Estimating the Risk of Malignancy in Adnexal Masses: Validation of the ADNEX Model in the Hands of Non-expert Ultrasonographers in a Gynecological Oncology Center in China

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Research

Keywords: ADNEX model, CA 125, diagnosis, ovarian tumor, ultrasonography

Posted Date: June 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-630532/v1

Abstract

Background:

The diagnosis of adnexal masses depends more on ultrasonography. This study aim to validate the diagnostic accuracy of the International Ovarian Tumor Analysis (IOTA) ADNEX model in the preoperative diagnosis of adnexal masses in the hands of non-expert ultrasonographers in a gynecological oncology center in China.

Methods:

This was a single oncology center, retrospective diagnostic accuracy study from 620 patients. All patients underwent surgery and the histopathological diagnosis was used as reference standard. The masses were divided into five types according to the ADNEX model: benign ovarian tumor, borderline ovarian tumor (BOT), Stage-I ovarian cancer (OC), Stages-II-IV OC and ovarian metastasis. Receiver-operating characteristics (ROC) curve analysis was used to evaluate the ability of the ADNEX model to classify tumors into different histological types with and without Cancer antigen 125 (CA 125) results.

Results:

Of the 620 women, 402 (64.8%) had a benign ovarian tumor and, 218 (35.2%) had a malignant ovarian tumor, including 86 (13.9%) with BOT, 75 (12.1%) with Stage-I OC, 53 (8.5%) with Stages-II-IV OC and 4 (0.6%) with ovarian metastasis. The AUC of the model to differentiate between benign and malignant adnexal masses was 0.97 (95% CI, 0.96–0.98). Performance was excellent for the discrimination between benign vs Stage II-IV OC, benign vs ovarian metastasis with AUCs of 0.99 (95% CI, 0.99-1.00) and 0.99 (95% CI, 0.98-1.00), respectively. Performance of the model was less effective at distinguishing between BOT and Stage I OC and between BOT and ovarian metastasis, with AUC of 0.54 (95% CI, 0.45–0.64) and 0.66 (95% CI, 0.56–0.77), respectively. When including CA125 in the model, performance in discriminating between Stages II–IV OC with stage I OC and ovarian metastasis were improved (AUC increased from 0.88 to 0.94, P = 0.01; 0.86 to 0.97, p = 0.01, respectively).

Conclusions:

The IOTA ADNEX model has excellent performance in differentiating benign and malignant adnexal masses in the hands of non-expert ultrasonographers with limited experienced in China. Between classification different subtypes of ovarian cancers, the model has difficulty to differentiate BOT from stage I OC, BOT from ovarian metastases.

Introduction

In Chinese women, the mortality rate of the three kinds of cancer is increasing year by year, including breast cancer, cervical cancer and ovarian cancer[1], In particular, most of the patients are asymptomatic in the early stage of ovarian cancer. The five year survival rate of patients with stage III-IV ovarian cancer is less than 30%, that of patients with stage II is about 70%, and that of patients with stage I is more than 90%[2]. The combination of early diagnosis and timely treatment is considered to be the key factor to optimize the survival rate[3,4]. We diagnose ovarian cancer as a benign tumor incorrectly may delay the timing of treatment and lead to inadequate treatment, on the contrary, it will make patient undergo more extensive treatment and increase the possibility of postoperative complications. It is very essential to make a correct diagnosis.

The diagnosis of adnexal masses depends more on ultrasonography. Some studies have reported that subjective evaluation of a tumor by an expert ultrasonographer is an excellent method for discriminating between benign and malignant adnexal masses[5–7]. It is necessary for doctors who are not so experienced to use a more objective method to assist in diagnosis. In order to characterize the ovarian tumors as benign or malignant, biomarkers combined with ultrasonography have been used to optimize the accuracy of diagnosis, including the risk of malignancy index (RMI). The International Ovarian Tumor Analysis group (IOTA) have presented a consensus on the terms, definitions and measurements used to describe the sonographic features of adnexal tumors[8] and standardized the description of ovarian lesions. Then IOTA developed and validated many models to discriminate between benign and malignant adnexal masses such as logistic regression model LR1, LR2, Simple Rules and so on[9,10]. In a meta-analysis[11], the ability of different methods to differentiate benign from malignant adnexal masses was compared. The results showed that IOTA Simple Rules and LR2 were superior to RMI and to all other methods included in the meta-analysis.

