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Research Article

Role of Risk Malignancy Index in Predicting Ovarian Malignancy and its Correlation with Histopathological Report

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Abstract: The aim of this study was to evaluate the accuracy of the Risk Malignancy Index in discriminating between benign lesions and malignant adnexal masses in gynaecologic practice by correlating with the postoperative histopathological report. The study was done in department of Obstetrics and Gynaecology at Cheluvamba Hospital, Mysore. During the period of May 2013 to August 2014 a total of 27 cases of adnexal masses were studied. On admission, detailed history and examination including preoperative laboratory work up was done. Pelvic USG scan and serum CA-125 done and Risk Malignancy Index (RMI-3) calculated for all patients. Post operatively histopathological reports collected and analyzed. Through the period of 1 yr 3 months, a total of 27 patients with adnexal mass were treated. Out of them 24 patients had benign and the remaining three had malignant adnexal masses. Each parameter constituting RMI was evaluated individually in order to determine its role in predicting malignancy. Of the 27 patients, 9 were menopausal. Whereas, the remaining 18 patients had regular menstrual cycle showing significantly more patients with malignant histopathology were in menopause. USG findings revealed a score of <2 in 19 cases and a score >2 in 8 cases. Further CA-125 of >35U/ml was seen in 5 cases, RMI was calculated using the formula (U*M*CA-125). High risk (RMI of >200) was seen in 4 cases, further narrowing the suspicion of malignancy more accurately in preoperative analysis of adenexal masses. RMI score using menstrual status, ultrasound score and serum CA-125 levels is a useful predictor in assessment of malignancy in ovarian tumors of epithelial origin.
Keywords: CA-125, Ovarian Malignancy, Risk Malignancy Index (RMI).

INTRODUCTION

Ovarian cancer is the third leading site of cancer among women in India, Varying between 5.4 and 8.0 per 100,000 populations in different parts of the country [1]. Screening for ovarian cancers pose challenges to clinicians as there is wide range of variables leading to their inaccurate interpretation. Over the years, many parameters have been evaluated to assess the risk like age, menopausal status, and size of tumor, family history, hormonal assay and immunological study. However in the year 1990, Jacobs *et al*. [2]. developed risk malignancy index (RMI) to standardize and improve preoperative evaluation. Calculating RMI is cost effectiveness and its application is easy. The original RMI (RMI-1) has been modified in 1996 (RMI2) [3] and again in 1999(RMI3) [4]. The difference between the new indices lies in the different scoring of ultrasound characteristics and menopausal status.

The aim of this study is to analyze pre and postoperative findings in patients with adnexal masses and to identify factors that may predict and influence the nature of the tumors .The study determines the role of RMI-3 to discriminate between benign and malignant ovarian masses so as to design appropriate referral and different therapeutic approaches.

MATERIALS AND METHODS

A study was conducted from May 2013 to August 2014 at Cheluvamba Hospital, a tertiary care center in Mysore. The study included 27 women randomly selected and admitted to the hospital for the evaluation and surgical treatment for adnexal masses. On admission, detailed history and examination was conducted. Parameters such as age of patient, symptoms at presentation, parity index, and previous history of similar complaints, family history and BMI are documented. Preoperative laboratory work up was sent for including CA-125.USG scan was done and significant parameters like size, loculation, bilaterality,

presence of solid components, ascites and intraabdominal metastasis are noted.

RMI was calculated for all patients. The RMI-3 was calculated using the formula

RMI = M ×U × serum CA-125.

(M) refers to the patient's menopausal status, (U) refers to the ultrasound score, and serum (CA-125) is the assayed level expressed in U/ml. Multilocularity, solid areas, bilaterality, ascites and intraabdominal metastasis score 1 point each.

A total of 2 or more points is recalculated into U=3, fewer than 2 points into U=1. Postmenopausal status is defined as more than 1 year of amenorrhoea. A score of M=3 is given to postmenopausal women and M=1 for premenopausal status. CA-125 (U/ml) was entered directly into the equation.

