Original Article

Pre-operative Assessment of Ovarian Tumor in Patients Presenting with Adnexal Mass on the Basis of Risk of Malignancy Index (RMI)

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Abstract

Background*:Ovarian cancer is the second most common gynaecologic cancer in developing countries. Five-year survival of ovarian cancer varies according to stages, hence, screening, detection and treatment in earlier stages are of great importance. The Scottish Intercollegiate Guidelines Network (SIGN) recommends use of Risk of Malignancy Index (RMI) for pre-operative assessment of ovarian tumours. It is a scoring system based on menopausal status, ultrasound findings, and serum CA 125 level in adnexal mass.*

Objective:*To investigate the accuracy of RMI as a predictive method of discriminating benign from malignant ovarian tumour.*

Methodology: *Fifty patients, 30 years or older, with adnexal mass, admitted for laparotomy in Obstetrics and Gynaecology Dept. from April'13 to September'13were randomly assigned in this cross-sectional descriptive study. RMI was calculated for each patient based on menopausal status, CA125 level and ultrasound findings of bilateral lesion, multilocular cyst, solid areas, ascites and metastases.*

Results*:Among 50 women, 18 cases (36%) were postmenopausal showing more malignant tumors (77.78%) in this group. Depending on histopathological reports, 82% benign and 18% malignant diseases.The best performance of RMI was obtained at cut-off value of 230 with sensitivity of 100%, specificity of 95.2%, positive predictive value (PPV) of 80% and negative predictive value (NPV) 100%.*

Conclusion:*Compared to previous studies, RMI was highly sensitive in detecting malignant disease, though not as specific in excluding benign lesions, particularly endometriosis.*

Key Words:
Adnexal mass, Menopausal status, RMI.

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Introduction

Adnexal mass refers to any mass occupying the region of uterine appendages including ovarian neoplasm, endometrioma, tubo-ovarian mass, myoma, ectopic pregnancy[1]. Ovarian tumor is the second most common gynaecologic cancer variant in developing countries causing huge mortality among women[2]. Peak incidence of epithelial ovarian cancer (EOC) is at 50-70 years subsequently declining to less than 2% after 80 years. About 30% of ovarian tumors in post menopausaland 7% in pre-menopausal are malignant[3].95% of women with ovarian cancer have non-gynaecological symptoms like abdominal distension, bloating, constipation, nausea, anorexia, or early satiety [4-7]. Standard management of EOC consists of aggressive surgical cytoreduction followed by chemotherapy. Extensive retrospective experience showed that optimal surgical debulking with no or less than 1 cm residual tumor is associated with improved patient outcome[8]. Considering diagnostic difficulties, RMI, an acronym for risk of malignancy index, was first described by Jacobs et al in 1990, to identify high risk patients in order to triage them accurately to specialist care. It is the product of menopausal status, trans abdominal ultrasound

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(TAS) score and serum CA125 (U/mL). During TAS, appearance and distribution of tumor, ascites, solidity is noted[9]. CA-125, a high molecular weight glycoprotein, is expressed by a large proportion of EOC. It is a well-established tumor marker for EOC and have an important role in diagnosis[10].However, sensitivity and specificity of this marker is poor. It is raised in approximately 50% of stage I EOC and in 75-90% of advanced diseases[11-16]. In menstruating women CA-125 may be elevated in many benign entities like fibroid, adenomyosis, endometriosis. Butin post-menopausal women, CA-125 is a good diagnostic tool, as their quiescent ovaries and endometrium do not secret such proteins[17].Jacobs I et al (1990) first applied RMI index among 143 patients with pelvic masses in London Hospital. In his study using RMI cut-off level of 200, sensitivity and specificity were 85% and 97% respectively. Patients with RMI score >200 had, on average, 42 times more risk of cancer and those with a lower value 0.15 times risk[9]. Hakanson et al have shown in their study that out of 1159 patients, there were 778 women had benign pelvic mass, 251 had malignant ovarian tumour and 74 had borderline variety. 56 patients were diagnosed with other forms of cancer. Sensitivity and specificity for ovarian cancer vs. benign pelvic mass for RMI > 200 were 92 and 82%, respectively. Corresponding positive and negative predictive values were 62 and 97%[8].

