

## Mini Review

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# Management of Adnexal Masses in Children and Adolescent Populations: Advocating for Ovarian Conservation

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## INTRODUCTION

When a young girl or adolescent presents to the Emergency Department with acute lower abdominal pain, it is not uncommon for a general surgeon to be consulted, as appendicitis is always top of the differential diagnosis. The management dilemma occurs when imaging reveals an adnexal mass in the setting of an acute abdomen. Historically, surgical management recommendations were for laparotomy with unilateral salpingo-oophorectomy, in an effort to avoid incomplete excision of cancer.<sup>1-3</sup> Laparoscopy has since replaced laparotomy as the surgical method of choice, however ovarian conservation procedures are often not considered unless a gynecologist is present. This goal of this article is to address the importance of ovarian conservation in adnexal masses in children and adolescents.

## BACKGROUND

The incidence of adnexal masses in children has been estimated at 2-5 cases per 100,000 patients per year, depending on the series.<sup>2,4,5</sup> The majority of these cases are benign, as malignancy rates have been quoted between 3.7 and 23.5%,<sup>2</sup> however ovarian cystectomy is still only performed in 61.4% of cases.<sup>3</sup> The differential diagnosis of adnexal masses lists both benign and malignant tumors (Table 1). Benign masses include cysts, endometriomas ("chocolate cysts"), mature cystic teratomas (dermoids), cystadenomas (serous or mucinous), ectopic pregnancy, or other benign neoplasms. One must also consider non-gynecological causes of pelvic masses including appendiceal abscess and pelvic kidney. Cysts are most common at 57.9%, with hemorrhagic corpus luteum cysts (26.4%) and follicular cysts (17.1%) being the most common types.<sup>6</sup> Torsion of the ovary or fallopian tube (with or without an associated mass) may lead to edema which can also appear as a mass on imaging studies. Malignant masses include epithelial, germ cell, sex cord, and metastatic tumors. While epithelial ovarian tumors are the most common malignancy when including all age groups, non-epithelial tumors are more common in women under 19 years of age.<sup>6,7</sup> The most commonly found malignancies are specifically immature teratomas and dysgerminomas.<sup>2,6</sup> Women greater than 15 years of age present more commonly with benign masses than those 15 or younger, with rates of malignancy estimated at 4.4 vs. 11.1%.<sup>2</sup>

## DIAGNOSIS

Although 8-13% of adnexal masses in children and adolescents less than 18 years of age are incidental, the majority of masses are identified due to symptoms. A thorough history and physical exam are an indispensable initial first step in evaluation. An estimated 57-60% of patients with a mass will have abdominal pain, and 22% will have a palpable mass.<sup>2,5</sup>

Additionally, 18% of patients may have menstrual irregularities and a small number

Benign	Neoplastic	Mature teratoma Cystadenoma (Serous or Mucinous) Fibroma Adenofibroma Thecoma Luteoma
	Non-neoplastic	Follicular cyst Hemorrhagic cyst Paratubal/Paraovarian cyst Endometrioma Torsion Ectopic pregnancy
Malignant	Epithelial	Cystadenocarcinoma (Serous or Mucinous) Brenner Endometrioid Clear cell Borderline (Low Malignant Potential)
	Germ Cell	Gonadoblastoma Dysgerminoma Endodermal sinus tumor Embryonal carcinoma Immature teratoma Ovarian choriocarcinoma
	Sex Cord-Stromal	Sertoli-Leydig Granulosa-Theca cell Gynandroblastoma
	Metastatic	Krukenberg (Gastrointestinal) Breast Endometrial Lymphoma

Table 1: Differential diagnosis of adnexal mass.

may even present with precocious puberty.<sup>5,7</sup> Pelvic ultrasonography, *via* transabdominal and transvaginal approaches, should be considered first line imaging, as it is widely available, low-cost, and non-invasive.<sup>7</sup> Transvaginal approach provides imaging of smaller masses as well as internal characteristics. Sonographic analysis should include largest diameter, gross morphology, and Doppler flow in the ovarian vessels. Internal morphology consistent with a heterogeneous or solid mass is more indicative of malignancy than a unilocular, homogenous cyst.<sup>8</sup>