The Assessment of Different NEoplasias in the adneXa (ADNEX) model is the first predictive multiclass model developed by IOTA and is able to differentiate between benign tumors, borderline tumors (BOTs), stage-I ovarian cancer (OC), stage II-IV OC and secondary metastatic ovarian cancers[12]. Preoperative characterization of an adnexal mass is of crucial importance for selecting the optimal management strategy and differential diagnosis of the mass by the ADNEX model may help to optimize management. In recent years, several studies have been reported the model has good to excellent performance in their populations[13–15]. Also in China, it has been reported had high accuracy in distinguishing between benign and malignant adnexal masses by expert ultrasonographers in a gynecological oncology center in Shanghai[16]. However, there are few studies validating the discriminative performance of the ADNEX model in the hands of non-expert ultrasonographers, it has great hope as a method for the correct classification of adnexal masses by ultrasonographers with limited experience.

The aim of our study was to evaluate the performance of the IOTA ADNEX model in the preoperative discrimination between benign, borderline, early and advanced stage invasive, and secondary metastatic tumors in the hands of non-expert ultrasonographers in a single oncology center in Beijing, China.

Methods

Study design and patients

This was a single center retrospective study for diagnostic accuracy conducted at a tertiary referral oncology hospital. From 1 January 2018 to 31 December 2019, seven hundred and sixty-eight patients with an ultrasound diagnosis of an adnexal mass were recruited from the Department of Ultrasound in Beijing Obstetrics and Gynecology Hospital in China consecutively.

The inclusion criteria were as follows: (1)patients presenting with at least one adnexal mass who underwent transvaginal or transrectal ultrasonography (supplemented with transabdominal if transvaginal is not sufficient); (2) the interval between operation and ultrasonography should not exceed 120 days. (3) The patient had no previous history of ovarian cancer. The exclusion criteria were as follows: (1) Cysts that were deemed to be clearly physiological and less than 3 cm in maximum diameter; (2) Previous bilateral adnexectomy. For bilateral adnexal masses, the mass with the most complex ultrasound features was included. If both masses had similar ultrasound morphology, the largest mass or the one most easily accessible by ultrasonography was included[17]. The study was approved by the Institutional Ethics Committee of Beijing Obstetrics and Gynecology Hospital Affiliated to Capital Medical University.

Two non-expert ultrasonographers at level 2 according to the EFSUMB classification who have successfully passed the IOTA certification test exam, assessed the sonographic tumor morphology based on the standardized manner previously published by the IOTA group[8]. All assessments were done prior to obtaining pathology result, and the ultrasonographers

were blinded to this outcome. The ultrasound machines used were Voluson E8 (GE Healthcare, USA) with 5.0–9.0 MHz transvaginal probes and 1.0–5.0 MHz transabdominal probes.

Clinical and ultrasound variables of the ADNEX model were recorded. Serum CA125(U/ml) levels were assessed 7 days before surgery using an Elecsys and Cobas E analyzers (Roche, Mannheim, Germany).

Reference standard

The histopathological diagnosis of the mass after surgical removal by laparoscopy or laparotomy was used as reference standard. Tumors were staged according to the World Health Organization (WHO) classification of tumors and malignant tumors are staged using the International Federation of Obstetrics and Gynecology (FIGO) standards[18]. In the final diagnosis, the masses were divided into five types: benign, BOTs, stage I OC, stage II-IV OC, secondary metastatic cancer.

Adnex Model

We input the variables needed by the ADNEX model into the web application ((http://www.iotagroup.org/adnexmodel/). The model includes nine variables in the: age (years), serum CA125 level (U/mL), type of center (oncology referral center vs non-oncology center), maximal diameter of the lesion (mm), maximal diameter of the largest solid part (mm), number of papillary projections (0, 1, 2, 3 or more than 3), number of cyst locules (≤ 10 vs > 10), acoustic shadows (yes or no), and ascites (yes or no) [12]. All ADNEX model parameters were logged objectively. Then the model can calculate the patient specific risk and relative risk of each subtype. With or without CA125 result, the model is able to calculate the malignant risk. This study compared the diagnostic accuracy of the model with or without CA125 result.

Statistical analysis

We analyzed data using R software. For statistical purposes, BOTs were considered malignant.

We compared clinical and sonographic features of adnexal masses of the ADNEX model using the chi-square test and Fisher's exact test for categorical data and the Mann–Whitney U-test for continuous data. In order to validate the ADNEX model with and without CA125 level, receiver–operating characteristics (ROC) curve analysis was performed. We calculated the area under the curve (AUC) with 95% CIs for basic discrimination between benign and malignant adnexal tumors using the total risk of malignancy (i.e., the sum of the estimated risks of the four malignant subtypes). AUCs of ADNEX model with and without CA125 level were computed for each pair of tumor types using the DeLong's test.

We calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) at progressive cut-off points for total risk of malignancy and at the cut-off point determined by ROC curve analyses of our data.

Statistical calculations were performed using 95% CIs, with $P < 0.05$ considered to be significant.

Results

Between 1 January 2018 to 31 December 2019, 768 patients with adnexal tumors were examined by ultrasonography before laparoscopy or laparotomy. 148women were excluded from the study because of pregnancy, failure to undergo surgery, incomplete clinical data, histological diagnosis of uterine lesion, diagnosis of an extragynecological tumor. Therefore, the final cohort consisted of 620 patients (Fig. 1).

Among them, 402 (64.8%) had a benign tumor, 218 (35.2%) had a malignant tumor, including 86 (13.9%) with BOT, 75 (12.1%) with stage I OC, 53 (8.5%) with stage II-IV OC, and 4 (0.6%) with ovarian metastases. The most common benign

tumors are serous cystadenoma and teratoma, while the most common malignant tumors are serous adenocarcinoma and clear cell carcinoma.

Clinical and sonographic features of adnexal masses in our cohort are shown in Table 2. The patients in the malignant group were older and had higher CA125 levels than those in the benign group. Prevalence of solid tissue, papillary projections and ascites are more common in the malignant group. Acoustic shadows are more common in benign tumor group. Besides these, prevalence of the features including the maximum diameter of the lesion and the largest solid component, more than 10 locules and presence of ascites were significant differences between benign and malignant masses. ($p<0.05$)

Table 1
Histopathological findings in 620 women with adnexal mass

Histological type	n (%)
Benign	402 (64.8)
Serous cystadenoma	115 (18.5)
Teratoma	111 (17.9)
Mucinous cystadenoma	81 (13.1)
Endometrioma	55 (8.9)
Fibrothecoma	15 (2.4)
Fibroma	7 (1.1)
Adenofibroma	2 (0.3)
Cystadenofibroma	2 (0.3)
Paraovarian cyst	6 (1.0)
Mesosalpinx cyst	4 (0.6)
Other ovarian benign lesion	4 (0.6)
Borderline	86 (13.9)
Serous	33 (5.3)
Mucinous	37 (6.0)
Endometrioid	2 (0.3)
Clear-cell	1 (0.2)
sex cord-stromal tumors	13 (2.1)
Primary Malignant	128 (20.6)
Serous adenocarcinoma	40 (6.5)
Clear cell carcinoma	31 (4.8)
Mucinous adenocarcinoma	28 (4.5)
Endometrioid adenocarcinoma	13 (2.1)
Serous/mucinous adenocarcinoma	7 (1.1)
Carcinosarcoma	3 (0.5)
Immature teratoma	3 (0.5)
Granulosa-cell tumor	2 (0.3)
Sertoli leydig	1 (0.2)
Ovarian metastasis	4 (0.6)

Table 2
Sonographic features of tumor in 620 women with adnexal mass

			Malignant (n = 218)				
	Benign	Borderline	Stage I OC	Stages-II–IV OC	metastasis	total	
Characteristic	(n = 402)	(n = 86)	(n = 75)	(n = 53)	(n = 4)	(n = 620)	p
Age (years)	31 (27–39)	38 (30–48)	47 (41–53)	48 (44–57)	57 (46–62)	44 (34–52)	< 0.001*
CA 125 (U/mL)	11.4 (8–17)	18 (10–28)	37 (15–83)	204 (53–547)	66 (28–137)	26 (13–74)	< 0.001 *
Max diameter of lesion (mm)	63 (50–83)	88 (53–121)	106 (71–148)	88 (64–143)	81 (63–108)	92 (64–133)	< 0.001*
Presence of solid tissue	44(10.9)	63(73.3)	70(93.3)	53(100)	4(100)	190(30.6)	< 0.001 †
Maximum diameter of largest solid component, if present (mm)	30 (13–48)	31 (21–49)	46 (31–80)	66 (57–79)	74 (48–107)	45 (26–67)	p = 0.001*
Papillary projections present	15(3.7)	45(52.3)	36(48.0)	28(52.8)	0(0)	109(17.6)	< 0.001‡
0	387(96.3)	41(47.7)	39(52.0)	25(47.2)	4(100)	109(17.6)	
1	11(2.7)	31(36.0)	23(30.7)	8(15.1)	0(0)	62(10.0)	
2	2(0.5)	7(8.1)	3(4.0)	4(7.5)	0(0)	14(2.3)	
3	1(0.2)	3(3.5)	4(5.3)	5(9.4)	0(0)	12(1.9)	
>3	1(0.2)	4(4.7)	6(8.0)	11(20.8)	0(0)	21(3.4)	
> 10 cyst locules	3(0.7)	15(17.4)	8(10.7)	4(7.5)	0(0)	27(4.4)	< 0.001 †
Acoustic shadows	121(30.1)	1(1.2)	5(6.7)	2(3.8)	0(0)	8(1.3)	< 0.001 †
Ascites	3(0.7)	4(4.7)	11(14.7)	30(56.6)	3(75.0)	48(7.7)	< 0.001 †

