

Clinical Performance of ADNEX (The Assessment of Different NEoplasias in the adneXa) Model in Early Diagnosis and Staging of Benign and Malignant Ovarian Tumors

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Abstract

Objective: To investigate the clinical value of ADNEX model in early diagnosis and staging of benign and malignant ovarian tumors. **Method:** 136 cases of ovarian cancer patients treated in our hospital were retrospectively analyzed using the ADNEX risk model and MRI data. The accuracy of the two diagnostic methods was compared with the results of pathological examination as gold standard. **Results:** For qualitative assessment, the accuracy and sensitivity of the ADNEX model were 78.70% and 93%, while the accuracy and sensitivity of MRI examination were 80.1%, and 90.7%, respectively. The diagnostic values of the two methods were not statistically different ($P > 0.05$). For ovarian tumor staging, the ADNEX model was significantly less accurate and specific for staging borderline tumor than MRI examination, although it had significantly higher sensitivity ($P < 0.05$). For tumors at other stages, there were no diagnostic differences between the methods ($P > 0.05$). **Conclusion:** ADNEX risk model has certain diagnostic and predictive value to distinguish benign from malignant ovarian tumors. It is useful to detect and exclude ovarian tumor. However, for early diagnosis, it is not accurate enough and further study is needed to validate this usefulness.

Keywords

Ovarian Cancer, ADNEX Risk Model, MRI Examination

1. Introduction

The incidence of ovarian cancer ranks the third in gynecological malignancies with the highest mortality [1]. Early diagnosis and cytoreductive surgery im-

prove 5-year survival rate [2] [3]. However, early screening and diagnosis of ovarian cancer is a hot but difficult spot in ovarian cancer research. The auxiliary diagnosis of ovarian cancer mainly includes the use of imaging examination and serum markers. Since ultrasound examination is simple and cost effective, it is most widely used in gynecological examination. To maximize the efficiency of early diagnosis of ovarian cancer, a number of ultrasound models have been proposed [4] [5] [6]. In 2014, the Assessment of Different NEoplasias in the adneXa (ADNEX) model was proposed to differentiate between benign, borderline, early and advanced stage invasive, and secondary metastatic tumors [7]. It can automatically provide differentiation between benign and malignant and tumor staging information on mobile devices or websites using clinical information and ultrasound data. At present, the clinical performance of the model has not been reported in China. The aim of this study is to investigate the clinical value of the model in the early diagnosis and staging of benign and malignant ovarian tumors.

2. Subjects and Methods

2.1. Subjects

223 cases of patients enrolled at the First Affiliated Hospital of Yangtze University from January 2011 to October 2015 with ovarian cancer were retrospectively analyzed. The patients were preoperatively diagnosed using color Doppler ultrasound and postoperatively confirmed pathologically to have epithelial tumors. Of them, 136 patients had ultrasound data for the ADNEX modeling and were examined using pelvic MRI examination. Among them, there were benign in 93 cases and malignant in 43 cases. The age ranged from 19 to 74 years with an average age of 45.6 years. MRI and pathological staging were performed based on 2013 FIGO [8]. Inclusive criteria: 1) From January 2011 to October 2015, we have admitted ovarian cancer to the Department of Obstetrics and gynecology in our hospital; 2) Histopathological diagnosis of ovarian tumors is clear, and the nature and pathological staging of ovarian tumors are determined; 3) Ovarian tumors are epithelial; 4) All the patients were examined by transvaginal ultrasound before operation. The ultrasonic image data can be read out or recorded, and all the index data needed for the ADNEX model can be read out; 5) MRI examination was performed before or after operation, with or without abdominal distension, abdominal pain and other clinical symptoms; 6) Preoperative serum CA125 examination is available or not. Exclusion criteria: 1) No MRI examination was performed before the operation; 2) Non epithelial ovarian tumor; 3) The ultrasonic inspection record is incomplete or missing image; 4) Exclusion of endometriosis, tuberculous peritonitis, tumors outside the reproductive tract (retroperitoneal neoplasms, rectal cancer, sigmoid colon cancer, etc.).