Serum markers are also used to identify malignancy to help with surgical planning and management; certain markers can help delineate type of tumor as well (Table 2). CA-125, used in monitoring of epithelial ovarian cancer in older women, is limited by the lack of specificity in this age group, as epithelial ovarian carcinomas are rare in children and adolescents. It is elevated in up to 1% of normal reproductive age women, as well as in women with confounding conditions such as endometriosis, first trimester pregnancy, Crohn’s disease and pelvic inflammatory disease.<sup>7</sup> Tumor markers that have been shown to be more associated with cancer in this age group include Alpha-fetoprotein (AFP, OR 9.60), Beta Human Chorionic Gonadotropin (βHCG, OR 5.93), and Lactate dehydrogenase (LDH, OR 225).<sup>5,9</sup> Additionally, thrombocytosis has been associated with ovarian malignancy in children and adolescents; as many as 33% of those with a germ cell tumor had thrombocytosis.<sup>10</sup> Most tumor markers can take several days to result and may not be of

use in an emergency setting.

Tumor Marker	Associated Malignancy
Ca-125	Epithelial ovarian tumors
AFP	Endodermal sinus tumors
LDH	Dysgerminomas Endodermal sinus
βHCG	Choriocarcinoma Polyembryoma
Inhibin, Mullerian Inhibiting Substance	Granulosa cell tumor

Table 2: Tumor markers.

Surgical excision is recommended for suspicious masses, positive markers, and benign cysts that are symptomatic, persistent beyond 4-6 weeks, greater than 5 cm in greatest diameter or if ovarian torsion is suspected.<sup>4</sup>

**MANAGEMENT**

The literature provides limited evidence-based recommendations for management of adnexal masses in children and adolescents, although more case series have been published as of late, in both Gynecology and Pediatric Surgery Journals. Historically, surgeons favored laparotomy with unilateral oophorectomy with or without removal of the fallopian tube.<sup>2,3,7,11</sup> Current literature indicates a significant trend over recent decades to-

wards laparoscopy and ovarian-conserving surgical procedures, such as ovarian cystectomy, in this age group.<sup>12</sup>

Berger-Chen and colleagues assessed the Perspective database and showed that since 2000, use of laparoscopy has increased from 32.1 to 57.9%, although these rates are affected by socioeconomic factors such as African-American race (OR 0.49) and geographic location in the Northeastern United States (OR 0.65).<sup>3</sup> Patients undergoing laparoscopy are 2 times more likely to have cystectomy performed.<sup>3</sup> Presence of a Gynecologist as primary surgeon increases use of laparoscopy and ovarian conserving surgery, as much as 8.7 times for all masses and 15 times for benign masses.<sup>12</sup> Gynecologists are more often involved when the patient is post-menarchal or greater than 15 years of age.<sup>12</sup>

Ovarian conservation is important, as women with a prior oophorectomy have a 3-15% risk of pathology or torsion in the contralateral ovary and more frequently will seek infertility consultation later in life.<sup>12,13</sup> Resistance to ovarian-conserving surgery has several factors contributing including surgeon's fear of malignancy, relative inexperience with adnexal masses, and in the case of ovarian torsion, risk of thromboembolic events and unrecoverable ischemia.<sup>2,11</sup>

To address this dilemma, criteria have been proposed to risk-stratify ovarian masses in order to facilitate the use of ovarian-conserving surgical techniques such as cystectomy.<sup>2,5,7,8,14</sup> These criteria aim to identify masses most likely to be benign and therefore are candidates for laparoscopic surgery with ovarian conservation. Papic and colleagues identified three criteria to isolate benign masses preoperatively, based on ultrasonography and serum markers: 1) maximum diameter less than 10 cm, 2) no solid components present on imaging studies, and 3) normal serum tumor markers, specifically alpha-fetoprotein (AFP, OR 9.60), beta human chorionic gonadotropin ( $\beta$ HCG, OR 5.93), and lactate dehydrogenase (LDH, OR 225).<sup>5</sup> A combined negative likelihood ratio calculated to be 0.01 is highly specific for benign masses, reducing risk of malignancy in the studied sample from an estimated pre-test probability of 20% to 0.25%.<sup>5</sup> Hermans and colleagues applied these criteria post hoc to a cohort of 111 patients with adnexal masses whom had already undergone surgery, resulting in a sensitivity of 40.91% and specificity of 100%. Preoperative application of these criteria would have prevented two laparotomies and seven oophorectomies, indicating that these criteria are sufficiently specific to rule out malignancy, however improving the sensitivity for benign masses may be able to further decrease the incidence of laparotomy and oophorectomy.<sup>2</sup> Rogers and colleagues performed a similar retrospective study, utilizing sonographic but no serum markers, which identified that 100% of malignant masses were greater than 8 cm with and complex on sonography, with a sensitivity of 36%, positive predictive value of 37.1%, and negative predictive value of 100%.<sup>14</sup> Application of these criteria to the retrospective cohort would have reduced open procedures by 40%.<sup>14</sup> A larger

