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Evaluating Efficacy: The ADNEX Model as a Predictive Tool for Ovarian Masses

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Abstract
Ovarian cancer ranks as the eighth most common cancer and the seventh leading cause of cancer-related deaths among women globally. In 2022, there were approximately 321,476 new cases and 248,305 deaths due to this malignancy. Often labeled as "silent killers," ovarian tumors present with vague symptoms, leading to late diagnoses. The current lack of effective screening methods necessitates reliance on radiological imaging and tumor markers like CA-125 for evaluation and diagnosis. The IOTA group's ADNEX model, introduced in 2014, represents a significant advancement in risk assessment for differentiating between benign and malignant ovarian tumors.

Aim
This study aims to evaluate the predictive accuracy of the ADNEX model for ovarian masses.

Material and Methods
Conducted over 18 months at Sree Balaji Medical College and Hospital in Chennai, India, this observational diagnostic study included 196 women presenting with adnexal masses. Exclusion criteria encompassed prior malignancy treatment and pregnancy. Data on demographic and clinical parameters were collected, followed by ultrasonography and CA-125 assessments. The ADNEX algorithm was applied to predict malignancy risk, and surgical specimens underwent histopathological evaluation. Statistical analyses, including ROC curve assessments, were performed using IBM SPSS software.

Results
The study population predominantly consisted of women aged 41-50 years, with benign lesions representing 70.9% and malignant lesions 18.3% of cases. CA-125 levels were below 35 IU/mL in 74% of participants. The ADNEX model showed high sensitivity (91.67%) and specificity (76.25%) in malignancy detection, with an area under the ROC curve of 0.933.

Discussion
The results align with previous studies confirming the ADNEX model's robust performance in distinguishing malignant from benign ovarian neoplasms. While the model demonstrated a strong sensitivity, it indicated a higher propensity for false positives, suggesting a need for further refinement in clinical settings.

Conclusion
The ADNEX model is a valuable tool for assessing ovarian masses, providing nuanced risk stratification that enhances clinical decision-making. Future research should explore its diagnostic accuracy across different ovarian cancer subtypes to validate its comprehensive applicability.

Keywords – *ADNEX model, ovarian malignancy, AUC*

INTRODUCTION

Globally, ovarian cancer is the eighth most common cancer and the seventh leading cause of cancer-related deaths among women.(1) In 2022, it was estimated that there were 321,476 new cases and approximately 248,305 deaths worldwide due to ovarian malignancy.(2)

Ovarian tumors are often termed "silent killers" due to their delayed presentation and vague, non-specific symptoms such as bloating, abdominal discomfort, pain, and changes in urinary or bowel habits. Currently, there is no proven screening method for early detection of ovarian cancer.

Radiological imaging, primarily ultrasonography, is used for evaluating ovarian masses. Tumor markers, particularly CA-125, alongside imaging and clinical evaluation, play a pivotal role in diagnosing ovarian cancers.

Preoperative scoring systems integrate these parameters to stratify malignancy risk, guide treatment decisions, and predict surgical outcomes. For benign lesions, the objective is to provide reassurance to the patient and manage based on clinical necessity, avoiding unnecessary or overly extensive surgical interventions. Conversely, in cases showing characteristics suggestive of ovarian malignancy, referral to a specialized center ensures optimal patient outcomes.

In 2014, the IOTA (International Ovarian Tumor Analysis) group introduced the ADNEX (Assessment of Different NEoplasias in the adneXa) model as a risk assessment tool for distinguishing between malignant and benign ovarianneoplasms.

This model represents the first of its kind to stratify risks across various categories, including benign tumors, borderline tumors, stage I invasive cancer, stage II-IV invasive ovarian cancer and secondary metastatic cancer.[3]

The ADNEX model incorporates 3 clinical predictors and 6 ultrasound predictors. According to the original study by the IOTA group, a cutoff probability of malignancy of 20% calculated by ADNEX was proposed to identify women withsuspected malignant lesions.[4]

The clinical Predictors include - age (years), type of center to which the patienthas been referred for ultrasound examination (oncology/not) and Serum CA-125 (U/mL), where as the 6 Ultrasound parameters are - proportion of solid tissue (%), maximal diameter of the lesion (mm), number of papillary projections (0, 1, 2, 3, >3), presence of acoustic shadows (yes/no), presence of more than 10 cyst locules (yes/no)and presence of ascites (yes/no). The model utilizes a multivariable logisticregression analysis to generate individualized risk probabilities, providing a numerical score that correlates with the likelihood of malignancy.