Final diagnosis is based on the histopathological of the surgical specimen. The results are tabulated and analyzed as follows.

RESULTS

During the above mentioned study period 27 women with adnexal masses were studied. Out of them 3 had malignant tumors and the remaining were benign. Histopathological analysis revealed 9 different types of masses. The malignancies consisted of serous cystadenocarcinoma, mucinous adenocarcinoma and granulosa cell tumor, one each. Of the benign tumors serous cystadenoma was most common constituting 40% of the total followed by mucinous cystadenoma 18.5%. The other benign masses include fibroma (n=1), dermoid (n=2) hemorrhagic cyst (n=2) and others (paraovvarian cyst, fimbrial cyst, mesenteric cyst). The mesenteric cyst was large with features suggestive of malignancy on sonological examination. The incidence of various histopathological diagnoses of adenexal masses is listed in Table 1.

There was no significant difference in histopathological diagnosis of tumors with regards to symptoms or parity.

Malignant lesions were more common in women over 60 years of age as in Table 2.

All malignant and borderline tumors were more frequent in postmenopausal women. Though all three malignant tumors were larger in size, large tumors were also common among serous and mucinous cystadenomas. The largest size was 35*28 cm, seen in granulose cell tumor as in Table 3.

Significant differences between the presence of loculations and the bilaterality of tumors did not help in differentiating between benign and malignant disease in our study. However the presence of solid elements and ascites hinted more toward malignant nature. None of the cases had any intraabdominal metastasis. Hence its relevance cannot be commented upon. The ultrasonographic parameters are tabulated in Table 4.

Both serum CA125 and RMI 3 were able to detect malignant ovarian masses with fair precision. Of the 3 malignant masses, high values of CA125 were present in all of them. However, CA125 was also found to be raised in 2 benign cases. When RMI was used along with CA125, all high risk cases showed malignancy. Intermediate risk, as determined by RMI, however turned out to be all benign in our study. The values are tabulated in Table 5.

Table1: Incidence of different types of adenexal mass

HPR	Number	Percentage
Benign		
Serous cystadenoma	11	40.7%
Mucinous cystadenoma	5	18.5%
Fibroma	1	3.7%
Dermoid	2	7.4%
Hemorrhagic cyst	2	7.4%
Other cysts	3	11.1%
Malignant		
Serous cystadenocarcinoma	1	3.7%
Mucinous cystadenocarcinoma	1	3.7%
Granulosa cell tumor	1	3.7%
Total	27	

Table 2: Age distribution

Age	Number
<30	5
30-45	10
45-60	5
>60	7

Table 3: Menstrual history

Menstural History		Size		
Regular	Menopausal	<5	5-10	>10
18	9	4	11	12

Table 4: Ultrasound characteristics

HPR	No.	Ultrasonographic Findings					U	
Benign		B'L	Loculation	Solid	Ascites	Meta	<2 U=1	>=2 U=3
Serous cystadenoma	11	1	5	2	1		8	3
Mucinous cystadenoma	5		1				5	
Fibroma	1						1	
Dermoid	2	1	1	2			1	1
Hemorrhagic cyst	2						2	
Other cysts	3		1	1			2	1
Malignant								
Serous cystadenocarcinoma	1		1	1	1			1
Mucinous cystadenocarcinoma	1		1	1				1
Germ cell tumor	1		1	1	1			1
Total	27	2	11	8	3		19	8

Table 5: CA-125 and RMI

HPR	No.	CA-125		RMI		
Benign		<35U/ML	>35U/ML	0-25	25-200	>200
Serous cystadenoma	11	10	1	7	4	
Mucinous cystadenoma	5	4	1	4	1	
Fibroma	1	1		1		
Dermoid	2	2			2	
Hemorrhagic cyst	2	2		2		
Other cysts	3	3		2		1
Malignant						
Serous cystadenocarcinoma	1		1			1
Mucinous cystadenocarcinoma	1		1			1
Germ cell tumor	1		1			1
Total	27	22	5	16	7	4