2.2. Methods

Ultrasound examinations were conducted using Philips ClearVue 580 system

and reported by the same physician. The married patients were examined by transvaginal examination, while the unmarried patients were examined by rectal examination. If the tumors were large, transabdominal examinations were performed.

MRI axial, sagittal and coronal scans were performed using GE Signal 1.5 T magnetic resonance imaging system. The field of view (FOV) was 28 - 36 cm and the layer thickness/spacing were 5 mm/1mm. T1WI was obtained using SE sequence at TR/TE: 350 - 550/10ms, with a matrix of $256 \times (192 - 128)$. The number of acquisition was 2. T2WI was generated using FSE sequence at TR/TE: 3000/108ms with a matrix of 320×224 . The number of scans was 4. The enhanced scanning was performed once at TR/TE: 80 to 150 ms/minimum with a matrix of $256 \times (192 - 224)$. The number of scans was 1. The contrast agent was acyclic, ionic gadolinium (GD-DTPA), used at a dose of 0.1 to 0.2 mmol/kg, injected at a rate of 2.5 ml/s rate through elbow vein.

Serum CA125 was detected using ADVIA Centaur XP automated chemiluminescence analysis system and associated kit (Siemens, Germany).

ADNEX modeling used 3 clinical indexes such as age, serum CA125 level and category of diagnosis and treatment center (whether the medical institutions had tumor diagnosis center) and 6 ultrasound parameters such as the maximum diameter of lesion, ratio of solid tissue, whether there were more than 10 cysts, the number of papillae, whether there were echoes or not and whether there were ascites or not. The sampling of images acquired with ultrasound is shown in **Figures 1(a)-(f)**. ADNEX model was accessed at <http://www.iotagroup.org/adnexmodel/>. Once relevant data were input, the property and staging of the tumor were automatically generated by the on-line ADNEX model software.

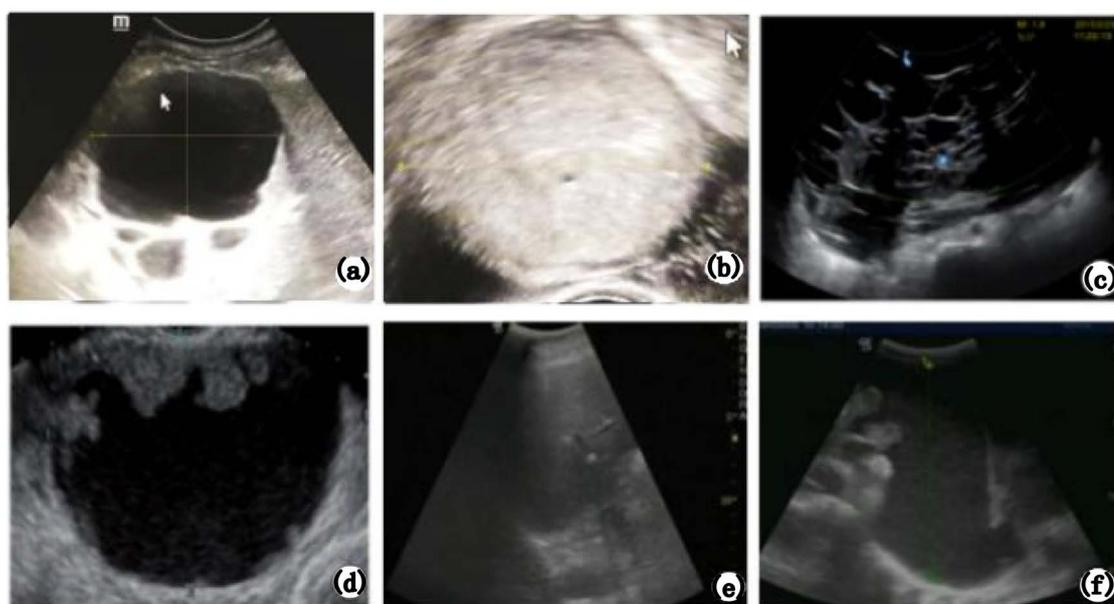


Figure 1. Collecting indicator for ADNEX model. (a) The maximum diameter of tumor (mm); (b) Measurement of solid tissue; (c) Count of cysts to see if they are more than 10; (d) The number of papillae (0, 1, 2, 3, >3); (e) Echo or not; (f) Ascites or not.