ADNEX model has shown high sensitivity and specificity in showing difference between benign and malignant ovarian tumors, with reported values ranging from 80% to 90% and 90% to 95%, respectively.[5]

AIM

The primary aim of my study is to study the predictive outcome of ADNEXmodel by IOTA for ovarian masses.

MATERIAL AND METHODS

This study is an observational diagnostic study, conducted at Department of Obstetrics and Gynecology at Sree Balaji Medical College and Hospital, Bharath University in Chennai, India over a period of 18 months (January 2022 – June 2023).

A sample size of 196 women were taken for this study. This study included all women who present with adnexal masses and were to be treated operatively according to standard guidelines. Patients treated conservatively, previously treated for malignancy, patient with secondary malignancies and pregnant women were excluded.

Detailed proforma with the demographic details. menstruation history, maritalhistory, obstetric history and past medical and surgical history was obtained. Patients' presenting complaints with history of present illness noted in detail. A detailed general, systemic, and pelvic examination was done and noted. Blood analysis for tumor marker (CA-125) and radiological investigation - ultrasonography of pelvic organs was performed as per clinical requirements. Pre - operative predictive scores were calculated according to ADNEX Algorithm for each patient.Specimens of all the women who have undergone surgery is collected and sent for pathology

and fixed using 10% formalin. . Information based on gross and histopathological findings also on the nature and type of ovarian tumor has been recorded. The data collected was analyzed the predictive value of ADNEX algorithm.

Statistical analysis was carried out using statistical packages for IBM SPSS vs 22 for Windows. ROC curve analysis was done to predict malignancy by ADNEX Algorithm. Diagnostic Indices were calculated of RMI and Adnex Scoring for malignancy. Two sided p values was considered as statistically significant at $p<0.05$.

RESULTS

In present study the largest proportion of patients with ovarian masses falls within the 41-50 years age range (40.9%), followed by the 31-40 years age group (31.1%). The lowest prevalence is observed among patients 20 – 30 years old (2.5%). This indicates that the majority of cases occur during the reproductive age range.

Table 1: Distribution of study participants according to age group

Age group	N=196	%
20 – 30 yrs	5	2.5
31 – 40 yrs	61	31.1
41 – 50 yrs	80	40.9
51 – 60 yrs	44	22.5
>60 yrs	6	3

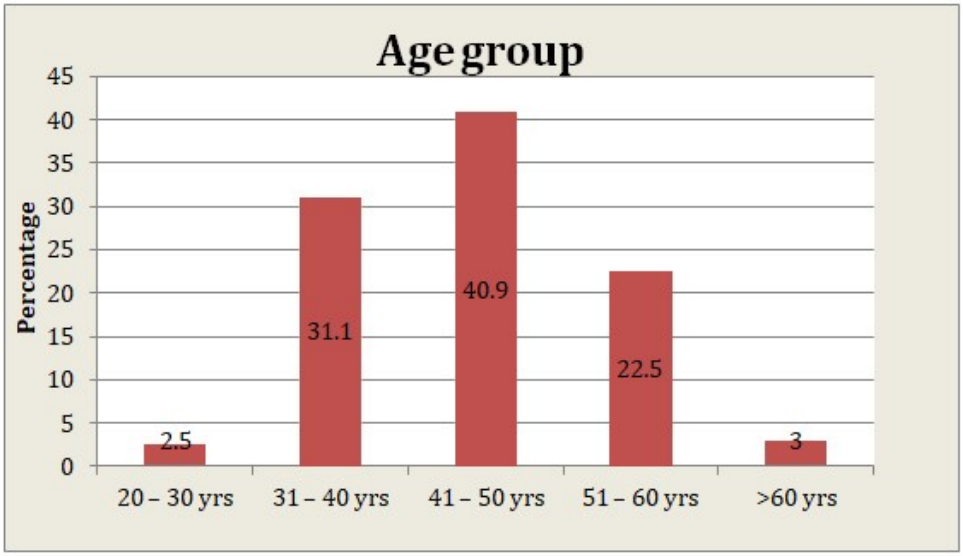

Table 1 illustrates the distribution of ovarian masses among different age groups.

The highest proportion of ovarian masses occurs in patients with parity 2 and above (85.20%), followed by parity 1 women (10.20%).

