VILNIUS UNIVERSITY
MEDICAL FACULTY

The Final Thesis

Ovarian Masses in Adolescents

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19.05.2023

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OUTLINE

KEYWORDS:
Ovarian masses; Adolescent females; Ovarian cysts; Ovarian tumors; Ovarian cancer; Benign vs Malignant; Incidence; Risk factors; Diagnosis; Medical treatment; Surgical Treatment; Fertility preservation; Prognosis; Outcome.

SUMMARY:

This literature review addresses the subject of ovarian masses in adolescents, aged 10-19. It explores the two primary classifications of ovarian masses, namely, non-neoplastic and neoplastic masses. These formations, while relatively rare, can have a significant impact on the health and well-being of affected individuals, emphasizing the importance of early diagnosis and proper management strategies. The review further differentiates the clinical presentations and treatment methods of ovarian masses between adolescent and adult females.

In conclusion, the review identifies that despite the low prevalence of ovarian tumors in adolescents, they are the most frequent reproductive organ tumors in this age demographic. It highlights the evolution of the medical approach from radical treatment towards more conservative, minimally invasive, and fertility-preserving methods such as laparoscopy. The review underscores the importance of individualized management strategies and emphasizes the need for additional research to better understand and optimize treatment approaches for this vulnerable patient demographic.

1. INTRODUCTION

1.1. Brief Background on ovarian masses in Adolescents

This literature review will analyze ovarian masses found in adolescent females, between the ages of 10 and 19. The ovaries are important endocrine organs that secrete hormones that are essential for the function and growth of reproductive organs in young females (1, 2). Ovarian masses are abnormal growths that can develop on or within the ovaries. They are relatively rare in adolescents and can be discovered incidentally during routine pelvic examinations or when adolescents experience symptoms such as abdominal pain or pressure, menstrual irregularities, etc. (1, 3).

Ovarian masses are categorized into two main groups: neoplastic and non-neoplastic. The non-neoplastic group, generally known as the "functional ovarian masses" or "ovarian cysts", are fluid-filled structures that can be categorized as simple or complex. They are commonly incidental findings on physical examination or imaging (3, 4, 5). Females in their adolescent years are in a stage of growth and development, meaning the ovaries are also beginning to actively grow and mature, making them more prone to mutation (6). When adolescent females are of reproductive age, most ovarian cysts are functional and benign as they are often related to the menstrual cycle. These cysts generally do not require surgical intervention; however, ovarian cysts can lead to complications such as pelvic pain, cyst rupture, hemorrhage, and ovarian torsion, which are considered gynecological emergencies that require prompt management (3). The neoplastic group entails the "ovarian tumors", which are divided into benign, malignant, and borderline. They are extremely rare in adolescents, accounting for only 1-2% of all childhood cancers, but are the most common reproductive organ tumors in adolescents (1, 2, 6, 7). They are usually asymptomatic but can occasionally cause an abdominopelvic mass or endocrine alterations (7). Moreover, an ovarian mass can often coincide with ovarian torsion which is defined as the complete or partial twisting of the ovarian vessels resulting in obstruction of blood flow to the ovary. This is seen as a gynecological emergency and therefore must be alleviated urgently to restore vital blood flow (3).

The clinical presentations, pathological classifications, and principles of treatment for ovarian masses vary between adolescent and adult women (6). Ovarian masses in adolescents can cause pain, menstrual irregularities, and other symptoms, and can have a significant impact on the physical, emotional, and social well-being of the affected individuals (3). Therefore, it is crucial to be aware of the symptoms and risk factors for an early diagnosis and proper management to ensure a good outcome and to prevent any potential complications (4). The management options may include conservative or surgical treatment, based on the type, size,

location, and malignancy of the ovarian mass while keeping in mind the importance of the preservation of fertility in this age population (3, 6).

1.2. Purpose and significance of this Literature review

This literature review aims to provide an overview of the current understanding of the prevalence, classification, and importance of proper handling of ovarian masses in adolescent females. Additionally, it aims to provide a basis of clinical guidelines for the diagnosis with the most effective current diagnostic methods. Most importantly, it aims to analyze and provide the state-of-the-art management of ovarian masses in adolescents to not only treat their ovarian mass but preserve fertility in these young patients.

1.3. Research Question

"What are the leading options and effects of different management strategies for adolescent females with ovarian masses to best preserve their fertility?"

2. LITERATURE SELECTION STRATEGY

The literature search for this literature review was conducted using the databases PubMed and Web of Science. The search was conducted between December 2022 and May 2023 and was limited to articles published in English. The search terms used included “ovarian masses,” “adolescents females,” “ovarian cysts,” “ovarian tumors,” “ovarian cancer,” “benign vs malignant,” “incidence,” “risk factors,” “diagnosis,” “medical treatment,” “surgical treatment,” “fertility preservation,” “outcomes” and “prognosis”.

The initial search yielded a total of ~250 articles. The titles and abstracts of these articles were screened for relevance, and articles that were not directly related to the topic of ovarian masses in adolescents were excluded, including many articles which spoke solely about adult ovarian masses. A total of 75 articles were selected for full-text review. The selected articles were then assessed for their quality using the following criteria: study design, sample size, study population, data collection methods, and potential sources of bias. Articles that did not meet the inclusion criteria, most commonly due to incorrect age population (neonates, adults, etc.) but also due to inaccessibility of the full-text pdf article, were excluded, leaving a final sample of 28 articles for inclusion in the literature review. The articles selected for inclusion in the literature review were mainly retrospective studies, with a small number of systematic reviews and prospective cohort studies. The sample sizes of the studies varied, with the largest study having a sample size of 752 and the smallest study having a sample size of 20, with the majority having a sample size of 50 to 150.

The study population was mostly from developed countries including the USA, China, Canada, Switzerland, and Turkey. The articles were published between 2017 and 2023. The final sample of articles was considered to be of high quality and relevant to the research question of the literature review.

3. EPIDEMIOLOGY & ETIOLOGY OF OVARIAN MASSES IN ADOLESCENTS

3.1. Incidence and Prevalence of ovarian masses in adolescent females

As stated above, ovarian masses are quite rare in the young female population. The annual incidence is estimated to be 2.6/100,000 (1, 8). There is an increasing incidence of ovarian masses in line with age and is markedly higher in girls over 12-14 years of age, constituting 17 to 44% of all ovarian pathologies in adolescents (1, 9). Approximately 10% of these ovarian masses are malignant while accounting for only 1% of all tumors in children and adolescents (1, 2, 10). That being said, ovarian tumors are the most common reproductive organ tumors in adolescents (1, 6, 7).

In several studies the obvious majority of ovarian masses were benign (~90%), divided more specifically into non-neoplastic cysts (~60%) and neoplastic benign tumors (~30%), while some were malignant (~7%), and very few were borderline (~2%) (8, 10, 11). Most ovarian masses in this age group are non-neoplastic cysts due to their irregular menstruation and frequent anovulation (11). Consistent with recent study findings, the most frequent benign ovarian neoplasms in adolescents include mature cystic teratomas (64.4%), along with the not-as-prevalent mucinous and serous cystadenomas and endometriomas (1, 11, 12). Unlike adults, ovarian malignancies in adolescents are derived from approximately 50-80% of germ cells, followed by epithelial cells, and lastly sex cord-stromal cells (11, 12, 13). The incidence of malignant tumors was found to be significantly higher in patients younger than 17 years than in those aged 18-20 years (14.5% vs. 10.7%, $p < 0.006$) (11).

Ovarian torsion is the most common complication in pediatric ovarian tumors (3-16%), causing 2.7% of all cases of acute abdominal pain, and represents the fifth most common gynecological emergency (3, 4, 7). Around 15% of ovarian torsions are found in the pediatric population, with two peaks in the frequency distribution. The majority (86%) are in the post-menarche period yet at a pre-pubescent age (~12 years) and the other peak, being less relevant for this review, is at the infantile age (1, 4). The explanation for this may be the longer ovarian pedicle in the pediatric population, giving a higher risk of torsion here compared to the adult population (1).

3.2. Risk factors and demographic characteristics associated with ovarian masses.

The risk factors for ovarian cyst formation that are relevant for adolescents include age, menstrual cycle disorders, endometriosis, hypothyroidism, PCOS, and less common but still relevant are cigarette smoking, and pregnancy (3).

The risk factors for ovarian tumors include age, genetics, (e.g., BRCA1/BRCA2 mutation), hormonal factors, and race. Hispanic women have a higher risk of benign tumors while Caucasian women have a higher risk of malignant & borderline tumors (8). Most ovarian tumors arise from somatic mutations from factors the patients acquired. Important predictors of ovarian malignancies remain the history of a first-order relative since inherited predispositions or germline mutations tend to follow an autosomal dominant pattern (14).

Due to anatomical reasons such as greater motility of the cecum, the slightly longer mesosalpinx and utero-ovarian ligament, as well as the greater relative space in the ipsilateral iliac fossa to the obturator region, there is a higher risk for females to develop ovarian masses and consequently, ovarian torsions on the right side (~65%) compared to the left side (30%), while only a few are localized bilaterally (~5%) (1, 4, 11). Although in 50% of cases, ovarian torsions occur in normal gonads, several studies found that abnormalities in the development of the fallopian tube or mesosalpinx as well as the presence of intrinsic ovarian or tubal pathologies, such as tumors, cysts, trauma, or recent surgery, are the main predisposing factors for ovarian torsions. The risk of ovarian torsion is further increased if the ovary is larger than 5cm in maximum diameter or 20 cm^3 larger than the contralateral (4, 7).

4. CLASSIFICATION OF OVARIAN MASSES IN ADOLESCENTS

4.1. Non-neoplastic ovarian masses

4.1.1. Functional ovarian cysts

Functional cysts are the most common ovarian cysts found in adolescents. They are also called “physiologic cysts” as the most common ones occur during the normal menstrual cycle and derive from ovulatory dysfunction (7). They may be found accidentally or in an emergency room when these patients complain of abdominal pain (9). Both follicular and corpus luteal cysts can turn into hemorrhagic cysts, but they are generally asymptomatic and spontaneously resolve without treatment (3).