Data are given as median (interquartile range) or n (%). P for benign vs malignant groups calculated using: *Mann–Whitney U-test, †chi-square test or ‡Fisher's exact test. OC, ovarian cancer.

Validation Of Iota Adnex Model

The diagnostic performance of the IOTA ADNEX model is presented in Fig. 2. The AUC of the model to differentiate between benign and malignant adnexal masses was 0.97 (95% CI, 0.96–0.98).

The performances of the IOTA ADNEX model with CA125 level at progressive cut-off points for probability of malignancy are shown in Table 3. Sensitivity was 87.06% (82.09–93.03) and specificity was 97.69% (91.03–99.23) at an optimal cut-off of 39.2% probability of malignancy.

Table 3
Performance of the ADNEX model in discriminating between benign and malignant tumors at progressive cut-offs for probability of malignancy

Cut-off	AUC (95% CI)	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)	PPV (95% CI) (%)	NPV (95% CI) (%)	LR+ (95% CI)	LR- (95% CI)	DOR
3%	-	97.51 (95.02–99.50)	69.49 (64.87–74.10)	62.22 (58.70-66.01)	98.22 (96.55–99.63)	3.20 (2.75–3.72)	0.04 (0.02–0.09)	80.00
5%	-	92.04 (88.05–95.52)	87.95 (84.62–91.03)	79.83 (75.30-84.16)	95.54 (93.33–97.49)	7.64 (5.82–10.02)	0.09 (0.06–0.15)	84.89
10%	-	88.06 (83.58–92.54)	94.10 (91.79–96.41)	88.61 (84.54–92.57)	93.92 (91.71–96.05)	14.93 (10.01–22.26)	0.13 (0.09–0.18)	114.85
15%	-	87.56 (82.59–92.04)	95.90 (93.85–97.69)	91.75 (88.02–95.31)	93.75 (91.57–95.84)	21.36 (13.18–34.61)	0.13 (0.09–0.19)	164.31
39.2%*	0.97 (0.96–0.98)	87.06 (82.09–93.03)	97.69 (91.03–99.23)	95.03 (84.07–98.35)	93.66 (91.41–96.24)	37.69 (18.09–78.53)	0.13 (0.09–0.19)	289.92

* Optimal cut-off, the maximum value of Youden index; AUC, area under receiver–operating characteristics curve; DOR, diagnostic odds ratio; LR+, positive likelihood ratio; LR–, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value

When tumors were classified into benign, BOTs, stage I OC, stage II-IV OC, secondary metastatic cancer, the model showed poor to excellent discrimination ability between the different subtypes, with AUCs varying between 0.54 and 0.99 when CA125 level was included in the model and between 0.50 and 0.99 without CA125 level (Table 4). And AUCs of the model in differentiating benign tumor from subtypes of malignant tumor are high. The AUC was 0.94 for benign tumors compared with borderline tumors, 0.98 for benign tumors compared with stage I OC, 0.99 for benign tumors compared with stage II-IV OC, and 0.99 for benign tumors compared with secondary metastatic cancer. The ability to discriminate between benign and stage II–IV tumors, benign and secondary metastatic tumors were near perfect for the model with and without CA125 (AUC 0.99). In comparison, the model had more difficulties discriminating between borderline and stage I tumors (AUC 0.54) and between borderline and secondary metastatic tumors (AUC 0.66). It was well able to distinguish stage II-IV cancer

from other malignancies (AUCs for stage II-IV cancer versus borderline tumors was 0.92, versus stage I cancer was 0.94, and versus secondary metastatic cancer was 0.97)

Table 4
Performance of the ADNEX model in polytomous discriminations between different types of adnexal mass, according to whether CA 125 level was included in the model