Methodology

This cross-sectional descriptive study was conducted at the Department of Obstetrics and Gynaecology of ShSMCH from April 01, 2013 to September 30, 2013.Fifty women, 30-75 years, admitted with adnexal mass (diagnosed either per abdominally or sonographically) for laparotomy, were randomly selected. Those who have suspected uterine malignancy or deny surgery are excluded. After taking informed consent, menopausal status, serum CA125 level and ultrasound findings of participants were registered. If there were no bilateral lesions, multilocular cyst, solid areas, ascites and abdominal metastases on TAS, it was termed as no abnormality (U=1), if any one abnormality was found it was termed as one abnormality (U=1) and >one abnormality was named as two (U=4). Laparotomy followed by histopathological analysis of specimens were done. RMI calculation was based on a simple regression equation where premenopausal status gave M=1 and postmenopausal M=4. CA125 level was applied directly into calculation. All statistical analyses were done in SPPS inc.version 11.5. Chi-square tests were used to test difference in age distribution, menopausal status and ultrasound score. Sensitivity, Specificity, Positive Predictive value (PPV) and Negative predictive value (NPV) were calculated for 3 cut-off values of RMI. Scoring should be carried out before laparotomy in assessing nature of mass. The best cut-off value was chosen according to the highest sensitivity with lowest false-positive rate.

Results:

Majority of the patients in this study were between 30-75 years with mean age being 40.7 years (SD 11.16 yrs) consisting of 32 (64%) pre-menopausal and 18 (36%) post-menopausal.

Table-I

Age distribution of patients (n=50)

Age distribution	Frequency	Percentage (%)
30-39 years	28	56
40-49 years	10	20
50-59 years	10	20
60-75 years	02	04
Total	50	100

Abdominal pain was complained by all patients followed by lump in 32 (64%), dyspepsia in 7 (14%) and constipation in 5 (10%) of patients. No abnormality on TAS was detected in 60%, one abnormality in 20% and two or more abnormalities in another 20%. 20 patients (40%) serum CA 125 fell within normal range (<35 U/ml).Pre-operative RMI value for assessment was taken as 200 and found 76% patients' RMI <200 and 24% had >200. Among 10 categories of histopathologically diagnosed masses, majority occupied two domains (28% serous cyst adenoma, 24% endometriosis). Benign conditions included: functional cysts (n=02), simple serous cyst (n=14), Dermoid cyst (n=04), Endometriosis (n=12), Mucinous cystadenoma (n=04), ectopic pregnancy (n=02) and parovarian cyst (n=04) whereas malignant tumors: Serous cystadenocarcinoma (n=2), Mucinous cystadeno-carcinoma (n=2), and secondary adenocarcinoma (n=4).

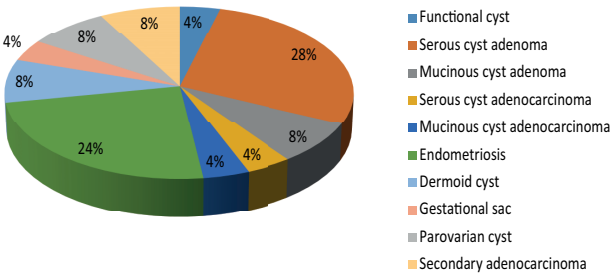

Fig.-1: *Pie chart showing histopathological variants of adnexal masses*

Though statistically insignificant differences were found between groups with benign and malignant pathology considering age (P value 0.074), menopausal status (P value 0.004), TAS score (P value .000) and CA 125 (P value .000), it was shown that higher proportions of malignant cases were associated with higher age, US score and serum CA 125.The best performance was obtained for RMI cut-off value of 230 with sensitivity 100%, specificity 95%, PPV 80% and NPV 100%.

Table-II

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for RMI

RMI cut-off value	Sensitivity	Specificity	PPV	NPV
150	100%	90%	71.4%	100%
200	100%	90.5%	66.7%	100%
230	100%	95.2%	80%	100%

2 serous cyst adenomas along with 2 endometriomas at RMI 200 and 2 serous cystadenomas at RMI cut off value 230 were recorded as false positive with no false negative cases in both RMI.

Discussion:

Among 50 women of this study, 64% were premenopausal.There were more malignant tumors (77.78%) in postmenopausal group (P=0.004) suggestive of cancer incidence rises with increasing age and in postmenopausal group. Result was similar with studies of Tahereh et al 63.2%, WatcharadaMoolthiya et al 60.8% and Samir et al 70%[17,18,19].

