ORIGINAL ARTICLE

IOTA Scoring and Tumor Marker Combination as a Tool to Decide on Minimally Invasive Approach for Adnexal Mass: A Review in Low-resource Setting of Islands

Pinky Sarasa Kumar Sahoo[1], Sudha Patil[2], Deepak Kumar[3], Sukesh Kumar Kathpalia[4], Nikhil R Nair[5]

Received on: 04 January 2023; *Accepted on:* 30 January 2023; *Published on:* 31 July 2023

Abstract

Background: Accurate preoperative initial evaluation of adnexal masses to distinguish between benign and malignancy is essential to plan the extent and surgical mode. The purpose of our study was to assess the effectiveness and precision of the international ovarian tumor analysis (IOTA) scoring model in low-resource settings of peripheral islands of India.

Material and Methods: A retrospective study of all cases operated for adnexal mass in our department between 2017 and 2021 was carried out in this medical college. Cases of adnexal mass were subjected to IOTA scoring, tumor markers, and clinical profile analysis and were classified as presumptively benign, malignant, or inconclusive to decide the mode of surgery. The diagnostic performance of the IOTA system was evaluated and different variables were analyzed.

Result: Among total of 53 patients, 32 (60.3%) could undergo laparoscopic management. Only one case of the borderline endometrioid tumor was missed as benign by the scoring system (3.1%). The sensitivity of the IOTA regression system was 93%, the specificity 83.78%, and the positive and negative predictive values were 71% and 96% respectively. The negative likelihood ratio was 0.07 and accuracy was around 86%. None of the cases needed intraoperative conversion.

Conclusion: International ovarian tumor analysis (IOTA) scoring system is a simple, clinically feasible diagnostic tool that accurately distinguishes benign from malignant adnexal pathologies and can guide in deciding on a laparoscopic approach.

Clinical significance: Benefits of laparoscopy can be provided even in low-resource setup by use of the IOTA ultrasonic scoring model.

Keywords: Adnexal mass, IOTA simple ultrasound rules, Laparoscopic management, Ovarian tumors, Tumor markers, Ultrasound.

Journal of South Asian Federation of Obstetrics and Gynaecology (2023): 10.5005/jp-journals-10006-2223

Introduction

In the evolving era of technology, most adnexal masses are being managed by minimally invasive techniques even when moderately large. By carrying out the operative procedure within the endo bag and using of Hassan entry technique it is possible to prevent any spillage and the possibility of port site metastasis. Adnexal mass constitutes lesions arising from the ovary, fallopian tubes, and para-tubal structures resulting in vaginal or abdominally palpable mass.[1] The pathology can range from benign to borderline, to frankly malignant or occasionally infective pathology.

There are multiple tools used to suggest the nature of the disease and here we want a tool that can be used to make an accurate preoperative diagnosis to distinguish between the benign from the malignant, in order to provide the extended benefits of laparoscopic surgeries even in peripheral setups. In our study, we propose to evaluate the efficacy of the International ovarian tumor analysis group (IOTA) ultrasonic scoring system for the same in a low-resource settings. We selected the above scoring system as it is a relatively simple, teachable, feasible method that can be adopted by most gynecologic units in the initial stages of evaluation.

The purpose of having a higher-accuracy diagnostic tool is to minimize the possibility of having an undiagnosed, unexpected malignant mass intraoperatively during the laparoscopy. According to a series of cases evaluated and managed laparoscopically by Nehzat et al. (1,011 women with adnexal masses) and Canis et al. (757 patients with 819 masses) the incidence of unexpected malignancy discovered when managing an adnexal mass was 0.4 and 2.9% respectively.[2,3]

[1,2,4,5]Department of Obstetrics and Gynaecology, Andaman and Nicobar Islands Institute of Medical Sciences, Port Blair, Andaman and Nicobar Islands, India

[3]Department of Community Medicine, Andaman and Nicobar Islands Institute of Medical Sciences, Port Blair, Andaman and Nicobar Islands, India

Corresponding Author: Nikhil R Nair, Department of Obstetrics and Gynaecology, Andaman and Nicobar Islands Institute of Medical Sciences, Port Blair, Andaman and Nicobar Islands, India, Phone: +91 9679562018, e-mail: nikhil.nair1798@gmail.com

How to cite this article: Sahoo PSK, Patil S, Kumar D, *et al*. IOTA Scoring and Tumor Marker Combination as a Tool to Decide on Minimally Invasive Approach for Adnexal Mass: A Review in Low-resource Setting of Islands. J South Asian Feder Obst Gynae 2023;15(3):292–296.