Discrimination	AUC (95% CI)		P
	ADNEX model with CA 125	ADNEX model without CA 125	
Benign vs malignant	0.97(0.96–0.98)	0.97(0.95–0.98)	0.07
Benign vs BOT	0.94(0.92–0.97)	0.94(0.91–0.97)	0.19
Benign vs Stage-I OC	0.98(0.97–0.99)	0.98(0.96–0.99)	0.21
Benign vs Stages-II–IV OC	0.99(0.99-1.00)	0.99(0.99-1.00)	0.03
Benign vs metastasis	0.99(0.98-1.00)	0.99(0.97-1.00)	0.24
BOT vs Stage-I OC	0.54(0.45–0.64)	0.50(0.41–0.60)	0.10
BOT vs Stages-II–IV OC	0.92(0.88–0.97)	0.89(0.88–0.97)	0.06
BOT vs metastasis	0.66(0.56–0.77)	0.52(0.29–0.75)	0.34
Stage-I OC vs Stages-II–IV OC	0.94(0.88–0.99)	0.88(0.80–0.96)	0.01
Stage-I OC vs metastasis	0.72(0.60–0.85)	0.54(0.21–0.86)	0.37
Stages-II–IV OC vs metastasis	0.97(0.93-1.00)	0.86(0.76–0.95)	0.01

Comparison of area under receiver–operating characteristics curve (AUC) of ADNEX model with vs without inclusion of CA 125 level using DeLong's test. BOT, borderline ovarian tumor; OC, ovarian cancer.

When including CA125 in the model, performance in discriminating between Stages II–IV OC with stage I OC and secondary metastatic tumors were improved (Tables 4 and 5). Validation AUCs increased from 0.88 to 0.94, p = 0.01 (stage II-IV OC vs metastatic cancer), from 0.86 to 0.97, p = 0.01 (stage II-IV OC vs stage I OC).

Table 5
Performance of the ADNEX model with vs without CA 125 level in discriminating between Stage-I OC vs Stages-II–IV OC and between Stages-II–IV OC vs metastasis

ADNEX model	AUC (95% CI)	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)	PPV (95% CI) (%)	NPV (95% CI) (%)	LR+ (95% CI)	LR- (95% CI)	DOR	* Optimal cut-off (%)	*P*
Benign vs Stages-II–IV OC										
With CA 125	0.99 (0.99-1.00)	100.00 (100.00-100.00)	98.97 (97.44–100.00)	92.73 (83.61–100.00)	100.00 (100.00-100.00)	97.09 (43.80-215.22)	0.00 (-)	0.00	42.95	0.03
Without CA 125	0.99 (0.99-1.00)	100.00 (100.00-100.00)	97.69 (96.15–99.23)	85.00 (77.27–94.44)	100.00 (100.00-100.00)	43.29 (22.70-82.57)	0.00 (-)	0.00	40.75	
Stage-I OC vs Stages-II–IV OC										
With CA 125	0.88 (0.80–0.96)	80.39 (68.63–90.20)	98.53 (95.59–100.00)	97.67 (92.68–100.00)	87.01 (80.95–93.15)	54.69 (7.78-384.48)	0.20 (0.11–0.35)	273.45	36.2	0.01
Without CA 125	0.94 (0.88–0.99)	84.31 (72.55–94.12)	98.53 (95.59–100.00)	97.78 (93.18–100.00)	89.33 (82.93–95.65)	57.35 (8.17-402.77)	0.16 (0.08–0.30)	358.44	30.55	
Stages-II–IV OC vs metastasis										
With CA 125	0.86 (0.76–0.95)	100.00 (100.00-100.00)	84.31 (72.55–92.16)	33.33 (22.22-50.00)	100.00 (100.00-100.00)	6.37 (3.50-11.61)	0.00 (-)	-	31.25	0.01
Without CA 125	0.97 (0.93-1.00)	100.00 (100.00-100.00)	96.08 (90.20–100.00)	66.67 (44.44–100.00)	100.00 (100.00-100.00)	25.51 (6.56–99.24)	0.00 (-)	-	15.2	

Comparison of AUC of ADNEX model with vs without inclusion of CA 125 level using DeLong's test. * Optimal cut-off, the maximum value of Youden index; AUC, area under receiver–operating characteristics curve; DOR, diagnostic odds ratio; LR+, positive likelihood ratio; LR–, negative likelihood ratio; NPV, negative predictive value; OC, ovarian cancer; PPV, positive predictive value.

