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Determination of efficiency of RMI3 and RMI4 in preoerative evaluation of adnexal tumors

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Abstract

Objective is to study was to compare the efficiency of Risk of malignancy index 3 and 4 (RMI3 and RMI4) in detection of ovarian malignancy. It was a prospective study conducted in department of obstetrics and gynaecology at Karnataka Institute of Medical Sciences, Hubli, where every patient in the study underwent ultrasonography, serum CA125, calculation of RMI3 and RMI4 was done and finally the sensitivity specificity, positive and negative predictive value was calculated based on histopathological analysis of the specimen postoperatively. The sensitivity of RMI3 is 87.95%, specificity is 75%, positive predictive value is 94.8%, negative predictive value is 54.54%, percentage of false negative is 12.04% and percentage of false positive is 25%. The sensitivity of RMI4 is 55.4%, specificity is 100%, positive predictive value is 100%, negative predictive value is 30.18%, percentage of false negative is 44.5% and percentage of false positive is 0%. Thus the study concludes that RMI3 is more sensitive then RMI4 for detection of malignancy but RMI4 has better specificity and positive predictive value.

Keywords: Determination, efficiency, RMI3, RMI4, adnexal tumors

Introduction

The burden of Ovarian malignancy in women healthcare seems to be high as most tumours are detected in late stages and thus they have poor survival ^[1]. Attempts have been made to find markers and methods to predict the nature of adnexal tumors so as to plan the management. Ultrasound findings were studied and several parameters were detected to predict malignancy ^[2]. Detection of CA125 levels can also serve an important marker for epithelial malignancy in the ovary ^[3]. Malignancy increases in incidence as age advances. It is the idea of Jacob to associate these three parameters and formulate the Risk of Malignancy Index (RMI) in an profound attempt to improve the detection of ovarian malignancy ^[4]. It was then modified by Tingustad in 1996 (RMI2) ^[5]. Again modified in 1999 (RMI3) ^[6]. Yamomoto incorporated size of the tumor in the formula and named it RMI4 ^[7]. The evaluation of adnexal tumours by RMI not only improves the rate of detection but also improve patient survival by optimising treatment. The objective of our study is to know and compare the efficiency of RMI3 and RMI4 in evaluation of adnexal tumors.

Materials and Methods

The study period was from June 2012 to August 2013 and women admitted to Karnataka Institute of Medical Sciences, Hubballi with adnexal mass during this period were chosen for the study. 100 women with adnexal masses met the inclusion criteria, out of this there was one drop out as patient was given neoadjuant chemotherapy and discharged and discontinued follow-up. Inclusion criteria was women presenting as adnexal masses and admitted for evaluation and management. Women already diagnosed as ovarian cancer by histopathology and have received chemotherapy were excluded from the study.

It was a prospective study. Name, age, complaints, parity, menopausal status, past and family history and associated medical condition of each patient were asked and systematically collected in the Performa.

General physical examination, systemic examination which included, cardiac system, respiratory system, per abdominal, per speculum, per vaginal and per rectal examination of all patients was done. Routine investigations, ultrasonography and serum CA125 levels were done in all patients. Ultrasonographic score was calculated as shown in table-1. All patients were subjected to laprotomy/laproscopy.

Total abdominal hysterectomy with bilateral salpingooophorectomy, cystectomy, unilateral or bilateral salpingooophorectomy were done in intra operatively benign appearing lesions and a surgical staging done for those with malignant masses with optimal debulking incuding total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. Histopathological analysis of the specimen was done.

The ultrasound was performed transabdominally by 5-2 MHz transducer of IU 22 Philips. A score was assigned for the following ultrasound features presence of multilocular cystic lesion, solid areas and size of the tumor, bilateral lesion, ascites, and intraabdominal metastasis. A total ultrasound score was thus calculated for each patient as shown in table-1. Tumor size (s) was measured by ultrasound for each patient. Postmenopausal status was defined as more than one year of amenorrhea or age older than 50 years in woman who had undergone hysterectomy and those less than 50 were taken as premenopausal. Serum samples were collected preoperatively and serum CA 125 levels were measured using Electrochemiluminescence immunoassay (ECLIA). Based on the data obtained RMI3 and RMI4 were calculated as follows

- RMI 3 (Tingulstad *et al.* 1999) = U x M x CA 125, where a total ultrasound score of 0 or 1 made U=1 and a score of >2 made U=3; premenopausal status made M=1 and postmenopausal M=3. The serum level of CA 125 was applied directly to the calculation ^[6].
- 2) RMI 4 (Yamamoto *et al.* 2009) = U x M x S (Size in centimeter) x CA 125, where a total ultrasound score of 0 or 1 made U=1 and a score > 2 made U=4. Premenopausal status made M=1 and postmenopausal status made M=4. A tumor size (Single greatest diameter) of <7 cm made S=1 and >7 made S=2. The serum levels of CA 125 was applied directly to the calculation.⁷

The histopathological diagnosis was considered the gold standard for definite outcome. All statistical analysis was performed using the SPSS version 17 (Trial version). Pearson chi-square test was used to test RMI3 and RMI4. The cut off for RMI3 was taken as 200 and RMI4 was taken as 400. Sensitivity was defined as the percentage of patients with malignant disease having a positive test result. The specificity was defined as percentage of benign disease having a negative test result. The positive predictive value was defined as the percentage of patients with positive test result having malignant disease and the negative predictive value was defined as the percentage of patients with a negative test result having benign disease and calculated.