2.3. Statistical Analysis

Data were processed using SPSS 17.0 statistical software. Enumeration data were tested using χ^2 test. The data were considered statistically different when P is <0.05 and were tested using a receiver operating characteristic curve (ROC).

3. Results

3.1. Distinguishment of Benign and Malignant Ovarian Tumors

Among the 136 cases, 93 and 43 (including were classified as benign and malignant), (including borderline malignant) based on FIGO (2013), respectively. Based on the ADNEX model software, 70 cases were benign, and 66 cases were malignant. The accuracy, sensitivity and specificity of the ADNEX model were 78.7%, 93%, and 72%, respectively, as compared to the FIGO system. The positive and negative predictive values were 60.6% and 95.7%, respectively (**Table 1**).

3.2. Staging of Ovarian Cancer by the ADNEX Model

Compared to the pathological results, the ADNEX model classified the tumors into five stages benign, borderline, I stage, II to IV stage and metastatic tumor (**Table 2**).

Table 1. The outcome of the ADNEX modeling on benign and malignant ovarian tumors.

Pathological examination	ADNEX modeling		Total
	Malignant	Benign	
Malignant	40	3	43
Benign	26	67	93
Total	66	70	136

Table 2. Prediction of tumor stage using the ADNEX model.

	Benign	Borderline	I stage	II to IV stage	Metastatic tumor
Accuracy (%)	78.6	86.0	91.9	86.8	93.4
Sensitivity (%)	72.0	50.0	25.0	90.9	14.3
Specificity (%)	93.0	87.8	96.1	86.0	97.7
Positive predictive value (%)	95.7	15.8	28.6	55.6	25.0
Negative predictive value (%)	60.6	97.4	95.3	98.0	95.5

Remark: ACC: Accuracy; SENS: Sensitivity, SPEC: Specificity; PPV: Positive predictive value; NPV: Negative predictive value.

3.3. Comparison of the ADNEX Model and MRI in the Diagnosis of Benign and Malignant Ovarian Tumors

Use the pathological results as gold standard, MRI detected 74 cases of benign and 62 cases of malignant tumors. The ROC analysis showed that the areas under the curve (AUC) in the ADNEX model and MRI data were 0.825 and 0.830, respectively (Figure 2). Statistical analysis showed that there were no significant difference between the two methods in the accuracy, sensitivity, specificity, positive predictive value and negative predictive value ($P > 0.05$, Table 3).

The AUC is 0.825 and 0.830 for the ADNEX model and MRI, respectively.