Discussion

In our study, we show that in the hands of non-expert ultrasonographers with limited experienced, the IOTA ADNEX model can distinguish benign and malignant masses and its performance level is similar to that achieved by experienced ultrasonographers in the original ADNEX validation study published by IOTA team[12]. Regardless of whether the CA125 level is included or not, IOTA ADNEX model has excellent ability in distinguishing benign and malignant masses in a China oncology center (AUCs of 0.97 with and without CA 125). Our results are also consistent with another Chinese validation study in which the model was validated by experts ultrasonographers[16].

Except BOT vs Stage I OC, BOT vs ovarian metastases, the ADNEX model showed good to excellent performance in distinguishing most of the subtypes of adnexal masses in our study (AUC ranged from 0.72 to 0.99), especially benign tumors and stage II-IV OC (AUC 0.99), benign tumor vs ovarian metastases (AUC 0.99), BOT vs Stage II–IV OC (AUC 0.92), Stage I OC vs Stage II–IV OC (AUC 0.94) and Stage II–IV OC vs ovarian metastases(AUC 0.97) which were consistent with the results of other studies[13,14,16,19]. The prediction of specific subtype of malignant tumors had lower performance. When discriminating between BOT from stage I OC and between borderline and secondary metastatic tumors, AUC were 0.54 and 0.66, respectively, which are both lower than the previous research results[13,14,16,19]. There are many overlapping features between BOT and OC, especially early-stage OC, so it is very challenging to differentiate them in clinical practice. The survival rate of borderline ovarian tumors confined to the ovary is high, almost 100% within 10 years[20]. BOT are often affected young women, one third of them are diagnosed under 40 years old, so fertility preserving therapy should be considered[21]. A meta-analysis showed that early OC women who underwent laparoscopic surgery had a lower incidence of complications and no significant difference in recurrence rates compared with those who underwent laparotomy[22]. For non-expert ultrasonographers with limited experienced,

with the help of the ADNEX model, it is helpful to identify the subtypes of ovarian tumors, except BOT vs Stage I OC, BOT vs ovarian metastases.

In our validation study, using a 15% cut-off value to define malignancy, ADNEX model achieved 87.6% sensitivity and 95.9% specificity, compared with 94.5% and 78.7% in the original study [12]. Although the sensitivity decreased, the specificity increased significantly, which helps to reduce the misdiagnosis rate of noncancer patients. In our clinical practice, we can choose the appropriate cut-off value according to the needs. According to the IOTA group studies results, a 10% risk cut-off for the ADNEX model is recommended for non-oncological centers. But, because of much higher percentage of malignant cases operated in oncology centers, we probably use much higher probability cut-off levels, i.e. 37% in this study. In our population, the IOTA ADNEX model indicated high positive and negative predictive value, which are slightly higher than other validation studies[14,15], thus it could be considered as an appropriate method for differentiating benign and malignant ovarian tumors in China.

The ADNEX model can make more personalized diagnosis of ovarian tumors by identifying the types of malignant tumors (borderline, primary stage I, primary II- stage IV or secondary metastatic). To help clinician choose the right treatment, choose conservative treatment, or plan the most appropriate surgical procedure (laparoscopic or open surgery) when surgery is needed, or prompt doctors to find the primary site of the tumor when masses are assessed as metastatic cancer. We have shown that the ADNEX model performs equally well in the hands of non-expert ultrasonographers with limited experienced compared to the initial study, But the differential diagnosis between BOT vs Stage I OC, BOT vs ovarian metastases need to be improved.

Strengths And Weaknesses

The main advantage of our study is that it is the first validation study in the hands of non-expert ultrasonographers with limited experienced in China. And the researchers have successfully passed the IOTA certification test exam so that we evaluated tumor morphology strict accordance with the IOTA consensus statement and with blinding for pathology results. Every patient in our center had a preoperative CA125 measurement using the same methodology.

The limitation of our study is that we are a retrospective study, which might have introduced selection bias. There are fewer cases of ovarian metastatic cancer, which can't guarantee that the ADNEX model can draw reliable conclusions when distinguishing it from other subtypes.

Conclusions

The IOTA ADNEX model has excellent performance in differentiating benign and malignant adnexal masses in the hands of non-expert ultrasonographers with limited experienced in China. Between classification different subtypes of ovarian cancers, the model has difficulty to differentiate BOT from stage I OC, BOT from ovarian metastases.

Abbreviations

IOTA: the International Ovarian Tumor Analysis; ADNEX model: the Assessment of Different NEoplasias in the adneXa model; BOT: borderline ovarian tumor; OC: ovarian cancer; ROC curve: Receiver-operating characteristics; AUC: the area under the curve; CA 125: Cancer antigen 125; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio;

Declarations

Ethics approval

The study was approved by the Institutional Ethics Committee of Beijing Obstetrics and Gynecology Hospital Affiliated to Capital Medical University.

