APPENDIX S5 OVARIAN CANCER

1.1. Standardized ultrasound report for ovarian cancer assessment

Ultrasound parameter	Description
Adnexal mass (describe the most complex mass or, in case of similar morphology, the largest one)	▪ Unilateral / bilateral ▪ Side of dominant mass: right, left, central ▪ Origin of the dominant mass: ovarian, paraovarian, fallopian tube, uncertain ▪ Morphology according to IOTA terms (Figure S2)[1]: unilocular, unilocular-solid, multilocular, multilocular-solid, solid ▪ Largest diameter (mm) ▪ Ovarian crescent sign: Present or Absent
Pattern recognition of dominant mass	▪ Benign/borderline/malignant ▪ Specific diagnosis
IOTA ADNEX model (with/without CA 125)	▪ CA 125 U/mL (if available) ▪ Risk of malignancy (subgroup of malignancy)[2, 3]
Intraperitoneal free fluid	▪ Present (pelvic, subdiaphragmatic, abdominal) ▪ Absent
Pelvic involvement	▪ Anterior compartment ▪ Posterior compartment > Recto-sigmoid carcinomatosis (serosa only / muscularis propria and deeper) If the pelvic side wall is affected, document the involved structures£
Upper Abdominal involvement	▪ Left diaphragm ▪ Splenic parenchyma / serosa / perisplenic ligaments ▪ Right diaphragm ▪ Liver parenchyma / serosa ▪ Lesser omentum and liver hilum ▪ Other visceral organs (gallbladder, stomach and duodenum, pancreas and others) ▪ Kidneys/ureters (if dilatation, the grading of hydronephrosis, distention of the renal sinus (grade 1), or the renal pelvis and calyces (grade 2), sacciform hydronephrosis and atrophy of renal parenchyma (grade 3)[4]
Anterior abdominal wall	▪ Present/absent involvement
Mesogastrium involvement	▪ Supracolic omentum ▪ Infracolic omentum ▪ Large and small bowel serosa and its mesentery ▪ Left and right paracolic gutter
Regional (pelvic and abdominal) lymph nodes£	Description of site, number, laterality Assessment by standardized VITA terms using the classification LN1 – LN5[5]: ▪ LN1: Normal finding ▪ LN2: Benign finding ▪ LN3: Indeterminate, probably benign finding ▪ LN4: Probably malignant finding ▪ LN 5: Malignant finding
Distant spread	▪ Distant lymph nodes (inguinofemoral / supradiaphragmatic; site, number, laterality if appropriate, lymph node status LN1-LN5)[5] ▪ Other distant spread (pleural parietal wall involvement right/left)
Pleural fluid (hydrothorax)	▪ Right/left
Other findings	▪ Related / unrelated gynecologic / non-gynecologic pathologies
Prediction of non-resectability (Figure S7)*	▪ Small bower carcinomatosis ▪ Root of the small bowel ▪ Stomach/duodenum ▪ Head/corpus of the pancreas ▪ Non-resectable liver metastases ▪ Hepatic hilum ▪ Non-resectable lymph node metastases
Staging system	▪ TNM and FIGO staging systems[6-8]

	▪ Comments and recommendations to additional diagnostic tests to the referring specialist and to multidisciplinary team meeting

[£]Pelvic side wall is defined as the parietal muscles of the pelvis, fascia, neurovascular structures, or skeletal portions of the bony pelvis.
**ESMO-ESGO markers of non-resectability. Non-resectable disease is defined by one or more markers published by the ESMO-ESGO consensus conference in 2019 (Figure S7)[9].*

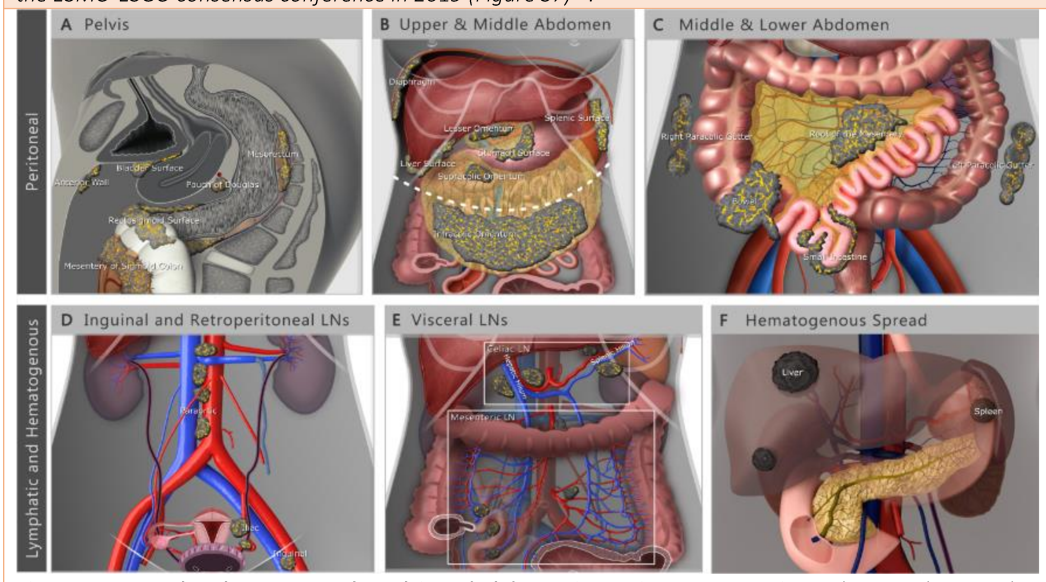

Figure S1 Protocol on how to scan the pelvis and abdomen in ovarian cancer staging. *Schematic diagram showing pelvic involvement with peritoneal carcinomatosis (A) parietal carcinomatosis in pouch of Douglas, visceral carcinomatosis in uterovesical fold and on the sigmoid colon, mesenteric carcinomatosis in the mesorectum and sigmoid mesocolon. Schematic diagram showing peritoneal carcinomatosis in upper quadrant (C) with parietal carcinomatosis on the diaphragm, visceral carcinomatosis on the liver, stomach and splenic surface and omental carcinomatosis including lesser (hepatoduodenal and hepatogastric ligaments) and greater omentum infiltration (the border of supra- and infracolic omentum is marked with dot-and-dash code according to the position of the transverse colon). Schematic diagram showing an example of peritoneal involvement in the middle abdomen (C) with parietal carcinomatosis in the left paracolic gutter, visceral carcinomatosis on the caecum and ileal loops and mesenterial involvement of the radix mesenterii of the small intestine. Schematic diagram showing inguinal and retroperitoneal iliac and paraaortic lymph node involvement (D). Schematic diagram of infiltrated visceral lymph nodes (E) containing coeliac and mesenteric lymph nodes. Schematic diagram of haematogenous spread in the liver and spleen (F).*
LNs, lymph nodes.