4.1.1.1. Follicular cysts

Follicular cysts are generally known to arise from gonadal hyperstimulation by the pituitary gland (7). Consequently, the follicles fail to rupture during ovulation because of a lack of physiological release from the ovum, either due to excessive FSH stimulation or

the absence of the usual LH surge at mid-cycle just before ovulation (7, 9). Follicular cysts can cause symptoms of precocious puberty (peripheral precocious puberty) and decreased frequency of menstruation due to excess estradiol production (3, 9). These cysts continue to grow because of hormonal stimulation and are usually “larger than 2.5cm in diameter with a smooth, thin-walled, and unilocular appearance” (3).

4.1.1.2. Corpus Luteal cysts

Corpus luteal cysts are thought to result from inappropriate central hemorrhaging. These cysts can be present during pregnancy but usually resolve by the end of the first trimester. These cysts usually “grow to ~3cm and can be complex or simple, thick-walled, or contain internal debris” (3).

4.1.2. Non-functional ovarian cysts

4.1.2.1. Endometrioma - "Chocolate cyst"

Endometriomas are benign estrogen-dependant cysts that arise from the ectopic growth of endometrial glands and stroma, called endometriosis (3). The ovaries are the most common site for endometriosis while 17-44% of patients with endometriosis have an ovarian endometrioma (15). Endometriomas are commonly referred to as “chocolate cysts” as they contain dark brown, thick, gelatinous aged endometrial fluid from the hormonally active endometrial tissue (3, 9). Ovarian endometriomas are classified into two types: Type I, “consisting of small primary endometriomas, which develop from surface endometrial implants”; Type II, “arising from functional cysts that have been invaded by ovarian endometriosis or Type I endometriomas”. On ultrasound, these cysts appear as a complex mass with “ground glass” internal echoes (3).

Ovarian endometriomas account for 35% of all benign ovarian cysts and have an overall low risk of malignant transformation, however, endometriomas do increase this risk in women with endometriosis (3, 15).

4.1.2.2. Theca Lutein cysts

Theca luteal cysts are “luteinized follicle cysts” that can develop due to overstimulation when human chorionic gonadotropin (hCG) levels are increased. These cysts generally occur in pregnant women and therefore are less commonly seen in adolescents as they are not very commonly pregnant in the developed world. Theca luteal cysts are also seen in women with multiple gestations, ovarian hyperstimulation, and gestational trophoblastic disease (3).

4.2. Neoplastic ovarian masses

Ovarian tumors can be benign or malignant and arise from the inappropriate overgrowth of cells from three cell lines: epithelial tissue cells, ovarian stromal cells, and “pluripotent” germ cells. Most ovarian tumors in adolescents originate from germ cells, while in adults the vast majority originate from epithelial tissue cells (9).

4.2.1. Benign ovarian tumors

4.2.1.1. Germ cells tumors

4.2.1.1.1. Mature Teratoma (Dermoid cyst)

A mature cystic teratoma is a type of germ cell tumor that contains well-differentiated derivatives from the three germ cell layers (i.e., ectoderm, mesoderm, and endoderm) developing as hair, muscle, teeth, or bone (9, 16). Mature cystic teratomas are the most common ovarian neoplasms in adolescents, with an increased incidence in the early teenage years. They represent approximately 50% of all pediatric ovarian tumors and up to 95% of primary ovarian germ cell tumors (9, 13, 16). The majority of teratomas are typically asymptomatic as they are slow-growing, and therefore commonly diagnosed incidentally with pelvic ultrasound (13). In children, mature teratomas often occur bilaterally (10-15%) (7, 9). Although mostly benign, mature teratomas can undergo a malignant transformation in 1 to 2% of cases (3, 16).

4.2.1.1.2. Immature Teratoma

Immature teratomas are much less common and are difficult to classify histologically since they may resemble mature teratomas microscopically. The key difference is the presence of immature embryonic tissue, derived from all the germinal sheets (endoderm, ectoderm, and mesoderm) and mixed with mature tissue. As it is mainly of neurogenic origin, the amount of immature neuroepithelial tissue determines the histological degree (7, 9). The newest publications state that immature teratomas are believed to be benign lesions in their pure form rather than having a tendency of "local malignancy" (9).

4.2.1.2. Stromal tumors

Stromal tumors arise from the ovarian stromal cells that produce hormones and can be benign or malignant.

4.2.1.2.1. Thecoma

Thecomas are sex cord-stromal tumors that arise from thecal cells. They are usually benign and are very rarely diagnosed in children. Thecoma tumors produce estrogen and progesterone which can also cause precocious puberty (7, 9).

4.2.1.2.2. Fibroma

Fibromas are tumors that arise from connective tissue cells (fibroblasts) that form the structural tissue of the ovary. They are very rarely diagnosed in children and are generally small, benign, and asymptomatic. In rare cases, fibromas may be associated with Meigs syndrome which includes pleural effusion and ascites (9).

4.2.1.3. Epithelial tumors

Epithelial tumors arise from the surface epithelium of the ovary. They are common in adults, accounting for 95% of ovarian tumors in adults, but rarely develop in adolescents (9).

4.2.1.3.1. Cystadenoma

Ovarian cystadenomas are common epithelial tumors in children and adolescents (7). The two most common types of cystadenomas are **serous (unilocular)** and **mucinous (multilocular)** cystadenomas. Serous tumors are the most common type of ovarian tumor in adults, which can also occur in adolescents. Cystadenomas are usually incidental findings but may reach enormous sizes, occupying the entire abdominal cavity, and causing pressure on the organs in the abdomen and chest (9, 17).

4.2.1.3.2. Endometrioid tumors

Endometrioid tumors are epithelial ovarian tumors that are made up of cells resembling the glandular lining of the uterus. They are rare in adolescents and can be either benign or malignant (17).

4.2.1.3.3. Brenner tumors

Brenner tumors arise from the epithelial lining of the ovary. They are generally benign, small, and asymptomatic as they are very slow growing (17).

4.2.2. Malignant ovarian tumors

4.2.2.1. Germinal ovarian tumors

Germinal tumors are the most frequent malignant tumors in children, making up 60 to 80% of all malignant ovarian tumors. (9)

4.2.2.1.1. Dysgerminoma

Dysgerminomas are the most frequent malignant germ cell tumors in children and adolescents. They arise from primordial germ cells, resembling the cells of a developing oocyte, and have an equivalent germ cell tumor of the testicle called Seminoma (7, 9). In its aggressive form, LDH (lactate dehydrogenase) and β-hCG (β-subunit of human chorionic gonadotropin) are indicative serum markers (7).

4.2.2.1.2. Yolk sac tumor (Endodermal sinus tumors)

Yolk sac tumors are rare, aggressive, fast-growing malignant tumors that resemble the yolk sac of an embryo. They account for approximately 20% of malignant ovarian germ cell tumors and 1% of all malignant ovarian tumors (6). They are often associated with ascites, abdominopelvic diffusion, and metastases. They produce αFP (alpha-fetoprotein), making this the indicative serum marker (7).

4.2.2.1.3. Embryonal carcinoma

Embryonal carcinomas often occur as part of a mixed tumor. This has led to false assumptions in the past, stating that it was endocrinologically active or that it produced β-hCG and αFP (9).

4.2.2.1.4. Choriocarcinoma

Choriocarcinomas are rare malignant germ cell tumors that are composed of malignant trophoblastic elements. They produce β-hCG (β-subunit of human chorionic gonadotropin), making this the indicative serum marker (9).

4.2.2.1.5. Gonadoblastoma

Gonadoblastomas are tumors that mostly form in dysgenetic gonads of people with disorders of sexual development (9).

4.2.2.1.6. Malignant mixed germ cell tumor

Malignant mixed germ cell tumors are mixed tumors, as is stated in the name. They can also produce αFP from their yolk sac tumor component (9).

4.2.2.2. Stromal ovarian tumors

Malignant stromal tumors constitute 6 to 17% of all malignant ovarian tumors. Stromal tumors arise from stromal cells (primary undifferentiated mesenchymal cells) that can differentiate into granulosa cells and theca cells in the female. Since they are hormonally active, they can cause precocious puberty or virilization (9).

4.2.2.2.1. Granulosa cell tumor

Granulosa cell tumors are the most common subtype of malignant stromal ovarian tumors. These are sex cord-stromal tumors are arisen from granulosa cells. They are generally slow-growing tumors that can produce estrogen and therefore can cause precocious puberty in adolescents (9).

4.2.2.2.2. **Androblastoma** (Sertoli-Leydig cell tumor)

Androblastomas are rare sex cord-stromal tumors that arise from Sertoli or Leydig cells that produce androgens which can cause masculinization in females (9).

4.2.2.3. Epithelial ovarian tumors

Epithelial tumors represent only 2% of all malignant ovarian tumors in adolescents. The incidence increases after 14 years of age, generally post-menarche, as their development may be triggered by hormonal stimulation (7, 9).

4.2.2.3.1. Cystadenocarcinomas

These are the malignant forms of cystadenomas, which can also be divided into serous and mucinous (9).

4.2.3. Other malignant neoplasms:

4.2.3.1. Borderline ovarian tumors (BOT)

Borderline tumors account for 10 to 20% of all epithelial ovarian tumors. These slow-growing tumors show reduced malignancy with a 5-year survival rate of 92% to 98% compared to epithelial ovarian cancer. Regardless, the earlier the diagnosis, the better the prognosis (6).

4.2.3.2. Polyembryoma

Extremely rare, aggressive, mixed germ cell tumor (9).

4.2.3.3. Metastases and infiltrations of another neoplasm (e.g., lymphoma)

The ovaries contain B- and T-cell lymphocytic lineages within cortical granulomas, which explain their potential for primary hematological malignancies. The incidence in children and adolescents is low compared to adults. The most common ovarian lymphomas found in children and adolescents are Burkitt's lymphoma or Burkitt-like lymphoma (14).