3.4. Comparison of the ADNEX Model and MRI in Tumor Staging

Using the pathological results as gold standard, the ADNEX model detected 70

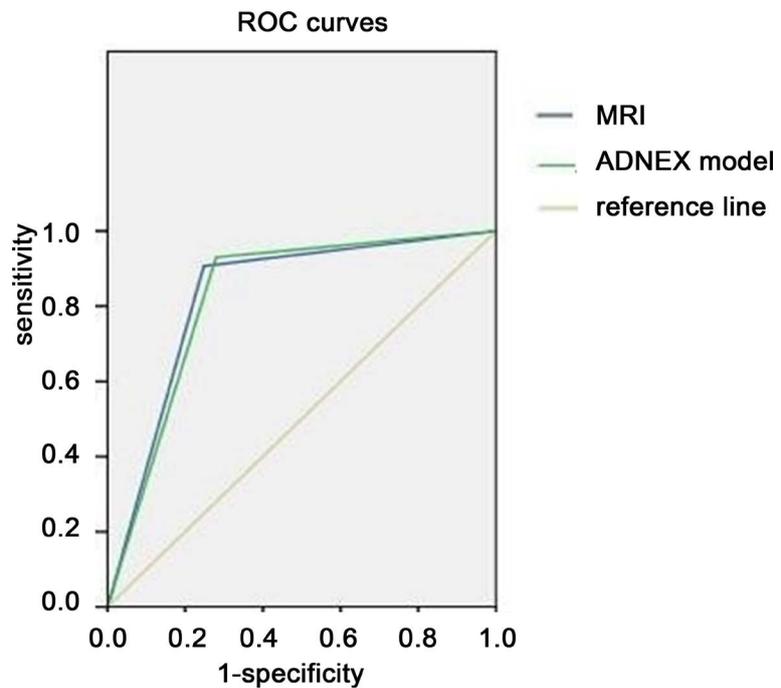


Figure 2. ROC showing the comparison of the ADNEX model and MRI in the detection of benign and malignant ovarian tumors.

Table 3. Comparison of the ADNEX model and MRI in differentiating benign and malignant ovarian tumors.

	ADNEX model	MRI	X ²	P
Accuracy (%)	78.7	80.1	0.09	0.764
Sensitivity (%)	93.0	90.7	0.156	0.693
Specificity (%)	72.0	75.3	0.249	0.618
Positive predictive value (%)	60.6	62.9	0.071	0.789
Negative predictive value (%)	95.7	94.6	0.098	0.755

benign, 19 borderline, 7 stage I, 36 stage II - IV and 4 metastatic tumors. MRI detected 74, 0 borderline, 18 stage I, 43 stage II- IV and 1 metastatic tumors. Compared with MRI, the ADNEX model has significantly lower accuracy and specificity, but significantly higher sensitivity for borderline tumor ($P < 0.05$). For other diagnostic outcomes, the results were similar between the two methods ($P > 0.05$, **Table 4**).

Table 4. Comparison of the ADNEX model and MRI in staging ovarian tumors.

Tumor stage	Diagnostic value	ADNEX model	MRI	χ^2	P
Benign	Accuracy (%)	78.6	80.1	0.09	0.764
	Sensitivity (%)	72.0	75.3	0.249	0.618
	Specificity (%)	93.0	90.7	0.156	0.693
	Positive predictive value (%)	95.7	94.6	0.098	0.755
	Negative predictive value (%)	60.6	62.9	0.071	0.789
Borderline	Accuracy (%)	86.0	95.6	7.44	0.006
	Sensitivity (%)	50.0	-	4.000	0.046
	Specificity (%)	87.8	100	17.049	-
	Positive predictive value (%)	15.8	-	-	-
	Negative predictive value (%)	97.4	95.6	6.26	0.429
I stage	Accuracy (%)	91.9	88.2	1.028	0.311
	Sensitivity (%)	25.0	62.5	2.286	0.131
	Specificity (%)	96.1	89.8	3.824	0.051
	Positive predictive value (%)	28.6	27.8	0.002	0.968
	Negative predictive value (%)	95.3	97.5	0.781	0.377
II to IV stage	Accuracy (%)	86.8	78.7	3.112	0.078
	Sensitivity (%)	90.9	81.8	0.772	0.380
	Specificity (%)	86.0	78.1	2.409	0.121
	Positive predictive value (%)	55.6	41.9	1.472	0.225
	Negative predictive value (%)	98.0	95.7	0.847	0.357
Metastatic	Accuracy (%)	93.4	94.1	0.063	0.802
	Accuracy (%)	14.3	-	1.077	0.299
	Sensitivity (%)	97.7	99.2	1.016	0.314
	Specificity (%)	25.0	-	0.313	0.576
	Positive predictive value (%)	95.5	94.8	0.059	0.808