Source of support: Nil

Conflict of interest: None

Materials and Methods

Our study was conducted at a teaching Medical college and hospital in remote peripheral islands of India. It was done as a retrospective record analysis to include all cases of adnexal masses

managed surgically at this center during 2017–2021, after approval by the Institutional ethics committee. Those presenting along with pregnancy and who were referred to a higher center were excluded. The sample size was decided by purposive sampling. As an institutional policy, all cases of adnexal mass were evaluated on the basis of clinical presentation, use of the IOTA scoring system (Table 1 and Fig. 1), and tumor markers as considered appropriate. On the basis of these three criteria the cases were grouped as (A) Presumptively benign; (B) Presumptively malignant; (C) Inconclusive. Tumor markers were done on a case basis and included CA125 (done for all the cases), carcinoembryonic antigen (CEA), lactate dehydrogenase (LDH), alpha-fetoprotein, and HCG were tailored depending on the case profile. Those presumed benign were subjected to laparoscopic management. The ones in the doubtful category were further evaluated by an expert radiologic evaluation which included computerised tomography or MRI. The group of patients in the inconclusive and presumptively malignant group were managed by laparotomy.

Table 1: Classification according to IOTA simple rules: Timmerman et al.

Classification	*Malignant characteristics*
M1	Irregular solid tumor
M2	Presence of ascites
M3	At least 4 papillary structures
M4	Irregular multilocular solid tumor with largest diameter ≥100 mm
M5	High Doppler blood flow (color score 4)
	Benign characteristics
B1	Unilocular
B2	Presence of solid components with largest component <7 mm
B3	Presence of acoustic shadows
B4	Smooth multilocular tumor with largest diameter <100 mm
B5	No Doppler blood flow (color score 1)

The case records of the three groups were analyzed in relation to the sociodemographic variables, tumor marker levels, the mode of surgery, the postoperative complications, the initial diagnosis whether benign, inconclusive, or malignant, and finally the histopathology report was taken as the gold standard. The data was analyzed by use of the SPSS software system. The efficacy of the IOTA screening method for preoperatively detecting benign or malignant lesions was calculated by use of performance tools like sensitivity, specificity, positive and negative likelihood ratio, positive and negative predictive value, and accuracy.

Result

The subjects in the study were aged between 12 years and 60 years. The median age in the laparoscopy group was 32 years, while in the laparotomy group, it was 46 years. The parity ranged from 0 to 3, most of them being para 2 (60%). About 32 women out of 53 (60.4%) could be selected for laparoscopic surgery while the rest were approached by laparotomy. At our center we are presently not able to access the frozen section facility. None of the patients needed a conversion from laparoscopy to open surgery. All the adnexal masses were more than 7 cm in diameter, the largest diameter being 15 cm. In the laparoscopic group, the CA125 value was less than 100 IU/mL in all the cases. In the laparotomic group, the CA125 value ranged between 10 and 2575 IU/mL. While those with benign pathology on histopathology had a of value less than 100 IU/mL. The five cases of the borderline ovarian tumor had CA125 value ranging between 100 and 500 IU/mL, while amongst the malignant epithelial ovarian tumor the highest values was 2527 IU/mL (Table 2).

On analyzing the preoperative classification grouping by the IOTA regression model, it was found that 32 out of total of 53 women were considered to be benign (60.37%), two (3.77%) were found to be inconclusive and 19 (35.84%) were considered malignant. When correlating with the final histopathology report, there were 37 cases that were benign in nature (69.81%), five cases (9.43%) of borderline ovarian tumors, and 11 cases (20.54%) were found to be malignant in nature. The individual breakup of the findings is

