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Original Research Article

The study of the correlation between international ovarian tumour analysis classification, risk of malignancy index and clinicopathological findings of adnexal masses

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ABSTRACT

Background: Adnexal masses of ovarian origin are of growing concern these days due to high fatality associated with ovarian malignancy because they are diagnosed at advanced stage due to vague symptoms and absence of recommended screening tests. The present study aimed to assess the prediction potential of IOTA classification and RMI to clinicopathological findings of adnexal masses and calculate the sensitivity and specificity of same.
Methods: This was a prospective observational study carried out on 96 non pregnant women presenting with adnexal mass to gynaecology OPD of a tertiary care hospital from 2020 to 2022. They were evaluated preoperatively with complete history, examination, ultrasound, and tumor markers. IOTA score and RMI was calculated for all patients. Following surgery, histopathology results were compared with preoperative evaluation. Statistical Analysis was done.
Results: Mucinous cyst adenoma was the most common benign ovarian tumour, serous cystadenocarcinoma being the most common malignant ovarian tumour. Patients with malignancy were older and mostly postmenopausal. IOTA was found better than RMI with higher sensitivity 98.5% and high PPV 98.5%. Similarly, IOTA had higher specificity 91.7% and higher NPV 91.7% for identifying and prediction of benign patients.
Conclusions: IOTA guidelines to describe sonographic features of adnexal masses have shown a high sensitivity and specificity for prediction of malignancy in adnexal masses and is a more reliable diagnostic tool over RMI tool for differentiation between benign and malignant adnexal masses.

Keywords: Adnexal masses, IOTA, Ovarian cancer, RMI

INTRODUCTION

Adnexal masses of ovarian origin are the most commonly encountered gynecological problem.[1,2] Of them, malignant epithelial ovarian tumors are associated with the highest mortality of all gynecological cancers.[3] Most ovarian cancers are diagnosed at advanced stages, with 5-year survival as low as 10% and the disease accounts for approximately half of all deaths related to gynecological cancer. Early diagnosis provides 5-year survival rate up to 90%.[4] Appropriate preoperative evaluation to discriminate between benign and malignant adnexal masses helps guide gynecologists refer women with suspected malignancies to a gynecologic-oncologist for appropriate therapy and optimal debulking, which is known to improve survival rate.[2] Pelvic ultrasound is the gold standard for ovarian masses diagnosis with 90% sensitivity and a specificity of 80%. However, only 50% of ovarian masses are characterized by sonography which makes need of an efficacious scoring system imperative.[5]

Different methods have been developed to predict the likelihood of malignancy in a pelvic mass found on

ultrasound.[6-9] Prediction models assist clinicians to determine the malignancy risk of ovarian cyst and decide the appropriate treatment pathways avoiding possible mistakes. They require an accurate description of the ultrasound image in order to characterize it as well as possible: lesion' size, unilocular or multilocular appearance, smooth tumor, presence of papillary projections and/or solid components and/or acoustic shadow, Doppler score and association with ascites.

The IOTA group (International Ovarian Tumor Analysis) developed clinically useful ultrasound criteria that can be used to classify most adnexal masses as probably benign or probably malignant: the IOTA classification based on ten ultrasound simple rules published by Timmerman in 2008 and validated by several other studies.[10-13] It has a reported sensitivity of 92% and specificity of 96%. IOTA simple rules are one of the best methods but are inconclusive in 25% of cases, where subjective assessment by an expert sonographer is recommended but may not always be available.

In order to improve test' performance, several multimodal prediction models are available to improve test' performance i.e., the RMI (Risk of Malignancy Index), the logistic regression models (LR1 and LR2) or the ADNEX (Assessment of Different Neoplasias in the adneXa) model of the IOTA group. Risk of Malignancy Index (RMI), which is a product of the ultrasound morphological features, menopausal status and serum tumour marker CA125. This has been recommended by the Royal College of Obstetricians and Gynaecologists (U.K.) guidelines. RMI has a pooled sensitivity of 78% and specificity of 87%.[14]

Knowledge of the specific type of adnexal pathology before surgery is likely to improve patient triage with a high accuracy, and it also makes it possible to optimize treatment. The correct identification of stage I cancer being particularly important. In advent of same the present study was planned to test the sensitivity and specificity of IOTA rules and RMI model as prediction models to discriminate between benign and malignant adnexal masses. An assessment of the correlation of two screening tests i.e., international ovarian tumour analysis (IOTA) classification and risk of malignancy index (RMI) to clinicopathological findings of adnexal masses was also done.