Table 2: Distribution of the study subjects based on the parity

Parity	N=196	%
Abortion 1	5	2.55
Nullipara	4	2.04
Parity 1	20	10.20
Parity 2 and above	167	85.20

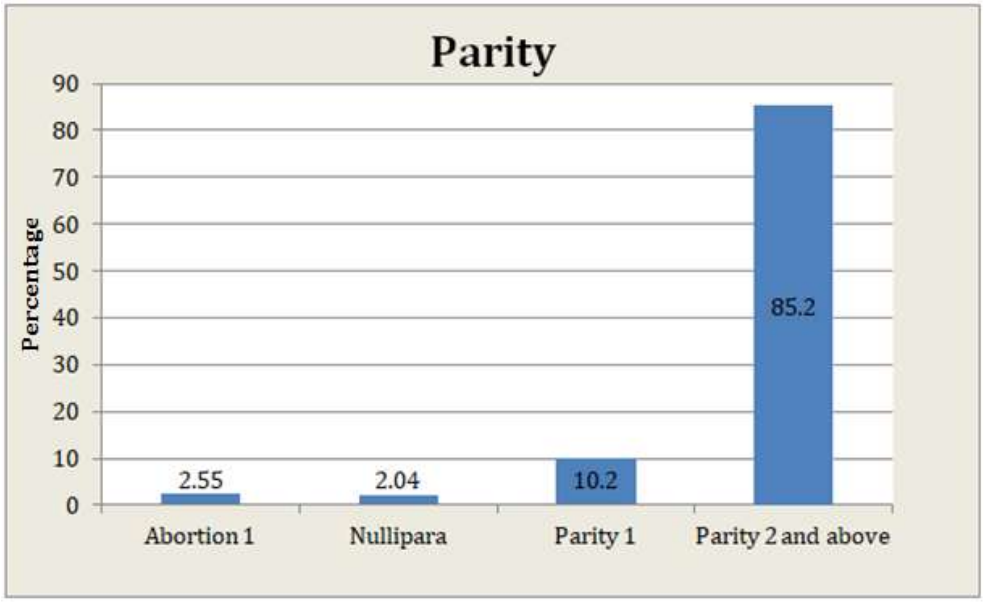

Table 2 presents the frequency distribution of parity status among patients diagnosed with ovarianmasses.

Out of 196 cases the majority, approximately 70.9%, are benign lesions,followed by malignant lesions, which account for 18.3% of cases.

Table 3: Distribution of the study subjects according to Nature of Ovarian Massbased on the Histopathological examination report

Nature of Ovarian Mass	N=196	%
Benign	139	70.9
Borderline	21	10.7
Malignant	36	18.3

The data shows that the highest percentage, nearly 74%, corresponds to CA – 125 levels being below 35 IU/mL.

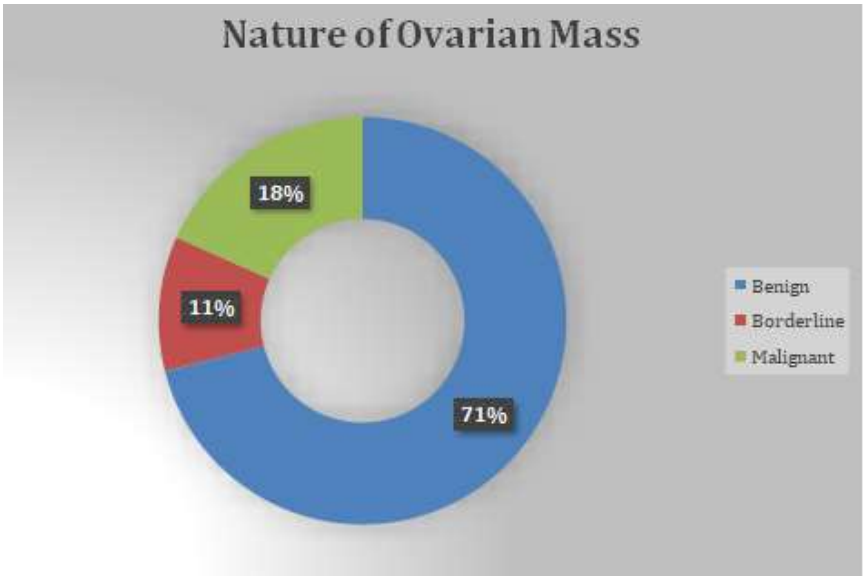

Table 3 outlines the nature of ovarian masses among study participants diagnosed with ovarianmasses.