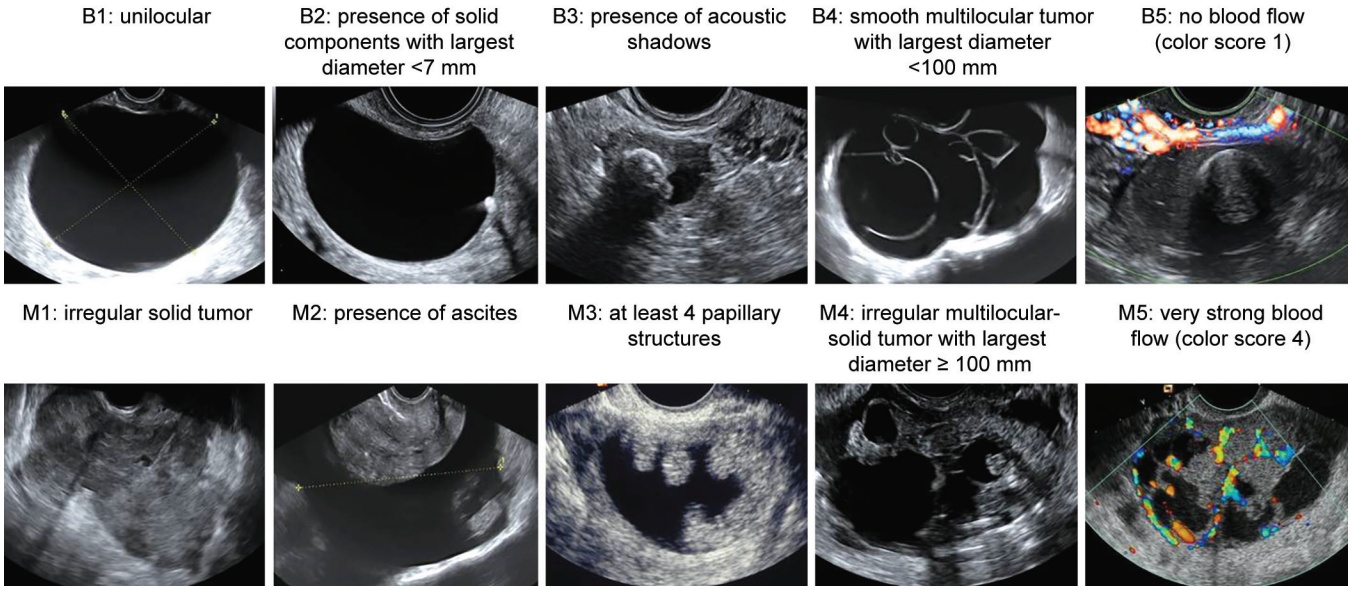

Fig. 1: Descriptors according to IOTA simple rules: Timmerman et al.

presented as a Flowchart 1. About 41% of all the adnexal masses were either benign cystadenoma or cystadenofibromas in our study, the largest group. The histopathologic distribution pattern is represented in Table 3.

It was observed that out of the 32 cases considered benign by the IOTA regression model, only one case of the borderline ovarian tumor was mistakenly classified as benign. There are 15 out of 16 truly borderline/malignant cases were correctly diagnosed as presumptively malignant or inconclusive by the IOTA system. Around six out of 21 cases (28%) were overly diagnosed as inconclusive or malignant by IOTA while in truth they were benign.

Hence, the sensitivity of the IOTA regression system in detecting malignant cases is 93.75% and the specificity is 83.78% with a positive likelihood ratio of 5.77 and a negative likelihood ratio of 0.07. The positive predictive value is 71% and the negative predictive value is 96%. The accuracy of this model was found to be 86.8%, considering this and a very low negative likelihood ratio, we can infer that when using IOTA for preoperative triaging the likelihood that a negative test (preoperative benign diagnosis) will eventually appear as malignancy in histopathology is very low.

Therefore in clinical practice, IOTA Regression Model appears an accurate tool to safely decide on a laparoscopic approach besides taking other clinical parameters into consideration.

Table 2: Ca125 level correlation with histopathology report and staging

Histopathology report	*Ca 125*	*Staging*
Non-epithelial ovarian tumor		
Mixed malignant germ cell tumor	35	II
Granulosa cell tumor	100	I
Borderline ovarian tumor		
Borderline serous ovarian tumor	142	IC
Mucinous borderline ovarian tumor	200	IA
Borderline serous ovarian tumor	220	IA
Mucinous borderline ovarian tumor	484	IA
Borderline endometrioid tumor	80	IA
Epithelial ovarian tumor/fallopian tube tumor		
Mucinous cystadenocarcinoma ovary	400	IA
Endometrioid adenocarcinoma left ovary	800	IC
Mucinous cystadenocarcinoma	800	II
Serous cystadenocarcinoma left fallopian tube	1028	III
Serous cystadenocarcinoma of ovary	1250	IB
High-grade serous carcinoma	1500	III
Adenocarcinoma ovary	2000	III
High-grade serous cystadenocarcinoma ovary	2000	III
Mucinous cystadenocarcinoma ovary	2527	III