Table S1 *Ultrasound checklist on tubo-ovarian cancer based the consensus of the authors*

1.2. FIGO / TNM staging system for tubo-ovarian cancer

FIGO	T	N	M	DEFINITION
I	T1	N0	M0	The cancer is only in the ovary (or ovaries) or fallopian tube(s) (T1). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IA	T1a	N0	M0	The cancer is in one ovary, and the tumor is confined to the inside of the ovary; or the cancer is in one fallopian tube, and is only inside the fallopian tube. There is no cancer on the outer surfaces of the ovary or fallopian tube. No cancer cells are found in the fluid (ascites) or washings from the abdomen and pelvis (T1a).
IB	T1b	N0	M0	The cancer is in both ovaries or fallopian tubes but not on their outer surfaces. No cancer cells are found in the fluid (ascites) or washings from the abdomen and pelvis (T1b).
IC	T1c	N0	M0	The cancer is in one or both ovaries or fallopian tubes and any of the following are present: The tissue (capsule) surrounding the tumor broke during surgery, which could allow cancer cells to leak into the abdomen and pelvis (called **surgical spill**). This is stage **IC1**. Cancer is on the outer surface of at least one of the ovaries or fallopian tubes **or** the capsule (tissue surrounding the tumor) has ruptured (burst) before surgery (which could allow cancer cells to spill into the abdomen and pelvis). This is stage **IC2**. Cancer cells are found in the fluid (ascites) or washings from the abdomen and pelvis. This is stage **IC3**.
II	T2	N0	M0	The cancer is in one or both ovaries or fallopian tubes and has spread to other organs (such as the uterus, bladder, the sigmoid colon, or the rectum) within the pelvis **or** there is primary peritoneal cancer (T2). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIA	T2a	N0	M0	The cancer has spread to or has invaded (grown into) the uterus or the fallopian tubes, or the ovaries. (T2a).
IIB	T2b	N0	M0	The cancer is on the outer surface of or has grown into other nearby pelvic organs such as the bladder, the sigmoid colon, or the rectum (T2b).
IIIA1	T1 or T2	N1	M0	The cancer is in one or both ovaries or fallopian tubes, **or** there is primary peritoneal cancer (T1) and it may have spread or grown into nearby organs in the pelvis (T2). It has spread to the retroperitoneal (pelvic and/or para-aortic) lymph nodes only. It has not spread to distant sites (M0).
IIIA2	T3a	N0 or N1	M0	The cancer is in one or both ovaries or fallopian tubes, or there is primary peritoneal cancer and it has spread or grown into organs outside the pelvis. During surgery, no cancer is visible in the abdomen (outside of the pelvis) to the naked eye, but tiny deposits of cancer are found in the lining of the abdomen when it is examined in the lab (T3a). The cancer might or might not have spread to retroperitoneal lymph nodes (N0 or N1), but it has not spread to distant sites (M0).
IIIB	T3b	N0 or N1	M0	The cancer is in one or both ovaries or fallopian tubes, or there is primary peritoneal cancer and it has spread or grown into organs outside the pelvis. During surgery, no cancer is visible in the abdomen (outside of the pelvis) to the naked eye, but tiny deposits of cancer are found in the lining of the abdomen when it is examined in the lab (T3a). The cancer might or might not have spread to retroperitoneal lymph nodes (N0 or N1), but it has not spread to distant sites (M0).
IIIC	T3c	N0 or N1	M0	The cancer is in one or both ovaries or fallopian tubes, **or** there is primary peritoneal cancer and it has spread or grown into organs outside the pelvis. The deposits of cancer are larger than 2 cm (about 3/4 inch) across and may be on the outside (the capsule) of the liver or spleen (T3c). It may or may not have spread to the retroperitoneal lymph nodes (N0 or N1), but it has not spread to the inside of the liver or spleen or to distant sites (M0).
IVA	Any T	Any N	M1a	Cancer cells are found in the fluid around the lungs (called a malignant pleural effusion) with no other areas of cancer spread such as the liver, spleen, intestine, or lymph nodes outside the abdomen (M1a).
IVB	Any T	Any N	M1b	The cancer has spread to the inside of the spleen or liver, to lymph nodes other than the retroperitoneal lymph nodes, and/or to other organs or tissues outside the peritoneal cavity such as the lungs and bones (M1b).

Table S2 *2014 FIGO and 2016 TNM staging system for tubo-ovarian cancer*[6, 7]

1.3. Methodology of ovarian mass characterization

Transvaginal ultrasound examination is the standard first-line imaging investigation for the assessment and characterization of adnexal pathology.[10] To standardize the description and sonographic evaluation of adnexal (ovarian, para-ovarian, and tubal) masses across different centers, the IOTA group has developed a universal nomenclature (Figure S2).[1]