5. DIAGNOSIS OF OVARIAN MASSES IN ADOLESCENTS

5.1. Clinical features of ovarian masses in Adolescents

5.1.1. Anamnesis

The primary anamnesis of adolescent patients must consist of basic age-related information including gynecological history (menarche; menstrual habits; volumes; dysmenorrhea); medical history; sexual history (rule out pregnancy; simultaneously indicate either transvaginal or transabdominal ultrasound examination); family history (genetic history) (3, 5, 14). The patient navigates the initial differential diagnosis and further investigational strategy (14).

5.1.2. Clinical symptoms

Clinical manifestations that ordinarily prompt medical attention include lower abdominal, often unilateral, pain (~ 75%), including acute abdominal pain caused by torsion; irregular menstruation (~ 30%); palpable pelvis mass (~12%); dysmenorrhea (3%), and abdominal distention (~2%) (1, 6, 11, 13). Further nonspecific symptoms that might coincide with ovarian masses include nausea, vomiting, fatigue, bloating, constipation, dyspareunia, and urinary incontinence, which can be secondary symptoms in relation to the mass torsion, expansion, and compression of nearby abdominal structures (4, 13, 14).

Some studies state that benign ovarian masses commonly present with lower abdominal tenderness while malignant ovarian masses present with palpable pelvis masses but other studies state that the symptoms correlate to the initial size and pathology, and not the malignant potential of the tumor (1, 14). The primary features of ovarian tumors are hormonal dysregulation, presenting most often as precocious puberty (30%). Depending on if it is a tumor that is secreting either male or female sex hormones, the subsequent manifestations may be hirsutism and virilization or menstrual abnormalities, endometrial pathology, etc. An additional presenting sign of ovarian pathology is ascites which is found in roughly one-third of patients with ovarian tumors (14). In case of an ovarian cyst rupture or ovarian torsion, the patient would most likely experience a sudden onset of acute severe pain almost always accompanied by nausea and vomiting (97.5%) (1, 3). It is relevant to mention that since torsions more commonly happen on the right side, the patients frequently have acute pain in the right quadrant of the abdomen, which can be mistaken for acute appendicitis (1, 4). The clinical diagnosis of ovarian masses is a challenge because most of the symptoms (abdominal pain, nausea, vomiting, etc.) are non-specific, making it difficult to differentiate between ovarian pathologies (1, 4, 14).

5.1.3. Physical Examination

The majority of ovarian cysts are incidental findings on physical exams or during pelvic imaging. Ordinarily, abdominal palpation and bimanual recto-abdominal or vaginal examinations are performed in sexually active patients for an accurate diagnosis (11). Amid the bimanual exam of the ovaries, palpation will help determine their location, shape (regular or irregular), size, consistency, level of tenderness, and mobility. Nevertheless, the pelvic examination has limited ability to reliably diagnose ovarian cysts, as they can be difficult to palpate depending on the patient's body habitus, examiner's experience, and pelvic anatomy (3). Since the ovaries are located deep in the pelvic cavity, it is challenging to detect early lesions. Moreover, adolescents often do not acknowledge the importance of regular physical examination and do not pay much attention to ovarian mass-related symptoms, therefore they generally do not seek medical advice until the mass is already large (6).

In the acute setting, if an ovarian torsion is present and persistent, the ovary can become necrotic, infected, cause peritonitis and eventually lead to the loss of the involved ovary (3, 4). Therefore, it is critical to promptly recognize and treat harmful ovarian masses along with persistent ovarian torsions as it is crucial for a better clinical outcome and preservation of the ovary and/or fallopian tube. Moreover, as pain is the most constant symptom of ovarian torsions and is poorly differentiated from other urgent conditions that affect the genitourinary and gastrointestinal system, the role of diagnostic imaging is fundamental and can play a key role in an acute setting to promptly evaluate and assist in electing the appropriate management (4, 7).

5.2. Diagnostics of ovarian masses in Adolescents

5.2.1. Laboratory studies:

When an ovarian mass is suspected, the physician should first perform a serum β-hCG or urine pregnancy test to rule out pregnancy before imaging and other possibly invasive examinations are done. In the complete blood count (CBC) the hematocrit and hemoglobin levels are necessary to evaluate for possible anemia caused by acute bleeding. A urinalysis is required to rule out urinary tract infections and kidney stones. Endocervical swabs should also be collected to assess for pelvic inflammatory disease (3).

Moreover, tumor markers can be helpful indicators and play a vital role in the preoperative detection of ovarian cancer (5, 18). These markers are either produced by the tumor itself or triggered by the host's response and confirm the presence, pathological nature, or malignant potential of the tumor. In asymptomatic children and adolescents, screening for

ovarian tumors is not advised. Adversely, the threshold is lower for screening patients when their family has genetic information suggestive of a predisposition to ovarian tumors (14).

In a study, it was found that alpha-fetoprotein (AFP) and ß-hCG tumor markers are highly specific in malignant tumors along with cancer antigen 125 (CA125) and lactate dehydrogenase (LDH) (1, 8). According to the American College of Obstetrics and Gynaecology, a CA125 level greater than 200 U/ml is concerning for malignancy in premenopausal patients (8). Additionally, the most reliable marker in mature cystic teratoma is cancer antigen 19-9 (CA19-9) (6). A summary of the most relevant tumor markers in ovarian masses, along with what they may indicate, is presented in Table 1.

Table 1	
Tumor marker	**Ovarian Tumor Diagnosis**
Alpha fetoprotein (AFP)	Yolk sac tumor Immature teratoma Embryonal carcinoma Sertoli-Leydig cell tumor
Beta-human chorionic gonadotropin (ß-hCG)	Choriocarcinoma Embryonal carcinoma Dysgerminoma
Lactate dehydrogenase (LDH)	Dysgerminoma
Cancer antigen 125 (CA125)	Epithelial ovarian tumors
Carcinoembryonic antigen (CEA)	Epithelial ovarian tumors
Human epididymis protein 4 (HE4)	Malignant and borderline epithelial ovarian tumors
Cancer antigen 19-9 (CA19-9)	Mature cystic teratoma
Inhibin A	Granulosa cell tumor
Calcium (Ca^{2+})	Sex cord stromal tumors

Table 1 – Summary of Tumor markers found in ovarian tumors (6, 18).

Nevertheless, one cannot exclude a malignancy based on normal serum tumor marker levels since only 50% of malignant tumors present with elevated serum tumor markers (11, 14, 19). Nor can one diagnose an ovarian tumor solely based on tumors marker since they can also be positive in other non-malignant and non-ovarian diseases, or be false positives, as 10% were in one study. Consequently, a new systemic method for the early diagnosis of ovarian cancer and new tumor markers, with high sensitivity and specificity, needs to be identified (5). Lastly, various body fluids, such as ascites or effusions, can be obtained via punctures and aspirated for cytological evaluation or flow cytometry. Flow cytometry is a less invasive technique that is significant for staging which supports a definitive diagnosis and further treatment (14).

5.2.2. Imaging studies:

5.2.2.1. Ultrasonography

Ultrasonography (US) is the first-line imaging method used in examining the pelvis of children and adolescents in a normal and emergency setting (4, 7, 11). The reasons for this are that ultrasonography is readily accessible, easy to use, has no harmful radiation, is non-invasive, does not require sedation, is diagnostically accurate, and is cost-effective (4, 7, 11). The transabdominal approach is favored in these young patients, but transvaginal probes may also be used in sexually active adolescents as it allows for better visualization of the endometrium and ovaries. For the transabdominal approach, the patient's bladder should be filled to move the bowel loops away from the preferred view (7).

Ultrasonography is also the first-line exam in ovarian neoplasms as it provides a valuable interpretation of the tumor to distinguish between benign and malignant masses (3, 7, 14). An ultrasound analyzes the lesion's dimensions, structural characteristics (cystic, solid, mixed, unilocular, multilocular), presence of pelvic free fluid, and assessment of the blood flow and vascularization (3, 7). The ultrasound should be performed on all patients before an operation since findings help guide the decision of how the patient should be managed; operatively or conservatively (6, 11). It is also very effective for monitoring smaller ovarian masses continuously to avoid unnecessary surgical treatment (11).

In a study, the diagnostic concordance between the initial ultrasound findings and the confirmed histopathology was rather significant (~83%) (11). Nevertheless, the diagnostic performance of ultrasound in evaluating ovarian masses can be primarily limited by the expertise of the sonographer (18).

5.2.2.2. Color Doppler ultrasound (CDUS)

The color Doppler ultrasound increases diagnostic accuracy, particularly in ovarian masses and ovarian torsions (7). In an ovarian torsion, the CDUS shows increased volume of the ovary, a round hyperechoic central stroma with multiple concentric hypoechoic vessels, resembling a target. The pathognomonic finding of ovarian torsion is a twisted vascular pedicle, also known as the "whirlpool sign", seen in Figure 1 (4, 7)

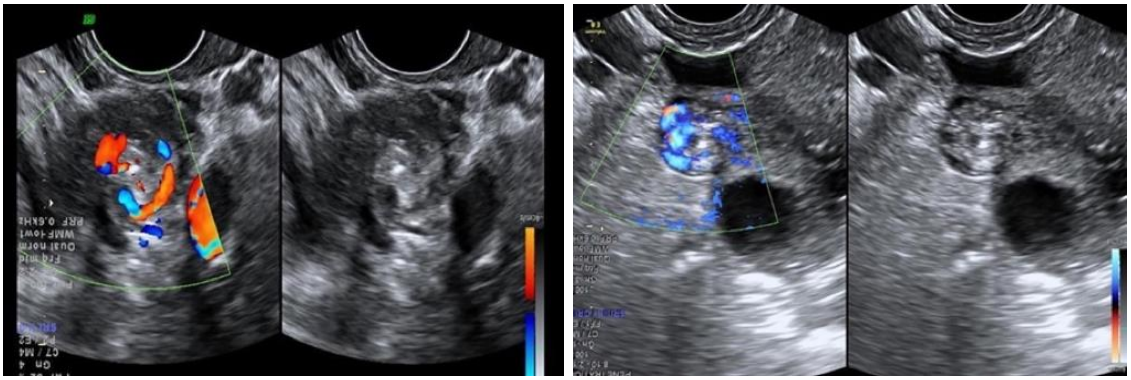

Figure 1 - Ultrasound images of ovarian torsion with the “whirlpool sign” (20).