Table 1:	Ultrasonographic	Scoring
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	Findings	Score
1	Unilocular simple cyst with regular fine wall or	
	lesion suggestive of dermoid	
	Multilocular cyst with regular and smooth wall	
2	(<3mm) or thick (>3mm) or solid homogenous tumor	1
	with hyperechogenic well defined wall	
3	Unilocular or multilocular cyst with fine wall or	
	irregularity in septa (thickness > 3mm)	
	Multilocular cyst with thick and irregular wall	
4	(irregularity <3mm) and or irregular septa or cyst or	4
	papillary irregularity > 3mm	
5	Complex lesion with predominance of cystic or solid	
	area without irregularity in surface	
6	Multiplicity : unilateral or bilateral lesion	10
7	Associated lesion	1
8	Wall expansive invasion > 3mm	2

Results

Out of 99 patients 17 were less than 30 years of age and only one had malignant lesion among them. Between 30 to 60 years 9 had invasive lesion and 47 had non invasive lesion. In age group more than 50 years 6 had invasive lesion and 20 had non invasive lesion as seen in graph-1 and graph-2. Age as individual factor is not significant in predicting type of adnexal mass.



Graph 1: Age Distribution of non invasive lesions.

In non invasive lesions 16 were below 30 years, 47 were between 30-50 years and 20 were more than 50 years.



Graph 2: Age distribution of invasive lesion

In invasive lesions only one was below 30 years, 9 were between 30-50 years and 6 were above 50 years.



Graph 3: The relation of size of tumor with type of lesion.

When tumor size of less than 7 taken as cut off, out of 23 patients, 22 had non invasive and 1 had invasive lesion. 76 of them had tumor size of 7 or more and among them 61 had non invasive and 15 had invasive lesion as seen in table-1 and graph-

8. Sensitivity, specificity, positive and negative predictive of tumor size was 26.5%, 93.75%, 95.65% and 19.73% respectively. Percent of false negative is 73.49% and percent of false positive is 6.25%.

Various types of invasive lesions were detected in histopathology. Out of 16 invasive tumors serous cystadenocarcinoma found in 7, mucinous cystadenocarcinoma in 2, papillary adenocarcinoma of fallopian tube in 1 patient, brenner tumour in 2, granulosa cell tumor in 2, krukenberg tumor in 1, yolk sac tumor in 1 patient. Among benign tumors or non invasive lesions, most commonly diagnosed was serous cystadenoma in 27 patients, mucinous cystadenoma in 19, teratoma in 5, salpingo-oophoritis in 4, ectopic pregnancy 1 patient, ovarian endometriosis in 1.26 had lesions in others category.

Among all patients who were evaluated for RMI3, 77 were benign and out of these 73 had non invasive lesion and 4 had invasive lesion in histopathology. 22 were malignant as assessed by RMI3 and 10 of them had non invasive lesion and 12 had invasive lesion in histopathology. The sensitivity of RMI3 is 87.95%, specificity is 75%, positive predictive value is 94.8%, negative predictive value is 54.54%, percentage of false negative is 12.04% and percentage of false positive is 25% as seen in table-2.

Among all patients who were evaluated for RMI4, 46 were benign and out of these all had non invasive lesion in histopathology. 53 were malignant as assessed by RMI4 and 37 of them had non invasive lesion and 16 had invasive lesion in histopathology. The sensitivity of RMI4 is 55.4%, specificity is 100%, positive predictive value is 100%, negative predictive value is 30.18%, percentage of false negative is 44.5% and percentage of false positive is 0% as seen in table-3.

Table 2: Correlation of RMI3 with histopathological report

RMI3		HPR		Total
		Non invasive	invasive	Total
Benign	199.00	73	4	77
Malignant	200.00	10	12	22
Tota	ıl	83	16	99

Table 3: Correlation of RMI4 with histopathological report

RMI4		HPR		Total
		Non invasive	invasive	Total
Benign	399.00	46	0	46
Malignant	400.00	37	16	53
Tota	l	83	16	99

Chi-square value: 16.54. P value is .000 (Significant)

Discussion

Our study was compared to study conducted in Department of Obstetrics and Gynecology of Gulhane Military Medicine Academy, Etlik 06010 Kecioren, Ankara, Turkey, conducted between October 1 2008, and February 3, 2010^[7]. It was also compared with the study conducted in Singapore ^[8]. Table-4 compares the efficiency of all RMI3 and RMI4 with those of other studies. Our study had higher sensitivity when compared to Gulhane military Academy and also a higher positive predictive value. The incidence of endometrioss was more in Singapore study, so the sensitivity of RMI in Singapore study was very less but had higher specificity

Table 4: Compration of RMI of present study with three other studies.

Study		Present study in KIMS	Gulhane military Academy, Turkey.	National university hospital, Singapore.
Sensitivity	RMI3	87.95	75	12.5
	RMI4	55.54	50	43.8
Specicificity	RMI3	75	87	90.1
	RMI4	100	98	78.8
PPV	RMI3	94.8	57	_
	RMI4	100	83	_
NPV	RMI3	54.54	93	
	RMI4	30.18	88	

Conclusions

RMI3 is more sensitive in detecting malignancy at a cut off of 200 as compared to RMI4 at a cut of 400. This suggests that RMI4 was not as efficacious in pre operative diagnosis at 400 cut off and the optimal cut off to be revised. RMI4 had a good positive predictive value compared to RMI3. Our study had a small sample size of 100 and also had the possibility of interobserver variability in ultrasound scoring and thus may be the confounding factor. RMI is definitely a good method of evaluating adnexal tumors and thus optimising the management and also help in right surgical approach and thus improved survival.

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