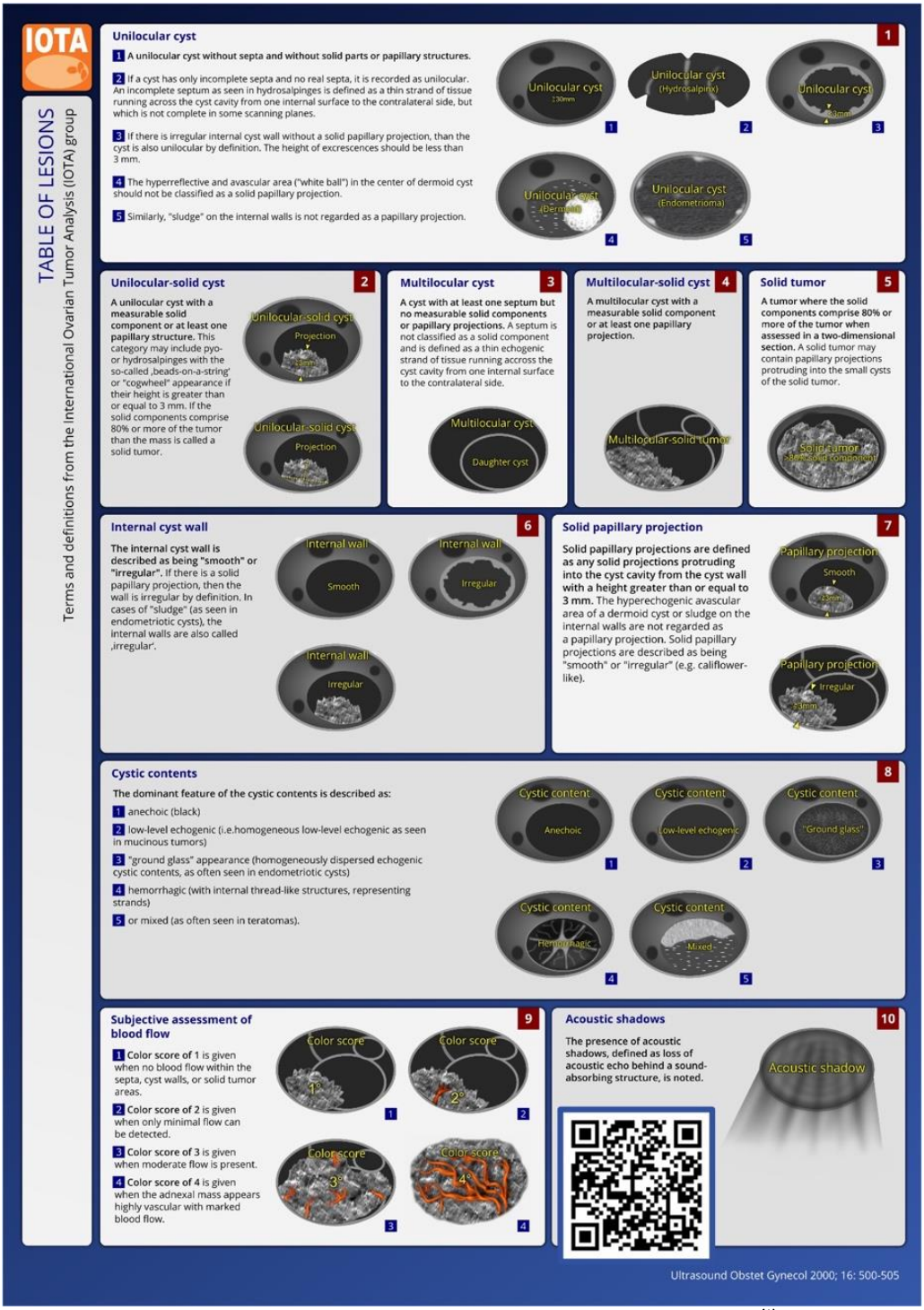

Figure S2 Terms and definitions from the International Ovarian Tumor Analysis (IOTA) group.[1]

1. Pattern recognition approach (subjective assessment of ovarian, para-ovarian, tubal tumors)

Subjective assessment by expert ultrasound examiners has excellent diagnostic performance to distinguish between benign and malignant ovarian tumors. In many cases, expert sonographers can narrow the diagnosis down to a specific histological subtype based on pattern recognition of pathognomic features associated with different tumor histotypes (Figure S3). These typical ultrasound features have been published in the series "Imaging in gynecological disease" Ultrasound in Obstetrics and Gynecology (https://obgyn.onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)1469-0705.IMAGINGINGYNECOLOGICALDISEASE). These features are also reported in the latest preoperative guidelines on ovarian cancer.[3]