Discussion

Adnexal masses are a common gynecologic problem encountered in clinical practice and about 10% and 16% of them will be requiring operative management.[4,5] Though the possibility of malignancy appears to range between 17% and 20% of these, the high mortality rate in women with ovarian malignancy mandates the use of highly

Table 3: Histopathologic distribution in our study

Sl. no.	*Histopathology report (out of 53 pt.)*	*N*	*%*
A	Benign adnexal pathology	37	69.81
	Cystadenoma/cystadenofibroma	22	41.51
	Serous cystadenocarcinoma adenoma of ovary	14	26.41
	Serous cystadenocarcinoma adenofibroma	3	5.66
	Mucinous cystadenocarcinoma adenoma ovary	4	7.54
	Mucinous cystadenocarcinoma adenofibroma ovary	1	1.88
	Ovarian fibrothecoma	1	1.88
	Functional cyst	2	3.77
	Hydrosalpinx	1	1.88
	Paraovarian cyst	4	7.54
	Mature cystic teratoma	4	7.54
	Endometriotic cyst ovary	3	5.66
B	Borderline ovarian tumor	5	9.43
C	Adenocarcinoma of the ovary/fallopian tube	8	15.09
	Serous cystadenocarcinoma ovary	4	7.54
	Mucinous cystadenocarcinoma ovary	2	3.77
	Endometrioid adenocarcinoma ovary	1	1.88
	Serous cystadenocarcinoma adenoma carcinoma fallopian tube	1	1.88
D	Germ cell tumors	3	5.66
	Granulosa cell tumor	1	1.88
	Mixed malignant germ cell tumor	2	3.77

Flowchart 1: Patient distribution based on IOTA and the histopathology outcome

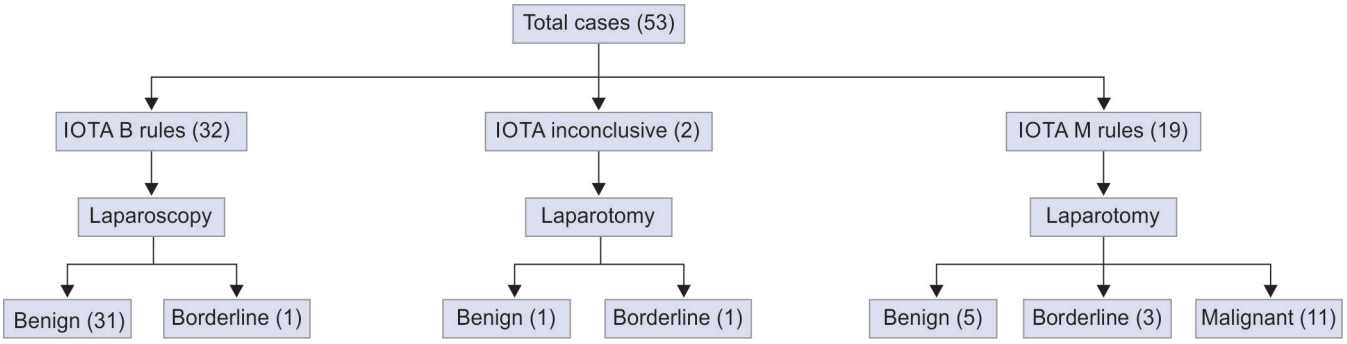

Table 4: Comparison of diagnostic performance of various modalities by different authors

	Sensitivity (%)	*Specificity (%)*	*Positive predictive value (%)*	*Negative predictive value (%)*	*AUC*	*Author*
RMI	78	80	60	90	0.88	Yanaranop et al.
ROMA	78	88	65	92	0.84	Yurkovetsky Z et al.
IOTA	93	83	71	96		Our Study
ORAD	94	66	80	89		Xie WT et al.

accurate triaging mechanisms in the preoperative assessment.[4,5] This will enable the application of oncologic principles in management or referral to a gynecologic oncology unit in case of a high probability of malignancy. The benefits of laparoscopy can be correctly applied to those deemed benign. The use of laparoscopic surgery may be associated with the risk of an intraoperative rupture of ovarian cystic masses.[6] In addition; port-site metastasis remains a major concern even in borderline ovarian malignancy.[7] Incidence of unexpected malignancy in laparoscopically managed adnexal masses has been quoted as 0.4, 1.5, and 2.5% in various studies respectively which was similar to our study's 3.1%.[2,3,7] When we use a higher accuracy diagnostic modality we can minimize the error. Hence the need for a relatively simple, clinically applicable, teachable diagnostic model that is accurate in its efficacy.