In the study 100% patients presented with abdominal pain and 64% with abdominal lump showing similar result by TayyibaWasim et al where abdominal pain was seen in 66% patients[20]. In a retrospective cohort study by Lataifeh et al with, abdominal pain and swelling were reported by 51% and 32% respectively in early stage and lump by 62% and pain by 44% in advanced stage[7]. This study do not differentiate symptoms among early and advanced cases.

In 80% cases USG revealed only unilateral adnexal mass scoring 1. All patients with U=1 had benign tumors; on the other hand, 90% of them who obtained U=4 were malignant in histopathology. Though there was a difference between these two groups (p value 0.000), it was not statistically significant. Tahereh et al[17] also showed, 98% patients with U score=1 had benign tumors with 65.4% patients with high score had malignancy and it

Table-III

Distribution of age, menopausal status, ultrasound score and S. CA125 in 50 women with benign (n=41) and malignant (n=09) adnexal mass.

Age (yrs)	Benign	Malignant	P value
30-39	26 (63.41%)	02 (22.22%)	
40-49	07 (17.07%)	03 (33.33%)	0.074[a]
50-59	06 (14.63%)	04 (44.44%)	
60-75	02 (4.88%)	0 (0%)	
Menopausal status			
Pre menopausal	30 (73.17%)	02 (22.22%)	0.004[b]
Post menopausal	11(26.83%)	07 (77.78%)	
Ultrasound score			
1	40 (97.56%)	0 (0%)	.000[c]
4	01 (2.44%)	09 (100%)	
S. CA125 value (u/ml)	Benign	Malignant	P value
>35	20 (48.78%)	0 (0%)	
35-100	15 (36.58%)	01(11.11%)	.000[d]
101-200	04 (9.75%)	02 (22.22%)	
201-400	02 (4.89%)	0 (0%)	
>400	0 (0%)	06 (66.67%)	

a= 4 cells (50%) have expected count less than 5. The minimum expected count is .36.
b= 1 cell (25%) have expected count less than 5. The minimum expected count is 3.24.
c= 2 cells (33.3%) have expected count less than 5. The minimum expected count is 1.80.
d= 8 cells (80%) have expected count less than 5. The minimum expected count is .36.

Table-IV

*Comparison of our Results with Previous Studies**

Study	No. of cases	Sensitivity	Specificity	PPV	NPV
Jacobs et al.1990	143	85.4	96.9		
Davies et al.1993	124	87.0	89.0		
Tingulstad et al. 1996	173	71.0	96.0	89	88
Manjunath et al. 2001	152	73.0	91.0	93.0	67.0
Andersen et al. 2003	180	70.6	87.7	66	90
Obeidat et al. 2004	100	90.0	89.0	96	78
Ulusoy et al. 2006	296	71.7	80.5	67	84
Tehereh et al. 2009	1159	89.5	94.7	71	98
Hakanson et al. 2012	159	92	82	62	97
Samir et al. 2011	140	86.67	92.5	89.66	90.24
Present study (RMI 230)	50	100	95.2	80	100

*Values were % given for RMI=200; PPV, positive predictive value; NPV, negative predictive value

was also statistically insignificant. Association of higher sonographic score with malignant cases was also supported by WatcharadaMoolthiya et al and Samir et al. Serum CA125 value >200 u/ml associated with malignant conditions was also supported by previous studies [17,18]. Main limitation of serum CA125 is its high value in benign diseases such as ovarian cysts, endometriosis and pelvic infection[21], reflected in present study. In this study out of 50 patients with adnexal mass,based on histopathological reports, less malignant cases (18%) were diagnosed than benign which is in concordance with previous studies [34,36].WatcharadaMoolthiya et al, stated in his study majority false positive cases were due to dermoid cysts and mucinous cyst adenomas while false negative cases were for borderline tumors, result not supported by this study**[18].**

At lower cut off values sensitivity increases at the expense of specificity, while at a higher cut off values specificity increases at the expense of sensitivity and more benign cases will be referred as malignant. These findings are important for clinical applicability of RMI. In the present study sensitivity of RMI (100%) to predict malignancy was higher than those reported by the previous studies[10,9,17,18,22,23]. One possible explanation is that we cannot differentiate early stage and borderline ovarian tumor.

Conclusion

This study demonstrated that RMI scoring is a simple and effective one in assessing nature of adnexal masses pre-operatively, despite some limitations. It guides the clinicians to determine which tumors will be operated by Gynaecologists/Gynae-oncologist and thereby improves patient's outcome.

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