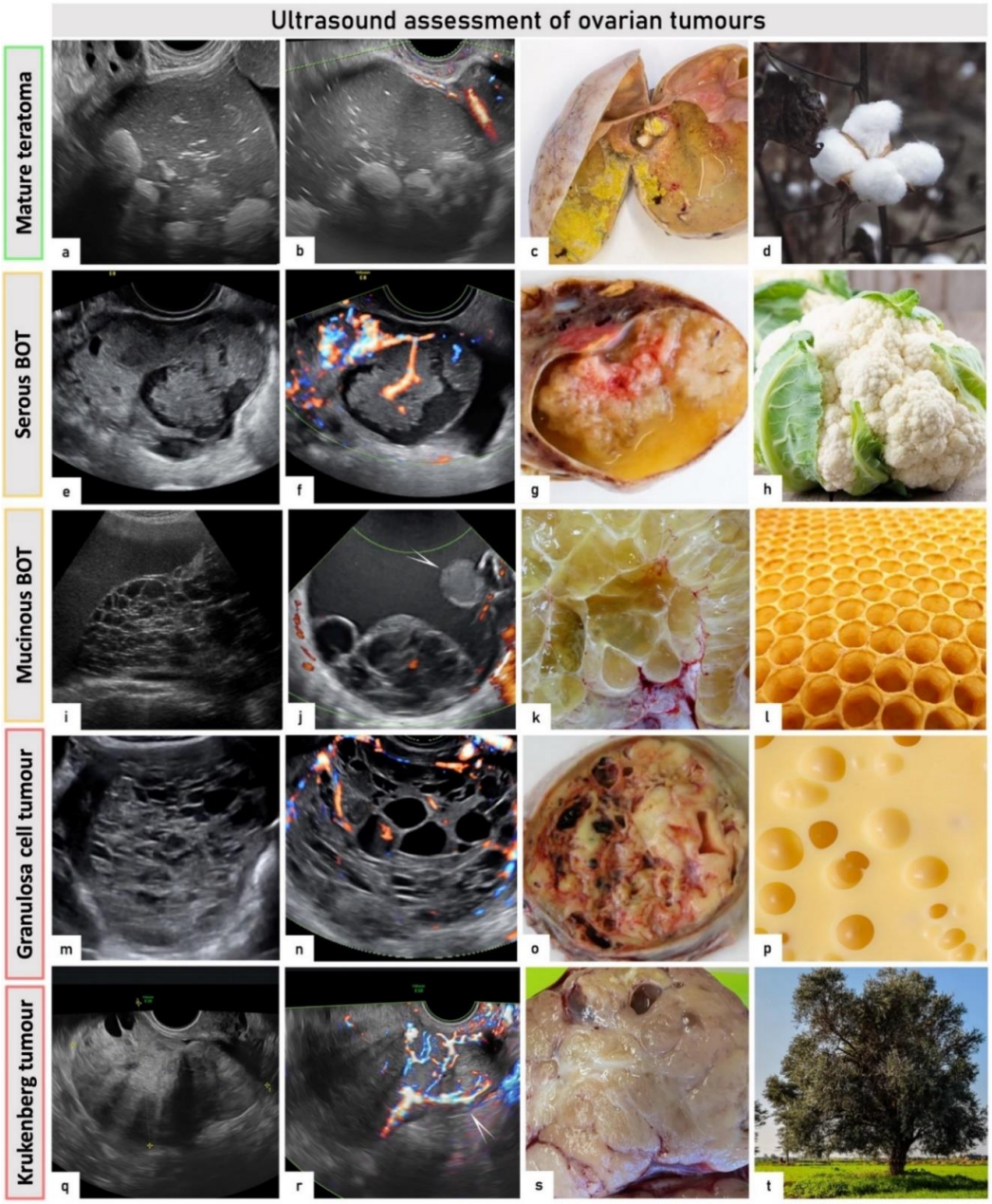

Figure S3 Subjective assessment of ovarian tumors based on specific features presented in the series "Imaging in Gynecological Disease". *The ultrasound images are shown beside the corresponding macroscopic appearence at the surgery and with objects that typically resenble the structure of these tumors. In the first line the ultrasound in gray-scale and with Power Doppler and pathological characteristics of benign ovarian teratomas are shown (a, b, c); they often have mixed content, including fat, hairs and sebeceous material that resembles cotton wool and are avascular (d).[11] The solid component of serous borderline tumors of the ovary (e, f, g) is sometimes similar to the oitline of a*

cauliflower (h).[12, 13] Mucinous borderline tumors have multiple locules containing intracystic fluid of variable echogenicity (dense mucinous content is marked with the arrow)(i, j, k) and mutliple densely packed daughter cysts resembling the appearance of a honeycomb (l).[12, 14, 15] Granulosa cell tumor of the ovary is often a solid tumor with small cysts (with low-level or ground-glass echogenicity fluid) dispersed within it (m, n, o) resembling swiss cheese (p).[16] Metastatic tumours to the ovary may have different features depending on the site of the primary. Krukenberg tumour (q, r, s) is an ovarian metastasis of a signet-ring cell tumor, usually being bilateral well-encapsulated solid tumor, fibroma-like (stripy shadowing due to desmoplastic reaction), but with typical perfusion patterns including ring-shaped vessels (arrow) surrounding the metastatic nodules[17] and a 'lead' vessel running into the tumor with a "tree-shaped" appearence.[16, 18]

2. Ultrasound-based diagnostic rules and risk prediction models

One of the most significant achievements of the IOTA Collaborative Group has been the development of the IOTA rules and risk prediction models based on the logistic regression analysis that can be used by non-experts in order to accurately differentiate between benign and malignant adnexal tumors.[18-21] The performance of IOTA rules and prediction models have been externally validated. [10, 22-24] Accurate diagnostic work-up is key in selecting optimal management for patients, allowing proper triaging of cases for conservative management, surgery in a district hospital, or specialised treatment in a gynaecological oncology centre. [25]

2.1. IOTA Simple Rules

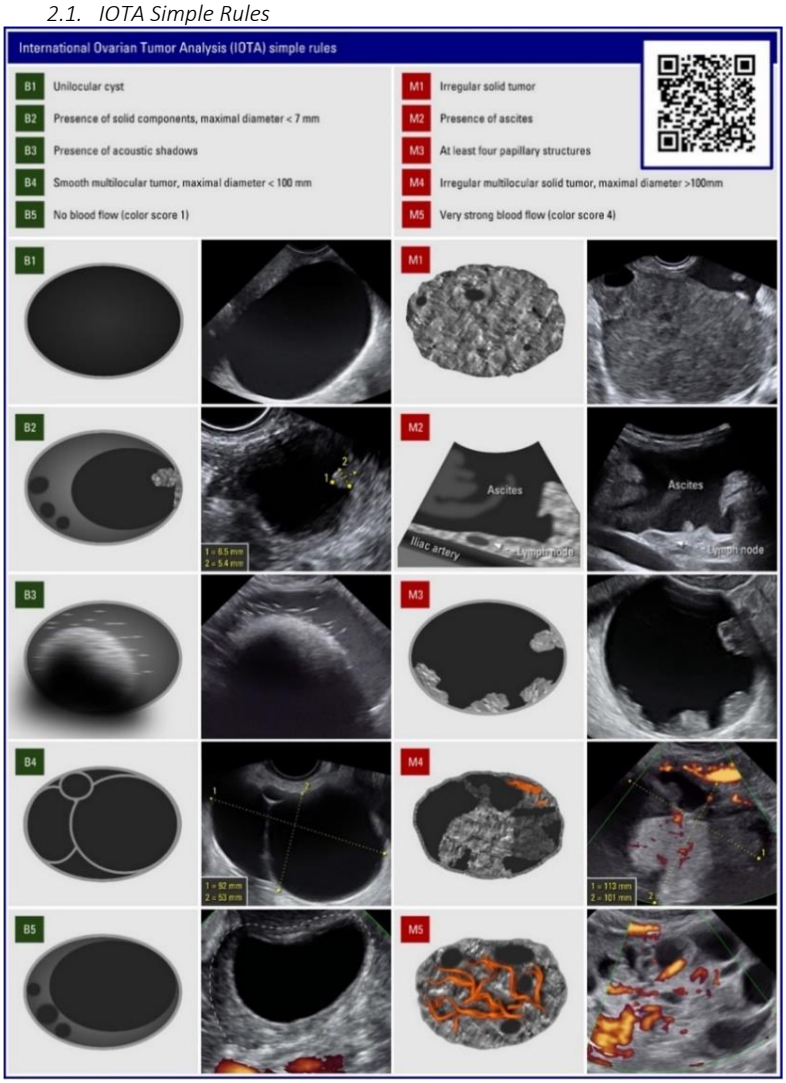

Figure S4 IOTA Simple Rules and IOTA Simple Rules Risk calculator (QR code). *Five benign (B1-5) and five malignant (M1-5) features. IOTA; the International Ovarian Tumor Analysis (IOTA) group.[18, 26]*

