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Maternal adnexal masses in pregnancy

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ABSTRACT

Maternal adnexal masses are increasingly detected during pregnancy, primarily due to the widespread use of ultrasound in obstetrics. Most of them are functional cysts that resolve spontaneously. Lesions visualized by ultrasound in adnexal topography may be retroperitoneal or intraperitoneal (non-gynecologic or obstetric/gynecologic formations, such as pregnancy-related masses, subserosal uterine fibroids or true adnexal lesions). The largest number of adnexal lesions do not change their ultrasound morphology in pregnancy. However, endometriomas may decidualize, mimicking borderline or stage I invasive ovarian malignancies. The patient management can be conservative (ultrasound surveillance) or surgery. The decision depends on a series of factors including the risk of malignancy. Until mathematical models have been widely validated in pregnancy, the International Ovarian Tumor Analysis Group recommends using simple benign descriptors and expert subjective assessment to predict the risk of maternal adnexal malignancy in pregnancy. In the future, artificial intelligence could be useful.

1. Introduction

Maternal adnexal masses are frequently incidental findings during pregnancy, being increasingly detected over the last few decades due to the widespread use of ultrasound in obstetrics, the technical development of sonographic equipment and the delay of childbearing to a more advanced maternal age [1,2]. In most cases, they are benign masses that resolve spontaneously. Unlike functional and spontaneously regressing formations, an adnexal lesion, as defined by the International Ovarian Tumor Analysis (IOTA) Group, is a portion of the ovary or an adnexal mass that is inconsistent with normal physiological function [3]. It persists and evolves according to its benign or malignant nature.

Ultrasound features suspicious for malignancy are present in a significant minority of maternal adnexal masses; however, malignant ovarian tumors rarely occur during pregnancy, complicating 1 in 15,000 to 1 in 32,000 gestations [4]. Appropriate diagnostic evaluation should provide a reliable prediction of the risk of malignancy as well as a prediction of the adnexal mass origin (gynecologic or non-gynecologic). Ultrasound is a fundamental tool for assessing adnexal masses due to its availability, low cost and reliability when employed by experienced sonologists or trained operators using validated prediction models/strategies [5]. In non-pregnant women, the IOTA models and strategies [especially the ADNEX (Assessment of Different NEoplasias in the adneXa) model] differentiate between benign and malignant adnexal tumors better than any other available alternative [5,6]. Correct classification of the adnexal masses is particularly critical during pregnancy because of the fetal and maternal risks associated with coexisting malignancies but also

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with surgical interventions, including those that are unnecessary and should definitely be avoided. Currently, there is no widely validated model/strategy for assessing the risk of malignancy in pregnant women with adnexal masses. Scientific research, primarily of the IOTA group and collaborators, is devotedly striving to achieve this goal.

The masses observed sonographically in the adnexal topography may actually be retroperitoneal or intraperitoneal, and these are not gynecologic or gynecologic (including uterine and true adnexal formations). The IOTA terms, definitions, and morphological classification [3] seem useful during pregnancy in characterizing the maternal masses of the adnexal origin [1]. This article focuses on the most frequent pregnancy-related and non-pregnancy-specific gynecologic masses detected during pregnancy. It intends to review their ultrasound features and provide a summary of available evidence on ultrasound-based approaches to malignancy risk assessment and patient orientation.

A non-systematic review of literature published in English until June 1st, 2024 was performed by searching PubMed using combinations of the following search terms: "adnexal mass" OR "adnexal masses" OR "ovarian mass", OR "ovarian masses" AND "pregnancy" OR "pregnant". Abstracts were reviewed, the most pertinent articles were included, and references of all included articles were also searched to find additional relevant information. The IOTA lexicon [3] was used to describe the ultrasound characteristics of adnexal masses.

2. Ultrasound features of functional and pregnancy-related maternal adnexal masses

Ultrasound examination of the ovaries in pregnant women, which are best visualized in the first trimester, practically always identifies unilocular cystic formations <5 cm that are consistent with normal ovarian function. Many of these are functional either **follicular** or **corpus luteum cysts** (Fig. 1) that resolve spontaneously during the pregnancy [7]. In patients who undergo ovulation induction, enlarged **hyperstimulated ovaries** are commonly observed, containing multiple follicular cysts with thin walls (Fig. 2A). Hyperstimulated ovaries regress spontaneously; however, they present an increased risk of hemorrhage and torsion [8]. While follicular, corpus luteum cysts and even hyperstimulated ovaries can be seen in both pregnant and non-pregnant women (including those who have failed to conceive), maternal adnexal masses unique to pregnancy comprise **theca lutein cysts** (also called **lutein cysts** or ***hyperreactio luteinalis***) and **luteomas**.

Hyperreactio luteinalis consists of multiple luteinized follicular cysts (Fig. 2B), resulting from hypersensitivity to human chorionic gonadotropin (hCG) or overstimulation by high hCG levels [2]. It may occur after ovarian stimulation and in a woman with gestational trophoblastic disease, a multifetal pregnancy or a gestation complicated by hydrops fetalis. Sonographically, *hyperreactio luteinalis* presents as bilateral multilocular ovarian enlargement, usually in the third trimester of pregnancy, and spontaneously resolves after delivery [2,8].