Funding

Not applicable

Consent for publication

Not applicable.

Availability of data and materials

The dataset supporting the conclusions of this article is included within the article and its additional files.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

WQQ and HP devised the study and wrote the main manuscript. WQQ, HP,

and DW collected the data. HP, WJJ, SC and YY performed the analyses. All authors contributed to the discussions. All authors read and approved the final manuscription.

Acknowledgements

Not applicable.

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Figures

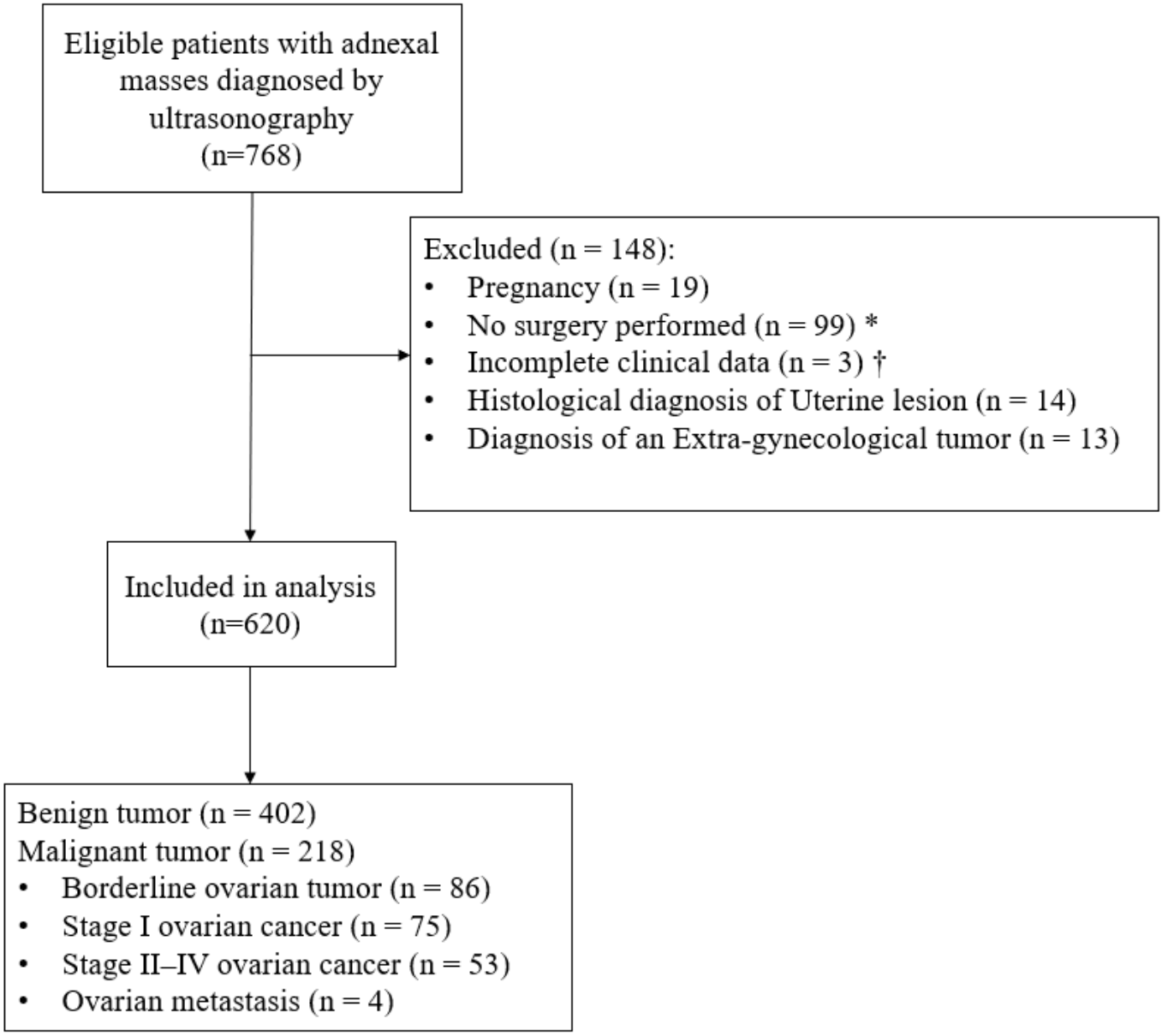

Figure 1

Flowchart showing enrolment of women with adnexal mass and reasons for exclusion. *No surgery performed in 99 patients because surgery was delayed due to neoadjuvant chemotherapy (n=34), patients were in poor physical condition, unable to accept surgical treatment (n=37), patients gave up the operation for personal reasons (n=28). † Incomplete clinical data refers to missing CA125 levels.