When we consider CA125 alone, it is found to be raised more than 35 kU/L in only 50% of stage I epithelial ovarian cancer and in 92% of advanced-stage ovarian cancer.[8] The search for better sensitivity and specificity resulted in evolving a panel of biomarkers by Yurkovetsky and colleagues encompassing CA125, human epididymis protein 4 (HE4), carcinoembryonic antigen (CEA), and vascular cell adhesion molecule-1 (VCAM-1).[9] This panel had a sensitivity of 86% in early-stage ovarian cancer and 93% in late-stage cancer at a fixed specificity of 98%.[9] With the help of HE4 in differentiating endometriotic masses from malignant ovarian masses in combination with other modalities.[10] The commercially available panel including HE4, CA125, and postmenopausal status is known as the risk of ovarian malignancy algorithm (ROMA). In 1990 the biomarker-based algorithm combining ultrasound as well, called the risk of malignancy index (RMI) was developed in order to identify those with a high probability of ovarian malignancy in women with adnexal masses. It included variables such as menopausal status, fixed threshold (≥35 U/mL) CA125 levels, and ultrasound findings in a logistic model. The sensitivity, specificity, and positive predictive value are 78, 95, and 82% repectively.[11] Similar performance values have been demonstrated by Indian authors in the context of women presenting with ovarian masses.[12,13] Addition of color Doppler to transvaginal ultrasound (TVUS) increases the sensitivity and specificity to 90%.[14]

In 2008 the international ovarian tumor analysis group (IOTA) developed a set of 10 simple descriptors and rules for benign ovarian appearances (B Rules) and malignant ovarian appearances (M Rules) by TVUS and the addition of color Doppler in the form of a logistic regression Model. These rules were applicable in 76% (386/507) of the tumors, where they had a sensitivity of 95% (106/112), a specificity of 91% (249/274), LR+ of 10.37, and LR– of 0.06.[15] The reproducibility of the above Model even in the hands of observers of variable experience has been proven by extensive external validation. Povilas Sladkevicius et al. demonstrated Interobserver agreement when classifying tumors as benign or malignant was 84% (98/117).[16–18]

Additionally, the ovarian-adnexal reporting and data system (O-RADS) was published by the American College of Radiology (ACR) and provides guidelines for ovarian management in high-risk categories.[19] It included O-RADS 0 (an incomplete evaluation); O-RADS 1 (the physiologic category, including a normal premenopausal ovary); O-RADS 2 (the almost certainly benign category, (<1% malignancy), O-RADS 3 (low risk of malignancy 1%–<10%), O-RADS 4 (intermediate risk 10–50%), O-RADS 5 (high-risk of malignancy >50%).

A comparative analysis of the diagnostic performances of the various modalities available is presented in Table 4.[9,19,20]

Conclusion

The most attractive attribute of the IOTA regression model is its simplicity in spite of high accuracy, making it an ideal initial triaging tool for differentiating benign from malignant adnexal masses. Those considered inconclusive or possibly malignant may need further expert radiologic evaluation. Thus IOTA model can be used to decide upon a laparoscopic approach for their management.

Limitations of the Study

The sample size of the study is minimal due to the lesser population of the outer island setting.