Luteomas arose from benign proliferations of luteinized cells forming sonographically detectable solid, vascularized and often

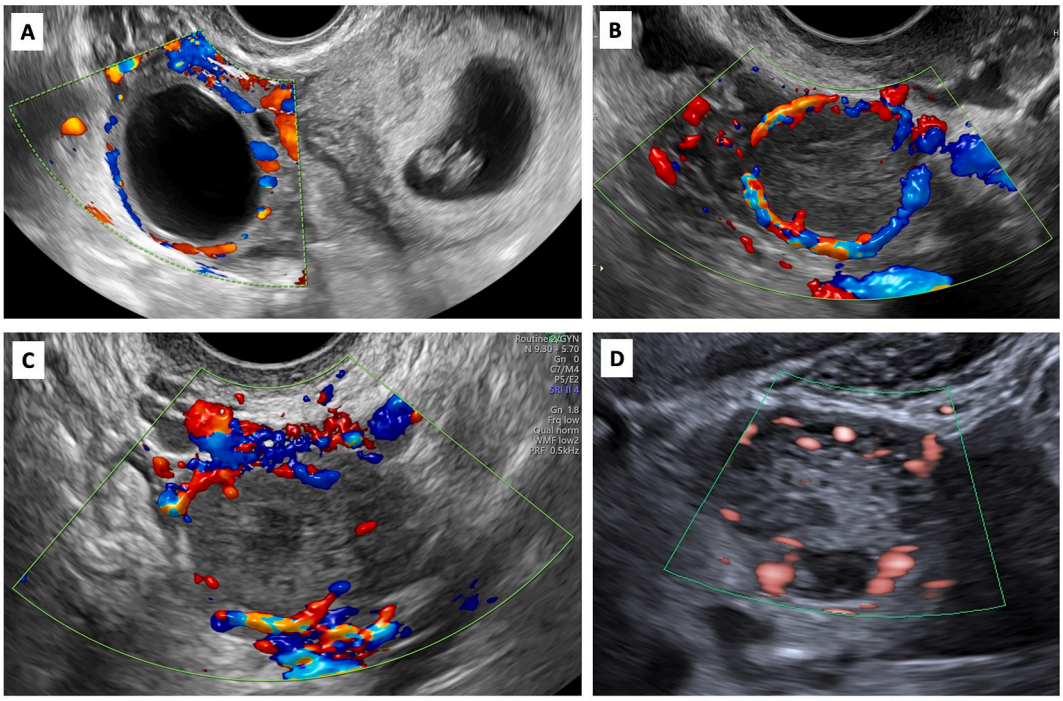

Fig. 1. Corpus luteum – various ultrasound presentations: A, cystic; **B,** cystic with intracystic clot formation; **C,** solid annular; **D,** solid. Peripheral vascular "ring of the fire" can be visualized using Color Doppler **(A–C)** and Power Doppler **(D).** (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

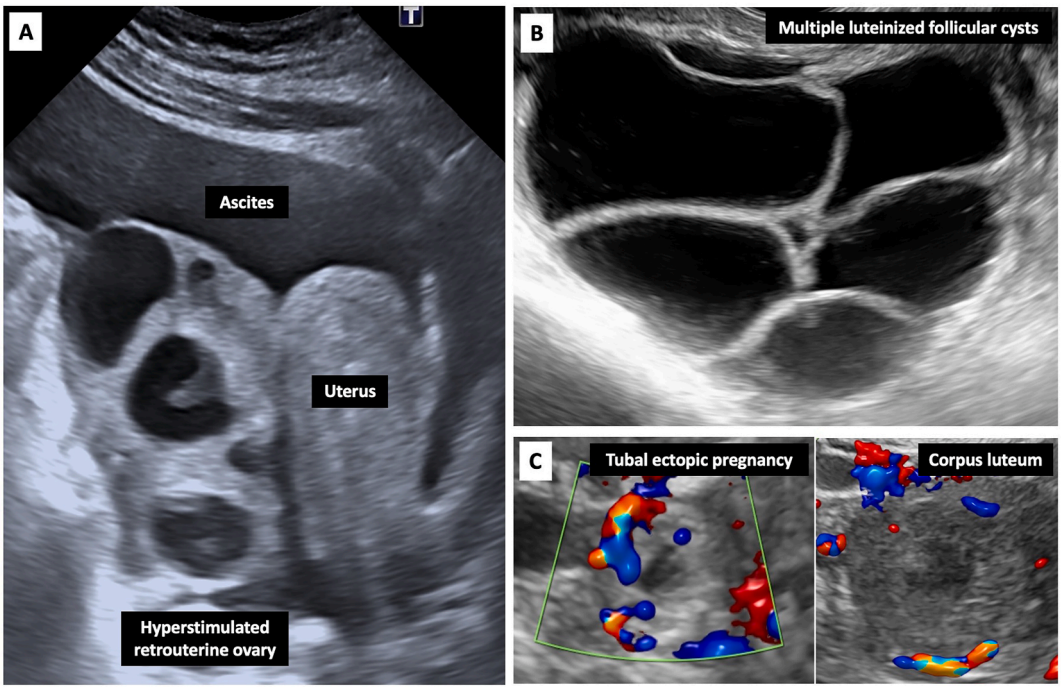

Fig. 2. Pregnancy-related maternal adnexal masses: A, hyperstimulated ovaries after ovulation induction; **B,** *hyperreactio luteinalis*; **C,** early tubal ectopic pregnancy (left) and corpus luteum (right) sharing similar ultrasound appearance.

bilateral ovarian masses [2]. They are typically diagnosed in later pregnancy, mimicking solid ovarian malignancies. Luteomas spontaneously regress after delivery. In up to 25 % of patients, luteomas are associated with maternal virilization (hirsutism); when it occurs, female fetus virilization is also evident in 60–70 % of cases [2].

