Original Article

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Role of Sonographic Gray-Scale Pattern Recognition in the Diagnosis of Adnexal Masses

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ABSTRACT

Introduction: Characterization of adnexal masses as benign or malignant is of utmost importance for optimal management and prognostication. Ultrasound examination plays an important role in the differentiation of adnexal masses. Various sonographic characteristics have been recognised to differentiate benign and malignant adnexal masses. Subjective evaluation of gray-scale ultrasound images by an experienced ultrasound examiner to discriminate adnexal masses is known as "pattern recognition".

Aim: To access the efficacy of pattern recognition at predicting an accurate histological diagnosis of adnexal masses.

Materials and Methods: All adnexal masses diagnosed clinically or during screening sonography were included in the study (n=136). Sonographic pattern recognition was performed and documented with specific diagnosis whenever feasible. Risk of Malignancy Index 3 (RMI3) score was also calculated. Results were compared with the gold standard histology. Chi-square test was used to assess the significance of the results and a p-value <0.05 was considered statistically significant.

Results: In the final cohort of 136 women, on pattern recognition, 91 were suspected to have benign adnexal masses and 45 were reported as malignant adnexal masses. However, on final histo-pathology, 94 patients had benign tumours and 42 patients had malignant disease. The benign group pattern recognition could render a specific diagnosis in 85.7% as compared to RMI3 pattern recognition conferred a sensitivity of 95.2% (RMI3 78.6%), with a slight compromise in the specificity (94.7% versus 96.8%).

Conclusion: Pattern recognition is a sensitive and specific sonographic tool in discriminating benign and malignant adnexal masses. Moreover, it is also useful in differentiating various benign adnexal masses.

Keywords: Benign, Malignant, Ultrasound examination

INTRODUCTION

Adnexal masses are one of the common challenges faced by a gynaecologist in day to day clinical practice. Characterization of these as benign or malignant is of utmost importance for optimal management and prognostication. Malignancy of the ovary is notoriously known for getting missed or misdiagnosed in early stages. With more than 225,000 new cases annually leading to 140,000 deaths, timely diagnosis of ovarian cancer remains a major health concern worldwide as well as a challenge [1,2].

The subjective evaluation of gray-scale ultrasound images by an experienced ultrasound examiner to discriminate adnexal masses is known as "pattern recognition". Pattern recognition can help to discriminate an adnexal mass as benign or malignant and at times to recognize a specific diagnosis as endometrioma, dermoid, mucinous cystadenoma, fibroma and likewise. This pattern recognition has been shown to accurately make a specific diagnosis in almost half of adnexal masses preoperatively [3]. The role of CA125 alone or in various combinations with sonographic tools has also been studied. Risk of Malignancy Index (RMI) which is scoring system, was developed to differentiate benign and malignant ovarian tumours, so as to facilitate timely management/referral. One of the most popular versions of this index is known as RMI3 [4]. Three-dimensional power Doppler is another modality which has been investigated in some studies [5].

As compared to the above mentioned modalities and scores, pattern recognition is a simple, cost effective gray-scale ultrasound based tool. It has recently attracted many investigators for triaging adnexal masses. It has been studied with varied combinations of other screening tools like RMI score or CA125 [6]. Therefore, this study was carried out to access the efficacy of pattern recognition alone at predicting an accurate histological diagnosis of adnexal masses.

MATERIAL AND METHODS

This prospective cohort study was carried out in a tertiary care center over a period of two years between January 2011-January 2013 on approval by Institutional Ethical Committee (IEC192/2011). All adnexal masses which were either diagnosed by history and examination or were incidentally diagnosed during preliminary sonography and now were planned for histological confirmation of diagnosis either following surgical removal or by biopsy were included in the study. All enrolled women provided written informed consent for participation. The investigator involved in pattern recognition during sonographic examination was not blinded to the history, clinical finding or any sonographic/laboratory work up done previously, to minimize the bias. Non gynaecological tumours and borderline ovarian tumour were excluded from the final analysis.

Sample Size Calculation

Anticipating 86% sensitivity for RMI with the precision of 10% at 95% confidence level a minimum of 46 malignant and 92 benign cases are required for this study [7].

A) Ultrasonography (pattern recognition): All sonographic examinations were performed with a transabdominal (5 MHz) and/or transvaginal (7.5 MHz) probes using Toshiba Nemio machine. Benign and malignant tumours manifest a characteristic appearance at gray-scale imaging known as "pattern recognition". Based on the subjective evaluation of the gray-scale ultrasound images by a single observer, the sonographer classified each tumour as probably benign or malignant. Whereever feasible, a specific diagnosis such as endometrioma, dermoid, paraovarian cyst, simple cyst, peritoneal inclusion cyst or hydrosalpinx was made [8].