4. Discussion

Ovarian cancer is a common malignant tumor in female reproductive systems, the incidence rate ranks the third and only seconds to cervical cancer and uterine cancer. Furthermore, the incidence has been increasing recently. It has been a hot but challenging spot to find effective early diagnosis method. The advantage of the ADNEX model is that it is designed specifically for predicting and staging benign and malignant ovarian tumors in a cost effective way. It uses conventional clinical information and ultrasound data for on-line prediction, irrespective of the availability of CA125 data. For ultrasound examination, data corrected by inexperienced physician are sufficient for modeling. MRI provides images at various directions and layers, and is especially suitable for soft tissue. It can display the relationship between the various organs in the pelvic cavity and guide surgical operation although the reports may be somewhat subjective.

4.1. The Clinical Significance of the ADNEX Model in the Diagnosis of Benign and Malignant Ovarian Tumors

It was reported that when the two sets of data were used for the diagnosis of benign and malignant ovarian tumors, the accuracy of the ADNEX model was 79.9%, and 81.3%, respectively [9]. We found that the accuracy, sensitivity and specialty of the ADNEX model were 78.70%, 93%, and 72%, respectively with the positive predictive value of 60.6% and negative predictive value of 95.7%. The accuracy is similar to the previous report. The accuracy, sensitivity, specialty, positive predictive value and negative predictive value of MRI were 80.1%, 90.7%, 75.3%, 62.9% and 94.6%, respectively. AUC was 0.825 and 0.830 for the ADNEX model and MRI, suggesting that both methods have excellent diagnosis value, although MRI is slightly better than the ADNEX model. Statistically, the two methods are the same in the tumor diagnosis. The outcomes of the ADNEX model showed that it is better for the detection and exclusion of ovarian tumors. It is clear that the ADNEX model is clinically valuable for the diagnosis of benign and malignant ovarian tumors as MRI technology.

4.2. The Clinical Significance of the ADNEX Model in Staging Ovarian Tumors

Traditionally, ovarian tumor staging is mainly depended on pathological examination, not on ultrasound data. The staging results based on the ADNEX model are similar to those reported previously [9]. The accuracy and sensitivity of the ADNEX model on early stage tumors were less than on late stage tumors. For early stage tumors, the ADNEX model and MRI are similar. For borderline tumor staging, the ADNEX model is less accurate and specific but more sensitive as compared with MRI ($P < 0.05$). For staging tumors at other stages, the outcomes from the two methods are slightly, and statistically insignificantly different ($P > 0.05$). Therefore, the ADNEX model is better at ovarian tumor staging, while MRI cannot directly stage the tumors, particularly for borderline tumor.

Although the ADNEX model is not perfect but it is a big step forward in tumor staging, despite its low sensitivity to early stage tumor. For better clinical use of the ADNEX model and higher qualitative assessment and staging of benign and malignant ovarian tumors, we have identified a number of shortcomings in the ADNEX model. For example, the age input has to be ≥ 14 ; the maximum diameter of tumor must be ≥ 8 mm. It is desirable to improve the model making it possible to accommodate the data outside the current range for better applicability. In addition, parameters used in the model may be expended to include indexes describing lymph node enlargement, nodes in pelvic cavity and posterior fornix, blood flow signal and resistance if any. Finally, due to the retrospective nature of the study, the ultrasound data parameters collected did not strictly follow what are required in the model, and some of the data were estimated. The limited sample size may also affect the diagnostic efficacy of the ADNEX model and MRI examination. It is likely that the model would have better diagnosis performance for differentiating benign and malignant ovarian tumors and their staging if the model is modified, clinical data are collected according to the model requirement, and further prospective study is conducted.

In conclusion, our study shows the ADNEX model is clinically value for differentiating benign and malignant ovarian tumors and their staging. It is useful for detection and exclusion of ovarian tumors, although its staging ability for early stage tumor needs further improvement and validation.

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