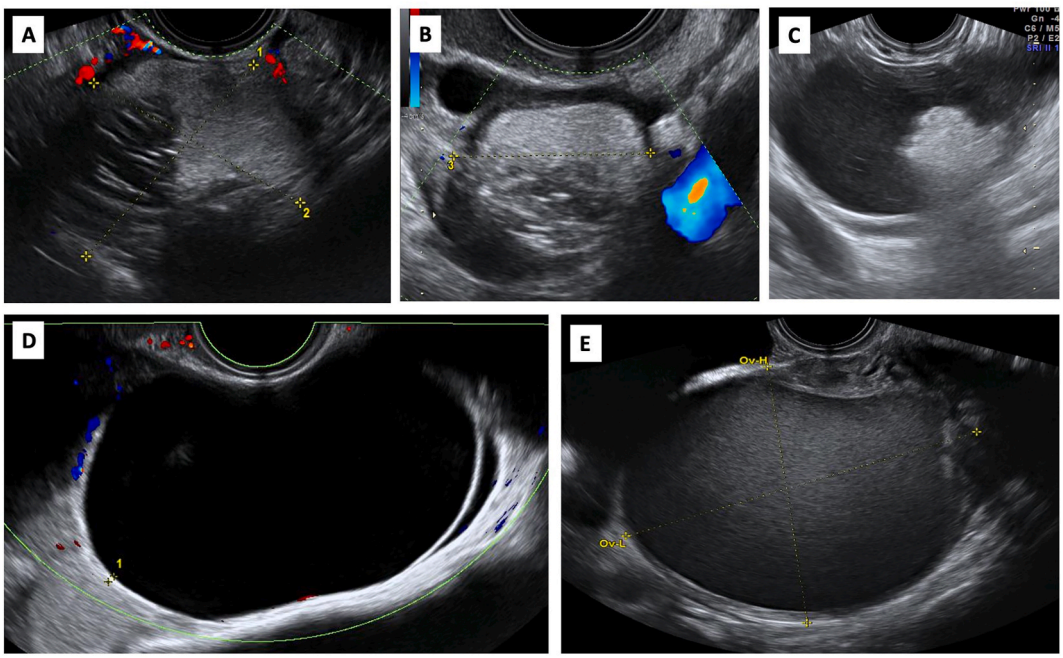

Fig. 3. Frequent benign maternal ovarian lesions: A, mature cystic teratoma (mixed echogenicity content with echogenic "dots and lines"); **B,** mature cystic teratoma (echogenic not vascularized "white ball"); **C,** mature cystic teratoma (echogenic "white ball" with acoustic shadowing); **D,** unilocular serous cystadenoma**; E,** endometrioma with typical "ground glass" content.

Another rare pregnancy-specific adnexal mass in women with intrauterine gestation is **extrauterine heterotopic pregnancy (tubal, ovarian, or abdominal)**. It is estimated to affect 1 in 30,000 spontaneous pregnancies [2] and 1 in 100 *in vitro* fertilization pregnancies [9]. The diagnosis of heterotopic pregnancy is easy to establish with ultrasound visualization of both intrauterine pregnancy and ectopic gestational sac with an embryo showing visible cardiac activity. The difficulty lies in differentiating an adnexal mass with a gestational sac but no visible embryo (which is often annular or solid, with a circumferential "ring of the fire" Doppler sign) from a corpus luteum (Fig. 2C) [10]. Additionally, amorphous echoic material corresponding to the blood clots and free fluid in the abdominal-pelvic cavity, if present, indicate intraperitoneal bleeding that may be due to an ectopic abortion or rupture of an ectopic pregnancy.

3. Ultrasound features of non-pregnancy-specific maternal adnexal masses

During pregnancy, any known histological types of adnexal masses may be observed, including ovarian lesions of epithelial, germ cell, sex cord-stromal or metastatic origin, Fallopian tube lesions and paraovarian/paratubal masses. Most adnexal lesions do not change their morphology or clinical behavior compared to the same entities in non-pregnant women. Of the adnexal masses that require surgical management or are removed at the time of cesarean delivery, dermoid cysts are the most common (32 %), followed by serous and mucinous cystadenomas (19 %) and endometriomas (15 %) [2]. Bilateral adnexal masses have been reported in up to 4 % of cases; of the published reports available to the authors, all bilateral masses in pregnancy were benign [11].

3.1. Benign gynecological masses

Mature cystic teratoma (*i.e.,* dermoid cyst) is a benign germ cell tumor that can include different combinations of mature endodermal, mesodermal, and ectodermal tissue, leading to great variability in histological and sonographic presentation. The most typical ultrasound appearance is a unilocular cyst with mixed echogenicity, acoustic shadows and the largest diameter <10 cm, evidenced in a premenopausal woman (Fig. 3A, B, and 3C) [12,13]. The mixed echogenicity content may include hyperechoic "dots and/or lines", representing hair in the cystic fluid (Fig. 3A), and an "echogenic white ball", corresponding to aggregation and compaction of hair and oily fluids (Fig. 3B and C) [12,13]. Complications related to dermoid cysts in pregnancy include torsion, rupture, obstruction of the birth canal and, very rarely, malignant transformation. However, it does not appear that these complications are increased in pregnancy [14].

Ovarian cystadenomas originate from the surface epithelium. Serous and mucinous types are the ones most often found in pregnant women [2]. **Serous cystadenoma** has a smooth external surface, one or more thin-walled locules, and clear liquid content, being bilateral in 15 % of cases, with an average size of 5–8 cm [15]. Sonographically, a typical serous cystadenoma is a unilocular cyst with anechoic content, smooth internal walls and largest diameter <10 cm (Fig. 3D) [12]. Some contain septations, whilst others small echoic (hemorrhagic) areas not attached to the cyst wall. **Mucinous cystadenoma** is classically a thin-walled, large and unilateral mass containing mucin, which appears on ultrasound as content with low-level echogenicity. Although it can be a unilocular, more frequently, it is a multilocular tumor of variable size, ranging from a few to over 30 cm [12,16].