series by Oltmann, et al. of 424 patients with surgically treated adnexal masses showed that malignancy was more common in patients age 1-8 years (OR 3.02) with complaints of a precocious puberty (as compared to pain, OR 4.8 and 5.67, respectively), and a heterogeneous or solid mass (OR 6.84 and 10.13) with a maximum diameter of greater than or equal to 8 cm (OR 19.0).<sup>8</sup> Tumor markers were only elevated in 54% of the malignancies in this cohort, and 6.5% of benign masses.<sup>8</sup> These data support using 8 cm as a diameter criterion, but diminish the impact of tumor markers on stratification. It should also be noted that criteria such as these often perform less well when replicated, but a sensitivity between 0.4 and 0.6 can be expected.<sup>15</sup>

The surgical procedure for ovarian cystectomy has been published previously and the technique is considered standard, however the learning curve is long.<sup>16</sup> The preferred procedure is to incise the thin ovarian tissue surrounding the cyst and then, using opposing graspers, strip the cyst wall from the adjacent ovarian tissue, resulting in complete enucleation, known as the "stripping technique." Dissection of difficult-to-peel areas may be performed sharply, bluntly, or with hydro-dissection. Hemostasis may be obtained using sutures or electrocautery, as despite mildly elevated FSH levels three months after cauterization, ovarian volume and antral follicle count return to normal values.<sup>17</sup> If there is concern for malignancy not appreciated preoperatively, frozen pathological analysis can clarify if intraoperative consultation to gynecologic oncology, if available, is necessary. Another point to consider is that adnexal masses may actually be associated with the fallopian tube as opposed to the ovary once directly visualized. Cystectomy is again the preferred surgical approach with ovarian conservation; the fallopian tube, if grossly distorted or involved with the mass, should be removed to prevent increased ectopic pregnancy risk in the future. Ovarian torsion, if encountered, may be untwisted, with cystectomy performed if a mass is present, and the ovary left in-situ regardless of the appearance; this procedure has been shown to be safe and effective since 1946.<sup>11</sup>

## SUMMARY AND RECOMMENDATIONS

Currently, recommendations for management of adnexal masses in children and adolescents should be as conservative of ovarian tissue as possible to reduce the risk of premature menopause and infertility. Preoperative workup should include:

- Thorough history and physical exam
- Transabdominal and transvaginal pelvic ultrasonography, including Doppler of the ovarian arteries, maximum diameter, and mass characteristics
- Serum markers for alpha-fetoprotein (AFP), beta human chorionic gonadotropin ( $\beta$ HCG), and lactate dehydrogenase (LDH)

If surgery is indicated, criteria with a high negative

likely ratio for malignancy should be applied with negative results leading to minimally invasive ovarian conserving surgery:

- Maximum diameter less than 8 cm
- No solid components to the mass
- Negative serum tumor markers

Surgical management should include ovarian cystectomy *via* enucleation for symptomatic benign neoplastic adnexal masses, persistent asymptomatic benign masses, and de-torsion for ovarian torsion. If tumor markers have not obtained or have not resulted given an acute abdomen, it has been advocated to still proceed with ovarian cystectomy unless highly suspicious on imaging studies. Unless malignancy is definitive on frozen pathology (which is rare), ovarian cystectomy is the approach of choice; it is preferable to perform a second staging surgery once final pathology verifies the malignancy which is in contrast to what is recommended in older women. Management of malignant masses may be minimally invasive or open, however consultation and referral to Gynecologic Oncology is recommended for oophorectomy and staging as appropriate.

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#### CONFLICTS OF INTEREST

Authors report no direct conflicts of interest for this manuscript.

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