Furthermore, the presence of effusion in the Douglas pouch and the uterus deviation from the side of the torsion is common (7). However, CDUS assessment in adolescent patients is not completely reliable when confirming or ruling out an ovarian torsion since the absence of arterial and venous flow in the ovary can be seen in non-pathological pediatric ovaries, and the "whirlpool sign" often goes undetected when using only a transabdominal CDUS (4). Vice versa, one cannot rule out an ovarian torsion when blood flow is present on a Doppler exam. This was confirmed by a study stating that over 60% of patients with right ovarian torsions have blood flow in the CDUS. The explanation for this may be an intermittent torsion or the double blood supply of the ovary (3, 7).

5.2.2.3. Contrast-enhanced ultrasound (CEUS)

The contrast-enhanced ultrasound uses microbubbles as a contrast agent, which allows for a real-time assessment of the difference in microvascular perfusion between lesions in a specific area (4, 21). The CEUS has better contrast resolution and “spatial definition”, resulting in better visualization of the ovaries. This allows for a more accurate distinction of the surrounding tissues and organs as well as free abdominal fluid (4). This technique increases the accuracy of diagnosis compared to conventional color and power Doppler ultrasound (21).

CEUS can be easily used in an emergency and routine clinical setting, providing advanced detection and characterization of different ovarian masses, consequently reducing the need for additional imaging examinations. In a study, the CEUS had an overall accuracy rate of 95% when detecting ovarian torsions, with a sensitivity of 94% and specificity of 100%. Regardless, there is limited data on this contrast medium and is still considered "off-label" in the pediatric population, so, therefore, it should be used with caution (4).

5.2.2.4. Magnetic resonance imaging (MRI) & Computer tomography (CT)

Magnetic resonance imaging (MRI) is used as a secondary imaging test when the ultrasound findings are inconclusive (7). An MRI provides additional details on tissue characterization, expansion, organ involvement, and possible differential diagnosis. It uses no ionizing radiation which is very favorable in pediatric patients. Nonetheless, it has limited availability, is very expensive, and requires either a complying patient or sedation (4, 7).

Computer tomography (CT) is an alternative to MRI with the advantage of being available in an emergency setting as it is performed more rapidly and does not require sedation. However, it causes exposure to ionizing radiation in pediatric patients which should be avoided when possible (4). An MRI or CT scan can help determine the nature of ovarian masses and the possibility of "metastatic involvement of pelvic and para-aortic lymph nodes" (11).

It is imperative to determine the possibility of malignant tumors with the valuable differential information from the clinical presentation, serum tumor markers, and these multimodal diagnostic methods for an appropriate diagnosis and subsequent treatment (11, 14). Radiologists play a vital role when interpreting images for differential diagnosis since the pathology among the adolescent population is noticeably distinct from the adult population. Although the first choice for screening is the abdominal ultrasound, a CT or MRI scan is important for preoperative planning along with post-adjuvant chemotherapy evaluation for residual disease (14).

5.2.2.5. Diagnostic Exploratory surgery

Alternatively, exploratory surgery may be used to assess the abdominal cavity when the definitive diagnosis is unknown but when an ovarian tumor or ovarian torsion is suspected. The importance of diagnostic laparoscopy is increasing since the ultrasound can lead to delays during examinations, false negative results, and incorrect localization of urgent findings, such as an ovarian torsion (1). In a study, exploratory surgery was the gold standard examination for identifying ovarian torsions (4).

5.3. Benign vs Malignant Diagnostics

When trying to distinguish between benign and malignant ovarian masses, a number of diagnostic tools mentioned above can be useful. The difficulty of preoperative distinction between benign and malignant masses can lead to incorrect surgical management. The combination of tumor markers and cytology of ascetic fluid can be a reliable diagnostic tool for

ovarian tumors, with high sensitivity (90%) and specificity (96.5%). Tumor markers in both blood and ascites are crucial in pre-operative diagnosis to differentiate between benign and malignant ovarian tumors (14). When analyzing the ultrasound images of the ovarian masses, certain criteria will help guide the differentiation and final diagnosis. An overview of the radiological features found in benign versus malignant ovarian tumors is summarized in Table 2.

Table 2		
Radiological information	**Benign**	**Malignant**
Size	<10cm	>10cm
Locality	Single lesion	Multiple lesions
	Unilateral	Bilateral
Consistency	Cystic	Solid
	Homogenous	Heterogenous
Shape	Well circumscribed	Invasive or metastatic
Calcifications	Not present	Present
Ascites	Generally, not present	Generally present

Table 2 – Radiological features of ovarian tumors (14).

5.3.1. DePriest and Ueland indices

These ultrasound scoring systems were developed to increase the accuracy of the preoperative ultrasound screening modality for malignancy. The DePriest index uses a morphology index (MI) which includes descriptions of the volume, wall structure, and septations. The Ueland index is a modified DePriest "two-factor" scoring system focussing on size and characteristics as seen in Table 3. Both indices have a scoring system from 0-10, consisting of volume plus structure findings. An index of ≤ 5 gives a high probability of a benign mass while ≥ 7 malignant mass (22).

Table 3

	DePriest Index			Ueland Index	
Points	Volume	Cyst wall Structure	Septa Structure	Volume	Tumor Structure
0	<10 cm^3	Smooth <3 mm thickness	No septa	<10 cm^3	Smooth wall, sonolucent
1	10–50 cm^3	Smooth >3 mm thickness	Thin septa <3 mm	10–50 cm^3	Smooth wall, diffuse echogenicity
2	>50–200 cm^3	Papillary projections <3 mm	Thick septa 3 mm–1 cm	>50–100 cm^3	Wall thickening, <3 mm fine septa
3	>200–500 cm^3	Papillary projections ≥3 mm	Solid area ≥1 cm	>100–200 cm^3	Papillary projection ≥3 mm
4	>500 cm^3	Predominantly solid	Predominantly solid	>200–500 cm^3	Complex, predominantly solid
5				>500 cm^3	Complex, solid and cystic areas with extratumoral fluid

Table 3 - DePriest and Ueland indices (22).

An additional radiological indicator of malignancy is the ovarian crescent sign (OCS). If this sign is present, displaying healthy ovarian tissue seen on the ipsilateral ovary in the

presence of an ovarian mass, it indicates a high probability of a benign lesion. Examples of OCS are shown in Figure 2 below.

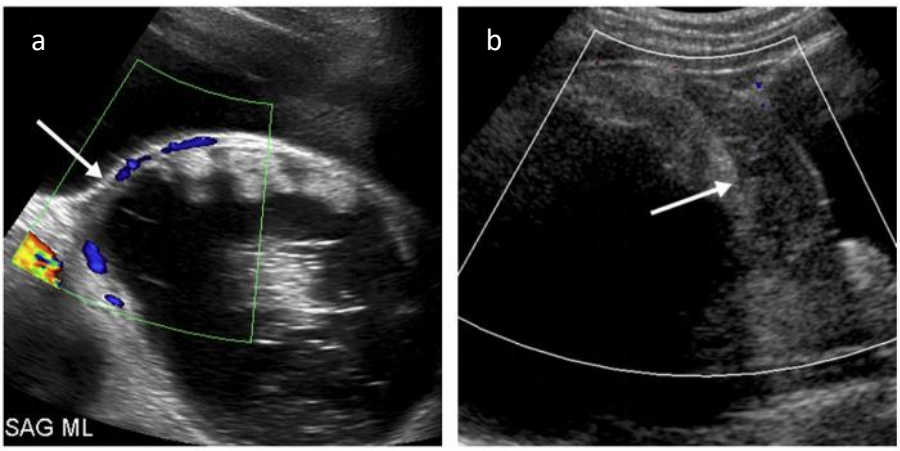

Figure 2 – Ovarian crest sign (OCS) (arrows) seen in cystic teratoma (a); ovarian torsion (b) (23).

Stankovic et al introduced an algorithm called the "Decision Tree System" (DTS) which is for the management of adnexal masses in children and adolescents. It consists of three rules that incorporate the Ueland Index (morphology index (MI) score), and the ovarian crescent sign (OCS) for risk stratification, as seen in Figure 3 (23, 24). The DTS illustrates a 93% sensitivity, 97% specificity, 86% positive predictive value (PPV), and 99% negative predictive value (NPV) of malignancy. This system is favorable in differentiating between malignant and benign masses in case of emergent surgery, permitting a higher rate of ovarian tissue preservation (22, 23).

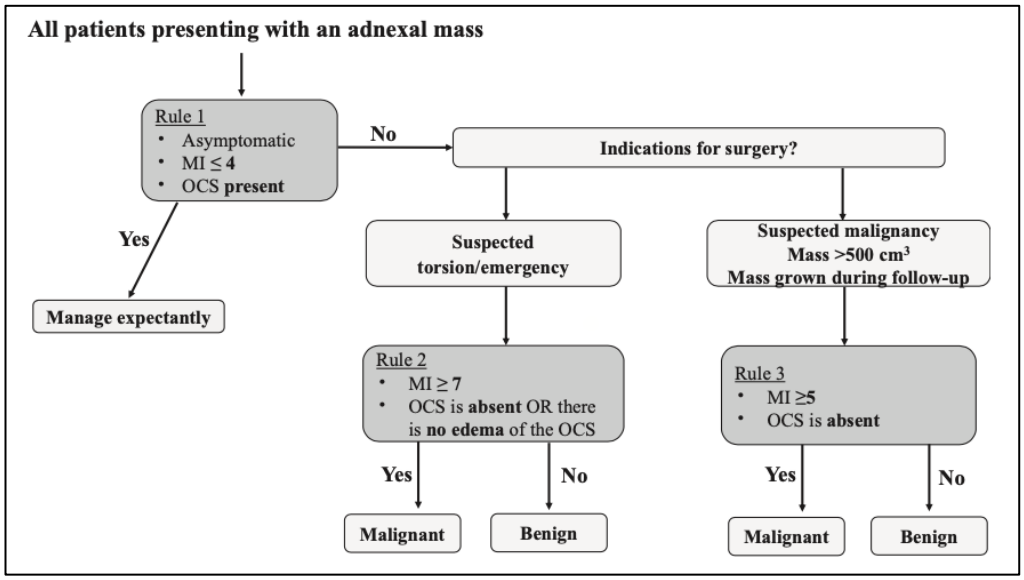

Figure 3 – The Decision Tree System. MI, morphology index; OCS, ovarian crescent sign (23).