Endometrioma is typically a unilocular cyst with "ground glass" echogenicity and the largest diameter <10 cm in a premenopausal woman [5,14]. The "ground glass" content corresponds to chocolate-like "old blood" inside the cyst cavity (Fig. 3E) [12]. This typical aspect can be observed in approximately 50 % of cases, while remaining endometriomas are considered sonographically atypical due to the presence of multiple locules, amorphous material within the cyst ("sludge"), hyperechoic wall foci or solid papillary structures [17,18]. One of the atypical endometrioma presentations is the **decidualized endometrioma,** occurring in pregnancy and corresponding to morphologic changes in a preexisting endometrioma, induced mainly by progesterone and involving hypertrophy of the endometrial stromal cells. The main ultrasound feature is the development of highly vascularized papillary projections with smooth

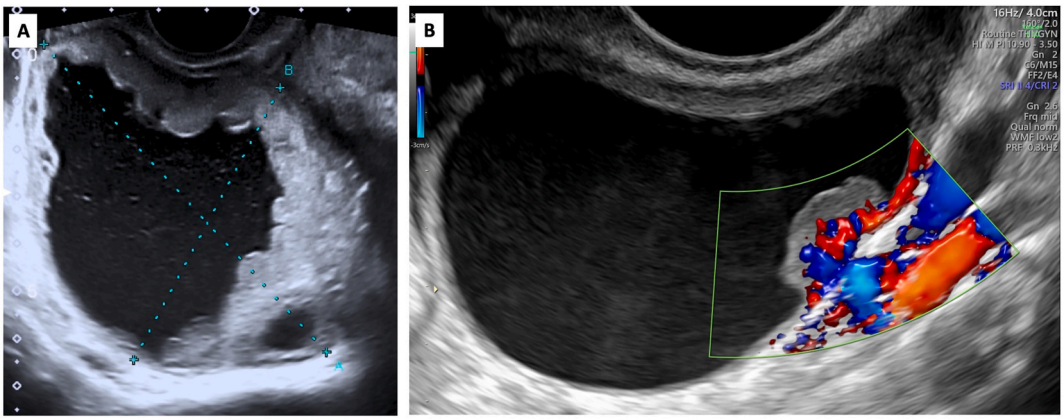

Fig. 4. Decidualized endometrioma: A, unilocular-solid lesion with multiple smoot papillary projections; **B,** unilocular-solid lesion with smooth and highly vascularized papillary projection.

contours (Fig. 4) [5,18,19]. Thus, unlike most other histological entities, endometriomas can change their appearance in the hormonal milieu of pregnancy, resembling borderline or early-stage invasive malignancies, in which papillary projections are also vascularized but their surface is often irregular [18]. Most of the papillary projections in decidualized endometriomas (85–90 %) regress in the postnatal period [20].

Regarding the tubal lesions, **hydrosalpinx** in pregnancy maintains the classic ultrasound features: elongated shape, incomplete septa, and anechoic content [21,22]. **Acute salpingitis** is identified as a unilateral or bilateral, elongated and richly vascularized solid mass, adjacent to the ovaries. **Pyosalpinx** is typically unilocular formation with anechoic or low-level content, characterized by thickening of the wall and the presence of incomplete septa (Fig. 5A) [22]. Due to inflamed and edematous septa, the "cogwheel sign" is often seen in the transverse section (Fig. 5A). **Tubo-ovarian abscesses** can be unilocular or multilocular, vary concerning their content echogenicity (anechoic, low-level, or "ground glass"), and may have solid-appearing areas with moderate to intense vascularity (Fig. 5B) [22].

Peritoneal, paraovarian/paratubal, and uterine masses which project to the adnexal areas may also be detected in pregnant patients. **Peritoneal pseudocysts (*i.e.,* inclusion cysts)** consist of collections of peritoneal fluid trapped in adhesions usually caused by previous pelvic surgery, pelvic inflammatory disease, or endometriosis. On ultrasound examination, they are described as unilocular or multilocular cysts (with complete, thin and mobile septa), that follow the contours of the pelvic wall and surrounding pelvic organs [23]. The ipsilateral ovary is visible in almost all cases, external to or entrapped within the cyst. The cyst contents are generally anechoic but may show low-level echogenicity [23]. **Paraovarian/paratubal cysts** arise in the broad ligament between the ovary and the fallopian tube. They appear as thin-walled unilocular anechoic masses, usually <5 cm, close to but separable from the ovary [24]. In nearly 30 % of cases, they show papillary projections. In almost all cases, it is possible to visualize the ipsilateral normal ovary and to detect movement of the cyst in the opposite direction to the ovary when the adnexal area is pushed with the vaginal probe ("split sign") [24].

Uterine fibroids are the most common solid pelvic neoplasms detected in pregnancy [21]. If subserosal and pedunculated (FIGO type 7), they can be confused with ovarian lesions, particularly when the vascular pedicle originating from the uterus is not clearly seen. The identification of a normal ovary and the "split sign" are of great importance in differentiating uterine fibroids or those arising from the broad ligament (**intraligamentary fibroids**) from ovarian tumors. *Red degeneration*, typically observed in pregnancy, is an

