SCORE is a good test to identify ovarian malignant tumors. So taking the cut off value of RMI 3 score of >190.5 for ovarian malignant tumor in this study sensitivity, specificity, positive predictive value and negative predictive value were 75%, 93%, 55% and 96% respectively [Figure-2].
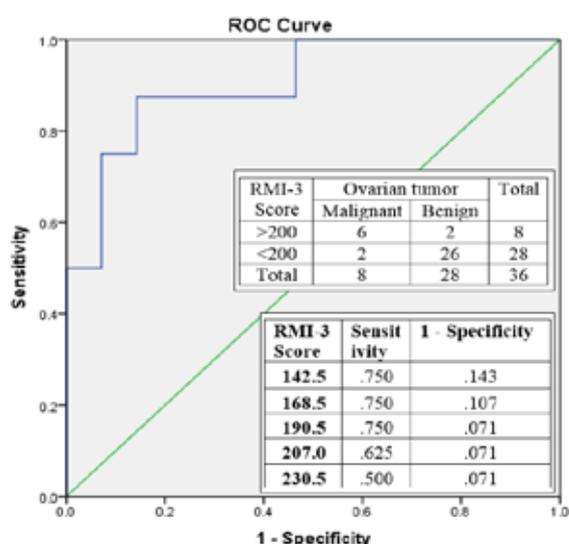

Figure-2: Relationship of OvarianTumor and RMI 3 Score

DISCUSSION

This study and other studies for ovarian tumors shows that 72-96% are benign and 4-30% are malignant.[12] So benign ovarian tumors are more common compared to malignant tumors.[12-15]

The mean age was 34 years for benign and 39 years for malignant tumors in this study. Higher proportion of cases in 40-50 years age group was malignant in nature.[12,13] Incidence of malignant ovarian tumors are higher in peri and postmenopausal women.[14,16] Parity has protective role for occurrence of ovarian carcinoma in postmenopausal women but this protective effect wanes with age.[15] OCP has protective role in development of ovarian cancer but alcohol and smoking do not increase risk of ovarian cancer.[17] The highest positive likelihood ratios were found for presence of abdominal mass; abdominal distension or increased girth; abdominal or pelvic pain; abdominal or pelvic bloating and loss of appetite.[18] Bimanual pelvic examination lacks accuracy as a screening test for ovarian cancer and as a way to distinguish benign from malignant lesions.[17]

Several studies showed higher frequency of epithelial tumor followed by germ cells but in this study the epithelial types are less than half. It may be due to small sample size.[12,18] Most of ovarian masses are cystic in nature as compared to solid and complex.[19]

The sensitivity, specificity, and the NPV of the diagnostic of RMI-3 were 83.3%, 88.46%, 94.52%, respectively using an RMI cut-off level of 200.[20] The best performance obtained for RMI-3 was at the cut-off point 236 with a sensitivity of 72.5%, a specificity of 98.2%, a PPV of 98.1%, NPV of 74.7%.[21] In various studies done in R.M.I -3 cut off level of 200 showed similar sensitivity specificity, PPV and NPV.[22-24] In our study done in PMWH taking histopathology to diagnose ovarian malignant tumor RMI 3 score >200 has sensitivity, specificity, positive predictive value and negative predictive value of 75%, 92%, 75%, 92% respectively. Area under curve (AUC) is 0.906, so RMI 3 SCORE is a good test to identify ovarian malignant tumors. So taking the cut off value of RMI 3 score of >190.5 for ovarian malignant tumor in this study sensitivity, specificity, positive predictive value and negative predictive value were 75%, 93%, 55% and 96% respectively.

CONCLUSIONS

Ovarian tumors are mostly benign with mean age of 35 years. Benign ovarian tumors were more common in younger group and malignant among peri and postmenopausal age group. Physical examination has limited role in differentiating benign from malignant ovarian tumors. Ultrasound characteristics can be used to categorize ovarian and adnexal masses but the sonographic appearance of an ovarian mass is not pathognomonic. The cut off value of RMI 3 score of >190.5 for ovarian malignant tumor in this study is a good diagnostic tool for pre-operative diagnosis of ovarian malignancy. This scoring system due to its simplicity can be used by the general gynecologists at the periphery to refer suspected ovarian cancers to oncological centers and thereby improving the survival and prognosis of women undergoing surgery for ovarian tumors.[25]

REFERENCES

1. Bray F, Trabert B. HHS Public Access. Int J Cancer.2018;140(11):2451–60.

2. Muhabat Q, Waheed F, Jabeen N. Clinical Presentation of Ovarian Tumors. Open J Obstet Gynecol. 2016;6:205–9.

3. Das P, Bast R. Early detection of ovarian cancer. J Natl Inst Heal Sci. 2010;2(3):291–303.

4. Hassan AY, Ellatif AAA, Darweesh FF. Two Dimensional Ultrasound and Doppler in Assessment of Adnexal Masses in Correlation to Histopathological Analysis. 2014;7(1):8–18.

5. Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol.1990O;97(10):922–9.

6. Tingulstad S, Hagen B, Skjeldestad FE, Onsrud M, KiserudT, Halvorsen T, et al. Evaluation of a risk of malignancy index based on serum CA125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. BJOG. 1996;103(8):826–31.

7. Tingulstad S, Hagen B, Skjeldestad FE, Halvorsen T, Nustad K, Onsrud M. The risk of malignancy index to evaluate potential ovarian cancers in local hospitals. Obstet Gynecol.1999;93:448–52.

8. Yamamoto Y, Yamada R, Oguri H, Maeda N, FukayaT. 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.

9. Hayam FM, Ashraf MQ, Hassan MKH. Assessment of the value of a Modified Risk of Malignancy Index (RMI) in preoperative discrimination between benign and malignant ovarian masses. Gynecol Obstet. 2016;6:417.

10. Valentin L. Prospective cross-validation of Doppler ultrasound examination and gray-scale ultrasound imaging for discrimination of benign and malignant pelvic masses. Ultrasound Obstet Gynecol. 1999;14:273-83.

11. Paropakar Maternity and Women's Hospital. Hospital Admission Record 2075.[Unpublished]

12. Jha R, Karki S. Histological pattern of ovarian tumors and their age distribution. Nepal Med Coll J. 2008;10(2):81–5.

13. Bindal J, Bankey S. Prevalence of ovarian tumours among ovarian mass lesions in Gajra Raja Medical College, Gwalior, India. Int J Reprod Contraception, Obstet Gynecol. 2017;6(9):3907–10.

14. Shen F, Chen S, Gao Y, Dai X, Chen Q. The prevalence of malignant and borderline ovarian cancer in pre- and post-menopausal Chinese women. Impact Journals. 2017;8(46):80589–94.

15. Mcguire V, Hartge P, Liao LM, Sinha R, Bernstein L, Canchola AJ, et al. Parity and Oral Contraceptive Use in Relation to Ovarian Cancer Risk in Older Women. Pubmed Cent. 2017;25(7):1–10.

16. Doubeni CA, Doubeni ARB, Myers AE. Diagnosis and Management of Ovarian Cancer. Am Acad Fam Physicians. 2016;93(11):937–45.

17. Ebell MH, Culp M, Lastinger K, Dasigi T. Examination as a Test for Ovarian Cancer. Am J Prev Med [Internet]. 2015;48(3):350–6.

18. Ebell MH, Culp MB, Radke TJ. A Systematic Review of Symptoms for the Diagnosis of Ovarian Cancer. Am J Prev Med. 2016;50(3):384–94.

19. Arunakumari B, Chandra AS. Diagnosis of Adnexal Masses Using Ultrasound and Magnetic Resonance Imaging for Proper Management. Asia Pacific J Heal Sci. 2016;3(4):279–84.

20. Vasudevan J, Nair V, Sukumaran S. Evaluation of risk of malignancy index in the preoperative assessment of ovarian tumors: Study from a tertiary care center. Saudi J Heal Sci. 2016;5(2):67–71.

21. Dora S, Dandapat A, Pande B, Hota J. A prospective study to evaluate the risk malignancy index and its diagnostic implication in patients with suspected ovarian mass. J Ovarian Res. 2017;10(55):1–9.

22. Ong C, Biswas A, Choolani M, Jen J, Low H. Comparison of risk of malignancy indices in evaluating ovarian masses in a Southeast Asian population. Singapore Med J. 2013;54(3):136–9.

23. Insin P. Evaluation of Four Risk of Malignancy Indices (RMI) in the Preoperative Diagnosis of Ovarian Malignancy at Rajavithi Hospital. Thai J Obstet Gynaecol. 2013;21(4):163–75.

24. Park J. Clinical utility of the risk of malignancy indices for preoperative differentiation between ovarian cancer and borderline ovarian tumor. Gynecol Oncol. 2019;154:188.

25. Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol. 1990;97(10):922–9.