B) Risk of malignancy index 3 (RMI3): This was calculated by multiplying the ultrasound score (U), menopausal status (M) and serum CA125 level {RMI 3 = U × M × CA125} [4]. If the RMI3≥200,

the diagnosis is suggestive of malignant ovarian tumour and if RMI3 is <200, it is diagnosed as benign tumour.

STATISTICAL ANALYSIS

The statistical analysis was done using SPSS version 22.0.0.0.The Pearson Chi-square test was applied to test the significance of differences of age, menopausal status and ultrasound score. The Mann-whitney U-test was applied when testing differences in distribution of CA125 among women with benign and malignant adnexal masses. A probability (p) value of <0.05 was considered significant.

RESULTS

A total of 140 women with an adnexal mass were enrolled. Four patients were excluded from the final analysis, as three of those had borderline pathology and one was diagnosed to have Gastro-Intestinal Stromal Tumour (GIST). Thus, the final study population included 136 women with adnexal mass. On pattern recognition, 91 patients were suspected to have benign adnexal masses and 45 patients were reported as malignant adnexal masses. However, on final histopathology, 94 patients had benign tumours and 42 patients had malignant disease. As histopatholgy is the 'goldstandard' to differentiate between benign and malignant pathology, analysis was performed and comparisons were done based on the final report.

Mean age of the study population (n=136) was 40.5 years. Mean age for malignant group is 46.5 years and benign group was 39.3 years. Nine patients in malignant group and 24 patients in benign group were nulliparous. Around 60% women in malignant group as compared to 25% in the benign group had attained menopause. The differences in age and menopausal status were statistically significant, as expected [Table/Fig-1].

Pattern Recognition

Among the 91 tumours recognised as benign by pattern recognition, a specific diagnosis was suggested in 85.7% (78/91). The proposed diagnosis was mucinous cystadenoma (19), serous cystadenoma (12), endometriotic cysts (17), dermoid cysts (12), fibroma (4), paraovarian cyst (4), peritoneal inclusion cyst (5), haemorrhagic cyst (2) and hydrosalpinx (3). Sixty eight (74.7%) of the proposed 78 diagnoses based on gray-scale imaging were correct [Table/Fig-2]. The incorrect diagnosis of three mucinous cystadenoma included two serous cystadenoma and another simple cyst. The incorrect diagnosis of four serous cystadenoma was of four mucinous cystadenomas. The incorrect diagnosis of one endometriotic cyst was of a granulosa cell tumour, the incorrect diagnosis of two haemorrhagic cysts comprised one each of peritoneal inclusion cyst and granulosa cell tumour. In 13 tumours, which were considered as benign no specific diagnosis could be ascertained.

Malignancy was suspected in 45 tumours with pattern recognition. Though five of these were benign by histopathology. In 45 malignant masses, a specific diagnosis was proposed in 35% (16/45) tumours [Table/Fig-3]. Out of those three proved to be wrong. The included two mucinous cystadenocarcinoma which turned out to be serous cystadenocarcinoma and fallopian tube carcinoma. One which was thought as borderline tumour was found to be endometrioma.

Pattern recognition suspected five benign cases falsely as malignant. It misdiagnosed two fibromas as malignant due to solid appearance. Two serous adenomas were misdiagnosed as malignant due to their solid papillary projections. Pattern recognition has identified two malignancies falsely as benign. Two granulosa cell tumours were misdiagnosed as benign due to their appearance as cyst with haemorrhage and ground glass appearance.

RMI3

The median RMI was 31 (Range: 6-1500) for benign tumours as compared to 943 (Range: 9-35,127) in malignant tumours. False positive RMI (RMI ≥200) was seen in three benign cases (3.2%). False negative RMI (RMI<200) was found in two cases of malignant ovarian tumour.

[Table/Fig-4] summaries the comparison of pattern recognition and RMI3 in the preoperative diagnosis of benign and malignant ovarian tumours.

DISCUSSION

Present study proves that the overall efficacy of pattern recognition is superior to RMI3 in differentiating benign and malignant adnexal masses. Pattern recognition not only differentiates benign and malignant tumours, it also confers a specific pathologic diagnosis. Specific diagnosis might not be much useful for malignant tumours as most of the times treatment is radical. However, it has big significance in differentiating various benign tumours and optimizing the management [3].