Orcid

Pinky Sarasa Kumar Sahoo https://orcid.org/0000-0001-5004-6275

References

1. Seshadri L. Benign diseases of the ovary and fallopian tube. In essentials of gynaecology. 2nd edition. New Delhi: Wolters Kluwer/Lippincott Williams and Wilkins; 2016. p. 167.
2. Nezhat F, Nezhat C, Welander CE, et al. Four ovarian cancers diagnosed during laparoscopic management of 1011 women with adnexal masses. Am J Obstet Gynecol 1992;167(3):790–796. DOI: 10.1016/s0002-9378(11)91591-9.
3. Canis M, Mage G, Pouly JL, et al. Laparoscopic diagnosis of adnexal cystic masses: A 12-year experience with long-term follow-up. Obstet Gynecol 1994;83(5 pt 1):707–712. PMID: 8164928.
4. Bullock B, Larkin L, Turker L, et al. Management of the adnexal mass: Considerations for the family medicine physician. Front Med (Lausanne) 2022;9:913549. DOI: 10.3389/fmed.2022.913549.
5. Rai R, Bhutia PC, Tshomo U. Clinicopathological profile of adnexal masses presenting to a tertiary-care hospital in Bhutan. South Asian J Cancer 2019;8(3):168–172. DOI: 10.4103/sajc.sajc_303_18.
6. Weber S, McCann CK, Boruta DM, et al. Laparoscopic surgical staging of early ovarian cancer. Rev Obstet Gynecol 2011;4(3–4):117–122. PMID: 22229064.
7. Matsushita H, Watanabe K, Yokoi T, et al. Unexpected ovarian malignancy following laparoscopic excision of adnexal masses. Hum Reprod 2014;29(9):1912–1917. DOI: 10.1093/humrep/deu162.

8. Dochez V, Caillon H, Vaucel E, et al. Biomarkers and algorithms for diagnosis of ovarian cancer: CA125, HE4, RMI and ROMA, a review. J Ovarian Res 2019;12:28. DOI: 10.1186/s13048-019-0503-7.
9. Yurkovetsky Z, Skates S, Lomakin A, et al. Development of a multimarker assay for early detection of ovarian cancer. J Clin Oncol 2010;28(13):2159–2166. DOI: 10.1200/JCO.2008.19.2484.
10. Yang S, Tang J, Rong Y, et al. Performance of the IOTA ADNEX model combined with HE4 for identifying early-stage ovarian cancer. Front Oncol 2022;12:949766. DOI: 10.3389/fonc.2022.949766.
11. Berek JS, Hacker NF. Ovarian Cancer – Tumor Markers and Screening. In: Berek and Hacker's Gynecologic Oncology. 6th edition. Philadelphia: Wolters Kluwer; 2015. p. 447–448.
12. Malla VG, Tuteja A, Singh P. Rethinking the role of serum cancer antigen 125 and risk of malignancy index in Indian women with ovarian masses: Newer perspectives and review of literature. J South Asian Feder Obst Gynae 2018;10(2):110–117. DOI: 10.5005/jp-journals-10006-1571.
13. Shekar NC, Dasappa P, Rangaiah N, et al. Evaluation of risk of malignancy index 5 - A new indicator in differentiating benign and malignant ovarian masses. J South Asian Feder Obst Gynae 2019;11(4):258–262. DOI: 10.5005/jp-journals-10006-1706.
14. Sohn C, Voigt H-J, Vetter K. Doppler ultrasound in gynecology. In: Doppler ultrasound in gynecology and obstetrics. Stuttgart: Thieme; 2004. p. 189.
15. Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. Ultrasound Obstet Gynecol 2008;31:681–690. DOI: 10.1002/uog.5365.
16. Timmerman D, Planchamp F, Bourne T, et al. ESGO/ISUOG/IOTA/ESGE consensus statement on preoperative diagnosis of ovarian tumors. Ultrasound Obstet Gynecol 2021;58(1):148–168. DOI: 10.1002/uog.23635.
17. Sladkevicius P, Valentin L. Interobserver agreement in describing the ultrasound appearance of adnexal masses and in calculating the risk of malignancy using logistic regression models. Clin Cancer Res 2015;21(3):594–601. DOI: 10.1158/1078-0432.CCR-14-0906.
18. Sayasneh A, Wynants L, Preisler J, et al. Multicentre external validation of IOTA prediction models and RMI by operators with varied training. Br J Cancer 2013;108(12):2448–2454. DOI: 10.1038/bjc.2013.224.
19. Xie WT, Wang YQ, Xiang ZS, et al. Efficacy of IOTA simple rules, O-RADS, and CA125 to distinguish benign and malignant adnexal masses. J Ovarian Res 2022;15(1):15. DOI: 10.1186/s13048-022-00947-9.
20. Yanaranop M, Anakrat V, Siricharoenthai S, et al. Is the risk of ovarian malignancy algorithm better than other tests for predicting ovarian malignancy in women with pelvic masses? Gynecol Obstet Investig 2017;82(1):47–53. DOI: 10.1159/000446238.