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# Comparison of Rmi (Risk Malignancy Index) and Simple Rules Risk Model In Evaluation of Adnexal Masses Taking Histopathology As Gold Standard

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## ABSTRACT

***Objective:*** To compare ultrasound grounded International Ovarian Tumor Analysis (IOTA) prediction models, specifically, the ADNEX models, the Simple Rules (SRs) and the Risk of Malignancy Index (RMI), for the adnexal masses' diagnosis before any surgical intervention

***Study Design:*** Cross-sectional analytical study

***Place and Duration of Study:*** Obstetrics and Gynecology Department. Pakistan Emirates Military Hospital, Rawalpindi, Pakistan from Aug 2019 to Jun 2020.

***Methodology:*** Five hundred and twenty-four patients took part in this cross-sectional Analytical study. All findings on ultrasound were evaluated and prognostic models were used. Histopathology findings were used as standard for comparison. Diagnostic performances of the prediction models were assessed by estimating sensitivities, ROC curves, negative predictive values and positive predictive values, specificities, diagnostic odds ratios and negative and positive likelihood ratios.

***Results:*** The ROC under curves (AUC) areas for ADNEX models were 0.94 (0.92-0.96, 95% CI) with CA125 and 0.94 (0.91-0.96, 95% CI) without CA-125 for RMI I-III It was expressively advanced than AUC: 0.83 (CI95%, 0.80 to 0.86), 0.82 (CI95%, 0.78 to 0.86 and 0.87 (CI95% 0.83 to 0.90) (all $p$ <0.0001). The CA-125 had a cut-off point of 10% in ADNEX model had the maximum precision (CI: 95%, 0.87 to 0.97) equated to other models. The SR model achieved 0.93 (95% CI 0.86 to 0.97) sensitivity and 0.86 (95% CI 0.82 to 0.89) specificity when not diagnosed was classified as definite (11.7%) malignant.

***Conclusions:*** ADNEX and Simple rules risk models were excellent for characterizing adnexal masses better than RMI in Pakistani patients.

**Keywords:** Adnexal mass; Benign masses; Transvaginal ultrasound

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## INTRODUCTION

Ovarian cancer has the most elevated death frequency and noticeably terrible anticipation among gynecological malignancies. The normal 5-year endurance rate for ovarian malignancies is <50%. It is important to precisely portray considerate and dangerous ovarian masses to upgrade treatment and improve endurance in patients with proper staging in ovarian tumors, and to prevent unnecessary surgical interventions and keep up fertility in patients with malignant ovarian tumors.[1-2] Transvaginal ultrasound is commonly utilized method for imaging in preoperative evaluation of adnexal masses. Ultrasound evaluation by Gynecological consultants have been considered as the best ways to evaluate adnexal masses in clinical practice.[3]

Distinctive ultrasound expectation models have been created to precisely recognize malignant and benign tumors on the grounds that the quantity of experienced examiners is deficient and isn't accessible in certain zones.[4] The malignancy index (RMI), representing CA-125 levels of menopausal status, ultrasound findings and serum cancer antigen (CA), is a prediction model proposed by several nationwide guidelines.[5]

In any case, the methods used to figure RMI are very tedious and their symptomatic viability is unacceptable. The IOTA introduced an accord on the ultrasound properties of adnexal tumors at the start of 20th century, and additional analytic models, including Simple Rules (SRs) or simple ultrasound-based rules model, Logistic Regression model and the Valuation of Diverse Neoplasia's in the adnexa (ADNEX) model.[6-8] The consequences of past outer approval examination have demonstrated that the SR model is difficult to utilize and has great indicative execution, however it is not reasonable for every genuine beneficiary.[9] The ADNEX model is perfect for

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the separation of harmful and amiable tumors and shows the phases of dangerous tumors.[10] Limited local data has been available in this regard. We therefore planned this study with the rationale to compare the ADNEX and SR models, as well as RMI, in their ability to distinguish amid malignant and benign expanding masses.

## METHODOLOGY

This cross-sectional study held in the Obstetrics and Gynecology department of Pakistan Emirates Military Hospital, Rawalpindi from March 2019 to March 2020. Non probability consecutive sampling technique was used to gather the sample for this study. Sample size was calculated by WHO sample size calculator by using population prevalence proportion of malignant adnexal masses as 12.7%.[10]

**Inclusion Criteria:** The patients who had a mass ≥ 1 cm with a diagnosis of adnexal mass on ultrasound were included.

**Exclusion Criteria:** If any patient was not ready to participate in the study or did not endure surgery with ovarian recurrence or had ectopic pregnancy or bilateral adnexectomy already or patients with incomplete clinical data were excluded.