METHODS

After approval from the institutional ethical committee (IEC), this prospective observational study was undertaken on 96 non-pregnant women with adnexal masses presenting to OPD and IPD at Department of Obstetrics and Gynaecology, B.J. Govt. Medical College, Pune from 2020 to 2022 (18 months). All women qualifying the inclusion criteria were enrolled for the study after taking an informed, written voluntary consent.

Inclusion criteria

All non-pregnant women with adnexal masses reporting to gynaecology outpatient department and willing to participate in the study and gave consent were included in the study.

Exclusion criteria

All women coming with histopathological report for further treatment and are found to have masses of uterine and GI origin were excluded from the study

Procedure

All gynaecological cases fulfilling the inclusion and exclusion criteria were selected from gynaecology OPD and gynaecology ward of tertiary health care centre under study. Detailed history (Chief complain, menstrual history, LMP, Obstetric history, H/O any medical illness, family history and socioeconomic status) of all cases was taken, examined thoroughly and investigated. We obtained informed, written voluntary consent from all patients before enrolment. We used a structured interviewer-administered proforma to collect demographic data and gynecological anamnesis and performed thorough general and perabdominal examination. Investigations done included complete blood count, renal function test, liver function test BSL profile, thyroid function test, Urine routine and microscopy and Serum CA-125 level. Ultrasonography (transabdominal or transvaginal) was done looking for size, septations, ascites, solid components and Doppler study.

We sent blood samples for tumor markers relevant to different age groups. International Ovarian Tumor Analysis and Risk of malignancy index (RMI) was done for different age groups and masses were classified as "likely malignant," "benign," or "indeterminate" (moderate) as per IOTA and benign and malignant as per RMI. We noted the intraoperative findings of each patient and sent tissue specimen for histopathology. Histopathologic findings were analyzed to make the final diagnosis and stage of the disease. International FIGO staging criteria (2014) was used for final staging of the disease. All the histopathologic examinations of the specimens were done by pathologists to whom the ultrasonographic findings, tumor markers, and intra-operative findings were not revealed. Histopathologic diagnosis was regarded as a gold standard for evaluation of results to classify malignant and benign mass.

Statistical analysis

All data were recorded on a structured pro forma and tabulated. Statistical analysis of the demographic data was performed using SPSS Software Version 20.0. The sensitivity and specificity of the IOTA classification and Risk of malignancy index (RMI) was calculated. The

collected data was analysed by using Chi square test and results were compiled. P<.05 was considered to be statistically significant.

RESULTS

Out of 96 patients evaluated, majority of patients i.e.,29 (30.2%) belonged to age group 30-40 years with 76 % in the reproductive age group of 20-49 years. The incidence of malignancy was found to be 15.6% in the present study. As per IOTA outcome a higher proportion i.e., 68 (70.8%) was for benign outcome followed by 16 (16.7%) which were inconclusive and the lowest proportion i.e., 16 (12.5%) was for malignant outcome respectively. The distribution of histologic types of adnexal masses in the present study showed the higher proportion of benign tumors i.e., 81 out of 96 (84.4%) with maximum 36 (37.5%) mucinous cyst adenoma. Whereas, amongst 15 Malignant tumours mucinous adenocarcinoma was most common with 7 (7.2%) (Table 1).

As per RMI outcome, most of the benign tumours were found in 30-40 years age group i.e., 25 (25 out of 29 i.e., 86.2%; 4 were malignant) with 13 (56.5%) benign tumours and 10 (43.5%) malignant. Similarly, in IOTA method max no. of patients i.e., 29 (benign: 23, inconclusive: 5, malignant: 1) belonged to 30-40 years, However, in histopathological test max no. of patients with benign tumors belonged to 30-40 years (28 benign 1 malignant). Results of all the three tests were in concurrence with each other with a slight variation which can be explained by the difference in the methodology used.

Table 1: Distribution on basis of RMI, IOTA & HPR outcome.

RMI outcome	Frequency	Percent
Malignant	24	25.0
Benign	72	75.0
Total	96	100.0
IOTA outcome		
Benign	68	70.8
Inconclusive	16	16.7
Malignant	12	12.5
Total	96	100.0
HPR outcome		
Benign	81	84.4
Malignant	15	15.6
Total	96	100.0

Benign lesions were significantly more common in patients below 50 years and malignant above 50 years. 8 out of 20 patients had malignant tumors with 4 in age group 60-70 years, 3 in age group 50-60 years and 1 in 80 years (Figure 1, Figure 2).