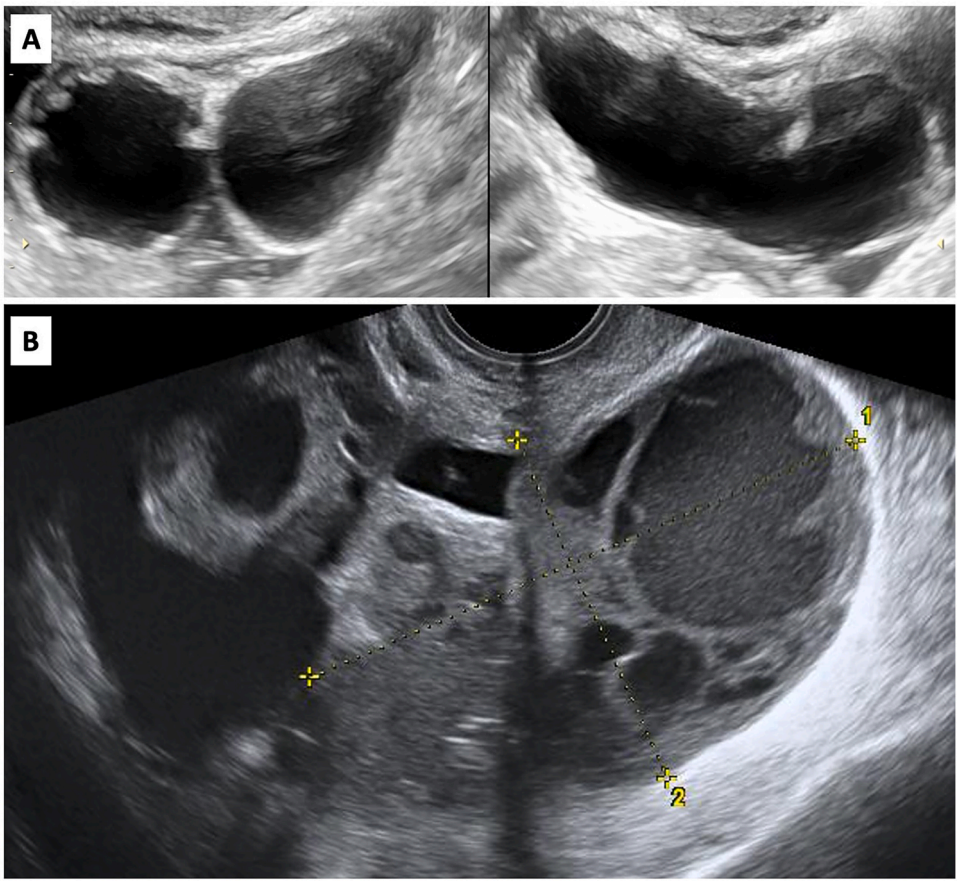

Fig. 5. Pelvic inflammatory disease: A, pyosalpinx; **B,** tubo-ovarian abscesses (ovary and Fallopian tube involved but cannot be clearly identified within the mass).

initial manifestation after fibroid infarction [25]. It may be sonographically unremarkable or result in a homogeneous low echogenicity, hyperechogenic lesion rim, and absent internal vascularity [26].

Finally, in some pregnant women presenting with acute pelvic pain (<1 %) [14], **adnexal torsion** can be observed as an enlarged edematous ovary when compared to the contralateral one, with or without antral follicles peripherally displaced and showing a hyperechogenic rim ("follicle ring sign") [27]. Twisted pedicle vessels may be visualized using Color or Power Doppler ("whirlpool sign"). Absent Doppler signals within ovarian parenchyma, representing ischemia, are observed in less than 50 % of cases [27]. During pregnancy, adnexal torsion occurs most frequently in the first trimester, probably due to the high prevalence of functional ovarian cysts. Twisted adnexa may or may not present a functional or tumoral mass.

3.2. *Malignant gynecological masses*

Approximately 2–4 % of adnexal masses in pregnancy are malignant [1,2,28]. A population-based study of nearly 5 million patients using California hospital records identified 87 cases of ovarian malignancies in pregnant women, 51 % of which were epithelial tumors, 39 % germ cell tumors, and 9 % *pseudomyxoma peritonei* [28]. Epithelial neoplasms were most commonly serous carcinomas, followed by mucinous, endometrioid, and clear cell carcinomas. Germ cell tumors were most commonly dysgerminomas, followed by malignant teratomas and endodermal sinus tumors. In a 2021 Italian study, among 65 pregnant patients undergoing surgery for suspicion of malignancy, symptoms or prevention of complications, 55 % (36 patients) had a diagnosis of malignancy (20 borderline ovarian tumors, 11 primary epithelial ovarian cancer, 1 recurrent ovarian cancer and 4 metastases to the ovary) [1]. Ovarian malignancy diagnosed during pregnancy is more likely to be of earlier stage and lower grade and is associated with more favorable outcomes than that diagnosed outside of pregnancy [2]. Ultrasound characteristics of malignant ovarian tumors are similar in pregnant and non-pregnant women, which applies to both epithelial and non-epithelial histological types [29].

Papillary projections appear to be the most typical ultrasound feature of **borderline serous ovarian tumors** (Fig. 6A), while the presence of solid components but few if any papillary projections is the most representative feature of **invasive serous malignancies** (Fig. 6B) [30]. **Borderline mucinous tumors** are most commonly large unilateral multilocular cysts with >10 locules (Fig. 6B), with