IOTA Simple Rules are currently broadly accepted and used in clinical practice to differentiate between benign and malignant adnexal tumors without the need of CA 125 level and sophisticated technologies (Figure S4).[18] Clinicians can classify about 80% of adnexal tumors based on the presence or absence of five benign (B1-5) and five malignant (M1-5) ultrasound features (Figure S4). Adnexal tumors are classified as benign (only B-features apply), malignant (only M-features apply) or inconclusive (no features apply, or both B- and M-features apply). The Simple Rules cannot replace training in ultrasonography and cannot compensate for poor quality ultrasound equipment.

Even basic tools, such as the IOTA terminology (Figure S2)[1] and Simple Rules (Figure S4)[18], must be implemented after robust training. This is evidenced by the poor to moderate interobserver agreement between non-experts and experts when utilizing IOTA terms (kappa = 0.39), and only moderate agreement when utilizing the Simple Rules (kappa = 0.50).[27] The Simple Rules are a useful triaging tool for further investigations but are inconclusive in approximately 20% of cases.[18, 28] In the remaining 80% of cases the benign/malignant category is correctly assigned but they do not offer a predicted risk of malignancy to form the basis of individualized clinical management. This was overcome when The Simple Rules Risk (SRrisk, 2016) calculation was developed incorporating also the type of medical center (oncology center vs other) into the logistic regression model, offering the predictive risk of ovarian cancer (IOTA Simple Rules and SRrisk calculator to diagnose ovarian cancer | Iota Group).[26]

2.2. IOTA ADNEX (Assessment of different neoplasias in the adnexa) model

The IOTA group also created the ADNEX model which, in addition to categorising tumors as benign or malignant, offers stratification of malignant tumors into four malignant subtypes: borderline, Stage I and Stage II-IV primary cancers and secondary metastatic tumors.[2] Serum CA 125 value improves discrimination between malignant tumor subtypes but has little effect on differentiating between benign and malignant masses.[24] The ADNEX model is based on a series of easy-to-assess sonographic features, so less experienced sonographers can potentially use this model more easily as compared to the Simple Rules or Simple Rules Risk model (Table S2). It has been externally validated on almost 5,000 cases of ovarian lesions showing that ADNEX with CA 125 was the best model, in comparison with the Risk of Malignancy Index (RMI), logistic regression model 2 (LR2) and Simple Rules Risk model (SRRisk), reliably distinguishing between benign and malignant lesions (AUC 0.94) with diagnostic performance ranging from AUC 0.75 to 0.98 for different tumor types.[24] Both the IOTA certificate and basic ultrasound skills should constitute obligatory requirements for implementation of the ADNEX model in practice. Health economic analysis indicates that the ADNEX model (malignancy risk threshold at ≥10%), may be cost-effective to guide referral decisions for women with suspected ovarian cancer in secondary care as sensitivity is strongly prioritised over specificity.[23]

ADNEX Model parameters	
Clinical parameters	Age
	Oncology center (referral center for gyn-oncol)
Ultrasound parameters	Maximal diameter of the lesion (mm)
	Maximal diameter of the largest solid part (mm)
	Presence of more than 10 locules
	Number of papillary projections
	Presence of acoustic shadows
	Presence of ascites (fluid outside pelvis)
Analytic parameter *(optional)*	Serum CA-125 (U/ml)

Table S2 *ADNEX Model parameters*
ADNEX, Assessment of Different Neoplasias in the adneXa.[2]

2.2. IOTA Simple Descriptors

Some adnexal lesions can be classified easily as benign or malignant just using the IOTA simple descriptors without the need of complex models and access to a computer. [29] If a benign simple descriptor applies to a tumor selected for surgery, the tumor is almost certainly benign (>99%), while >92% of tumors corresponding to a malignant simple descriptor are truly malignant.[30] In clinical practice, if an ovarian cyst

is checked against the benign descriptors and one of these applies, the mass could be classified as benign (risk of malignancy <1%), if none applies, a mathematical model could be used to estimate the risk of malignancy. For this reason Landolfo et al. conducted a multicenter study including 4905 patients, validating the two-step strategy (benign simple descriptors followed by ADNEX model) for the assessment of adnexal masses.[31] For this purpose, the authors modified the original benign descriptors[29] by limiting the largest tumor diameter to be < 10 cm for all four benign descriptors (Figure S5).[31] The malignant simple descriptors[29] were not used in the two-step strategy. Modified benign simple descriptors were applicable to 37% of the masses with 99.3% of true positives. The two-step strategy based on ADNEX without CA 125 showed an excellent accuracy (AUC= 0.94).[31]