5.3.2. International Ovarian Tumor Analysis - IOTA

The International Ovarian Tumor Analysis created ultrasound guidelines and an ADNEX risk model which estimates the probability that an adnexal tumor is benign,

borderline, malignant, or secondary metastatic cancer (8). The IOTA "simple rules" (IOTA-SR) is a guideline that is widely used in clinical practice and includes ten variables that are classified into two groups for the identification and characterization of benign and malignant adnexal masses (18). IOTA SR has been validated in numerous studies demonstrating the highest value in predicting preoperative differentiation of adnexal tumors with a sensitivity of 94% and specificity of 95% (18, 25). The ADNEX model uses nine variables consisting of three clinical and six ultrasound variables (8, 25). Numerous reports have shown that a combination of IOTA simple rules combined with CEUS and tumor markers has more significant diagnostic value in predicting malignancy in ovarian cancer than the approaches individually (18, 26).

5.3.3. Ovarian-Adnexal Reporting and Data System (O-RADS)

Ovarian-Adnexal Reporting and Data System (O-RADS) was recently published by the American College of Radiology (ACR) and provide guidelines for improving the ultrasound risk assessment of malignancy to reduce or eliminate uncertainty in ultrasound reporting and provide management recommendations for each risk category (21). However, the diagnostic performance of the O-RADS has not been validated; therefore, its utilization still needs to be verified (18).

5.4. Differential Diagnosis

The differential diagnosis of ovarian masses is highly important since the management and particularly the surgical treatment rely on it. The basis of the differential diagnosis is the specific clinical manifestations, elevated serum tumor marker levels, distinctive imaging findings, and finally histological examination. All lesions require a thorough histopathological analysis and staging to determine the definitive diagnosis (14, 19).

Generally, there are gynecological and non-gynecological differential diagnoses for ovarian masses. Figure 4 indicates the most relevant ovarian gynecological differential diagnoses in adolescents. Other gynecological differential diagnoses include paratubal cyst, hydrosalpinx, tubo-ovarian abscess, subserosal pedunculated leiomyomas, and ectopic pregnancy (3, 12, 27). Relevant non-gynecological differential diagnoses include appendicitis; diverticulitis; pelvic kidney, peritoneal pseudocysts; gastrointestinal masses; urinary tract infection; nephrolithiasis; psoas abscess, etc. (3, 27).

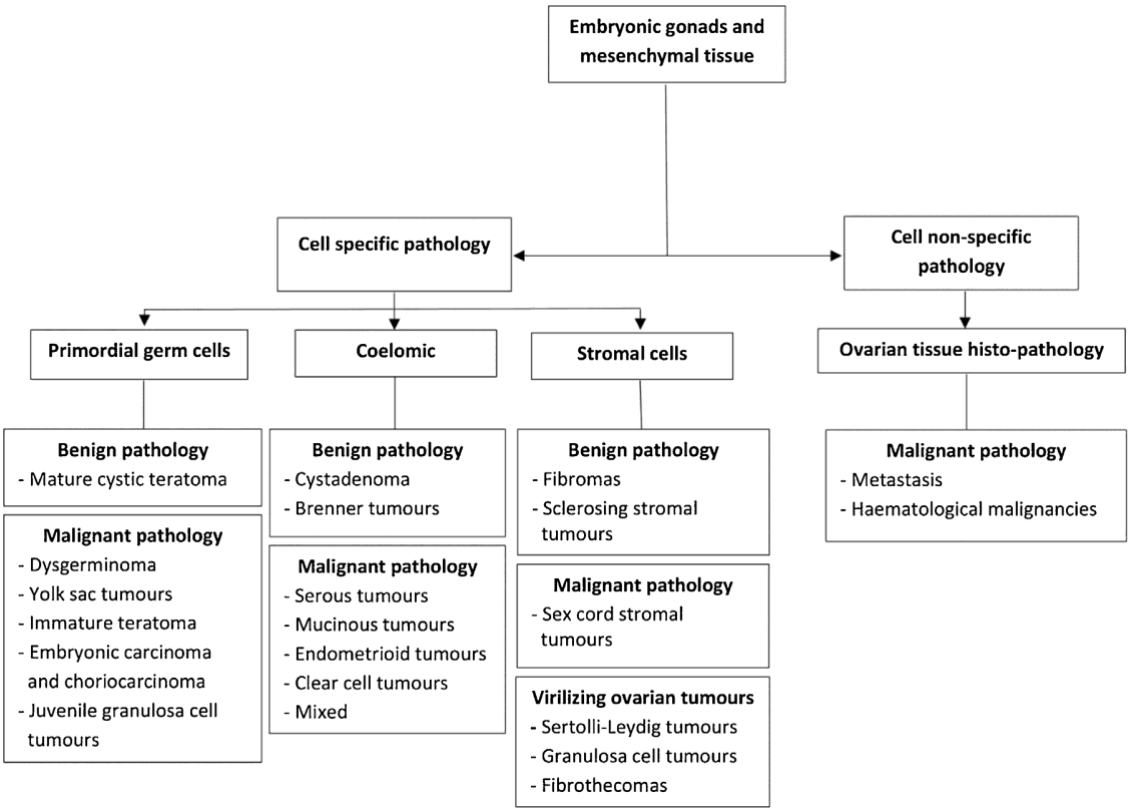

Figure 4 – Illustration of the main ovarian gynaecological differential diagnosis' (14).

6. MANAGEMENT OF OVARIAN MASSES IN ADOLESCENTS

6.1. Medical and Surgical management options

Managing ovarian masses in adolescents involves ethical considerations that can impact a patient's medical, emotional, and psychological well-being, including their identity, fertility, family planning, and sexual health (14). Differing from adult women who already have children, adolescents have a life-long expectancy after treatment, so keeping both functional gonads for reproduction is of utmost interest (19).

Considering the diverse clinical presentation and various potential causes, the management requires multidisciplinary teamwork from obstetrician/gynecologist; gynecologic oncologist; pediatric oncologist; infertility & reproductive endocrinologist; general surgeon; radiologist; and pathologist (3, 14). Aside from the medical specialists, guidance from caretakers, social services, psychologists, religious representatives, and ethics committee representatives should be provided (14). This extensive list of specialists brings a vast amount of expertise which will ensure the election of the most adequate and optimal management.

Genetic counseling is imperative when a genetically linked disease is diagnosed. This would include long-term monitoring, potential prevention, and interventions, as well as family counseling. This is necessary as it can have both immediate and long-term effects on the affected

individual, as well as their potential future children or other family members. The main goal would be to help patients and their families understand the nature of the disease, the likelihood of inheritance, and the possible risks and benefits of different management strategies (14).

The primary aspects of management revolve around the potential diagnosis, objectives of the intervention, avoidance of co-morbidities, preservation of fertility, and to a lesser extent, the aesthetic appearance of the incision in these young females (14). Multiple different treatment options are available, but the management is ultimately determined by the age of the patient, the size of the mass, and the risk factors for malignancy (3). If the ovaries cannot be preserved, then the cessation of secondary sexual characteristics and infertility are likely (2).

Concisely, the management should be curative, fertility and reproductive function preserving, minimally invasive, and sensitive to the psycho-emotional effect on this "vulnerable" population and all while mitigating morbidity (14).

6.1.1. Conservative therapy

Deciding whether conservative therapy is the best management can be difficult. In adolescent patients with ovarian masses, the initial approach should always be conservative. The management of asymptomatic cysts is typically based on their size and complexity sonographically (5). When an ovarian cyst is considered benign, and the patient is asymptomatic, expectant management with close surveillance via ultrasound is preferred (3). Without intervention, the majority of simple cysts decrease in size or resolve spontaneously after 4-6 months (3, 5, 11, 12). On the contrary, if the cyst does not resolve after numerous menstrual cycles in post-menarche adolescents, it is doubtfully a functional cyst and further diagnostics will be necessary (3).

6.1.2. Medical therapy:

The final diagnosis dictates whether and what type of medical intervention is required (14). According to the ESHRE 2022 guidelines, the first-line drug therapy for endometriomas in adolescents younger than 16 years is hormonal contraceptives or progestogens (systemically or via Intrauterine device) as this is safe and effective. This hormonal treatment may be used adjunctively pre- and postoperatively when surgery is considered necessary (6, 28). Supportive medical therapy using estrogen replacement medication is imperative in the case of bilateral oophorectomy (14). Chemotherapy in adolescents is controversial since there are tumors, such as yolk sac tumors or epithelial ovarian tumors, that are highly sensitive to

chemotherapy or that supposedly "require" chemotherapy after an operation, however, many studies illustrate that chemotherapy and radiotherapy increase infertility rates (6, 19).

Pediatric studies state that solely surgery, with a completely resected tumor regardless of tumor grade, is curative, whereas in adult women with ovarian malignant tumors, postoperative chemotherapy is the standard of care. In incompletely resected tumors the role and the rate of relapse with chemotherapy in adolescents are not well assessed, accentuating the need for improved collaboration between adult and pediatric teams (19).