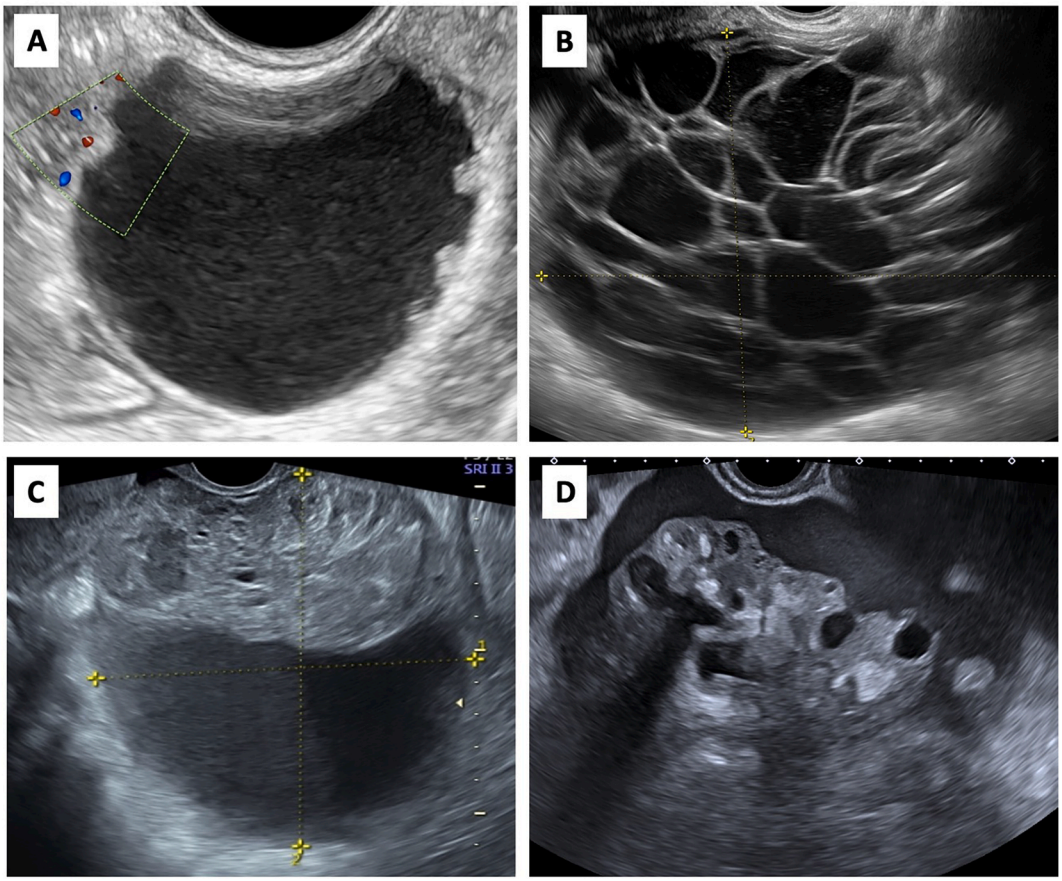

Fig. 6. Maternal ovarian malignancies: A, borderline serous ovarian tumor with vascularized papillary projections; **B,** borderline mucinous ovarian tumors with >10 locules; **C,** invasive mucinous ovarian malignancy with large solid component, no papillary projections and "ground glass" content; **D,** immature teratomas with characteristic heterogeneous ("bizarre") solid component.

no clear definition of solid nodule or papillary projection, and with a well-defined multilocular nodule ("honeycomb nodule") [16]. Most **invasive mucinous cancers** contain solid components (Fig. 6C) and have a multilocular-solid ultrasound morphology [16]. **Endometrioid ovarian malignancies** are often large, unilateral, multilocular-solid, or solid tumors [31]. Endometrioid carcinomas developing from endometriosis differ from those without previous endometrioma, being usually unilateral cysts with papillary projections and no ascites [31]. **Clear cell carcinomas** are most commonly diagnosed at an early stage and typically appear as large unilateral masses with solid components [32]. Clear cell cancers developing from endometriosis more often present ground-glass echogenicity of cyst content [32].

Dysgerminomas typically occur in 20 to 30-year-old patients, being large, solid, lobulated and highly vascularized adnexal masses [33]. **Immature teratomas** are characterized by a large variability of the differentiated and undifferentiated tissues that make them up. On ultrasound examination, they are large unilateral adnexal masses, cystic with a large solid component or purely solid, with poor or moderate vascularization [34]. The most specific feature is the very characteristic heterogeneous ("bizarre") echogenicity of the solid component, with hyperechoic areas, spots and cystic spaces, with or without acoustic shadows (Fig. 6D) [34].

To summarize, malignancy should be suspected during pregnancy when multilocular-solid or solid tumors are sonographically visualized. Malignancy should also be considered as a possibility when unilocular-solid cysts with irregular papillary projections increase in size and the number of projections during gestation.

4. Ultrasound-based patient management

Management of a pregnant woman with an adnexal mass may be conservative (ultrasound surveillance) or surgical. The choice is tailored according to (1) patient clinical presentation (symptoms and signs), (2) ultrasound criteria (mass size, morphology and associated findings) and (3) obstetric criteria (gestational age and obstetric comorbidities). Conservative management of adnexal masses is preferable in asymptomatic patients given the risks associated with surgical interventions performed during pregnancy, such as fetal growth restriction, preterm delivery and maternal surgical complications [35,36]. Surgery is indicated in women with suspected cyst-related complications or invasive malignancy [1]. For instance, adnexal torsion requires urgent surgical treatment in both non-pregnant and pregnant patients. However, the risk of torsion during pregnancy is very low (0.5–0.7 %) [14].

Focusing on the risk of malignancy, the selection of asymptomatic patients for safe expectant management relies on accurate imaging classification of maternal adnexal masses. Ultrasound assessment plays a critical role in discrimination between benign and malignant ovarian masses with very high accuracy in non-pregnant women, based on subjective assessment by experienced ultrasound examiners and mathematical models [6,37–39]. However, a very reduced number of studies have been published so far on the performance of ultrasound to differentiate ovarian masses during pregnancy. A meta-analysis of studies from 2021, assessing ultrasound accuracy in detecting ovarian malignancy during pregnancy, reported the overall pooled sensitivity, specificity, positive likelihood ratio and negative likelihood ratio of 64 % (95 % CI: 30–88 %), 88 % (95 % CI: 64–97 %), 5.6 (95 % CI: 1.2–25.4) and 0.4 (95 % CI: 0.15–1), respectively [40]. As previously pointed out, ultrasound characteristics may be misinterpreted during pregnancy, primarily in women with endometriomas due to influences of the hormonal environment (endometrioma decidualization) [19].

In a retrospective single-centered study, Testa et al. looked for the malignancy rates in each of the IOTA ultrasound morphological categories [1]. The prevalence of malignancy was 0 % (0/37) in unilocular cysts, 27 % (4/15) in multilocular, 35 % (11/31) in unilocular-solid, 70 % (14/20) in multilocular-solid and 70 % (7/10) in the solid lesions. Based on these findings, the authors designed an algorithm for counseling patients in their referral oncology center (https://ijgc.bmj.com/content/31/6/899.long).