Table 4: Distribution of the study subjects based on the values of CA-125

CA -125	N=196	%
<35	145	74.0
>35	51	26.0

The ADNEX scores among participants in the study shows that benign lesions (<20% cutoff) make up the majority, approximately 63.8% of cases, with malignantlesions (≥20% cut off) accounting for 36.8%.

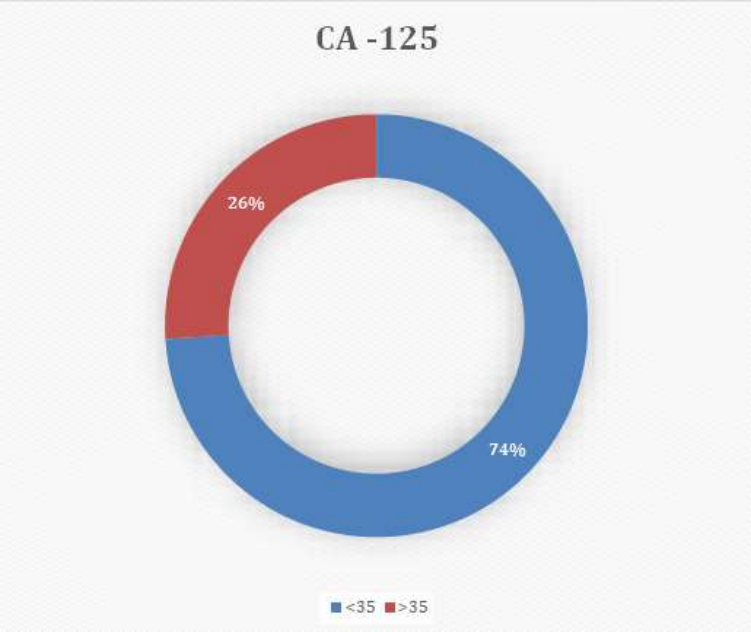

Table 4 presents the distribution of tumor marker CA – 125 levels among patientsdiagnosed with ovarian masses.

Table 5: Distribution of the study subjects based on the values of ADNEX Scoring

ADNEX scoring	N=196	%
<20 %	125	63.8
>20 %	71	36.8

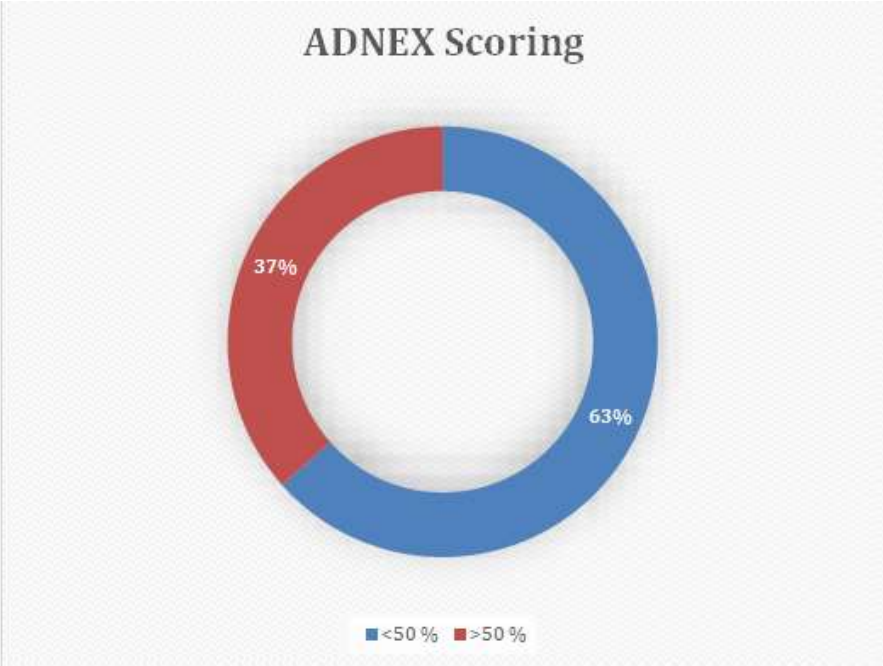

Table 5 summarizes the ADNEX scores among participants in the study.

ASSESSMENT OF ADNEX SCORING SYSTEM TO PREDICT MALIGNANCY

According to our study, with ADNEX model, we identified 33 true positive cases and 122 true negative cases, with 3 false positives and 38 false negatives observed as well.