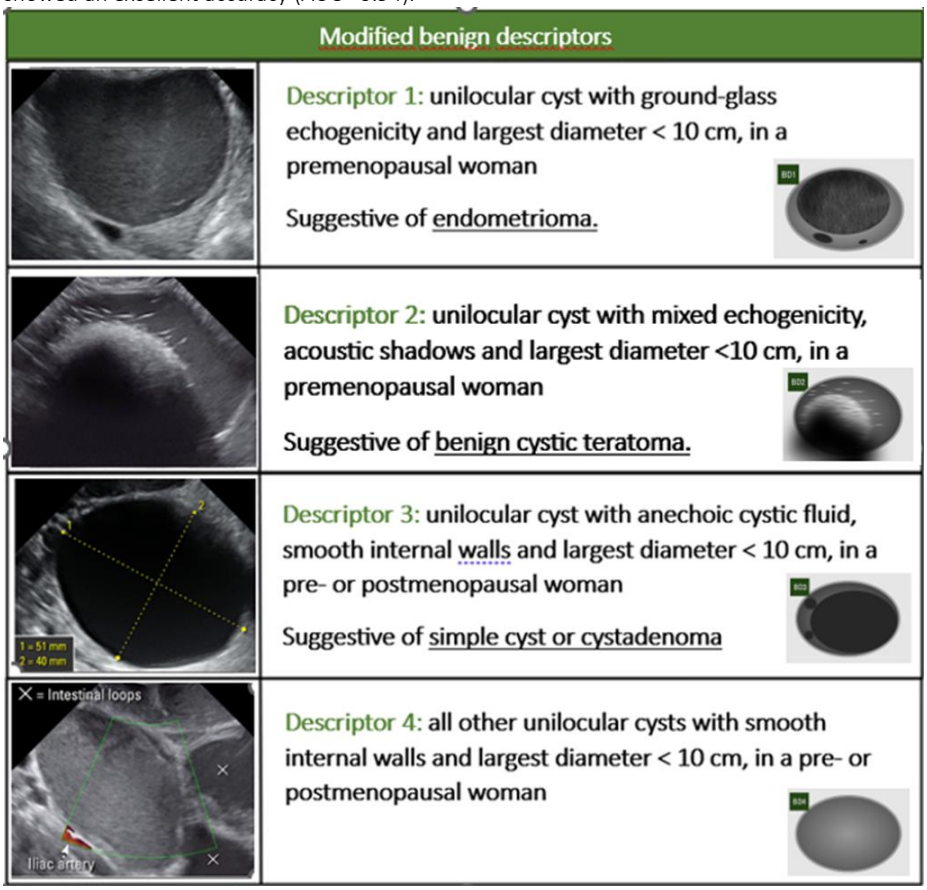

Figure S5 IOTA modified benign simple descriptors. IOTA, International Ovarian Tumor Analysis.[31]

2.3. O-RADS-US lexicon (the Ovarian-Adnexal Reporting and Data System for Ultrasound)

In 2018, the standardized O-RADS US lexicon for ultrasound was published under the direction of the American College of Radiology.[32] The consensus-driven lexicon included all the relevant descriptors and definitions of the characteristic ultrasound appearance of normal ovarian findings and ovarian/para-ovarian/tubal lesions using similar terms to those used in the IOTA models.

2.4. O-RADS-US risk stratification classification and management system

The ultimate objective of O-RADS US lexicon was to stratify the risk of malignancy for consistent follow-up and management in the clinical practice. In 2020, authors introduced six O-RADS categories: O-RADS 0, an incomplete evaluation; O-RADS 1, the physiologic category (normal premenopausal ovary); O-RADS 2, the almost certainly benign category (<1% risk of malignancy); O-RADS 3, lesions with low risk of malignancy (1% to <10%); O-RADS 4, lesions with intermediate risk of malignancy (10% to <50%); and O-RADS 5, lesions with high risk of malignancy (≥50%).[33] Assigning different risk categories using O-RADS descriptors or IOTA-ADNEX model, patients can be selected for individualized treatment pathways. A retrospective study by Hack et al externally validated the O-RADS system, finding that ADNEX performed better than O-RADS ultrasound descriptors, with a statistically different accuracy of 95% vs 91%, respectively (P = 0.01).[34] A recent retrospective external validation study and prospective observation study by Timmerman Jr. et al found that both the O-RADS lexicon and the IOTA two-step strategy can be used to stratify patients into risk

groups, with similar sensitivity (92% vs 91% respectively) and specificity (80% vs 85%) for high-risk tumors (i.e. O-RADS 4-5).[35] However, the observed malignancy rate in O-RADS 2 category was more than 1% (1.1%), while the corresponding result for the IOTA two-step strategy was 0.9%. Prospective external validation of the O-RADS descriptors and triage system using these O-RADS descriptors and/or two-step strategy is, however, still a subject of ongonig research. At present, the IOTA collaborative group has proposed the use of its two-step strategy approach, assigning one of the O-RADS categories to guide the management and selection of patients for referral to a dedicated gynecological oncology centre (Figure S6).

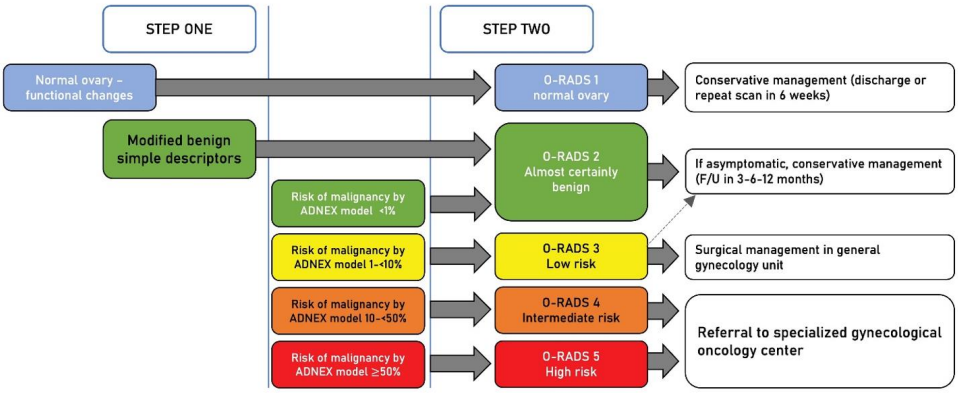

Figure S6 Algorithm for the management of patients with adnexal mass according to the "two-step" strategy based on modified benign simple desciptors and ADNEX. *An adnexal lesion is the part of an ovary or an adnexal mass that is judged from an assessment of ultrasound images to be inconsistent with normal physiologic function.[1] Adnexal lesions are assessed as (1) almost certainly benign (modified SD can be applied or ADNEX model calculated risk of malignancy is <1%), which are indicated for conservative management, (2) low-risk of malignancy (1-<10%) when surgery can be performed at level 2 hospital (or conservative management can also be an option), (3) intermediate risk (10 to <50%) and (4) high risk of malignancy (≥50%) where timely referral of patients to gynecologic oncology centre is advised.[3, 33] SD, simple descriptors. ADNEX, Assessment of Different Neoplasias in the Adnexa; F/U, follow-up.*