Table 1
Ultrasound-based strategies and scoring systems for adnexal masses assessed in pregnant patients.

Study reference	Study characteristics	Strategy/systems	Sensitivity	Specificity
Lee et al., 2021 [41]	Single institution Prospective 236 patients 13 malignancies BOT excluded	Sassone Lerner IOTA ADNEX (14 % cut-off)	69 % 77 % 62 %	85 % 69 % 85 %
Czekierdowski et al., 2021 [42]	Single institution Prospective 36 patients 9 malignancies (2 BOT)	IOTA SRR IOTA ADNEX (20 % cut-off)	100 % 78 %	37 % 70 %
Rabiej-Wronska et al., 2022 [43]	Single institution Prospective 153 patients 12 malignancies	IOTA SR	92 %	69 %
Barcroft*et al.*, 2024 [14]	Multicenter Retrospective 267 patients 11 malignancies (all BOT)	IOTA two-step strategy[a]	90 %	65 %

Abbreviations: ADNEX, Assessment of Different NEoplasias in the adnexa model; **BOT**, border-line ovarian tumor; **IOTA**, the International Ovarian Tumor Analysis Group; **SR,** Simple Rules; **SRR**, Simple Rules Risk model.

[a] The IOTA two-step strategy involves the use of simple benign descriptors (BDs) to classify adnexal masses without any computer support in the first step, and ADNEX in the second step, if BDs cannot be applied.

Ultrasound-based scoring systems and strategies, which were originally developed for malignancy prediction in non-pregnant women with adnexal masses but also assessed in pregnant patients, include the Sassone and Lerner systems, IOTA Simple Rules (SR), IOTA Simple Rules Risk (SRR) model, IOTA ADNEX models as well as the IOTA two-step strategy [14,41–43]. Their performance is presented in Table 1. So far published validation studies in pregnant women present limitations such as the retrospective character or the reduced number of included patients (Table 1).

To facilitate correct classification of adnexal masses by less experienced ultrasound examiners, the IOTA group defined 4 simple benign descriptors (BDs) [5], presented in Table 2, in addition to the development of the ultrasound-based mathematical models, such as ADNEX [38,44]. In a study by Barcroft et al., BDs were applied to 68.9 % of maternal adnexal masses during pregnancy (184/267); of these only one lesion (border-line ovarian tumor) was misclassified as benign (1/184, 0.5 %) [14]. The IOTA two-step strategy involves the use of BDs to classify adnexal masses without any computer support (the first step) and ADNEX (the second step) if BDs cannot be applied [5]. The two-step strategy accurately distinguished benign from malignant adnexal masses in a large cohort of non-pregnant women (n = 4905, AUC 0.95) [5]. Pregnancy-induce morphological changes of endometriomas overlap with ultrasound features of borderline ovarian tumors and early-stage invasive ovarian cancer, likely contributing to the poor performance of the ADNEX model in pregnancy [18,19]. Although the IOTA two-step strategy and ADNEX are currently considered the most appropriate tools in non-pregnant patients, larger prospective multicenter studies are required to validate the IOTA diagnostic models in pregnancy. Ongoing "Prospective Validation of the ADNEX Model for Discrimination Between Benign and Malignant Adnexal Masses in Pregnancy: p-IOTA" (https://clinicaltrials.gov/study/NCT05974618) is one such study. Until ADNEX/other models or strategies have been validated in pregnancy, the IOTA group recommends using BDs and expert subjective assessment, where BDs cannot be applied [14]. In the future, ultrasound-based strategies combined with artificial intelligence could be useful to support the classification of adnexal masses by less experienced ultrasound examiners.

While expert ultrasound assessment generally provides sufficient information about the risk of maternal adnexal malignancy in pregnancy, magnetic resonance imaging (MRI) is useful as a secondary imaging modality, evaluating the extent of suspected cancer [2]. MRI can be also valuable for characterizing non-gynecologic (*e.g.* gastrointestinal-related) processes, as well as in doubtful clinical situations when it is desirable to share professional experience and responsibility by cross-interpreting imaging findings [*e.g.* very large tumor, degenerating uterine (subserosal) fibroids, suspected adnexal torsion, etc.] [2]. T2-weighted imaging and especially diffusion-weighted imaging are useful even without gadolinium-based contrast which should be avoided in pregnant women for fetal safety [45]. Computed tomography (CT) and ^{18}F-FDG positron emission tomography (PET), although not absolutely contraindicated in pregnancy, are largely avoided because of fetal ionizing radiation exposure [46,47].

In addition to imaging, clinicians may require dosing of maternal serum tumor markers while managing patients with strongly suspected ovarian cancer. Cancer antigen 125 (CA-125), the most frequently examined epithelial ovarian malignancy marker, is physiologically elevated in pregnancy, especially in the first trimester and immediately following delivery [48]. The markers that are not affected by normal pregnancy are carcinoembryonic antigen (CEA; a marker for epithelial tumors), carbohydrate antigen 19-9 (CA19-9; a mucinous epithelial tumor marker), inhibin B and antimüllerian hormone (markers for granulosa cell tumor), and lactate dehydrogenase (LDH; a marker for dysgerminoma, which may be also elevated in preeclampsia/HELLP syndrome) [2,48]. Human chorionic gonadotropin (hCG; a marker for some germ cell neoplasms, particularly choriocarcinoma) is physiologically very increased in pregnancy and useless as a tumor marker. Alfa fetoprotein (AFP; another marker for some germ cell neoplasms, such as immature teratoma and endodermal sinus tumor) is physiologically increased in normal pregnancy, abnormally increased in "open" neural tube defects, and decreased in Down Syndrome [48]. Extremely elevated AFP values (>10,000 ng/mL) should prompt concern for a germ cell tumor, especially pure endodermal sinus (yolk sac) tumor [2].