Table 6: TP, FP, FN, TN of ADNEX for predicting Malignancy

ADNEX Score	Malignancy		Total
	Present	Absent	
Present (Score>20%)	33 (TP)	38 (FP)	71
Absent (Score <20%)	3 (FN)	122 (TN)	125
Total	36	160	196

In the current study, our analysis of the RMI scoring system revealed a highersensitivity (91.67%, CI: 77.53% to 98.25%) compared to specificity (91.25%, CI: 68.89% to 82.61%).

Table 7: Sensitivity and Specificity of ADNEX for predicting Malignancy

Statistic		
	Value	95% CI
Sensitivity	91.67%	77.53% to 98.25%
Specificity	76.25%	68.89% to 82.61%

It was found that the area under the curve is 0.933 with SE = 0.024 and 95%CI from 0.885 to 0.980 for ADNEX.

Table 8: ROC Curve analysis of ADNEX to predict malignancy

Area under curve(AUC)	Std. Error	P value	95% Confidence Interval	
			LowerBound	UpperBound
0.933	0.024	<0.001**	0.885	0.980

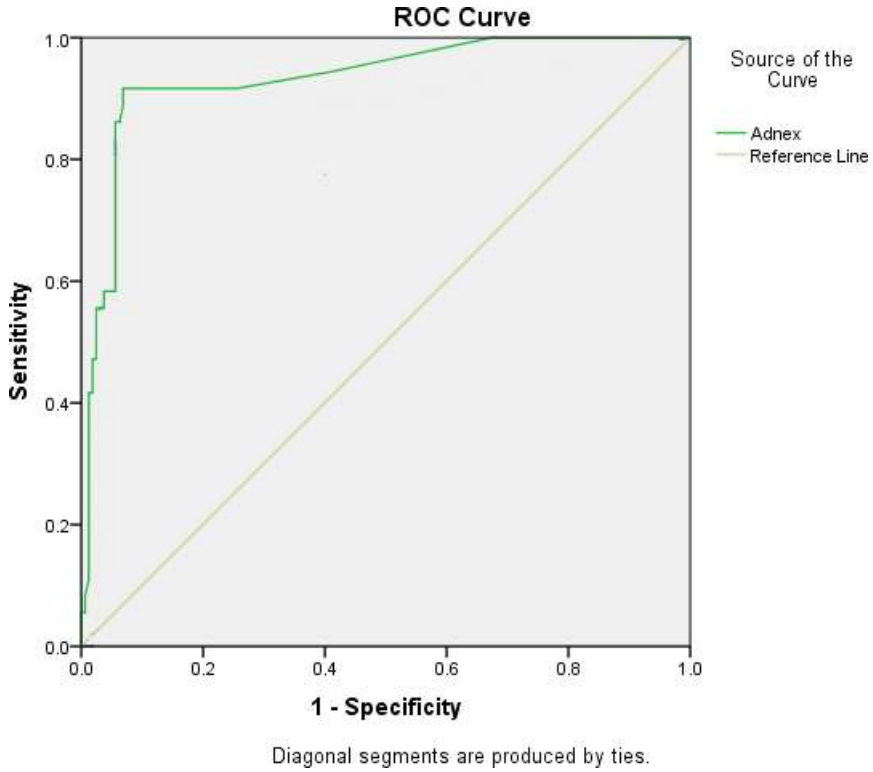

Figure 1. The ROC curve obtained by ADNEX

DISCUSSION

In this study, the majority of ovarian masses occurred in patients aged 31-40 years (30.3%), followed by those aged 41-50 years. Similar age distributions were reported in other studies. Patil et al. found that 50% of ovarian masses occurred in the 31-40 age group then it was seen in the 41-50 age group.[6] Priya MHF et al. observed a mean age of ovarian mass diagnosis similar to our study within the reproductive age group.[7] Sharadha et al. also noted a similar age distribution with ovarian masses diagnosed predominantly in the reproductive age group.[8] Jagadeeshwari et al. and Verma et al. similarly reported a higher frequency of ovarian tumors in the 31-40 age group, consistent with our findings.[9,10] Bhuyan et al. also reported a higher frequency of ovarian masses among the reproductive agegroup, aligning with our study's findings.[11]

In this current study, ovarian tumors were more prevalent in multiparous women, maximum in women with parity – 2 and above being 85.20%. Similar patterns were reported in studies by Shahin Rashid et al. and Vaidya et al.[12,13] Parous women under 55 showed a decreasing trend in ovarian neoplasm riskcompared to nulliparous women.