6.1.3. Surgical management:

The surgical indications for ovarian masses include large, complex, or symptomatic cysts, a suspected ovarian torsion, a persistent ovarian mass, acute abdominal pain, and suspected malignancy (5). The incision size must correlate to the chosen surgery, the size of the tumor, and whether additional exploration and sampling of tissue and lymph nodes will be necessary (14). Abdominal scars can cause psychological issues in adolescents, requiring more attention and justification than in adults (19).

The surgical treatment of ovarian masses in adolescents is controversial in this age group since fertility-preserving methods are a priority while the oncological principles should not be compromised (1, 11). Ovarian-sparing surgery is considered the favored approach for both cystic and solid lesions when there are no symptoms (i.e., abdominal pain) or signs (i.e., palpable mass) indicating a malignancy since there is a very low incidence of malignancy in this age group (1, 5, 10). According to several studies, the gold standard in the management of benign ovarian masses is minimally invasive laparoscopy, or, in recent years, robotic surgery (5, 19). Laparoscopy has many widely recognized advantages including small incisions, lower incidence of surgical site infection, reduced recovery time, excellent intraoperative visualization in the smaller pelvis of adolescents, minimal risk of adhesion, minimal blood loss, greater cost-effectiveness, and fewer postoperative complications (10, 11). The disadvantages of laparoscopy are the extended duration of surgery instigating increased exposure to general anesthesia causing a higher risk of internal organ and blood vessel damage (3).

Recent studies state that the treatment of choice for a mature ovarian teratoma, cystadenoma, and borderline ovarian tumor in adolescents is no longer open or laparoscopic oophorectomy, but instead, ovary-sparing due to the “very low risk of recurrence and malignancy” (13, 19). Figures 5 and 6 depict excised mature and immature teratomas.

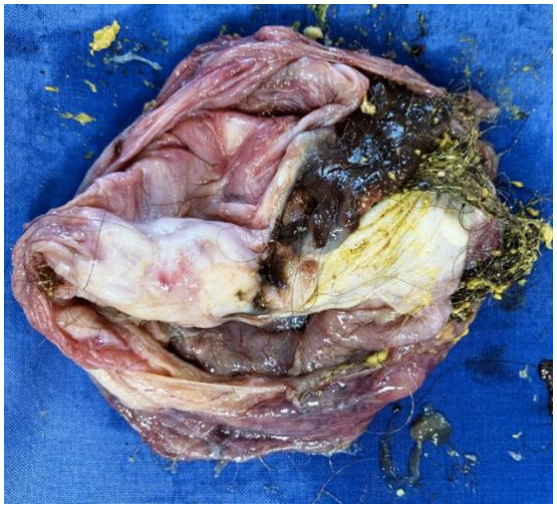

Figure 5 - Excised Cystic Teratoma with visible deposits of sebum and hair (19).

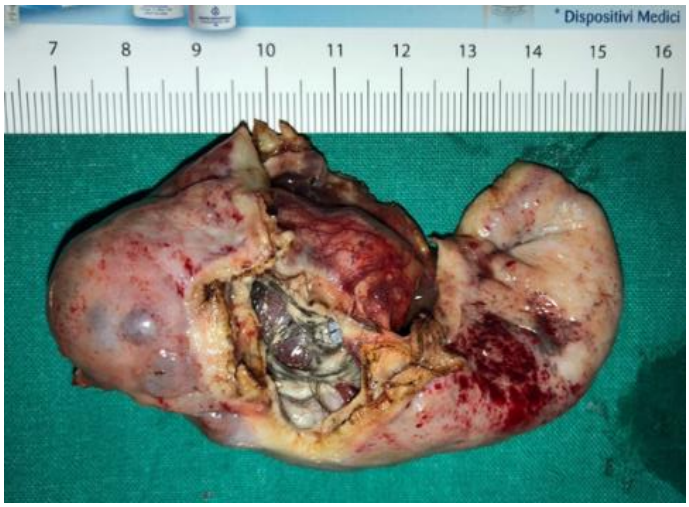

Figure 6 – Excised Immature teratoma (5).

The management of ovarian torsions has also changed in recent years to detorsion with or without cystectomy rather than oophorectomy, to preserve fertility potential since follicular activity may continue (1, 3). Ovarian fixation is a debated topic since some experienced surgeons support it in cases with relapsing torsions, while others are concerned that fixation could disturb the ovary and communication between the ovarian follicles and the fallopian tube (1).

Although the ovary-preserving laparoscopic approach is the preferred procedure in benign masses, laparotomy remains the treatment of choice in larger, potentially malignant masses and acute tumor-induced ovarian torsion (1, 13). Malignant ovarian tumors require exploratory staging surgery and potentially salpingo-oophorectomy for the complete surgical removal of the tumor (11). In a hemodynamically unstable patient, laparotomy is also preferred as it allows for rapid access and direct visualization of the affected structures (3). In some cases, laparotomy may be recommended in addition to laparoscopy when the mass is too large to be removed by the port site when puncturing the mass in the endo-bag is not sufficient to reduce its size (14).

Oophorectomy is indicated when there is confirmation of malignancy or tissue necrosis due to ovarian torsion, as seen in Figure 7 (10). If an oophorectomy is planned, the patient and their parents should be informed of the hypothetical alternative fertility preservation options. These include oocyte cryopreservation ("egg freezing") and ovarian tissue cryopreservation with pregnancy rates ranging between 4-60% (14).

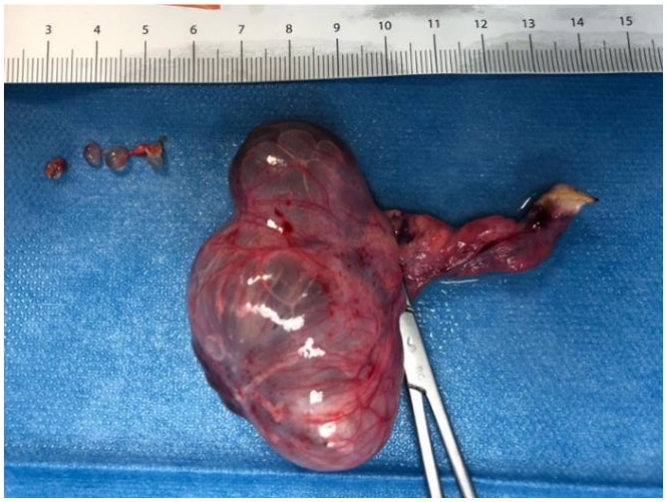

Figure 7 - Laparoscopic oophorectomy after ovarian torsion (5).

Intraoperatively, the use of sealing devices for dissection is favorable for surgeons as it controls bleeding and refrains from using metal clips on vessels, as shown in Figure 8 (5). Ovarian cyst aspiration can help reduce the volume of the cyst, resulting in decreased risk of cystic fluid overflow or cystic rupture along with improved visualization intraoperatively (19, 6). In order to avoid the dissemination of potentially malignant cells, the lesion should be removed with a laparoscopic endo-bag through the port site. This is the safest and simplest way to avoid spilling (5, 14). Performing a frozen section ("cryosection") examination is a crucial procedure that allows for a rapid intraoperative diagnosis of the lesion, which aids in further immediate and postoperative management (14).

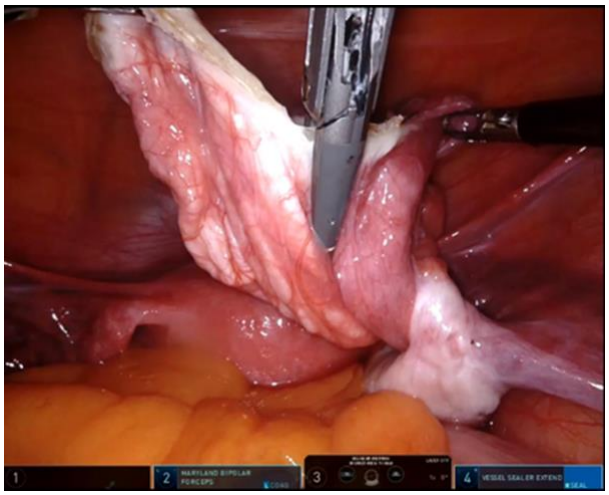

Figure 8 - Use of sealing device in robotic removal of ovarian mass (5)

In recent years, robotic surgery has become more popular internationally. A study comparing robotic versus laparoscopic staging for early cancer revealed a significantly reduced operative time in robotic surgeries, while the approximate blood loss was

comparable (6). Furthermore, a new visualization system using ICG (Indocyanine Green) enhanced fluorescence technology was introduced in minimally invasive laparoscopic and robotic surgeries of ovarian masses, as seen in Figure 9. The ICG system has proven to be useful to better visualize the ovarian mass margins, analyze ovarian vascularization and possible ischemic damage after detorsion, and evaluate lymph nodes in case of malignancy. A study showed that the ICG system not only reduces the mean operative time by nearly 40% but was also able to spare healthy ovarian tissue and reduced the number of total oophorectomies. The downside to the ICG system is the limited availability of such costly and specific equipment that requires separate software (5).

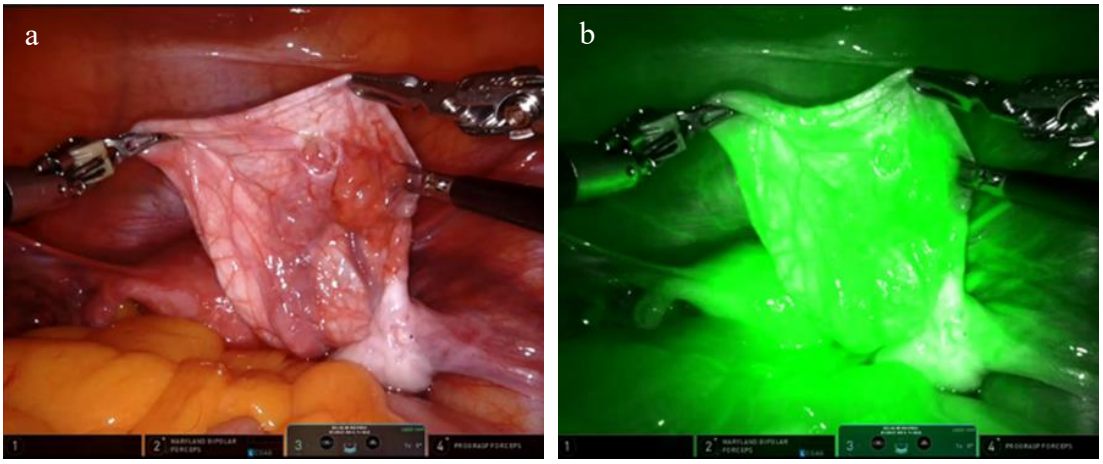

Figure 9 - The role of ICG system to check vascularization of the ovary after detorsion: (a) without ICG; (b) with ICG view (5).