SR models, RMI (I-III) variants and diagnostic performance of ADNEX were assessed in the women operated on to eradicate adnexal masses at the Obstetrics and Gynecology department.

Preoperative transvaginal ultrasound was performed on all patients. Transabdominal ultrasound examination was achieved when a malignant tumor was assumed and the mass was very huge to be assessed only by transvaginal ultrasound. After the examination on ultrasound, we used the three RMI variants and ADNEX model to compute the risk of cancer without knowing the histological results. When more than one adnexal mass was detected, we analyzed with complex ultrasonographic morphology and selected the largest mass when the masses had similar morphological properties. Formerly to the ultrasound examination, clinical data was gathered regarding the age of patient, menopause, former cancers and ovarian cancer family history. Patient preoperative CA-125 levels were also assessed.

The ADNEX model consists of 9 markers with 3 clinical variables and six ultrasonic variables. After an objective presentation of all predictors, malignant or benign mass probability indicators are displayed numerically or graphically. Because this was the first multi-class predictive model for adnexal masses, it had been shown that the mass will be an Ovarian Cancer stage I, borderline ovarian tumor (BOT), Ovarian Cancer stage II-IV, or metastasis are accessible. The versions available for ADNEX model can exclude or include CA-125 levels, and in this study, we assessed the ADNEX model predictive accuracy with and deprived of CA-125.The SR model contains a set of guidelines grounded on 5 features of ultrasound that show benign (B features) and 5 malignant (M features). Its labelled as benign lesion if ≥ 1 B-characteristic is existing in the nonappearance of any M-features, and if ≥ 1 M- characteristic is existing in the nonappearance of any B-features was taken as malignant. If both M and B and clinical signs are existing or if no topographies are contemporary, the model vintages an indecisive result. 3 main types of the RMI scoring system (RMI-III, RMI-II and RMI-I) were used to combine ultrasound results, CA125 serum levels and determine menopause status.

Tissue samples gained through operation were analyzed by a group of pathologists specializing in gynecological pathology examinations. The WHO cancer classification strategies were applied for Tumor's classification. The stages of malignant tumors are determined by means of the criteria of International Federation of Gynecology and Obstetrics.

Diagnostic performance measures including specificity, sensitivity, PPV and NPV, diagnostic probability rates (DOR) and positive and negative probability rates were considered to assess the classification of malignant or benign tumor models by cut off points from earlier researches. The ultrasound and CA-125 levels associated clinical characteristics related with malignant and benign tumors were related; To analyze categorical data; Fisher's exact and Chi-square test were used and for continuous data; Mann-Whitney U test was applied. Statistical analyzes were achieved with version 15.2.2 MedCalc Statistical Software and SPSS version 22.0. BOTs were measured malignant for statistical analysis. All statistical calculations were done using CI of 95% and the p-value of less than 0.05 value was measured significant statistically.

## RESULTS

Initially 591 women were approached to participate in the study but after the application of inclusion and exclusion criteria 524 patients were included with 385(73.5%) benign masses and

139(26.5%) malignant lesions. Table-I shows histological results. Most commonly seen tumor was endmetrioma 106(74.8%). Sclerosing ovarian tumors 02(0.4%) and ovarian lymphomas 02(0.4%) were least commonly seen in our study participants.