Fig. 7 summarizes the management of pregnant patients with adnexal masses based on clinical presentation and ultrasound findings.

5. Conclusion

Obstetric sonologists and pelvic imagers should be familiar with the ultrasound morphologies of maternal adnexal masses in pregnancy because they are frequent. Their correct interpretation is fundamentally important for counseling patients, choosing the most appropriate therapeutic options and avoiding unnecessary interventions. In the spectrum of adnexal formations observed in the first trimester, functional formations predominate, and they self-resolve during pregnancy. The most common true adnexal lesions are benign, having similar ultrasound characteristics in both pregnant and non-pregnant women, just like the much rarer borderline and invasive malignancies. An exception is decidualized endometrioma, which, due to the appearance of vascularized papillary projections, resembles a borderline or early-stage invasive malignancy. The evolution and detailed characterization of papillary

Table 2
Modified IOTA benign descriptors (associated risk of malignancy <1 %).

	Simple benign descriptor
D1	Unilocular tumor with ground-glass echogenicity and maximum diameter <10 cm in premenopausal woman (suggestive of endometrioma)
D2	Unilocular tumor with mixed echogenicity, acoustic shadow and maximum diameter <10 cm in premenopausal woman (suggestive of benign teratoma)
D3	Unilocular tumor with anechoic echogenicity, regular internal walls and maximum diameter <10 cm (suggestive of cystadenoma or simple cyst)
D4	Unilocular tumor with regular walls and maximum diameter <10 cm

Abbreviations: D, descriptor; **IOTA**, the International Ovarian Tumor Analysis Group.

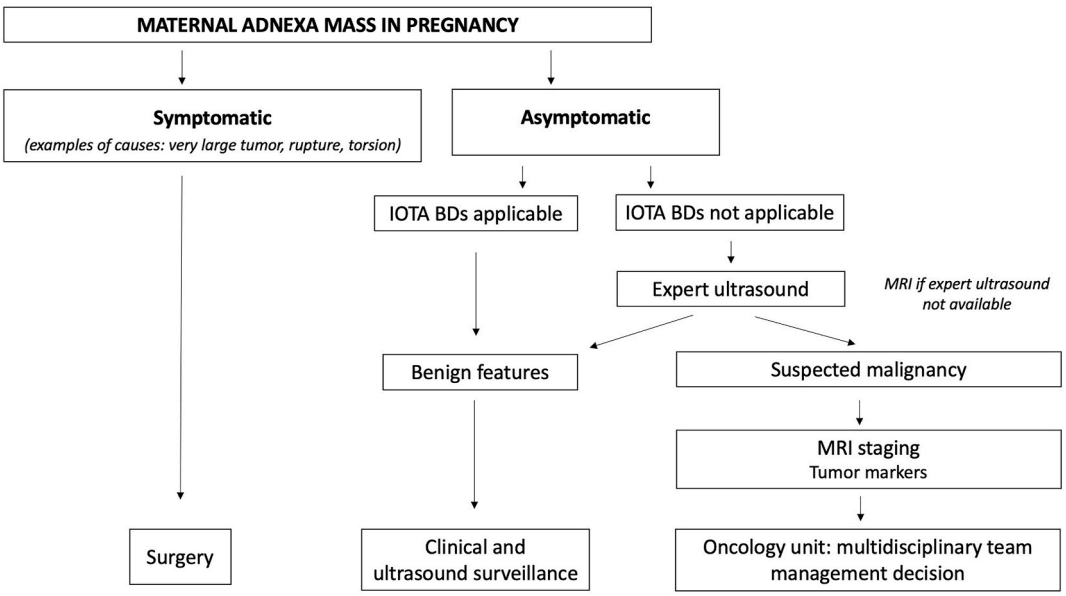

Fig. 7. Management of pregnant patients with adnexal masses.
Abbreviations: BD, modified benign descriptor; **IOTA**, the International Ovarian Tumor Analysis Group, **MRI**, magnetic resonance imaging.

projections may help in differentiating these lesions. Malignancy should be suspected when multilocular-solid or solid tumors are visualized, as well as when unilocular-solid cysts with papillary projections increase in size and the number of projections during gestation. The IOTA BDs, in the first line, and expert subjective assessment, when BDs cannot be applied, are recommended to be used to assess the risk of maternal adnexal malignancy. Prospective, adequately powered studies are needed to validate mathematical models and new strategies that would be useful for less experienced examiners.

CRediT authorship contribution statement

Dusan Djokovic: Conceptualization, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Patrícia Pinto:** Investigation, Methodology, Writing – review & editing. **Inês Reis:** Investigation, Methodology, Writing – original draft, Writing – review & editing.

Practice points

- Until mathematical models have been widely validated in pregnancy, use the IOTA simple benign descriptors (BDs) and expert subjective assessment to predict the risk of maternal adnexal malignancy.
- Be familiar with the ultrasound morphology of functional formations and the most frequent lesions such as mature teratomas, cystadenomas or infectious formations.
- Keep in mind that endometriomas may change during pregnancy, including the appearance of rounded, smooth, richly vascularized papillary projections in the first trimester; their size and vascularization increase in the second trimester, and the lesion shrinkage in the third trimester.
- Consider a borderline ovarian tumor in patients with a unilocular-solid cyst characterized by vascularized papillary projections with an irregular surface, with no evidence of morphological changes during the first half of pregnancy.
- Consider invasive malignancy in pregnant women with (a) solid or (b) multilocular-solid adnexal masses or (c) unilocular-solid cysts with papillary projections that increase in size and the number of papillations from the first trimester during gestation.

Research agenda

- Largescale prospective multicenter validation of the IOTA ADNEX model and novel scoring systems/mathematical models in pregnant women with adnexal masses
- Development of combined ultrasound/artificial intelligence-based approaches for maternal adnexal masses in pregnancy

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