In present study, prevalence of benign, borderline and malignant tumors were 70.9%, 10.7% and 18.3% respectively. We can observe a higher prevalence of benign tumors followed by malignant and borderline. In the study done by SanthoshKumar et al. the similar findings were observed that is benign was highest in number when compared to borderline and malignant.[14] Similar findings were observed in the Pilli et al. study, Koonings et al. study and by Rujuta Javdekar et al.[15,16,17]

CA-125 is the predominant tumor marker used to evaluate ovarian malignancies. The standard cutoff value for CA-125 is set at 35 U/mL. In our study, 76.02% of women had CA-125 levels below this threshold, while 23.98% had levels exceeding 35 U/mL. Similar findings were reported in studies conducted by Mongkol Benjapibal et al. and E L Moss et al.[18,19]

In our investigation of the ADNEX model, we studied 71 women who had anADNEX score exceeding 20%. Among these, 33 cases were correctly identified as true positives, indicating accurate detections, while 38 cases were falsely identifiedas positive, reflecting instances where the model incorrectly indicated a positive result.

In contrast, we observed 125 women with an ADNEX score below 20%, with122 cases accurately identified as true negatives, and 3 cases incorrectly identified as false negatives.

In terms of statistical metrics, our study achieved an Area Under the Curve (AUC) of 0.933, demonstrating the ADNEX's overall accuracy in distinguishing between positive and negative cases.

This aligns closely with findings from studies by El Maraghy et al. (AUC: 0.864) and Huong et al. (AUC: 0.956).[20,21] Yang et al. also reported a comparable AUC of 0.925 in their study.[22] Study conducted by Froyman et al. showed AUC ofADNEX being 0.940, and Vilendecic et al. having observed with AUC of ADNEX as 0.914. [23,24] Ben Van Calster et al. in their study also observed similar results ofAUC of 0.940 for ADNEX model.[25]

Specifically, across these studies, the AUC for ADNEX typically exceeded 0.900, indicating its robust performance as a predictive scoring system for distinguishing between benign and malignant ovarian neoplasms. Therefore, based on our study and the cumulative evidence from the literature, ADNEX appears to offer superior predictive outcomes over the RMI scoring system for ovarian masses.

Additionally, our analysis revealed a specificity of 76.25%, indicating the proportion of true negative results correctly identified by the ADNEX, and a sensitivity of 91.67%, indicating the proportion of true positive results accurately detected by the ADNEX. El Maraghy et al. reported sensitivities of 91%, Huong et al. reported 89.2%, and Wang et al. reported 90.6%. These studies also reported specificities of 65%, 94%, and 90.6%, respectively.[20,21,22]

These findings suggests that the ADNEX model more reliably detects true positive cases (patients with ovarian cancer) than it does true negative cases (patientswithout ovarian cancer). This imbalance indicates the model's tendency to prioritizesensitivity (identifying positives) over specificity (avoiding false positives), potentially influencing its diagnostic performance and accuracy in clinical settings. These findings underscore the effectiveness and performance metrics of the ADNEXmodel as evaluated in our study.

CONCLUSION

The primary aim of my study is to study the predictive outcome of ADNEX model by IOTA for ovarian masses. The ADNEX model emerges as a superior option in this comparative analysis. Developed by the IOTA group, ADNEXintegrates multiple clinical predictors and ultrasound parameters to provide a nuanced risk assessment. Its ability to categorize adnexal masses into various malignancy probabilities, including different stages of malignant tumors, enhances clinical decision-making and potentially reduces unnecessary interventions.

One of the limitations of this study is that the diagnostic methods were validated solely on patients who underwent surgery, which may not represent the entire spectrum of patients with ovarian masses encountered in clinical practice. Additionally, a notable strength of the ADNEX model is its classification into four subtypes of ovarian cancer. However, in this analysis, comprehensive diagnostic data for all four subtypes in 2 × 2 tables could not be extracted. Therefore, our discussion focused solely on the diagnostic accuracy in distinguishing ovarian cancer from benign tumors. Future studies should investigate the diagnostic accuracy of the ADNEX model across different subtypes to provide a more comprehensive assessment.

ETHICAL COMMITTEE

Consent was obtained or waived by all participants in this study. InstitutionalEthical Committee, Sree Balaji Medical College and Hospital issued approval002/SBMC/IHEC/2022/1799.

CONFLICTS OF INTEREST

In compliance with the ICMJE uniform disclosure form, all authors declarethe following:

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