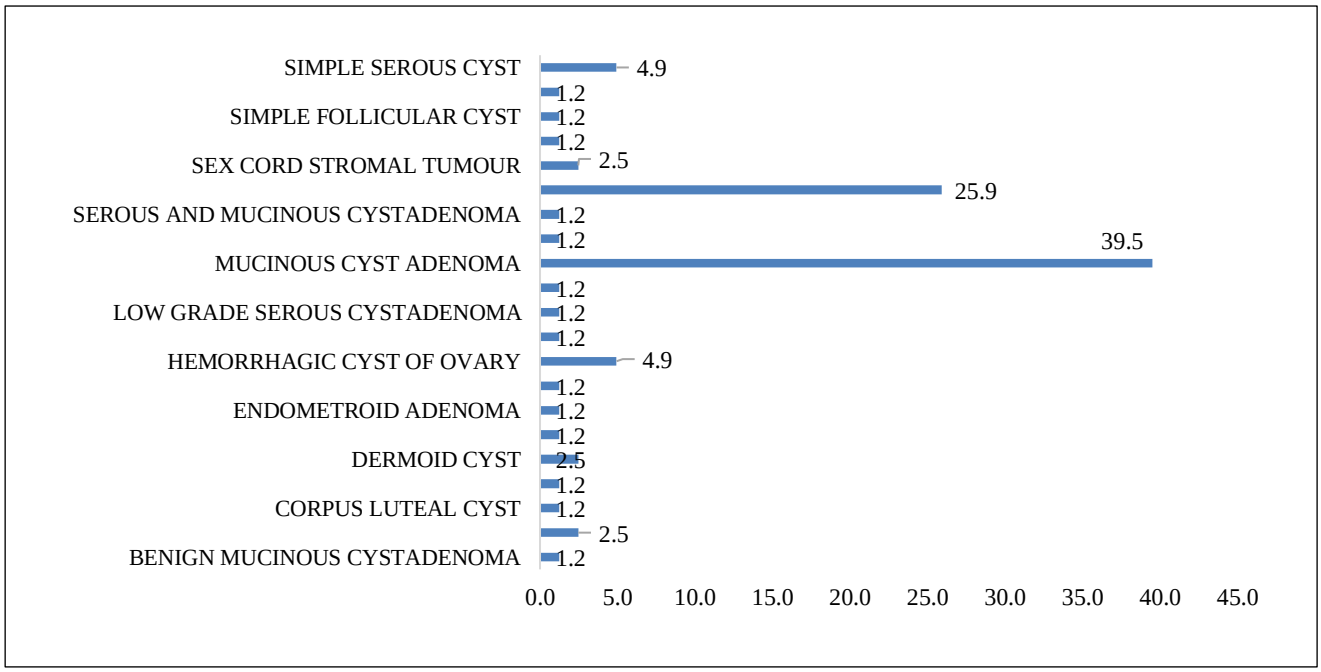

Figure 1: Distribution on basis of HPR report for benign cases.

Higher specificity 85.2% and higher NPV 95.8% OF RMI method shows that this can be used as method for identifying the benign patients. Hence, we can conclude that RMI method is more accurate in identifying and prediction of the negating benign cases as compare to identifying and prediction of positive malignant cases.

Higher sensitivity 98.5% and high PPV 98.5% suggestive that IOTA can be used as method for identifying and prediction of malignant patients. Similarly, higher specificity 91.7% and higher NPV 91.7% of IOTA method shows that this can be used as method for identifying and prediction of benign patients (Table 2).