**Table-I: The Histological Consequences of 524 Adnexal Masses and Its Distributions**

| The adnexal masses Histological types | n(%) |
|---|---|
| Endometrioma | 106(20.20%) |
| Benign | 392(74.8%) |
| Teratoma | 54(10.3%) |
| Serous cystadenoma | 74(14.1%) |
| Hydrosalpinx | 37(7.1%) |
| Mucinous cystadenoma | 35(6.7%) |
| Mesosalpinx cyst | 15(2.9%) |
| Fibrothecoma | 20(3.8%) |
| Cystadeno fibroma | 7(1.3%) |
| Par-ovarian cyst | 16(3.1%) |
| Adenofibroma | 5(1%) |
| Fibroma | 7(1.3%) |
| Peritoneal mesothelioma | 4(0.8%) |
| Brenner tumor | 5(1%) |
| Sclerosing stromal tumor | 2(0.4%) |
| Sertoli-Leydig cell tumour | 3(0.6%) |
| Other ovarian benign lesion | 21(4%) |
| Tuberculosis | 2(0.4%) |
| Serous | 15(2.9%) |
| Borderline | 35(6.7%) |
| Endometrioid | 4(0.8%) |
| Mucinous | 15(2.9%) |
| Serous adenocarcinoma | 48(9.2%) |
| Primary ovarian malignant | 73(13.9%) |
| Endometrioid adenocarcinoma | 11(2.1%) |
| Clear cell carcinoma | 16(3.1%) |
| Sertoli-Leydig cell tumor | 3(0.6%) |
| Mucinous adenocarcinoma | 4(0.8%) |
| Granulosa cell tumor | 3(0.6%) |
| Carcinosarcoma | 3(0.6%) |
| The ovary diffuse large B cell lymphoma | 2(0.4%) |
| Seromucinous adenocarcinoma | 2(0.4%) |
| Stromal carcinoid of ovary | 2(0.4%) |
| Small cell neuroendocrine carcinoma | 2(0.4%) |
| Gastric cancer | 11(2.1%) |
| Metastasis | 21(4%) |
| Cholangiocarcinoma | 3(0.6%) |
| Appendiceal adenocarcinoma | 4(0.8%) |
| Pancreatic cancer | 3(0.6%) |
| Breast cancer | 3(0.6%) |

## DISCUSSION

We looked at the symptomatic presentation of ADNEX models just as SR and RMI. RMI was the primary clinically utilized prognostic model and was the most generally utilized model in numerous locales.[11] Nevertheless, the results of our study indicated that the ADNEX model performed better than each of the three RMI variations in recognizing the kind of harmful masses. The ADNEX model, which does exclude CA-125, has a higher AUC (both 0.94) for RMI variations than those made in the 0.82 to 0.87 territory.[12] The ADNEX model indicated better symptomatic execution and higher affectability than RMI in our investigation. Hereafter, the ADNEX model may recognize preoperative adnexal masses better than other models in Pakistani patients.

**Table-II: Ultrasound Features and Clinical Characteristics For 524 Patients with Adnexal Masses**

| Features | Benign (n = 385) | Malignant (n = 139) | *p*-value |
|---|---|---|---|
| Age in years | 51(41-61) | 64(52-73) | < 0.001a |
| Premenopausal | 294(76.4%) | 72(51.8%) | |
| Menopausal status | | | |
| CA125 (U/mL) | 20(21-48) | 64(28-527) | < 0.001a |
| Postmenopausal | 110(28.6%) | 86(61.9%) | |
| Maximal diameter of lesion (mm) | 66(54-82) | 88(60-136) | < 0.001a |
| Presence of solid tissue | 127(33.0%) | 126(90.6%) | < 0.001b |
| Family history of ovarian cancer | 0(0.0%) | 21(15.1%) | 0.013c |
| Presence of papillary projections | 58(15.1%) | 65(46.8%) | < 0.001b |
| Proportion solid tissue if present (mm) | 41(27-56) | 54(30-75) | < 0.001a |
| 0 | 346(89.9%) | 93(66.9%) | |
| 1 | 40(10.4%) | 32(23.0%) | |
| 2 | 25(6.5%) | 22(15.8%) | |
| 3 | 24(6.2%) | 24(17.3%) | |
| 3 | 26(6.8%) | 44(31.7%) | |
| > 10-cyst locules | 30(7.8%) | 41(29.5%) | < 0.001b |
| Ascites | 21(5.5%) | 54(38.8%) | < 0.001b |
| Acoustic shadows | 62(16.1%) | 0(0.0%) | < 0.001c |

Preoperative assessments utilizing the SR model were strong with an exactness of 0.93 (CI95% 0.86 to 0.97) and a sensitivity of 0.86 (95% CI 0.82 to 0), 89) for adnexal masses with dubious ordered conclusions as pernicious; These outcomes are like the results of studies done in the past by Knafel et al. and Auekitrungrueng et al. in 2016 and 2019 respectively.[13-14] The IOTA SR model was perceived by clinicians as a viable prescient model for adnexal masses and was suggested for use in the 2011 Green-Top Strategies. As of late, the College of Obstetrics and Gynecology has incorporated the SR model in clinical practice rules for appraisal and treatment of adnexal

masses. In light of the accord in regards to the primary precisely thinks about the ultrasound-based IOTA and