1.4. Methodology of tubo-ovarian cancer staging and prediction of non-resectability

Systematic ultrasound examination in suspected tubo-ovarian malignancy includes assessment of the primary tumor and evaluation of tumor spread in the pelvis, abdomen, inguinal lymph nodes and other locations as indicated. Further assessment of extra-abdominal sites is required in patients with extensive retroperitoneal lymphadenopathy, extensive diaphragmatic carcinomatosis, malignant hydrothorax, pleural carcinomatosis or other extensive spread (e.g., peripheral lymph nodes infiltrations). A detailed description of all sites affected by tumor, with special emphasis on sites which are not easily resectable, is necessary to plan individualized treatment and predict chances of complete cytoreduction. Incidental findings during preoperative imaging related to tumor complications such as intestinal obstruction, hydronephrosis, venous thrombosis among others should also be noted.[36]

For staging, a systematic approach combining transvaginal and transabdominal evaluation is recommended to provide information on pelvic and abdominal sites affected by tubo-ovarian cancer spread.[37] A detailed review on how to scan gynecological cancers for staging (methodology, terminology, clinical implementation) has been published.[4] The abdominal sites infiltration which frequently contribute to suboptimal surgical results are summarized in Figure S7. A diagnostic work-up with the best available imaging methods, depending on the local expertise, should be used to assess the disease extent according to the ESGO-ESMO guidelines 2019, to predict resectability (Figure S7).[9]

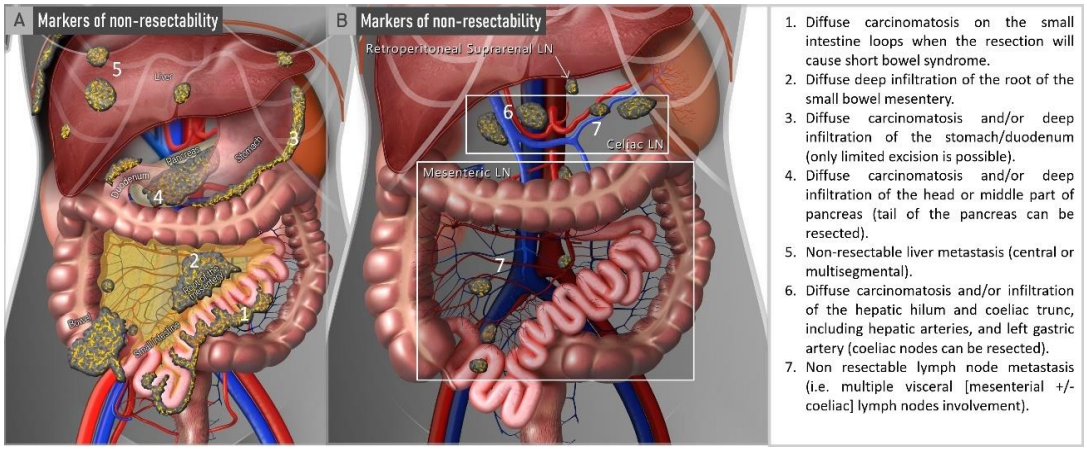

Figure S7 Graphical illustration of the imaging findings indicating non-resectability in ovarian cancer. *Non-resectable disease is defined by one or more markers published by the ESMO-ESGO consensus conference in 2019[9]. ESGO, European Society of Gynaecological Oncology; ESMO, European Society for Medical Oncology*

Radiological ovarian cancer staging ought to be documented using a systematic checklist (Table S1).

Supplemental references

[1] Timmerman D, Valentin L, Bourne TH et al. Terms, definitions and measurements to describe the sonographic features of adnexal tumors: a consensus opinion from the International Ovarian Tumor Analysis (IOTA) Group. *Ultrasound Obstet Gynecol*. 2000;**16**: 500-5.

[2] Van Calster B, Van Hoorde K, Valentin L et al. Evaluating the risk of ovarian cancer before surgery using the ADNEX model to differentiate between benign, borderline, early and advanced stage invasive, and secondary metastatic tumours: prospective multicentre diagnostic study. *BMJ*. 2014;**349**: g5920.

[3] Timmerman D, Planchamp F, Bourne T et al. ESGO/ISUOG/IOTA/ESGE Consensus Statement on pre-operative diagnosis of ovarian tumors. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2021;**31**: 961-82.

[4] Fischerova D. Ultrasound scanning of the pelvis and abdomen for staging of gynecological tumors: a review. *Ultrasound Obstet Gynecol*. 2011;**38**: 246-66.

[5] Fischerova D, Garganese G, Reina H et al. Terms, definitions and measurements to describe sonographic features of lymph nodes: consensus opinion from the Vulvar International Tumor Analysis (VITA) group. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2021;**57**: 861-79.

[6] Prat J, Olowaiye AB, Bermudez A et al. Ovary, Fallopian Tube, and Primary Peritoneal Carcinoma. In: Amin MB, ed. *AJCC Cancer Staging Manual*. Switzerland: Springer International Publishing AG Switzerland 2016:689.

[7] Prat J. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*. 2014;**124**: 1-5.

[8] Gibb RK, Olawaiye AB, Bhosale PR et al. Vulva. In: Amin MB, ed. *TNM Classification of Malignant Tumours*. Switzerland: Springer International Publishing AG Switzerland 2016:641.

[9] Colombo N, Sessa C, Bois AD et al. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. *Int J Gynecol Cancer*. 2019.

[10] Meys EM, Kaijser J, Kruitwagen RF et al. Subjective assessment versus ultrasound models to diagnose ovarian cancer: A systematic review and meta-analysis. *Eur J Cancer*. 2016;**58**: 17-29.

[11] Heremans R, Valentin L, Sladkevicius P et al. Imaging in gynecological disease (24): clinical and ultrasound characteristics of ovarian mature cystic teratomas. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2022;**60**: 549-58.