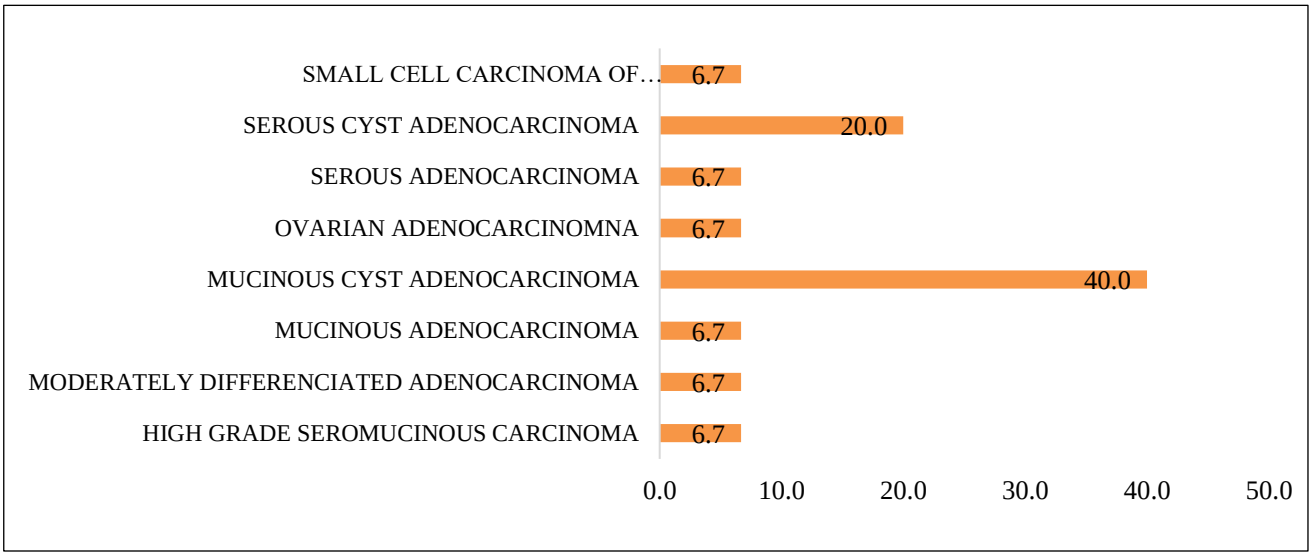

Figure 2: Distribution on basis of HPR report for malignant cases.

Table 2: Sensitivity and specificity of RMI and IOTA method.

RMI outcome	HPR outcome		Total
	Benign	Malignant	
Malignant	12	12	24
	14.8%	80.0%	25.0%
Benign	69	3	72
	85.2%	20.0%	75.0%
Total	81	15	96
	100.0%	100.0%	100.0%
Sensitivity	80.0%		
Specificity	85.2%		
PPV	50.0%		
NPV	95.8%		
IOTA outcome	HPR outcome		Total
	Benign	Malignant	
Benign	67	1	68
	98.5%	8.3%	85.0%
Malignant	1	11	12
	1.5%	91.7%	15.0%
Total	68	12	80
	100.0%	100.0%	100.0%
Sensitivity	98.5%		
Specificity	91.7%		
PPV	98.5%		
NPV	91.7%		

DISCUSSION

In the present study we compared the accuracy of two promising methods of detecting ovarian malignancy i.e., RMI (Risk Malignancy Index) and IOTA (International Ovarian Tumour Analysis) method and compared it with the histopathological findings which is considered as the gold standard method for diagnosing ovarian malignancy. It is already known that operative findings are gold standard for determining the origin, size and laterality of adnexal masses. But it is an invasive technique. So, the quest for seeking a non-invasive yet accurate diagnostic method led to the present research.

Majority of patients i.e., 29 (30.2%) belonged to age group 30-40 years with 76 % in the reproductive age group of 20-49 years. This was in concurrence with studies done Rai et al, Badkur et al which also showed that adnexal masses occur with maximum frequency in reproductive age group i.e., 20-49 years.[15,16] This suggest that prevalence of benign and malignant adnexal masses was more common in reproductive age group and a significant linear trend of increasing age and higher chances of malignancy was also observed.

As per RMI outcome, the higher proportion i.e., 72 (75.0%) was for benign outcome and the lower proportion i.e., 24 (25.0%) was for malignant outcome respectively. It has been suggested that low RMI score was significantly associated with benign lesions and high RMI score with malignant lesions. The study done by Rai et al showed that RMI had correlation in diagnosing epithelial ovarian malignancies.[15] High RMI in post-menopausal women having adnexal mass is usually associated with malignancy. Thus, RMI can be used as a valuable indicator for early diagnosis of malignancy in adnexal mass. However, as per IOTA outcome which is more of evidence-based test, a higher proportion i.e., 68 (70.8%) was for benign outcome followed by 16 (16.7%) which were inconclusive and the lowest proportion i.e., 16 (12.5%) was for malignant outcome respectively.