6.2. Long-term follow-up management

Given the possibility of future relapses or the development of a similar ovarian tumor on the contralateral side, the patient will necessitate long-term follow-up monitoring.

The follow-up monitoring should include a clinical analysis, biological monitoring, and pelvic ultrasound (13, 19). Tumor markers can also be used as follow-up parameters in long-term screening for the potential relapse of certain ovarian cancers, such as malignant germ-cell tumors and epithelial tumors (1, 13, 14). The recommended follow-up for mature teratomas (dermoid cysts) is yearly with ultrasound until potential surgical removal, while for endometriomas it is first 6 to 12 weeks after the initial imaging, then also yearly until potential surgical removal (3). On the ultrasound follow-up, the majority of simple cysts decrease in size or resolve spontaneously within 4-6 months without intervention (3, 5, 11, 12).

A constructive overview of the steps in the management of ovarian masses is shown in Figure 10.

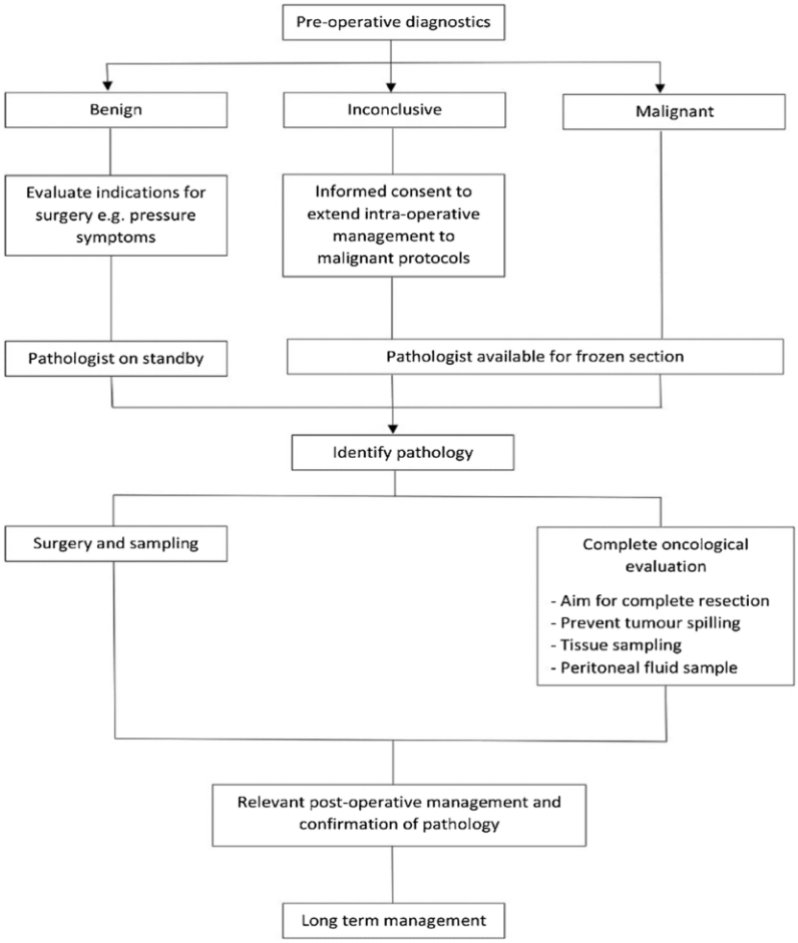

Figure 10 - Diagram illustrating an overview of the management of ovarian masses (14).

6.3. Outcomes and Prognosis for adolescent females with ovarian masses

Most asymptomatic, benign ovarian cysts resolve spontaneously and have a good prognosis, like follicular cysts which resolve spontaneously 70-80% of the time (3). Ovarian teratomas are commonly benign and also have an excellent prognosis (13). In the case of endometriomas, the recurrence rate of endometriosis post laparoscopic cystectomy is between 9% and 15% at 3 and 5 years, respectively. Dermoid cysts and endometriosis rarely have malignant development, but in those few cases, it is associated with a very bad prognosis. The overall survival in less aggressive tumors with low malignant potential is ~86% at five years. However, the prognosis is usually poor if there is suspicion of malignancy since this is usually detected in advanced stages (3).

In a 25-year retrospective study on the laparoscopic and robotic management of ovarian masses in neonates, children, and adolescents, it was found that in most cases they were able to remove the mass and spare the ovary, which lead to excellent long-term results and low rates of recurrence (5, 11). The long-term ultrasound follow-up a decade later confirmed that these patients had developed normal ovaries after removing the ovarian mass and preserving the

ovarian tissue (5). Another study supports that if more than 1.5cm of ovarian tissue is preserved, menstruation is found to be normal and pregnancy rates can reach over 70% (6).

The outcome and the probability of adverse events are better when these patients are managed by a multidisciplinary team, as mentioned above (3).

7. CONCLUSIONS

7.1. Summary of key findings and important considerations

In conclusion, ovarian masses in adolescents are very rare and predominantly benign. Although ovarian tumors only account for 1% of all tumors in children and adolescents, they are still the most common reproductive organ tumors in this age group (1, 2, 6, 7, 10). They can be discovered incidentally or when symptoms such as abdominal pain or pressure, menstrual irregularities, and other unspecific symptoms are experienced (1, 3).

Of all ovarian masses, the most common among adolescents are the non-neoplastic cysts (60%), including the functional follicular and corpus luteal cysts. Among the neoplastic ovarian masses, the most common are benign mature teratomas (dermoid cysts) (8, 10, 11).

The occurrence, clinical presentation, and histological characteristics of ovarian tumors in adolescents differ from those in adults, requiring an appropriate therapeutic approach (6, 19). Adolescents should have regular physical examinations and visit a doctor promptly when they experience ovarian symptoms. The main diagnostic tools for differential diagnosis include ultrasound imaging and tumor markers (6).

In recent years, the management of ovarian masses in adolescents has shifted from a "radical and mutilating" method to a conservative and minimally invasive, fertility-preserving method. Laparoscopy has become the gold standard in benign ovarian tumors since ovary preservation has become a very high priority (1, 11, 19). Laparoscopic and robotic ovary-sparing tumor removal in adolescents has led to excellent long-term results with low rates of recurrence and an overall good prognosis (5, 11). The Indocyanine Green enhanced fluorescence technology is an advanced intraoperative visualization system that substantially reduces the mean operative time and total oophorectomies (5). Studies have proven that in young patients where ovarian tissue was preserved, the long-term ultrasound follow-up found normal ovaries with menstruation and fertility (5, 6). This reinforces the importance and purpose of these trends. To ensure the best outcome in this age population, each patient requires very thorough diagnostic differentiation, and a personalized management plan (3, 14, 19).

Nevertheless, further studies are needed to define the best treatment approach for this vulnerable patient population (13).