[12] Fischerova D, Zikan M, Dundr P, Cibula D. Diagnosis, treatment, and follow-up of borderline ovarian tumors. *Oncologist*. 2012;**17**: 1515-33.

[13] Franchi D, Boveri S, Fruscio R et al. Imaging in gynecological disease (8): ultrasound characteristics of recurrent borderline ovarian tumors. *Ultrasound Obstet Gynecol*. 2013;**41**: 452-8.

[14] Fruscella E, Testa AC, Ferrandina G et al. Ultrasound features of different histopathological subtypes of borderline ovarian tumors. *Ultrasound Obstet Gynecol*. 2005;**26**: 644-50.

[15] Moro F, Zannoni GF, Arciuolo D et al. Imaging in gynecological disease (11): clinical and ultrasound features of mucinous ovarian tumors. *Ultrasound in obstetrics &*

gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2017;**50**: 261-70.
[16] Van Holsbeke C, Domali E, Holland TK et al. Imaging of gynecological disease (3): clinical and ultrasound characteristics of granulosa cell tumors of the ovary. *Ultrasound Obstet Gynecol*. 2008;**31**: 450-6.
[17] Fischerova D. Metastatic Ovarian Tumors (Clinical Setting and US). In: Saba L, ed. *Ovarian Neoplasm Imaging*. New York: Springer Science+Business Media New York 2013.
[18] Timmerman D, Testa AC, Bourne T et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol*. 2008;**31**: 681-90.
[19] Timmerman D, Testa AC, Bourne T et al. Logistic regression model to distinguish between the benign and malignant adnexal mass before surgery: a multicenter study by the International Ovarian Tumor Analysis Group. *J Clin Oncol*. 2005;**23**: 8794-801.
[20] Van Calster B, Van Hoorde K, Valentin L et al. Diagnosing ovarian cancer using the ADNEX risk model from the International Ovarian Tumour Analysis group: differentiating between benign, borderline, stage I invasive, advanced stage invasive, and secondary metastatic tumours. *BMJ (in print)*. 2014.
[21] Timmerman D, Van Calster B, Testa A et al. Predicting the risk of malignancy in adnexal masses based on the Simple Rules from the International Ovarian Tumor Analysis group. *Am J Obstet Gynecol*. 2016;**214**: 424-37.
[22] Kaijser J, Sayasneh A, Van Hoorde K et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis. *Hum Reprod Update*. 2014;**20**: 449-62.
[23] Westwood M, Ramaekers B, Lang S et al. Risk scores to guide referral decisions for people with suspected ovarian cancer in secondary care: a systematic review and cost-effectiveness analysis. *Health Technol Assess*. 2018;**22**: 1-264.
[24] Van Calster B, Valentin L, Froyman W et al. Validation of models to diagnose ovarian cancer in patients managed surgically or conservatively: multicentre cohort study. *Bmj*. 2020;**370**: m2614.
[25] Wynants L, Timmerman D, Verbakel JY et al. Clinical Utility of Risk Models to Refer Patients with Adnexal Masses to Specialized Oncology Care: Multicenter External Validation Using Decision Curve Analysis. *Clin Cancer Res*. 2017.
[26] Timmerman D, Van Calster B, Testa A et al. Predicting the risk of malignancy in adnexal masses based on the Simple Rules from the International Ovarian Tumor Analysis group. *Am J Obstet Gynecol*. 2016;**214**: 424-37.
[27] Meys E, Rutten I, Kruitwagen R et al. Simple Rules, Not So Simple: The Use of International Ovarian Tumor Analysis (IOTA) Terminology and Simple Rules in Inexperienced Hands in a Prospective Multicenter Cohort Study. *Ultraschall Med*. 2017;**38**: 633-41.
[28] Timmerman D, Ameye L, Fischerova D et al. Simple ultrasound rules to distinguish between benign and malignant adnexal masses before surgery: prospective validation by IOTA group. *BMJ*. 2010;**341**: c6839.
[29] Ameye L, Timmerman D, Valentin L et al. Clinically oriented three-step strategy for assessment of adnexal pathology. *Ultrasound Obstet Gynecol*. 2012;**40**: 582-91.
[30] Testa A, Kaijser J, Wynants L et al. Strategies to diagnose ovarian cancer: new evidence from phase 3 of the multicentre international IOTA study. *British journal of cancer*. 2014;**111**: 680-8.
[31] Landolfo C, Bourne T, Froyman W et al. Benign descriptors and ADNEX in two-step strategy to estimate risk of malignancy in ovarian tumors: retrospective validation on IOTA 5 multicenter cohort. *Ultrasound Obstet Gynecol*. 2022.

[32] Andreotti RF, Timmerman D, Benacerraf BR et al. Ovarian-Adnexal Reporting Lexicon for Ultrasound: A White Paper of the ACR Ovarian-Adnexal Reporting and Data System Committee. *J Am Coll Radiol*. 2018;**15**: 1415-29.
[33] Andreotti RF, Timmerman D, Strachowski LM et al. O-RADS US Risk Stratification and Management System: A Consensus Guideline from the ACR Ovarian-Adnexal Reporting and Data System Committee. *Radiology*. 2020;**294**: 168-85.
[34] Hack K, Gandhi N, Bouchard-Fortier G et al. External Validation of O-RADS US Risk Stratification and Management System. *Radiology*. 2022;**304**: 114-20.
[35] Timmerman S, Valentin L, Ceusters J et al. External Validation of the Ovarian-Adnexal Reporting and Data System (O-RADS) Lexicon and the International Ovarian Tumor Analysis 2-Step Strategy to Stratify Ovarian Tumors Into O-RADS Risk Groups. *JAMA Oncol*. 2023;**9**: 225-33.
[36] Fischerova D, Burgetova A. Imaging techniques for the evaluation of ovarian cancer. *Best Pract Res Clin Obstet Gynaecol*. 2014;**28**: 697-720.
[37] Fischerova D, Zikan M, Semeradova I et al. Ultrasound in preoperative assessment of pelvic and abdominal spread in patients with ovarian cancer: a prospective study. *Ultrasound Obstet Gynecol*. 2017;**49**: 263-74.