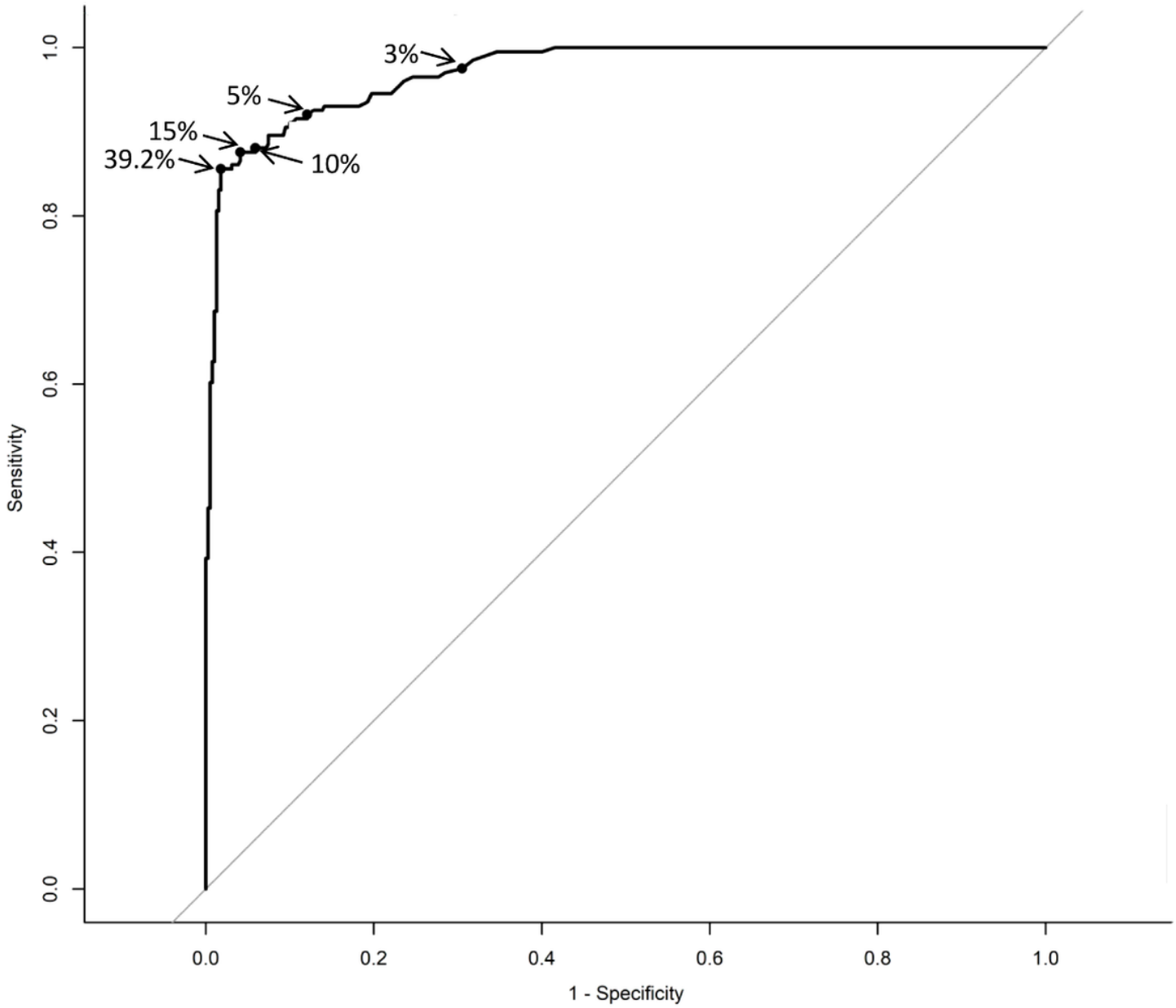

Figure 2

Receiver-operating characteristics (ROC) curves for performance of International Ovarian Tumor Analysis ADNEX model in discriminating between benign and malignant adnexal masses. Optimal cut-off (the maximum value of Youden index) was 39.2% for probability of malignancy, at which sensitivity was 87.06%, specificity was 97.69%, positive predictive value was 95.03%, negative predictive value was 93.66% and area under ROC curve was 0.925. Cut-offs of 3.0%, 5.0%, 10.0% and 15.0% are also indicated.