A recent study even tried to find out the sensitivity of pattern recog-

Characteristics		Total no. of patients n=136(%)	Benign group n=94(%)	Malignant group n=42(%)	p-value
Mean age (range) in years		41.5 (14-75)	39.3 (16-63)	46.5 (14-75)	0.04
Median age		42	36	48	
Parity	Nulliparous	33 (24.3)	24 (25.5)	9 (21.4)	0.09
	Parous	103 (75.7)	70 (74.5)	33 (78.6)	
Menopausal status	Pre menopausal	88 (64.7)	71 (75.5)	17 (40.5)	<0.001
	Post menopausal	48 (35.3)	23 (24.5)	25 (59.5)	

[Table/Fig-1]: Demographic characteristics of the study population.

Ultrasound characteristics	Number n = 91 (%)	USG specific diagnosis	Histological diagnosis
Multiloculated ovarian cyst	26 (28.5)	Mucinous cystadenoma (19)	Mucinous cystadenoma (16) Serous cystadenoma (2) Simple cyst (1)
		No specific diagnosis (7)	Infarcted ovarian cyst (2) Chronic oophoritis (2) Pyosalpinx (1) Torsion ovary (1) Mucinous cystadenoma (1)
Ground glass appearance	17 (18.7)	Endometriotic cysts (17)	Endometriotic cysts (16) Granulosa cell tumour (1)
Clear cyst	13 (14.3)	Serous cystadenoma (12)	Serous cystadenoma (8) Mucinous cystadenoma (4)
		No specific diagnosis (1)	Torsion ovary (1)
Solid tumours	9 (9.4)	Fibroma (4)	Fibroma (4)
		No specific diagnosis (5)	Fibroma (1) Haemorrhagic cyst (2) Ruptured corpus luteal cyst (2)
Cysts with bright echoes with posterior acoustic shadowing	7 (7.7)	Dermoid cysts (7)	Dermoid cyst (7)
Cysts with hyperechoic lines	5 (5.5)	Dermoid cysts (5)	Dermoid cyst (5)
Spider in a web appearance	5(5.5)	Peritoneal inclusion cyst (5)	Peritoneal inclusion cyst (5)
Unilocular cyst with normal ovary adjacent to the cyst	4(4.4)	Paraovarian cyst (4)	Paraovarian cyst (4)
Reticular lacy network	2 (2.2)	Haemorrhagic cyst (2)	Peritoneal inclusion cyst (1) Granulosa cell tumour (1)
Unilocular with incomplete septation	3 (3.3)	Hydrosalpinx (3)	Hydrosalpinx (3)

[Table/Fig-2]: Diagnosis of benign adnexal masses (n=91) based on pattern recognition compared with histology.

Ultrasound characteristics	Number n = 45 (%)	USG specific diagnosis	Histological diagnosis
Multilocular with solid area	11 (24.4)	Mucinous cystadeno-carcinoma (4)	Mucinous cystadenocarcinoma (2) Serous cystadenocarcinoma (1) Fallopian tube carcinoma (1)
		No specific diagnosis (6)	Serous cystadenocarcinoma (6)
		Borderline tumour (1)	Endometriotic cyst (1)
Unilocular cyst with solid area which has irregular borders	10 (22.2)	No specific Diagnosis (10)	Clear cell tumours (3) Mucinous cystadenocarcinoma (1) Serous cystadenoma* (2) Serous cystadenocarcinoma (1) 3 - Endometrioid tumour (3)
Unilocular, solid with papillae	4 (8.8)	Serous cystadeno-carcinoma (4)	Endometrioid tumour (1) Serous cystadenocarcinoma (3)
Multilocular, solid area with papillae	5 (11.1)	No specific diagnosis (5)	Serous cystadenocarcinoma (5)
Solid tumours	15 (33.3)	Germ cell tumour (6)	Dysgerminoma (2) Yolk sac tumour (2) Mixed germ cell tumour (1) Granulosa cell tumour (1)
		Sexcord stromal tumour (1)	Sertoli leydig cell tumour (1)
		No specific diagnosis (8)	Endometrioid tumour (4) Serous cystadeno carcinoma (1) Steroid cell tumour (1) Fibroma (2)

[Table/Fig-3]: Diagnosis of malignant adnexal masses (n=45) based on pattern recognition compared with histology.
RMI – Risk of Malignancy Index.