**Table-III: Diagnostic Efficacy of The Prediction Models For Discernment Among Malignant And Benign Adnexal Masses**

| Valuation criteria | tAUC | Sensitivity | Specificity | Positive predictive value | Negative predictive value | LR+ | LR- | DOR |
|---|---|---|---|---|---|---|---|---|
| ADNEXN125 | 0.95(0.92–0.97) | 0.94(0.88–0.98) | 0.75(0.70–0.80) | 0.79(0.74–0.84) | 0.93(0.88–0.96) | 3.61(3.01-4.32) | 0.10(0.06–0.21) | 40.1 |
| ADNEX125 | 0.95(0.93–0.97) | 0.94(0.88–0.98) | 0.77(0.73–0.82) | 0.81(0.76–0.85) | 0.93(0.88–0.96) | 3.94(3.21–4.73) | 0.10(0.04–0.23) | 43.77 |
| MAL+ SRs | Nil | 0.94(0.87–0.98) | 0.87(0.83–0.90) | 0.88(0.83–0.92) | 0.93(0.89–0.96) | 5.92(5.05–7.83) | 0.10(0.06–0.17) | 71.43 |
| SRs + BE | NA | 0.70(0.61–0.78) | 0.97(0.94–0.98) | 0.95(0.91–0.98) | 0.77(0.71–0.81) | 15.83(9.67–25.94) | 0.33(0.26–0.43) | 49.54 |
| RMI-I | 0.88(0.84–0.91) | 0.56(0.47–0.65) | 0.94(0.91–0.97) | 0.90(0.84–0.95) | 0.68(0.63–0.73) | 9.01(5.34–11.21) | 0.49(0.44–0.60) | 15.87 |
| RMI-II | 0.84(0.81–0.87) | 0.62(0.53–0.71) | 0.93(0.90–0.96) | 0.90(0.84–0.94) | 0.71(0.66–0.76) | 7.96(5.43–11.76) | 0.43(0.34–0.53) | 19.03 |
| RMI-III | 0.83(0.79–0.87) | 0.54(0.45–0.64) | 0.95(0.92–0.97) | 0.91(0.85–0.96) | 0.68(0.63–0.74) | 9.31(5.92–13.59) | 0.51(0.46–0.64) | 19.7 |

worldwide beneficiaries of enhancements, the SR model was proposed as the fundamental analytic methodology.[15] The SR model is anything but difficult to put in clinical training and can be utilized for around 77-90% of adnexal masses. In our examination, the SR model was utilized in roughly 86.8% of patients. At the point when gynecological ultrasound authorities were not accessible, it was understandable to characterize tumors as harmful after dubious analyses utilizing the SR model. In any case, this methodology might be one-sided because of the nearness of threatening tumors in the populace, and about portion of patients with a mellow conclusion may encounter pointless intercessions.[16-17] In Pakistan, the last indicative system of the subsequent stage is required, particularly in progressively inaccessible and less created regions where the quantity of experts in the field of gynecological ultrasound is lacking. Our study results demonstrated that 64 conventions have tumors with unrecognized findings in the wake of applying the SR convention to the ADNEX model, with or deprived of CA-125, and up to 3 RMI variations. Similar phenomenon was described by Perrone et al. in 2020.[18] The AUC of prognostic models for tumors with uncertain conclusions was not extraordinary and might be because of constrained sample size. With regards to distinguishing harmful neoplasms among undiscovered masses, the ADNEX model gave somewhat advanced AUC and DOR than the 3 RMI variations. At the point when gynecological ultrasound pros are not accessible, further research is required to decide whether the ADNEX model is a 2nd-stage demonstrative system for adnexal tumors with questionable analyses.[18,19] This is one of the main investigations in the patient populace in Pakistan that RMI prognostic models with the IOTA accord revelation, which is the quality of the examination. We additionally included conceivably chose and unassigned patients and just patients with complete information were incorporated.

## LIMITATIONS OF STUDY

There were multiple limitations in this study. This was a single focus configuration, may cause examining predisposition and breaking point the relevance of results to different locales.19 What's more, in our investigation, ultrasound assessments were not performed by individuals with various instructive encounters. Further studies are required at different indicative habitats with fluctuating degrees of ultrasound ability in Pakistan.

## CONCLUSION

As a result, our results exhibited that the SR and ADNEX models did well in distinguishing between malignant and benign metastatic masses, and both models were better than RMI.

**Conflict of Interest:** None.

**Funding Source:** None.

**Authors' Contribution**

Following authors have made substantial contributions to the manuscript as under:

AC & DES: Data acquisition, data analysis, critical review, approval of the final version to be published.

K & ZT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

IT & SA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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