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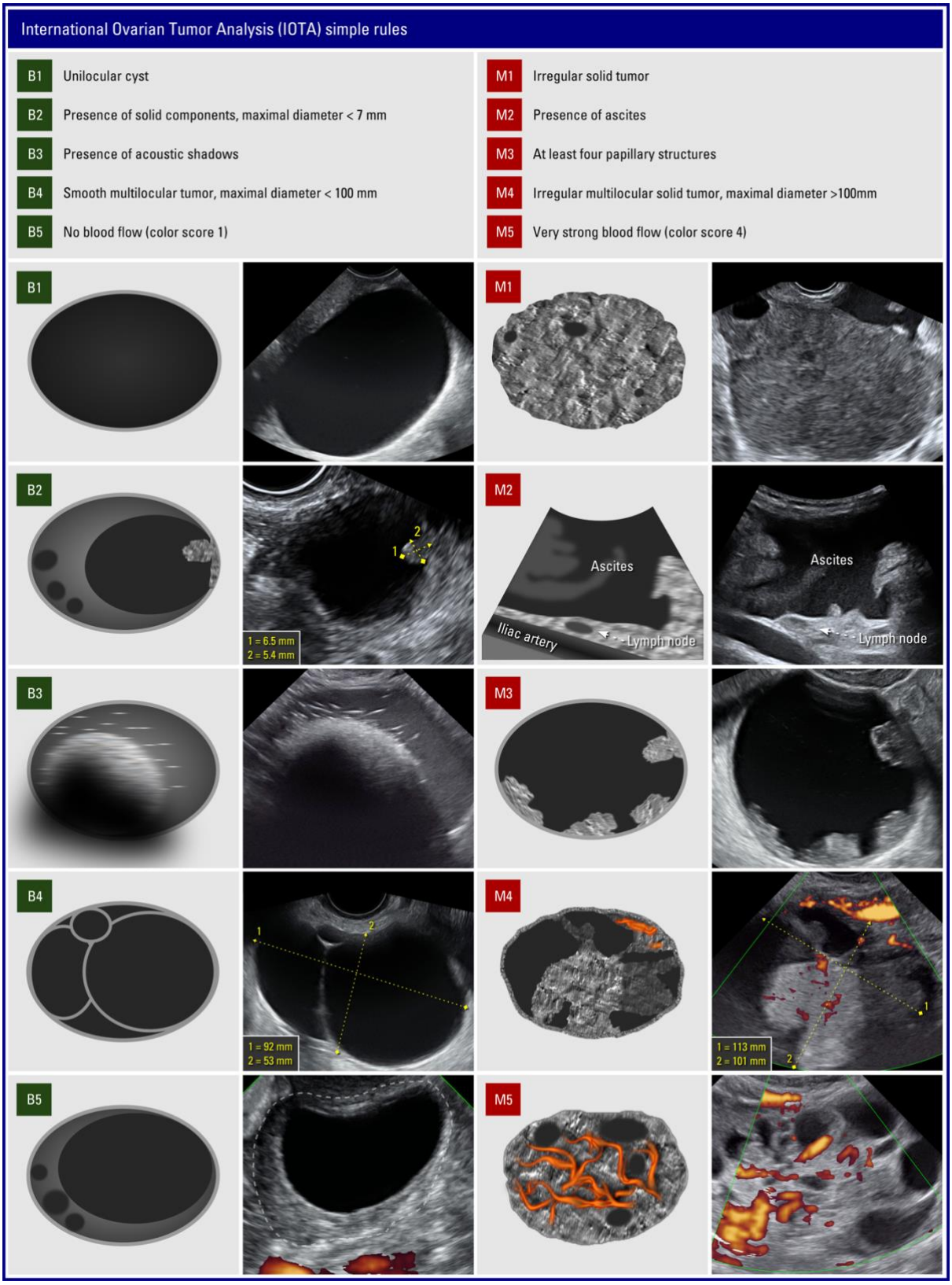
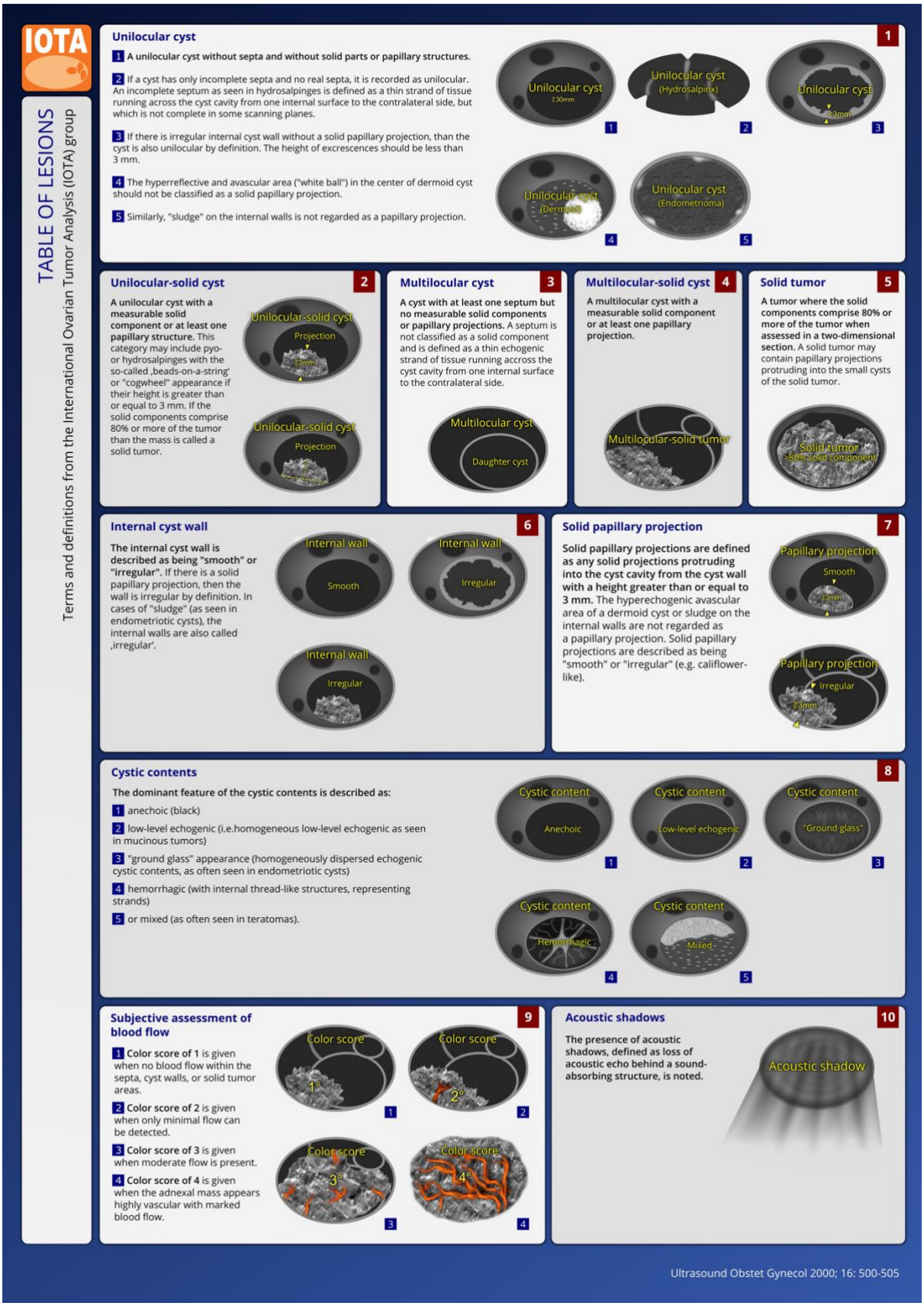
SUPPLEMENTARY MATERIAL:

A collection of the International Ovarian Tumor Analysis (IOTA) guidelines for additional review.

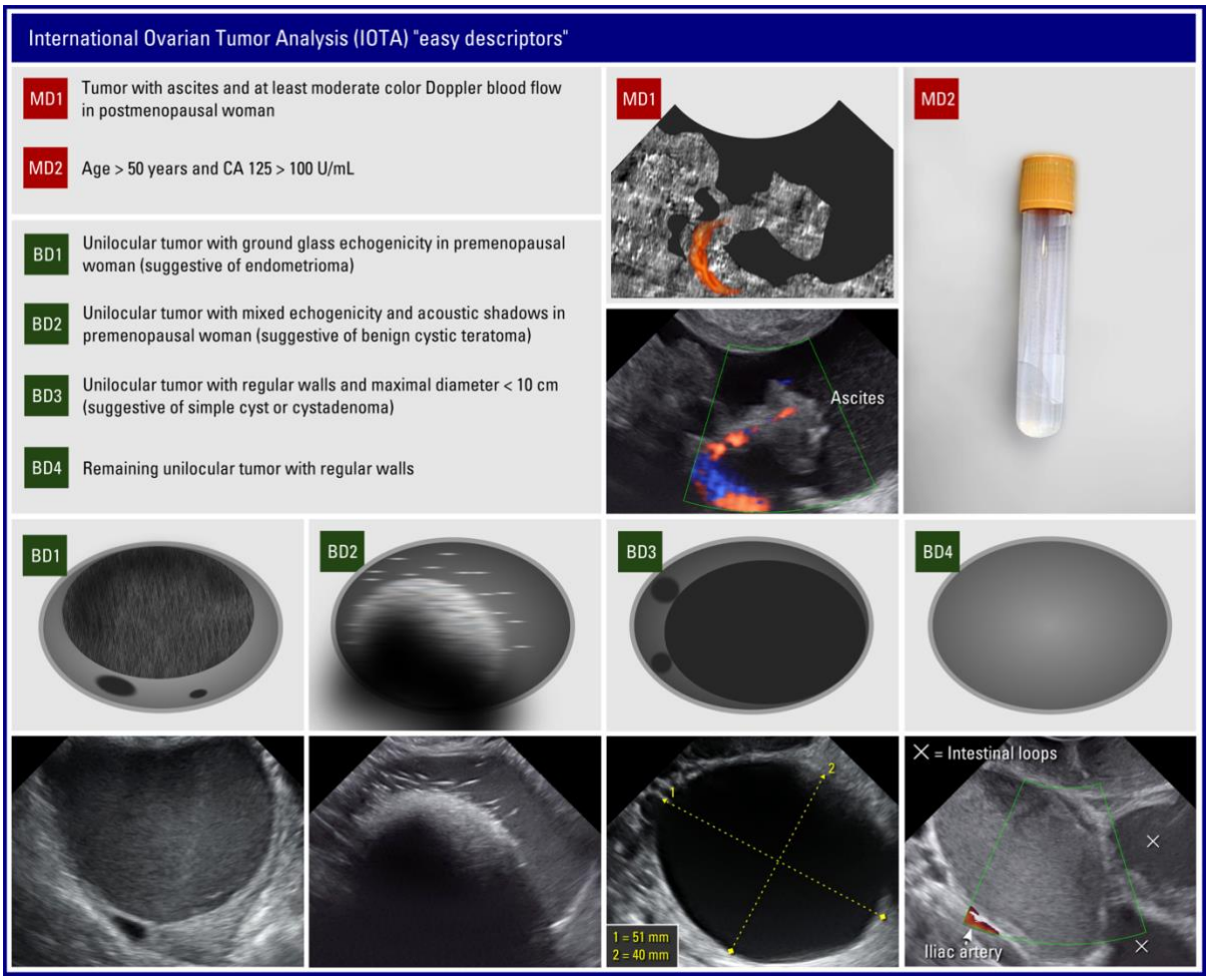
1. **International Ovarian Tumor Analysis (IOTA) "simple rules"** (25)



2. International Ovarian Tumor Analysis (IOTA) "Table of Lesions" (25)



3. **International Ovarian Tumor Analysis (IOTA) "easy descriptors"** (25)



4. **International Ovarian Tumor Analysis (IOTA) "ADNEX model"** (25)

IOTA - ADNEX model

1. Age of the patient at examination (years)
2. Oncology center (referral center for gyn-oncol)?
3. Maximal diameter of the lesion (mm)
4. Maximal diameter of the largest solid part (mm)
5. More than 10 locules?
6. Number of papillations (papillary projections)
7. Acoustic shadows present?
8. Ascites (fluid outside pelvis) present?
9. Serum CA-125 (U/ml)

calculate Clear