Table 6: Scoring system

Variable	Scoring system			
	RMI 1	**RMI 2**	**RMI 3**	**RMI 4**
Menopausal Status (M)				
Premenopause	1	1	1	1
Postmenopause	3	4	3	4
Ultrasound Score (U)				
Multilocularity	No feature=0			
Bilaterality	1 feature=1	<1 feature=1	<1 feature=1	<1 feature=1
Solid	>1feature=3	>1 feature=4	>1 feature=3	>1feature=4
Ascites				
Intraabdominal metastasis				
Serum CA-125	Absolute level (U/ml)			
Calculation of RMI1,2,3 =M*U*CA-125 Calculation of RMI 4=M*U*CA_125*S (single greatest diameter of tumor size (cm). If size <7cm, S=1; if >7 cm, S=2)				

DISCUSSION

Ovarian tumors can occur at any age in a woman's life but they differ in type, being mostly germ cell tumors in childhood, functional cysts in the reproductive age group and becoming increasingly malignant towards and after menopause. Most cases are diagnosed at advanced stage where prognosis is poor.

Serum CA-125 was earlier used as an independent marker for preoperative evaluation [5]. The main limit of CA125 is that it may be high in benign

disease such as ovarian cysts, endometriosis and pelvic infection. The combination of serum CA125 with menopausal status, other tumor markers and ultrasound parameters increases the discriminating power of the method for the two types of ovarian pathology.

Many versions of RMI have been used over the years to predict the tumor nature. The 4 versions of RMI used are summarized in Table 6 [6]. RMI 1 give ultrasound score (u=0) when none of USG features are presenting, completely eliminating the importance of CA-125. RMI 2 and 4 have been less evaluated than RMI 3. Hence we have used RMI 3 in our study.

HE4 (Human Epididymal Protein) is another serum marker recently being evaluated for cancer prediction [7]. Even in the first stages of ovarian cancer (stages I and II), HE4 is over-expressed and mainly found in serous, endometrial and clear-cell cancers. Value more than 70pM (as suggested by Moore et al) is suspicious of malignancy.

The ROMA (Risk of Ovarian Malignancy Algorithm) algorithm integrates the HE4 assay, the CA125 assay and the menopausal status of patients in order to evaluate the malignancy risk of a pelvic mass. Using ROMA the predictive index is calculated by the following equation [8]:

Premenopause PI = – 12.0 + 2.38*ln(HE4) + 0.0626*ln(CA125);

Postmenopause PI = – 8.09 + 1.04*ln(HE4) + 0.732*ln(CA125);

Where, ln is the natural logarithm

ROMA was determined using the following equation:

ROMA (%) = exp (PI)/[1 – exp(PI)]*100.

Based on the above equation, 13.1% and 27.7% as the cutoff points for pre- and postmenopausal patients, respectively.

Other markers like CA 19-9, CA-15.3, CEA, ESR, OVA1 is under evaluation. 3D ultrasound, Doppler and MRI has been used to improve the imaging modalities in complex vascularised adenexal masses [9].

For proper diagnosis, some poorly differentiated malignant serum tumors require immunohistochemistry investigations with a panel of antibodies including CK7, CK20, Estrogen, progesterone receptors and oncoprotein p53 can be used postoperatively.

CONCLUSION

The early diagnosis of ovarian cancer is still a challenge to gynecologist. In the recent years there has been an explosion of potential markers that aid in their prediction. Most of them need further studies and clinical trials. However currently, the results show the RMI improves the ability of the preoperative diagnosis of any adnexal mass.RMI helps to categorize the women with adnexal masses to be referred to oncology centre. Calculating RMI is a non invasive, cost-effective and simple to apply in any primary health care set up.

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