The RMI and IOTA outcome were correlated with Histopathological findings to assess the accuracy of the two methods. The histopathological findings reported a higher proportion i.e., 81 (84.4%) was for benign outcome and the lower proportion i.e., 15 (15.6%) was for malignant outcome respectively. The incidence of

malignancy was found to be 15.6% in the present study. This was similar to the study done by Acharya et al, Rai et al.[17,15] However, Sharadha et al and Javdekar et al reported an incidence of 4.1% and 9.5% respectively Both studies were done in India and reported a low incidence compared to our study.[18,19] However, Badkur et al, in their study done in Northern India reported incidence of malignancy among adnexal masses was 19.3%.[16] The high incidence of malignancy seen in our study could be due to referral bias since our hospital is a tertiary centre catering gynaecologic-oncology service.

The distribution of histologic types of adnexal masses in the present study showed the higher proportion of benign tumours i.e., 81 out of 96 (84.4%) with maximum 36 (37.5%) mucinous cyst adenoma. Whereas, amongst 15 Malignant tumours mucinous adenocarcinoma was most common with 7 (7.2%). The results were in concurrence with results of study done by Badkur et al, who reported that benign adnexal masses constitute 80.96% and malignant masses constitute 19.04% of all adnexal masses.[16] The most common is benign ovarian masses (42.85%). Similarly, Rai et al, in their study reported 15% of women presenting with adnexal mass had an ovarian malignancy.[15] Epithelial ovarian cancers accounted for a majority of them, the rest being metastatic from other primaries.

Benign lesions were significantly more common in patients below 50 years and malignant above 50 years. 8 out of 20 patients had malignant tumors with 4 in age group 60-70 years, 3 in age group 50-60 years and 1 in 80 years. This was in concurrence with results of studies done by Rai et al, Acharya et al and Badkur et al.[15,18,16] Women above 50 years were shown to have significantly increased risk of ovarian malignancy. We recommend screening women above 50 years for ovarian malignancy when they present to the clinic with suggestive symptoms because there is a lifetime risk of 1-1.5% of having ovarian cancer.[20,21]

In our study, we have used RMI for preoperative evaluation to differentiate benign and malignant adnexal masses. The accuracy of RMI to differentiate between the two was statistically significant overall as well as specifically for epithelial ovarian cancers. However, few cases were wrongly classified which resulted in overall low sensitivity. The higher sensitivity 80% and moderate PPV 50% shows that RMI method can be used as method for identifying the malignant patients. Similarly, higher specificity 85.2% and higher NPV 95.8% OF RMI method shows that this can be used as method for identifying the Benign patients. Hence, we can conclude that RMI method is more accurate in identifying and prediction of the negating benign cases as compare to identifying and prediction of positive malignant cases.

Preliminary findings given our limited sample size suggest our current method of calculating RMI scores for preoperative prediction of epithelial ovarian malignancy is of only moderate efficacy. This could have been due to use of only gray-scale ultrasound. These findings were similar to Badkur et al.[16]

Further, we also analyzed the efficacy and efficiency of IOTA and it showed higher sensitivity 98.5% and high PPV 91.7% suggestive that IOTA can be used as method for identifying and prediction of malignant patients. Similarly, higher specificity 98.5% and higher NPV 91.7% of IOTA method shows that this can be used as method for identifying and prediction of benign patients. Hence, we can conclude that IOTA method is equally accurate in identifying and prediction of the negating benign cases as well as identifying and prediction of positive malignant cases and thus holds better sensitivity and specificity over RMI method. As reported by Abbas et al, combining gray-scale ultrasound with color Doppler study and incorporating International Ovarian Tumor Analysis (IOTA) rules to describe sonographic features of adnexal masses have shown a high sensitivity and specificity for prediction of malignancy in adnexal masses.[21]

The main limitations of the study were its hospital-based nature which predisposes to referral bias and increased prevalence of malignancies compared to the general population.

CONCLUSION

Whilst the outcomes for patients with ovarian cancer clearly benefit from centralised, comprehensive care in dedicated cancer centres, unfortunately the majority of patients still do not receive appropriate specialist treatment. Any improvement in the accuracy of current triaging and referral pathways whether using new imaging tests or biomarkers would therefore be of value in order to optimise the appropriate selection of patients for such care. In Conclusion, International Ovarian Tumor Analysis guidelines to describe sonographic features of adnexal masses have shown a high sensitivity and specificity for prediction of malignancy in adnexal masses and is a more reliable diagnostic tool over RMI tool for differentiation between benign and malignant adnexal masses.

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