Final Diagnosed as per histopathology	Malignant (42)	Benign (94)	Test efficacy
RMI			Sensitivity: 78.6% Specificity: 96.8% PPV: 91.7% NPV: 91%
RMI ≥200	True malignant-33	False malignant-3	
RMI<200	False benign-9	True benign-91	
Pattern recognition			Sensitivity: 95.2% Specificity: 94.7% PPV: 88.9% NPV: 97.8%
Benign pattern	False benign-2	True benign-89	
Malignant pattern	True malignant-40	False malignant-5	

[Table/Fig 4]: Comparison of RMI 3 versus pattern recognition.

Sl. No.	HPE	Meno-pausal status	Specific tumour marker	U x M x specific tumour marker	Original RMI
1	Stage 3 dysgerminoma	Pre-menopausal	LDH = 4387 IU/L	3 (solid tumour with ascites) x1x4387 =13,161	3 x 1 x 13.2 =39.6
2	Stage 1 dysgerminoma	Pre-menopausal	LDH = 2064 IU/L	1x1x2064 =2064	1 x 1 x 11.8 =11.8
3	Stage 1 yolk sac tumour	Pre-menopausal	AFP=26,957 ng/ml	1 x 1 x 26,957 =26,957	1 x 1 x 133 =133
4	Stage 3 yolk sac tumour	Pre-menopausal	AFP=9423 ng/ml	3(solid tumour with ascites) x1x9423 =28,269	3 x 1 x 390 =1170
5	Stage 3 mixed germ cell tumour	Pre-menopausal	AFP=984 ng/ml	3 (solid tumour with ascites) x 1 x 984 = 2,952	3 x 1 x 108 =324

[Table/Fig-5]: RMI score incorporating specific tumour marker instead of CA125.
HPE- Histopathological evaluation, LDH- Lactate dehydrogenase, AFP- Alpha fetoprotein, U- Ultrasound Score, M- Menopausal Status, RMI- Risk Of Malignancy Index.

nition in the specific diagnosis of benign adnexal masses [9,10]. They found that the highest sensitivities were achieved with simple cysts (100%) and hydrosalpinx (100%). This was followed by mature teratomas (88%), endometriomas (75%), ovarian fibromas (88%), tubo-ovarian abscesses (88%) and serous cystadenocarcinomas (82%). Serous cystadenomas were misdiagnosed most commonly (40.5%). In our study, however five cases of serous cystadeno-carcinoma having sonographic pattern of 'multilocular, solid area with papillae' could not be diagnosed with confidence. The sensitivity of subjective assessment in diagnosing adnexal torsion in the aforementioned study was 54%. Similarly in our study too, both the cases of adnexal torsion were not given any specific diagnosis.

On excluding the ten cases of non epithelial origin from our study sample, the sensitivity of RMI3 increased from 78.6% to 94% with a specificity of 96.8%. Thus, it can be inferred that the efficacy of RMI3 is equal to pattern recognition in identifying epithelial ovarian cancers.

More or less similar efficacy has been reported for RMI3 in other recent studies too (sensitivity of 85%, a specificity of 91%, a PPV of 60%, and a NPV of 97.8%) [11-13]. Pattern recognition confers a sensitivity of 95.2% as compared to 78.6% by RMI3, with a slight compromise in the specificity (94.7% versus 96.8%). The reason for a lower sensitivity of RMI3 may be due to the fact that CA125 is usually not much elevated in stage I disease, which is a determinant in RMI3 index calculation [14]. Another interesting observation was made by Lennox GK et al., that the scoring systems for triaging ovarian malignancies do not perform well in patients with stage I disease where endometriod and clear cell histologies predominate [12]. Similar trend was seen in our study too where RMI score was not found to be similarly efficient for early stage or non epithelial ovarian cancer. We realized that six of the nine malignant cases which were misdiagnosed as benign by RMI3, were non epithelial in origin. So in case if we have suspicion by sonography and RMI is not matching, it is worthy to test for other tumour markers and then replacing CA125 in RMI with the specific tumour marker [Table/Fig-5].

LIMITATION

Though the sample size here is inadequate to propose for the substitution of a specific tumour marker instead of CA125 in non epithelial tumours. Further prospective studies with large number of non epithelial tumours are required to validate this proposal.

CONCLUSION

Pattern recognition was superior to RMI3 for discriminating benign and malignant adnexal masses. RMI3 was not able to identify epithelial ovarian cancer stage I, germ cell tumours, and sex cord stromal tumours. RMI3 may be useful when experienced sonographer is unavailable.

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